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Symposia, Oral and Poster Presentation Abstracts

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Symposia

Post-stroke dementia

Symp1-1
Incidence and development of cognitive impairment after stroke

D. Leys
Lille, France

Objectives: to determine the incidence of cognitive impairment after stroke and the underlying mechanisms.

Methods: literature review.

Results: Dementia is one of the major causes of dependency in stroke patients. The prevalence of dementia in stroke patients is likely to increase in the future. The risk of dementia is doubled after stroke. Patient-related variables associated with an increased risk of dementia after stroke are increasing age, low education level, dependency before stroke, pre-stroke cognitive decline without dementia, diabetes mellitus, atrial fibrillation, myocardial infarction, epileptic seizures, sepsis, cardiac arrhythmias, congestive heart failure, silent cerebral infarcts, global and medial temporal lobe atrophy, and white matter changes. Stroke-related variables associated with an increased risk of dementia after stroke are severity, volume, location, and recurrence of stroke. Dementia in stroke patients may be due to vascular lesions, Alzheimer pathology, or summation of these lesions. The cause of dementia after stroke varies between studies according to the mean age of patients, ethnicity, criteria used, and duration of follow-up after stroke. In western populations, the proportion of patients with presumed Alzheimer's disease amongst those with dementia after stroke varies between 19 % and 61 %. Stroke patients with dementia have higher mortality rates, and are more often functionally impaired.

Conclusions: Post stroke cognitive decline is frequent and can be due to both Alzheimer pathology and stroke lesions.

Disclosure: Nothing to disclose.

Symp1-2
Amyloid, ischemia and inflammation in post-stroke dementia

V. Hachinski
London, Canada

Objectives: To discuss one of the mechanisms of cognitive deterioration after stroke.

Methods: The experimental method involves a rat model of Alzheimer disease (amyloid deposition) and cerebral infarction. The clinical methods are the use of ligands for amyloid deposition and microglial activation in humans by positron emission tomography.

Results: We found that an infarct in the presence of amyloid experimentally was larger and it grew as opposed to it being smaller and shrinking in control animals. Similarly inflammation was greater in the animals with amyloid in the brain and it flared, as opposed to settling down as it did in control animals. Treatment with anti-inflammatory and antioxidant agents resulted in the mitigation of the histological changes and behavioral consequences. Preliminary clinical studies suggest that there is a better correlation between the cortical amyloid deposition and the 6 month cognitive status than with the initial cognitive status and that there is a better correlation between white matter inflammation and cognitive status in 6 months than there is with the initial cognitive status.

Conclusions: The interaction between ischemia, amyloid and inflammation offers an opportunity for a treatable mechanism to prevent or minimize post-stroke cognitive impairment.

Disclosure: Nothing to disclose.

Symp1-3
Imaging morphologic, metabolic and molecular changes responsible for post-stroke dementia

W.-D. Heiss
Cologne, Germany

Aging leads to a small loss of cortical neurons, but to a significant reduction of synapses, dendrites and myelinated fibers. These age-related changes may cause some cognitive impairment, brain atrophy and frontally accentuated diffuse decrease in metabolism. In pathological disorders leading to dementia, most frequently degenerative Alzheimer's disease, cerebrovascular disease or a combination of both, the changes are more severe, affect predominantly specific regions and result in significant loss of neurons. The differential diagnosis of these disorders is based on symptoms of cognitive and memory impairment and is supported by results of neuropsychological tests and of imaging. Whereas computed tomography and magnetic resonance imaging are able to detect morphologic lesions, these modalities cannot determine functional consequences of the underlying pathologies. Positron emission tomography allows imaging of the localized and/or diffuse metabolic disturbances responsible for cognitive impairment and dementia, and is effective in differentiating vascular from degenerative dementia, as Alzheimer's disease. It can also detect inflammatory changes and their interaction with amyloid depositions for the development of mixed dementias after stroke. Imaging of neurotransmitters and of synaptic function additionally yields insight into disease specific pathophysiology. Combined PET-studies of amyloid deposition and microglia activation as an indicator of neuroinflammation indicate that mainly cortical amyloid deposition, which is correlated with gray matter inflammation, predicts post-stroke cognitive impairment. In subcortical white matter amyloid deposition does not play a significant role for cognitive impairment in contrast to inflammation. Modulation of inflammation and/or amyloid deposition might open a way for prevention of cognitive impairment after stroke.

Disclosure: Nothing to disclose.

Symp1-4
Therapeutic concepts to prevent or ameliorate cognitive impairment after stroke

D. Inzitari
Florence, Italy

Stroke is associated with a substantially increased risk of subsequent cognitive impairment or dementia. A number of pre-stroke factors may contribute to Post Stroke Cognitive Impairment (PSCI), including older age, prior cognitive dysfunctions, previous stroke, recent infections, and selective risk factors such as hypertension, diabetes and Apoe 4 allele. Acute phase complications such as fever, hyperglycemia or seizures were also reported to be associated with PSCI risk. Concurrent chronic small vessel disease changes including white matter changes, silent infarcts, or microbleeds may interact with the effect of acute infarct lesions.

Following the multi-infarct concept, the factor most strongly associated with PSCI risk is likely stroke recurrence. Among patients with atrial fibrillation risk of dementia after stroke proved over twofold increased. Consequently the best prevention of PSCI is logically based on the best prevention of recurrent stroke. Successful

reperfusion after ischemic stroke, and the best patients management during the acute phase, may be important aiming at preventing PSCI. Regarding PSCI prevention or treatment to be started after stroke, BP lowering or other risk factors control may contribute by slowing progression of concurrent small vessel alterations. Studies are in progress investigating comprehensive and adherent risk factors control. There are clues suggesting that motor rehabilitation, specific domains interventions (against aphasia, spatial neglect, executive or attention dysfunctions), as well as physical activity combined with aerobic exercise might help ameliorating cognitive performances in stroke patients. No selective drug was proven conclusively as effective on improving cognitive performance after stroke.

Disclosure: Grants for research: Bayer Italy S.p.A.

Status epilepticus

Symp2-1
Definitions, epidemiology and outcome

E. Trinka
Salzburg, Austria

Status epilepticus is one of the most common neurological emergencies. With an incidence rate of 20–60/100,000/year and its mortality of around 20 % emergency management and effective treatments are needed. The definition of status epilepticus has varied over time and can be defined as "the failure of the mechanism responsible for seizure termination leading to continue seizure activity that mildly to long-term consequences including neuronal death, neuronal injury and alterations of neuronal networks, depending on the type and duration of status epilepticus". It is important to emphasise that the duration, when a seizure is most likely to be prolonged, depends on the type of status. There is current evidence that a generalized tonic–clonic seizure exceeding 2–3 min is likely to go on into status epilepticus. Thus, the definition of 5 min has been widely accepted to designate a condition as status epilepticus and treated as such with all available emergency measures. The causes of status epilepticus may be divided in the common, and the uncommon ones. In the developed countries of the industrial world cerebrovascular accidents, traumatic brain injury, intoxication and epilepsies are the most common causes. In the developing world infections are the prevailing cause of status. The uncommon causes deserve special attention, because identification of the causes and its proper causal treatment is important for prognosis of SE. Uncommon causes, such as autoimmune encephalitides and inflammatory diseases might respond well to immunosuppressant, while rare infections and metabolic disorders must follow another treatment strategy. Most treatment protocols worldwide follow a staged approach for generalized convulsive status epilepticus, which includes benzodiazepines as first line agents, followed by intravenous antiepileptic drugs (levetiracetam, valproic acid, phenytoin and lacosamide). If seizures persist patients should be further treated in the neurological intensive care unit. Due to the lack of randomized controlled trials at this stage, pure empirical treatment is the predominant method used. Barbiturates, benzodiazepines, propofol and ketamine are widely used with different enthusiasm of intensivists and neurologist. The outcome depends on the duration of status and its cause. The main negative predictors are old age, symptomatic etiology, long duration and deep coma. Several scores to predict the negative outcome are currently under clinical evaluation.

Disclosure: E. Trinka has acted as a paid consultant to Eisai, Ever Neuropharma, Biogen Idec, Medtronics, Bial, Lundbeck, and UCB. He has received research funding from UCB, Biogen-Idec, Sanofi-Aventis, FWF, Jubiläumsfond der Österreichischen National bank and Red Bull. He has received speakers honoraria from Bial, Eisai, GL Lannacher, Glaxo Smith Kline, Böhringer, Viropharma, Actavis, and UCB.

Symp2-2
Pharmacotherapy: initial and established status epilepticus

H. R. Cock
London, UK

After over two decades of largely retrospective and small case series, (with the noteable exception of the Treiman study of 1998) a drive towards evidence based treatment of convulsive status epilepticus (CSE) has gained considerable momentum in the last few years. Whilst age and etiology remain the primary predictors of outcome, prompt control (within 1–2 h) now established as an important predictor. There is also now good evidence and agreement that Midazolam (buccal, in and out of hospital) and Lorazepam (intravenous) should be used in preference to diazepam in initial status, and that for second line agents, there are several efficacious alternatives. Speed and adequacy of treatment, which in turn may be reflected in familiarity with the drug, are probably more important than which drug is used on current evidence, although both valproate and levetiracetam are gaining favour over (fos)phenytoin. This is despite CSE being an unlicensed indication, but reflects ease of use, better side effect profiles and what looks like at least equivalent efficacy (Yasiry & Shorvon Metaanalysis, Fig. 1; HC review Fig. 2). A long awaited adequately powered randomized controlled trial (ESETT) to provide good quality comparative efficacy and safety data is now in the late stages of development, pending confirmation of funding. International guidelines on both sides of the Atlantic reflect current evidence, yet considerable variation in practice still exists both between and within countries. Lacosamide is also emerging as a possible alternative. Newer initiatives include technological advances making the possibility of rapid EEG in the emergency department tantilizingly close, and a proposal to consider earlier intubation and anaesthesia than is currently typical. Neuroprotection, beyond that directed at the etiology, remains a relatively distant prospect, and there is still considerable work to be done on how best to implement evidence based practice more widely.

Disclosure: Dr Cock has received hospitality and/or honorarium from the manufacturers of all currently licensed AEDs. Full disclosed over the last 5 years is at http://www.whopaysthisdoctor.org/.

Symp2-3
Immunity and inflammation in status epilepticus

M. Seeck
Geneva, Switzerland

In recent years, an increasing number of auto-antibodies (AB) are detected in the CSF and serum of patients with new onset epilepsy. Some of these patients develop status epilepticus (AB-SE), convulsive or non-convulsive, necessitating intensive care. From several case reports and few small series it became evident that AB-SE is a severe but often reversible condition. However, the delay of treatment effect of immune-modulating drugs or plasmapheresis is variable, and we do not yet know the optimal treatment algorithm. If AB-SE has a paraneoplastic origin, outcome appears to be better if the tumor can be successfully treated. We will review most frequent clinical presentations related to distinct antibodies, as well as relevant diagnostic and therapeutic approaches. AB-SE is probably still under-diagnosed. Only increased awareness will shorten the still considerable delay to diagnosis, and ultimately to treatment, hopefully related to an overall better prognosis of AB-SE.

Disclosure: During the last 2 years, Dr Seeck received consultant fees from UCB and EISAI.

Symp2-4
Refractory and super-refractory status epilepticus (ICU management)

A. Rossetti
Lausanne, Switzerland

Status epilepticus (SE) not responding to an initial treatment with benzodiazepines and one antiepileptic drug defines the condition of refractory status epilepticus (RSE); it occurs in about 1/3 of patients with SE, and is related to a high morbidity and mortality. While there is a wide consensus on attempting a prompt control of RSE, scarce evidence is available to support the choice of specific treatments and strategies. In particular, the delicate balance between the aim of aborting ongoing seizures on the one side, and the risk of treatment-related side-effects on the other, represents a very challenging issue. Of note, age and etiology are the major independent outcome SE predictors (which should always be actively addressed), while existing studies are controversial regarding the specific prognostic impact of SE treatment.

Most expert guidelines recommend that RSE treatment strategies should be adapted to the clinical situation: in order to minimize complications, focal RSE without major consciousness impairment should be approached without coma induction, at least initially; conversely, a rapid escalation towards pharmacological coma and EEG-verified seizure control should be undertaken in generalized-convulsive forms. For this purpose, midazolam, propofol or barbiturates represent the most popular compounds. Should RSE continue despite this step, the so-called super-refractory SE may be managed with several additional treatments, such as other anesthetics, further antiepileptic drugs, immunomodulatory agents, ketogenic diet, or non-pharmacological approaches (e.g., electroconvulsive treatment, hypothermia). Prolonged SE treatment lasting for weeks or months may sometimes still result in a good functional outcome; therefore, it is mandatory not to stop SE treatment unless a clearly irreversible brain damage is proven.

Awaiting well-designed studies of these conditions, it seems reasonable to tailor the therapeutic management to the underlying biological background of each patient.

Disclosure: Nothing to disclose.

Peripheral neuropathies: present and future

Symp3-1
Genetic neuropathies: chances for treatment

R. Martini
Würzburg, Germany

Genetic neuropathies of the Charcot-Marie-Tooth type 1 are presently not treatable. Previous studies from our laboratory have shown that in models for three distinct forms of Charcot-Marie-Tooth neuropathy, phagocytosing macrophages mediate demyelination and perturbation of axons. One important mediator is monocyte chemoattractant protein-1 (MCP-1; Ccl2) which is expressed by mutant Schwann cells. Another important cytokine is colony-stimulating factor-1 (Csf-1), expressed by endoneurial fibroblasts and essential for macrophage-mediated demyelination and axonopathy. Based on these findings, we considered the possibility that attenuating macrophage-related peripheral nerve inflammation could be a putative option to ameliorate disabling symptoms associated with CMT-1. As a first approach, we orally treated three distinct CMT-1 models with a novel and highly selective Csf-1-receptor (Fms kinase) inhibitor (provided by Plexxikon Inc.), which was tested in a phase 1 clinical trial for the treatment of rheumatoid arthritis. In all models investigated, a high concentration of the inhibitor led to a robust decline of macrophages in the peripheral nerves, accompanied by an alleviation of demyelination, as revealed by electron microscopy and electrophysiological recordings. However, at the doses initially applied, a reversible and subclinical reduction of the compound muscle action potentials (CMAP) was also detectable. By step-wise reduction of the inhibitor concentration, we could preserve CMAP while still substantially attenuating macrophage numbers in nerves and spinal roots. Studies are now under way which focus on the pathological and clinical outcome of respective long-term treatments. In another approach, we injected human adipose derived mesenchymal stem cells (MSCs) isolated from lipoaspirate into tail veins of Cx32-deficient mice, a model for CMT-1X. Single injection of these immune modulatory xenografts caused macrophage attenuation and mild preservation of myelin. Future experiments are designed to optimize the treatment regime in order to receive an even more robust and persistent treatment effect in the mouse model. Our experiments demonstrate that attenuating phagocytic macrophages in peripheral nerves might be a promising chance for treatment of inherited neuropathies of the CMT-1 type.

Disclosure: Supported by German Research Foundation (DFG, MA 1053/6-1); Plexxikon Inc. (USA) and CMT Association, USA. A. v. H was an ERASMUS student from the University of Antwerp, Belgium (local co-supervisor: Vincent Timmerman).

Diagnosis and treatment of diabetic neuropathy: Can we do better?

Rayaz A. Malik.
Manchester, UK

Not received

Disclosure: Not received.

Symp3-2
Immune-mediated neuropathies: how to optimise treatment?

P. A. van Doorn
Rotterdam, The Netherlands

Guillain-Barré syndrome (GBS) in most cases is a post infectious and potentially life-threatening heterogeneous disease. The main characteristics are rapidly progressive symmetrical weakness of the extremities and low or absent tendon reflexes. About a quarter of patients develops respiratory insufficiency, many patients have signs of autonomic dysfunction and pain. Prognostic models are now available that help to accurately predict the chance that an individual patient will require artificial ventilation, and to predict the probability to walk unaided after half a year. These simple models are ready to use, at or soon after hospital admission, and may help making important clinical decisions. Additional models are under construction. Treatment is with intravenous immunoglobulin (IVIg) or plasma exchange. Despite this treatment, the prognosis is still cumbersome in a substantial proportion of patients. Therefore new treatment trials have been started. About 10 percent of GBS patients will have a treatment related deterioration (TRF), requiring a repeated treatment course. Other patients initially diagnosed as GBS will turn out to have acute-onset chronic inflammatory demyelinating polyradiculoneuropathy (A-CIDP). This condition may indicate a switch to maintenance IVIg or to steroid treatment. For CIDP is has been shown that steroids, IVIg and plasma exchange are effective. Recent trials evaluated pulse high-dose steroid treatment in comparison with IVIg. Follow-up studies in CIDP found some factors related to the initial IVIg treatment response and to the requirement of long-term treatment. These studies may help to further optimise treatment in these immune-mediated neuropathies.

Disclosure: Nothing to disclose.

Symp3-3
Amyloid neuropathies: treatment

D. Adams
Kremlin-Bicêtre, France

Amyloid neuropathies (AN) are progressive and life-threatening sensorymotor and autonomic neuropathy. As amyloidosis are systemic diseases, each newly diagnosed AN case should be screened also for cardiological and nephrological impairment but also for ocular manifestations in transthyretin FAP (TTR-FAP) or hematological involvement for Light-chain amyloidosis (AL-amyloidosis).

Treatment of AN includes anti-amyloid therapy, symptomatic therapy (i.e. for sensorimotor and autonomic neuropathy, visceral involvement), and treatment of endstage organ failure (cardiac, renal).

Anti-amyloid therapy:

i) For TTR-FAP, it includes liver transplantation (LT) to remove the main source of variant TTR, TTR-kinetic-stabilizers (tafamidis, diflunisal) to stabilize the tetrameric TTR and inhibit release of amyloidogenic monomers. Indications for these treatments depend on the stage of the neuropathy, the variant TTR, the age of the patient and severity of organ involvement. Pacemaker implantation should be discussed in case of significant conduction disorder. Heart or kidney transplantation must be discussed in endstage cardiac or renal failure in stage 1 neuropathy.

LT has better results in early onset (<50 yo) V30 M TTR-FAP, allowing to double median survival and to stop progression of the disease in most of cases. Recently, Tafamidis (Vyndaqel®) obtained marketing authorisation in Europe in stage 1 (walking unaided) of the disease to delay progression of the disease and diflunisal showed also the ability to slow progression of the disease in TTR-FAP in many variants and varied stages of the disease. Two phase 3 clinical trials are actually testing TTR gene silencing approach with RNAi or antisense oligonucleotids in order to block hepatic synthesis of both variant and wild type TTR, this latter being also pathogenic in late onset TTR-FAP.

ii) In AL amyloid neuropathy, treatment is based on chemotherapy to control the underlying plasma clone that produces amyloidogenic light chain (LC); the association of an alkylating agent with high-dose dexamethasone is considered as the current reference treatment. The hematological response may be checked by serial measurements of serum free LC. Survival in AL amyloidosis depends on amyloid heart disease, and haematological response to treatment.

Enhancing the clearance of amyloid deposits with monoclonal antibodies against human serum amyloid P component (hu-SAP Mab) is another strategy. SAP is a ubiquitous non–fibrillar plasma glycoprotein in amyloid deposits. A phase 1 study is ongoing in UK in patients with amyloidosis to assess the safety and efficacy. In case of positive results, this approach could be applicable to amyloid neuropathy.

In conclusion: treatment of AN considerably improved during the past 20 years and benefit of major scientific and medical advances; many clinical trials are in progress and could end in combination therapies.

Disclosure: Consultant for ISIS, Consultant for ALNYLAM, Conference speaker in symposium by PFIZER.

Sunday, 1 June

Plenary Symposium: Hot topics in neuroscience

PlenSymp1
Immunology: The gut-lung-brain connection in CNS autoimmunity

H. Wekerle
Martinsried, Germany

Brain-specific autoimmune T cell clones are normal components of the immune repertoire. In most people they remain dormant throughout life, only in patients with autoimmune demyelination, as supposedly in MS, they become activated and attack their target tissue. We have studied the events triggering brain autoreactive CD4+ T cells in a transgenic mouse model featuring spontaneous development of relapsing-remitting encephalomyelitis. The transgenic autoimmune T cells are activated in the gut associated lymphatic tissues dependent on an interaction with components of the commensal gut flora. Germfree mice are fully protected against spontaneous disease development, while colonization of such animals with commensal bacteria leads to prompt induction of disease. Triggering of autoimmunity is not a global property of all gut floral components, but is restricted to discrete subpopulations. Importantly, diet, which profoundly imprints the microbiota, also strongly acts on the triggering phase of brain autoimmunity. We shall discuss consequences for understanding the pathogenesis of human multiple sclerosis, and potential therapeutic uses of these findings.

Disclosure: Nothing to disclose.

PlenSymp2
Optogenetics in Neurology

A. Adamantidis
Berne, Switzerland

Understanding the biological basis of neurological disorders affecting the nervous system is crucial to the development of therapeutic strategies. The heterogeneity of cell types in the central nervous system and their complex wiring into circuits has often limit both clinical and experimental progress in translational medicine. Recently, the optogenetic technology has opened new perspective to identify the functions of those circuits in health and disease. Optogenetics represents a versatile approach to probe the function of neural circuits in animal model of human pathologies. Combined with electrophysiological, optical or behavioral methods, the use of optogenetics recently identified cellular substrates of disease symptoms, including arousal/sleep, anxiety/depression, addiction, fear, autism and parkinsonism. This lecture will provide the audience with up-to-date information and illustration of optogenetic principles and applications in experimental neurology.

Disclosure: Nothing to disclose.

PlenSymp3
Prion disease (accumulation of proteins)

A. Aguzzi
Zurich, Switzerland

Transmissible spongiform encephalopathies (TSEs) are inevitably lethal neurodegenerative diseases that affect humans and a large variety of animals. The infectious agent responsible for TSEs is the prion, an abnormally folded and aggregated protein that propagates itself by imposing its conformation onto cellular prion protein (PrPC) of the host. PrPC is necessary for prion replication and for prion-induced neurodegeneration, yet the proximal causes of neuronal injury and death are still poorly understood. Prion toxicity may arise from the interference with the normal function of PrPC, and therefore understanding the physiological role of PrPC may help to clarify the mechanism underlying prion diseases. I will discuss the evolution of the prion concept, how prion-like mechanisms may apply to other protein aggregation diseases, the events occurring during neuroinvasion, and the possible scenarios underlying brain damage. If time allows, I may also briefly review potential antiprion therapies and current developments in the realm of prion diagnostics.

Disclosure: Nothing to disclose.

PlenSymp4
The frontotemporal dementias: new insights

M. N. Rossor
London, UK

The frontotemporal dementias (FTD) have always provided a rich source of study into brain/behaviour relationships due to the strikingly selective pattern of neuronal degeneration that can occur and is exemplified by semantic dementia associated with TDP 43 deposition in neuronal networks underpinning semantic as opposed to episodic memory. Semantic dementia is one of the three prototypic FTD syndromes, the others being behavioural variant and progressive non-fluent aphasia (PNFA) which is also being fractionated into more fine-grained classifications. The syndromic classifications are mirrored by neuropathological classifications derived from the emerging analyses of the molecular neuropathology. The correspondence between a particular clinical presentation and the underlying molecular pathology is variable. A significant proportion of patients with FTD have a family history, and in approximately 20 % the disease is inherited on an autosomal dominant basis. Importantly, the familial form shares many of the characteristics, both clinically and neuropathologically, with sporadic disease. The identification of three main disease genes, and additional rare mutations have revolutionised our understanding of FTD. C9ORF, which is the commonest underlying mutation, may present both as behavioural variant FTD and amyotrophic lateral sclerosis, offering particular insights into factors that might determine the selective vulnerability of the underlying networks. The study of autosomal dominant disease also allows pre-manifest observations, as has been successfully pursued with familial Alzheimer's disease (the DIAN study), and it is possible to demonstrate an important pre-clinical phase of biochemical and imaging changes which may precede a diagnosis by many years. A number of potential therapeutic candidates, some of which would involve repurposing current drugs that have been shown in vitro to be of potential value, provide optimism for intervention in the important therapeutic window at a pre-manifest stage.

Disclosure: The author received grant funding from MRC, National Institute of Health research (NIHR); he is Vice President of the UK Alzheimer Society; he is NIHR National Director for Dementia Research; he is on a Servier DMC for an Alzheimer drug.

Monday, 2 June

Alzheimer prevention and uncommon causes of dementia

Symp4-1
Prevention of Alzheimer's disease

P. Scheltens
Amsterdam, The Netherlands

Alzheimer's disease is the most common form of dementia. Dementia is the fastest increasing health problem for society in the coming 30 years. This is a challenge for all health care systems in Europe and concerns neurologists because it will be becoming the most significant brain disorder in the future.To date, most progress has been made in diagnosing the disorder and new guidelines are present that allow for use of biomarkers to identify the disease process in its earliest presentation.No effective causal treatment exists yet, hence more attention is given to preventive measures. The talk will distinguish between primary and secondary prevention and will review existing data.

Disclosure: Nothing to disclose.

Symp4-2
Immune mediated dementias

J. M. Schott
London, UK

The last decade has seen major advances in our understanding of immune mediated syndromes associated with cognitive impairment. Whilst paraneoplastic forms of limbic encephalitis have been recognized for many years, the discovery that antibodies directed against the voltage-gated potassium channel complex can produce a sub-acute and potentially treatable limbic encephalopathy usually in the absence of an underlying tumour was a seminal finding. Subsequent studies have extended the phenotypic spectrum associated with this condition notably to include faciobrachial dystonic seizures which can precede the development of cognitive decline; defined specific antigenic targets (LGI1, CASPR2 and contactin-2) within the potassium channel complex which go some way towards explain some of its heterogeneity; and explored clinical outcomes and potential treatment options. The second major breakthrough was the identification of antibodies directed against NMDA-receptors as the cause of a distinctive encephalopathy, initially in young women with ovarian teratomas. Over time, the phenotype of this syndrome has been extended and now includes men, older women, and individuals without evidence of neoplasia; and considerable inroads have been made in defining its pathophysiology and how best it should be treated. As well as these two conditions, a range of other, rarer, antibody-mediated encephalopathies, including those associated with antibodies directed against AMPAR, GABA-B, GAD and Glycine receptors are now recognised. In parallel with these sub-acute, potentially treatable, if relatively rare syndromes, an emerging body of evidence from pathological, genetic, imaging and basic science research has implicated the inate immune system as playing an important role in the aetiology of the much commoner neurodegenerative dementias. In this talk I will provide a clinical overview of the antibody mediated encephalitides, with a particular focus on their cognitive features, identification, and treatment, as well as briefly outlining the evidence for a role for immunity in the pathogenesis of Alzheimer's disease.

Disclosure: Nothing to disclose.

Symp4-3
Rare dementias

S. Sorbi
Florence, Italy

Uncommon dementias indicate a wide heterogeneous group of rare disorders causing cognitive impairment and are generally characterized by an early age at onset. Uncommon causes of dementia comprise a wide number of very rare and often misdiagnosed disorders, including late-onset forms of childhood metabolic inborn errors, inflammatory disorders, infectious diseases and toxic-metabolic abnormalities.

Thus, uncommon dementias greatly overlap the concept of young-onset dementia. i.e. early-onset forms of common neurodegenerative dementia, such as familial Alzheimer's Disease, dementia associated with other neurological disorders (Huntington's disease, myotonic dystrophies, autosomal dominant cerebellar ataxia or hereditary spastic paraparesis), or late-onset forms of childhood conditions, such as mitochondrial disorders, lysosomal storage disorders and leuko-dystrophies. Potentially reversible etiologies, including inflammatory disorders and infectious or toxic-metabolic abnormalities, can also play a part in the causes of rare dementia.

It should be noted that information on the frequency of uncommon dementias among the elderly is not available, while the little epidemiological data available on young-onset dementia comes from restricted geographical settings. Clinical data on most of them are based only on a single case report, and often diagnosis is challenging due to the clinical heterogeneity among and within the various disorders. Thus, a complete list of un-common dementia is not possible. The creation of diagnostic categories, even if arbitrary, can help clinicians make differential diagnoses and may reduce diagnostic errors, which is of great importance since disease modifying therapies are available in some cases. Creation of a regional or national registry may be useful to make a real estimate of the prevalence of uncommon dementia and to improve our clinical knowledge overall.

Disclosure: Nothing to disclose.

Symp4-4
Parkinsonism associated with cognitive impairment

M. Emre
Istanbul, Capa, Turkey

An association between Parkinsonism and dementia can occur in a number of primary degenerative dementias as well as in some symptomatic forms. Primary degenerative dementias presenting with this association are mainly tauopathies and synucleinopathies, characterized by accumulation of tau or alpha-synuclein protein (Lewy bodies) in abnormal forms. Alpha-synuclein or Lewy-body related dementias are by far more common, they constitute the second most frequent cause of dementia following Alzheimer disease. The prototypical forms are Dementia with Lewy Bodies (DLB) and Demantia associated with Parkinson's disease (PD-D), there are, however, also mixed forms such as "Lewy-body variant of Alzheimer's disease". Clinically Lewy-body related dementias are characterized by a predominance of executive dysfunction, early and disproportinate impairment in visual-spatial functions, less severe amnesia and prominent behavioral symptoms such as hallucinations. The clinical profile of cognitive and behavioral symptoms may be determined by the amount of concomitant Alzheimer-type pathology, which often is co-existent to varying degrees, particularly in patients with DLB. Biochemically the most prominent abnormalitiy in PD-D and DLB is a cholinergic deficit, cholinesterase inhibitors have been shown to provide some benefits in both conditions.

Disclosure: Nothing to disclose.

Multiple sclerosis: an unmet need

Symp5-1
Understanding the natural history of MS progression

A. Scalfari
London, UK

Prognosis of MS has been puzzling clinicians for decades. In relapsing remitting (RR) MS, the disability progression seems to occur in two independent stages, separated by a clinical watershed of irreversible moderate disability (DSS 3/4), which heralds the conversion to secondary progressive (SP) MS in most of cases. Once the progressive phase supervenes, the evolution of the disease becomes relatively stereotyped and not influenced by the previous clinical history, implying that the long-term outcome is mainly determined before the onset of progression. The concept is further reinforced by the similar rate of disability accumulation, between primary and SP MS patients. However, at individual level the evolution of the progressive phase remains considerably variable and what differentiates slow from rapid "progressors" needs to be elucidated. Recent analysis of the London Ontario database suggested that, early in the disease course, the axonal degeneration might become disconnected from the phasic inflammatory processes. Total (occurring during the RR phase) and late (occurring after the second year) inflammatory attacks did not influence the outcome. In contrast, a high number of early relapses (occurring during the first 2 years) associated with a faster development of severe disability, secondary to an increased probability of experiencing the progressive course. In addition the age at onset of the RR phase affects the disease course, by increasing the risk of converting to SP MS. Groups older at onset attain progression and clinical endpoints in significantly shorter times. Therefore, the onset of the SP phase is the key determinant of the long term prognosis. Age at onset and early relapses frequency are the two strongest predictors of the latency to SP. The outcome severity is regulated by mechanisms tied to the onset of progression, which are likely to be active during the early stage of the disease, the most plausible window of therapeutic opportunity.

Disclosure: I received honoraria and travel support from Teva and Biogen.

Symp5-2
Pathophysiology of progression

C. Stadelmann
Göttingen, Germany

Progressive MS is characterized by insidious clinical worsening without important relapse or MRI activity. Immunomodulatory drugs do not adequately prevent disability progression in the chronic disease phase. Pathologically, the progressive phase of MS is characterized by a predominance of inactive or chronic active lesions as opposed to actively demyelinating lesions, widespread cortical demyelination and increasing axonal loss and neuronal dysfunction. However, more recently, important meningeal lymphocytic infiltration has been reported to accompany the chronic disease phase. Nevertheless, our understanding of the pathogenesis of progressive MS is still limited. This presentation will summarize our current knowledge on the pathophysiologic mechanisms operating in the chronic progressive disease phase.

Disclosure: Nothing to disclose.

Symp5-3
Biomarkers (including predictors/MRI)

G. Giovannoni
London, UK

Objectives: Biomarkers are used in MS to aid in the diagnosis of MS by helping to exclude alternative diagnoses. More recently, with the introduction of disease modifying therapies, biomarkers are being increasingly used to help monitor the underlying MS disease processes, aid in predicting the future course of MS and helping reduce the risk of disease modifying therapies.

Methods: Professor Giovannoni will use case studies to demonstrate the utility of biomarkers that are in current clinical practice to help diagnose, predict the clinical course, response to treatment and to help manage disease-modifying therapies with appropriate pharmacovigilance procedures.

Results: MRI and spinal fluid monitoring are being increasingly used to assess the response or lack of response to disease-modifying therapies. The current strategy of treat-2-target of no evident disease activity (NEDA) relies on frequent MRI assessments. The incorporation of brain atrophy and possibly spinal fluid neurofilament levels into the definition of NEDA promises to improve the long-term clinical outcome of people with MS. The use of biomarkers for pharmacovigilance is being increasingly used in MS; for example, the detection of antibodies to JC virus and the introduction of an anti-JCV antibody index have reduced the number of cases of PML in patients with MS on natalizumab.

Conclusions: MS is a complex disease. Biomarkers are helping predict the clinical course of MS and are being increasingly used to monitor the response to treatment and to maximise the safety of patients on specific therapies.

Disclosure: Prof. Giovannoni has received compensation for participating on Advisory Boards in relation to clinical trial design, trial steering committees and data and safety monitoring committees from: Abbvie, Bayer-Schering-Healthcare, Biogen-Idec, Canbex, Eisai, Elan, Fiveprime, Genzyme, Genentech, GSK, GW-Pharma, Ironwood, Merck-Serono, Novartis, Pfizer, Roche, Sanofi-Aventis, Synthon-BV, Teva, UCB-Pharma and Vertex-Pharmaceuticals.

Symp5-4
Future therapeutic strategies

G. Comi
Milan, Italy

The recent approval by European Medicines Agency (EMA) of three new disease modifying drugs for relapsing remitting multiple sclerosis (RRMS) characterised by different mechanisms of action and different safety/efficacy profile represents a significant progress in the treatment of the relapsing phase of the disease. Quite interesting results also emerged for clinically isolated syndromes. Long term follow up of clinical trials exploring the efficacy of beta interferons and glatiramer acetate confirmed the importance of an early treatment with clear benefits still persisting after many years of treatment. Moreover results of the ORACLE study, exploring the efficacy and safety of oral cladribine and the TOPIC study testing teriflunomide in early multiple sclerosis indicate the importance of immunosuppression to target the peripheral immune dysfunction. At the same time the significant advances in risk minimisation for natalizumab and fingolimod now allow to try to individualize treatments using predictive and prognostic factors, with the aim to maintain the patients in the condition of freedom from disease activity. Unfortunately, quite different is the situation for the progressive forms of multiple sclerosis. In this case, the key mechanisms underlying the phenomenon of progression are far from being fully understood. As a consequence a treatment for this phase of the disease does not exist. New hopes are now open by the Progressive MS Alliance (PMSA) a joint initiative of some National MS Societies involving in a coordinate effort many European and North American labs and MS centres.

Disclosure: Received personal compensation for consulting services and/or for speaking actitivies from Novartis, Teva, Genzyme, Merck Serono, Biogen, Bayer, Actelion, Almirall and Serono Symposia International Foundation.

Evolving concepts in movement disorders: EFNS/ENS/MDS-ES Symposium

Symp6-1
Early diagnosis and biomarkers in PD

W. Poewe
Innsbruck, Austria

Slowing of disease progression remains the single most important unmet need in the treatment of Parkinson's disease (PD). However, numerous clinical trials over the past 20 years failed or produced inconclusive results. Reasons for such failures include shortcomings of current disease models to detect target engagement and perform target validation of potential interventions as well as difficulties in choosing clinical endpoints and the lack of reliable biomarkers sensitive to disease progression. In addition, target populations for neuroprotective or disease-modifying trials have been those with early, clinically established PD. Recent research has provided substantial evidence that the pathology underlying PD likely begins years before the first manifestation of classical motor signs of PD. It is therefore conceivable that disease-modifying or neuroprotective interventions targeting the earliest phases of PD might offer greater potential for disease modification as compared to later stages. Idiopathic REM-sleep behavior disorder, hyposmia, depression, constipation have all been associated with an increased risk to later develop classical motor PD and might represent "pre-motor" stages of the illness. In addition, genome-wide association studies have identified several PD risk alleles while potential proteomic markers for PD risk are currently under investigation. Imaging may be another tool to identify at-risk populations for PD, either via preclinical abnormalities in functional dopaminergic imaging using dopamine transporter SPECT or PD susceptibility via transcranial ultrasound of the midbrain. A recent, population-based, prospective study has shown a highly significantly increased risk to develop PD in healthy subjects showing midbrain hyperechogenicity on transcranial ultrasound. There is emerging evidence that a combination of markers may be able to define at-risk populations for PD who could be entered into future "neuropreventive" trials.

Disclosure: Nothing to disclose.

Symp6-2
Movement disorders moving beyond the motor phenotype

H. Reichmann
Dresden, Germany

Clinically, Parkinson's disease (PD) is mainly characterized by motor symptoms such as bradykinesia, rigidity, tremor and postural instability. The clinical diagnosis of this disease is based on these cardinal symptoms. In addition, it has become increasingly apparent that PD patients also suffer from non-motor symptoms which impair their quality of life quite considerably. Non-motor symptoms consist of

disturbances of olfaction, sleep and the autonomic nervous system. Furthermore, although James Parkinson claimed in 1817 in his report "An Essay on the Shaking Palsy" that "the senses and the intellect are uninjured", we now know that this statement does not hold true. There are many PD patients with neuropsychiatric symptoms such as anxiety, depression and dementia. Gambling and sexual abnormalities were recently added to this list.

It was the work of Braak et al. who showed that the first morphological abnormalities such as Lewy bodies and deposition of α-synuclein occur not in the substantia nigra, but in the olfactory bulb and in the nc. vagus and the glossopharyngeus and also in the salivary glands and the enteric nervous system of the gastrointestinal system.

For this reason it is not surprising that impairment of olfaction is a very common feature of idiopathic PD. We and others could show that up to 90 % of all PD patients present with hyposmia and most patients report that this loss of olfaction occurred quite some time before the first motor disturbances were present.

Depression in PD is a very common phenomenon which is predominantly caused by degeneration of monoaminergic neurotransmitter systems and by fronto-cortical dysfunction. Neuropathological findings show a loss of neurons of the noradrenergic Nc. coeruleus and also a loss of neurons of the serotonergic nc. Raphe in some patients, which highlights that it is not only reactive behaviour which causes depression. Depression affects at least 40–50 % of PD patients and it may even precede the motor symptoms. This is the case in 30 % of all patients with PD and depression. Depression in PD is usually of mild-to-moderate intensity and suicide is rare. Symptoms of dysautonomia are a common occurrence in Parkinson's disease (PD). Constipation is one of the commonest non-motor symptoms in Parkinson's disease and can precede development of the disease. Nocturnal sleep disturbance occurs in 60–98 % of PD patients and is often severe. REM sleep behaviour disorder (RBD) represents a parasomnia characterised by loss of the normal skeletal muscle atonia during REM sleep, thus enabling patients to physically enact their dreams, which can often be vivid or unpleasant. Besides these early non-motor symptoms patients suffer from urinary incontinence, sexual dysfunction, profuse sweating, drooling of saliva. Neuropsychiatric problems include fatigue, apathy, psychosis and dementia which underlines that non-motor symptoms give rise to a highly disturbed quality of life and for that reason need our attention and new treatment options are needed.

Disclosure: Professor Reichmann was acting on Advisory Boards and gave lectures and received research grants from Abbott, Abbvie, Bayer Health Care, Boehringer/Ingelheim, Brittania, Cephalon, Desitin, GSK, Lundbeck, Merck-Serono, Novartis, Orion, Pfizer, TEVA, UCB Pharma, and Valeant.

Symp6-3
Controversies in tremor classification

K. P. Bhatia
London, UK

The commonest cause of pathological tremor is essential tremor (ET). However, it has proved difficult to identify genetic mutations causing ET, particularly because other causes of tremor continue to be misdiagnosed as ET. Dystonia and dystonic tremor remain an enigmatic issue. Whether subjects with dystonia or Parkinson's disease (PD) carry an increased genetic risk of developing ET, or vice versa, is controversial. In addition, the notion of a separate disorder of benign tremulousparkinsonism (BTP) has been debated. An overview will be provided including difficulties within the current classification of tremor and a suggestion for new classification in view of the above controversies.

Disclosure: Nothing to disclose.

Symp6-4
Future of DBS in movement disorders

G. Deuschl
Kiel, Germany

Deep brain stimulation has been admirably successful in the past decade. The problem of fluctuating Parkinson's disease has found a new solution for those patients having limited comorbidity and few cognitive problems. Many hitherto untreatable tremors and primary dystonias can be successfully treated. Severe tics, obsessive–compulsive disorder and many other general neurological diseases can be addressed. Nevertheless, many questions are still unanswered and the potential for future improvements is huge. The timing for surgery in Parkinson's disease is still one of the main issues. We do not know the very long-term course of patients treated with DBS. New indications are still under development as for example the medication-resistant focal dystonias and particularly the secondary dystonias. Technological development in this field has just begun. As the circuit consequences of pathology are further explored the interventions may become more customized and the stimulating paradigms can adapt. Closed-loop stimulation will be one of the hot topics of the future. Another area of research must be the perception of this treatment by the patients and their caregivers. We know that some patients have only limited improvement of their life quality despite favorable motor improvement. DBS has introduced a new dimension for the neurologist's capabilities to treat their patients. This also comes with new educational challenges for the neurologist of the twenty-first century.

Disclosure: GD has received lecture fees from UCB, Medtronic and Desitin and has served as a consultant for Medtronic, Sapiens, Boston Scientific and Britannica. He received royalties from Thieme publishers. He is a government employee and he receives through his institution funding for his research from the DFG, BMBF and Medtronic.

Headaches: an update on neurobiology, genetics and management

Neurobiology of the transformation from episodic to chronic headache

T. Jürgens
Regensburg, Germany

Disclosure: Not received.

Symp7-1
Genetics and neurobiology of conditions causing migraine and stroke (CADASIL, Col4A1, HRNS, FHM)

C. Ayata
Charlestown, USA

Epidemiological and neuroimaging studies have unequivocally shown that migraineurs are at increased risk for stroke. Although the mechanisms underlying this association are unknown, a number of diverse genetic conditions predispose to both migraine and stroke, such as mutations in NOTCH3 (CADASIL), COL4A1, TREX1 (RVCL), and mitochondrial genes (MELAS), providing important clues to the pathophysiology. Among these, CADASIL, RVCL, and mutations in COL4A1 are all characterized by cerebral small vessel disease and white matter degeneration implicating vascular dysfunction, whereas MELAS relates to mitochondrial energy metabolism as potential mechanisms for migraine with or without aura. In addition, higher risk of stroke in monogenic familial migraine syndromes

provides further insight into causality. Altogether, this talk will provide an overview of the genetic conditions, pathophysiological implications and recent experimental data to dissect the mechanisms.

Disclosure: Nothing to disclose.

Strategies in the management of chronic headache patients

J. Schoenen
Liège, Belgium

Not received

Disclosure: Not received.

Symp7-2
Acute headache units

A. Ducros
Paris, France

Objectives: Providing the audience with an update about acute headache units.

Methods: The lecture will be based on the experience gained in the Parisian acute headache unit that was launched in 2000, and where more than 10000 acute headache patients are seen every year.

Results: Academic acute headache units have three main goals. Their first aim is to provide the best possible management to patients with acute headaches. The most challenging part of this management is to identify serious secondary causes in patients presenting with isolated headaches. Therefore, acute headache units require an easy access to emergent investigations for patients suspected of a serious secondary cause, including cerebral and cervical imaging, and emergent blood and CSF analysis. Moreover, a neurology department with a stroke unit and a neurosurgery department are needed to hospitalise patients. Second, an acute headache unit is a unique tool for practical medical teaching. Due to its large recruitment, such a unit gives interns and fellows the opportunity to become familiar with almost all primary and secondary headache forms within a few weeks. For example, in the Parisian headache unit, a mean of 15–20 patients are admitted every week for cluster headache, and a patient with idiopathic intracranial hypotension is admitted every 2 weeks. Finally, an acute headache unit offers the opportunity to set up specific research programs focused on some infrequent headache disorders, either primary or secondary, on diagnosis strategies and procedures, and on acute pain-relieving treatments.

Conclusion: Acute headache units may be part of academic headache centres providing the centre has enough headache doctors to put on duty.

Disclosure: I serve as associate editor of Cephalalgia, as member of the editorial advisory board of The Journal of Headache and Pain. I received travel and meeting expenses from Almirall, Merck, Baush&Lomb and Pfizer, received travel expenses and/or honoraria for le.

New therapeutics on the horizon

Symp8-1
Stroke

S. Davis
Parkville, Australia

Thrombolysis with intravenous tPA up to 4.5 h after stroke onset is the major pharmacological strategy in acute ischemic stroke. A major challenge is to substantially increase rates of thrombolysis and deliver earlier therapy. Telestroke is therefore an expanding strategy. The ischemic penumbra lasts many hours beyond the current 4.5 h window and can be detected by multimodal MRI or CTP. In both cases, mismatch between the perfusion lesion and ischemic core represents a potential opportunity for intervention in patients treated at late time windows, to evaluate new therapies, the 20 % of patients with "wake-up stroke" and for patients who do not respond to standard IV tPA. Patient selection with advanced multimodal imaging, more effective devices and earlier treatment times are goals of current trials. We are testing IV tPA in patients with persisting penumbra at later times (4.5–9 h and wake-up stroke) in EXTEND. Newer and more selective thrombolytic therapies include Desmoteplase and Tenecteplase. These IV lytics are being tested in delayed time windows, with imaging used to better select potential treatment responders. Another strategy is to enhance the effects of IV tPA with transcranial ultrasound (the Clotbuster Trial).Endovascular thrombectomy ("clot retrieval") is an attractive approach, with higher rates of recanalization than IV therapy with new-generation devices, but currently awaits level 1 evidence. In our EXTEND-IA trial, we are testing the benefits of endovascular thrombectomy in patients who have routine IV tPA, who have the dual target of a penumbra and an occluded artery.Despite many trials, no neuroprotective strategy has been confirmed to date. There is considerable interest in hypothermia and more innovative trial design, such as ambulance-based therapy.

Disclosure: Nothing to disclose.

Symp8-2
Multiple sclerosis

K.-M. Myhr
Bergen, Norway

It has been a revolution in treatment options and strategies in multiple sclerosis (MS) during the last decades. The first big step came along with the introduction of self-injectable medications of interferon beta-1b/1a and glatiramer acetate in the mid-1990s. These medications gave a relapse-rate reduction of about 30 % compared to placebo, and a modest effect on disability progression as measured by Expanded Disability Status Scale (EDSS).

The next big step came with the introduction of the first monoclonal antibody in 2006. Monthly intravenous infusions with natalizumab improved the efficacy to almost a 70 % reduction in the relapse rate accompanied with a more pronounced effect on disability progression. But this treatment also introduced the life-threatening risk of developing progressive multifocal encephalopathy (PML) that needed strategies for risk stratification.

Fingolimod became the first oral medication in 2011 without injection associated side effects and without the need for frequent hospital based infusions. Although no available head-to-head comparisons, the efficacy of fingolimod seems probably somewhat less than for natalizumab. Even though fingolimod is not associated with increased risk for PML, risk stratifications related to heart diseases and macula oedema are needed.

Recently, another two oral treatments became available for MS-treatment. Teriflunomide (2013) equals the efficacy on relapses as for the injectable medications, but perhaps with more convincing efficacy on disability progression showed by two phase-III studies. Dimethyl fumarate (2014) seems to approach similar efficacy on relapse rate as for fingolimod, and has also shown effects on disability progression.

The second monoclonal therapy came in 2013 with alemtuzumab, which reduce the relapse rate of about 50 % compared to high dose interferon beta 1a, and has higher impact on disease progression. But this therapy may also have serious and potential life-threatening autoimmune induced side effects that need monthly long-lasting blood and urine screenings.

MS is in the early phase dominated by inflammatory destruction of myelin and axons accompanied by lesser degrees of degeneration. Focus has probably therefore been on anti-inflammatory treatment

strategies, and all available therapies seem to have their major mode of actions through anti-inflammatory mechanisms. But neuro-protective therapeutics are also needed, and increasing focus on these aspects seems to evolve. Stimulation of repair processes is another strategy—and emerging therapeutics are also focusing on these aspects.

Personalized medicine driven by biomarkers with high sensitivity and specificity is another important strategy for improved therapy. Early diagnosis and early treatment initiation with highly effective therapies guided by biomarkers will hopefully be the standard of care in MS in the near future.

Disclosure: KM Myhr has received honoraria for lecturing, participation in advisory boards or pharmaceutical company-sponsored clinical trials and travel support from: Allergan, Almiral, Bayer Schering, Biogen Idec, Novartis, Merck-Serono, Roche, Sanofi-Aventis and T.

Symp8-3
Epilepsy

T. Marson
Liverpool, UK

The last 20–30 years has seen the development of new generation of antiepileptic drugs, with more than 15 products reaching the market. These new drugs provide a much wider range of treatment options for patients, and some have proven advantages over standard treatments with respect to adverse effects and pharmacokinetics. However, there is little evidence that these new drugs have had an impact on longer term patient outcomes as 30–40 % of patients continue to have seizures despite optimum treatment. This may not be surprising given the heterogeneity of epilepsy with respect to aetiology and the fact that current drugs are 'anti-seizure' and have no known effect on the underlying biology of epilepsy. It is important therefore to reflect on antiepileptic drug development paradigms and consider how the next step change in antiepileptic treatment might emerge. Six scenarios will be considered in this presentation, which include strategies to use existing treatments more efficiently as well as the development of new drugs. Most scenarios look at a quite distant horizon.

1. Continued development of anti-seizure drugs. A number of potential new drugs are in development using long standing paradigms. Trials are mainly in patients with refractory focal epilepsy. It is unlikely that such drugs will have a significant impact on patient outcomes.
2. Stratified medicine: efficacy. Significant resource is being spent through international collaborations and consortia to try and identify biomarkers (genetic and others) for seizure outcomes with existing antiepileptic drug treatments. Such biomarkers would allow identification of the most effective drug for an individual.
3. Stratified medicine: safety. Genetic biomarkers have already been identified for severe skin hypersensitivity reactions to carbamazepine in Asians and Caucasians. Similar developments may prevent the occurrence of a range of serious adverse effects with a range of drugs.
4. Antiepileptic and disease modifying treatments. We urgently need treatments that influence the underlying biology of epilepsy. These would prevent the development of epilepsy following brain trauma, or alter brain biology once epilepsy has occurred to remove the propensity to unprovoked seizures. Drug targets include inflammatory pathways. Progress is challenged by our continued lack of understanding of the basic biology of the epilepsies, and challenges in trial design.
5. Drug transporter blockers. The drug transporter hypothesis suggests that antiepileptic drugs are pumped away from the epileptogenic zone, although the importance of this hypothesis is still not satisfactorily proven. Drugs that block drug transporters might improve antiepilepetic drug efficacy.
6. Brain stimulation. Vagus nerve and deep brain stimulation are accepted treatments for refractory epilepsy. Other brain stimulation treatments are in development for patients with refractory epilepsy. This includes stimulation of the cerebral cortex.

Disclosure: Nothing to disclose.

Symp8-4
Treatment of hereditary myopathies: a close horizon

Z. Argov
Jerusalem, Israel

Introduction: Treatments of myopathies due to genetic defects have recently advanced to the point of human trials (active or in preparation).

Aims: To review several approaches for therapies giving examples that have reached registered human trials.

Data: The first approach is metabolic treatment to bypass a specific genetic defect (e.g. sialic acid in GNE myopathy). The second is pharmacotherapy of the pathological consequences of a hereditary myopathy either by reducing a specific abnormal accumulation (e.g. trehalose in OPMD) or preventing secondary increase of connective tissue (e.g. halofuginon in DMD). The third is bypassing the genetic defect by manipulating the RNA (e.g. exon skipping in DMD). A more complicated approach is the introduction of the normal gene (or a modified form) to compensate for the presence of a defective one. This fourth approach is being tried by using viral vectors for local or systemic administration (e.g. using AAV mediated therapy in DMD and LGMD2C). A liposomal introduction has been tried too (GNE myopathy, single case). The last strategy to be discussed is to introduce the wild type gene using stem cell therapy, an approach that started to move into clinical trials (although currently given only locally in OPMD).

Conclusions: All these approaches have limitations which will be mentioned but each carry a potential promise in these degenerative neuromuscular disorders.

Disclosure: The speaker has ad hoc consultant agreement with Ultragenyx and Bioblast.

Oral sessions

Ageing and dementia 1

OS1101
Assessing brain system dysfunction in amnesic mild cognitve impairment through MRI-based connectomics

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Introduction: To investigate the topological organization of functional brain network connectivity in patients with amnesic mild cognitive impairment (aMCI).

Methods: Graph theoretical analysis was applied to resting state fMRI from 45 aMCI patients and 32 healthy controls. Functional connectivity between 90 cortical and subcortical brain regions was estimated using bivariate correlation analysis and thresholded to construct a set of undirected graphs. Measures of global and local network organization were obtained.

Results: Small-worldness was verified in both groups. Functional brain networks in aMCI patients were characterized by a significantly higher hierarchy compared with controls. Compared to controls, aMCI patients did not show hub regions in the right hippocampus,

anterior cingulate and calcarine cortices bilaterally, and left putamen and caudate nucleus. Compared with controls, aMCI patients showed increased betweeness centrality in the posterior cingulate cortex bilaterally, left angular, inferior parietal and supramarginal gyri, and right superior medial frontal cortex.

Conclusions: The global organization of functional networks is relatively preserved in aMCI, except for an increased hierarchy of the brain functional networks. High hierarchy suggests a high sub-modular decomposition of the functional networks, which is thought to be negatively related with the span of control acted by the central module. On the contrary, local functional network organization is altered in aMCI showing a loss of major hubs in the regions typically hit by the disease and evidence for increased connectivity locally within the parietal and frontal lobes. Graph analysis provides additional insights into the physiology of early changes in Alzheimer's disease.

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OS1102

Cytokine gene expression in peripheral cells from patients with frontotemporal lobar degeneration due to *GRN* and *C9ORF72* mutation

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Introduction: Mutations in progranulin (*GRN*) and *C9ORF72* genes are common causes of familial Frontotemporal Lobar Degeneration (FTLD). Our main aim is to evaluate the expression of inflammatory factors in peripheral cells from *GRN* and *C9ORF72* carriers as compared with sporadic FTLD and controls.

Methods: Sabiosciences PCR array containing 84 common cytokines was used to investigate the expression profile of cytokines in 3 *C9ORF72* FTLD symptomatic expansion carriers, 3 *GRN* symptomatic mutation carriers, 3 GRN asymptomatic carriers, 3 sporadic FTLD patients and 3 age-matched controls.

Results: We observed a general down-regulation of cytokines expression levels in *C9ORF72* symptomatic expansion carriers compared with controls. In particular, IL8, IL4 and TNFSF4 expression levels showed a significant downregulation (−8.03; −2.55 and −2.32 fold regulation, respectively, $P < 0.05$) compared to controls. The same trend characterized *GRN* mutation carriers compared to controls, even in a stronger fashion. On the contrary, considering cytokine profiling of sporadic cases compared to controls, the opposite trend was observed. Results showed a general up-regulation of cytokines expression levels, in particular, IL12A, IL5 and VEGFA expression levels were significantly over-expressed in sporadic cases (1.81, 3.59 fold and 1.51 fold regulation over controls, respectively, $P < 0.05$). No de-regulated cytokines were observed in asymptomatic *GRN* carriers.

Conclusions: This is the first attempt to characterize the cytokine profile of *GRN* and *C9ORF72* expansion carriers. Preliminary results showed opposite trend of cytokines expression levels between *GRN* and *C9ORF72* FTLD carriers and sporadic patients compared with controls, suggesting different pathogenic pathways between mutation carriers and sporadic FTLD.

Disclosure: Nothing to disclose.

OS1103

Mild cognitive impairment with suspected non AD pathology (SNAP): prediction of progression to dementia

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Introduction: Alzheimer's disease (AD) is believed to feature amyloid deposition, followed by neurodegeneration, and clinical symptoms. However, a minority of patients show neurodegeneration but no amyloidosis ("suspected non-AD pathophysiology"- SNAP). Aim of this study was to investigate AD biomarker predictors of progression to dementia in SNAP patients with mild cognitive impairment (MCI).

Methods: CSF Abeta-42, hippocampal volume on MRI, and cortical metabolism on FDG-PET were measured in 188 MCI patients followed for at least one year. MCI patients were categorized based on biomarker abnormality: biomarker negative (MCI-BN), MCI-SNAP (no amyloid pathology, with neurodegeneration), and MCI-AD (amyloid pathology, with or without neurodegeneration). In MCI-SNAP and MCI-AD groups, risk and time to progression to AD dementia were assessed.

Results: Thirty-six MCI-BN, 27 MCI-SNAP and 125 MCI-AD were included. MCI-SNAP showed lower prevalence of APOE-ε4 carriers ($p = 0.011$) and progressors ($p = 0.185$) than MCI-AD. In MCI-SNAP, hypometabolism was comparable to MCI-AD, while hippocampal atrophy was more severe ($p < 0.0001$) (Table 1). MCI-SNAP and MCI-AD had comparable MMSE score loss and risk of progression to dementia (HR = 4.04 vs 5.36). In MCI-AD, hypometabolism predicted risk of progression (HR = 3.32, $p < 0.0001$) and hippocampal atrophy predicted risk (HR = 1.86, $p = 0.009$) (Table 2) and time-to-progression ($p = 0.009$). In MCI-SNAP, hypometabolism predicted risk. (HR = 6.71, $p = 0.008$) and time-to-progression ($p = 0.044$). Unexpectedly, shorter time-to-progression was predicted by less atrophic hippocampi ($p < 0.001$)(Table 3).

Conclusions: Our findings suggest that in MCI neurodegeneration with no amyloidosis is associated with a specific risk progression profile, and confirm the high-value of FDG-PET as biomarker of progression in MCI, independent of amyloid pathology.

Disclosure: Nothing to disclose.

OS1104
Abnormalities of fixation, saccade and pursuit in posterior cortical atrophy

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Introduction: Patients with posterior cortical atrophy have impairments in visuo-perceptual and visuo-spatial processing associated with atrophy of the parietal and occipital lobes. Here we present the first detailed and systematic study of oculomotor function in this patient group, describing the particular characteristics of oculomotor abnormalities in posterior cortical atrophy.

Methods: We recorded fixation, saccade and smooth pursuit eye movements in 20 patients with posterior cortical atrophy using an infrared pupil tracking system, 12 patients with typical Alzheimer's disease, and 22 healthy controls.

Results: Posterior cortical atrophy patients showed a higher frequency of large saccadic intrusions during fixation compared to both healthy controls and typical Alzheimer's patients. Saccades were hypometric, significantly shorter than those of healthy controls and typical Alzheimer's patients, and smooth pursuit significantly impaired in PCA.

Conclusions: This study establishes the oculomotor abnormalities present in posterior cortical atrophy for the first time, describing features unique to this condition and features in common with typical Alzheimer's disease. The cognitive mechanisms and neurological basis for this impairment are discussed, with the features observed suggesting that both visual cognition and automatic oculomotor mechanisms can be impaired in this patient group.

Disclosure: Nothing to disclose.

OS1105
Early diagnosis of dementia campaign in a population of elderly people in Athens

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Introduction: Athens Association of Alzheimer's Disease and Related Disorders in collaboration with the Memory Clinic of HYGEIA hospital organized a project to promote early diagnosis of dementia. Free memory screening was offered to people over 65 years living in the community and without a diagnosis of dementia.

Methods: Neurologists and cognitive psychologists examined the participants. Demographics, medical history and reasons for taking the examination were recorded. Cognitive tests performed were: Mini Mental State Examination (MMSE), Clock Drawing Test (CDT), MOCA 5 words and Geriatric Depression Scale (GDS).

Results: 1800 elderly people participated in memory testing. Mean age was 73 years (60−93 years). 70.1 % reported memory dysfunction as the reason for taking the examination. Mean MMSE score was 26.5 (±3.5) and 82 % of the participants scored over 24. Mean CDT was 5/10 (±3.3). Age and education level were significant predictors of MMSE score.

According to GDS scores, 66 % of the participants had no depression, 22 % had mild depressive symptoms while 12 % showed severe depression. Those diagnosed with cognitive decline or depression were referred to Memory Clinics.

Conclusions: Memory complaints of the participants on the project were not related to actual memory deficits but more to bad mood and anxiety.

Age had a negative impact on MMSE scores while higher education was associated with increased MMSE scores.

Disclosure: Nothing to disclose.

OS1106
Overview on the clinical development of the PET imaging agent florbetaben to assist in the clinical diagnosis of cognitively impaired subjects

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Introduction: The clinical diagnosis of Alzheimers Disease is wrong in up to 30 % as detected by autopsy studies. Efforts have been taken to reliably detect beta-amyloid (Aß) plaques in the brain during life. The 18F-labelled stilbene-derivative florbetaben binds to Aß with high affinity and can be used for PET imaging. The clinical development program comprised the investigation of florbetaben in 884 subjects to study its safety, diagnostic performance and efficacy.

Methods: Regulatory approval required the proof of florbetaben binding to Aß-plaques. A phase 3 study was designed accordingly: Elderly end-of-life subjects, who consented to donate their brains post mortem, were imaged with florbetaben during life. The correlation of the cortical grey matter PET signal to the presence or absence of Aß-plaques was investigated post mortem.

Results: In this histopathology study, 216 subjects with diagnoses of AD, other or no dementia were enrolled. In 74 autopsied subjects, a sensitivity of 98 % and specificity of 89 % was determined. Out of 57 subjects with a clinical diagnosis of AD, 44 subjects (77 %) showed presence of Aß in histopathology. In 43 of these 44 subjects Aß-plaques were detected by PET. In 11/13 subjects with clinical diagnosis of AD and in 13/14 subjects with other or no dementia but without Aß-plaques, the PET images were correctly read negative.

Conclusions: Although the detection of Aß-plaques does not establish a diagnosis of AD, the reliable exclusion of Aß should encourage the physician to search for other causes of cognitive decline and tailor available treatment options.

Disclosure: Andrew Stephens is employee if Piramal Imaging. Florbetaben (NeuraCeqTM) is an investigational PET amyloid imaging agent currently under review by the U.S. Food and Drug Administration and recommended for approval in the European Union by the CHMP.

Cognitive neurology and neuropsychology

OS1107
Predictors of driving performance in individuals with MCI: preliminary results

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Introduction: Mild Cognitive Impairment (MCI) represents a transitional stage between normal aging and dementia with no or only minimal impairment in everyday activities. Recent research suggests that individuals with MCI may have altered driving abilities. The scope of the present research is to investigate the association of neurological and neuropsychological measures with indexes of driving performance in individuals with MCI.

Methods: A CDR score of 0.5 was required for the diagnosis of MCI. Additional inclusion criteria were the presence of a valid

driver's license and regular car driving. Sixteen individuals with MCI attending our Memory Clinic participated in the study. The collection of the data included:

(a) detailed clinical, medical and neurological assessment,
(b) extensive neuropsychological assessment, and
(c) a driving simulation experiment.

Outcome measures were driving speed, number of crashes, and reaction time in unexpected incidents.

Results: A regression model that included as predictors general cognitive functioning (MMSE) as well as balance and movement coordination explained 55.9 % of the variance in driving speed, $R^2 = .559$, $F(2,13) = 8.25$, $p = .005$. Measures of general cognitive functioning (MMSE), visuospatial memory and processing speed explained 77.3 % of the variance in number of crashes, $R^2 = .773$, $F(3,10) = 11.35$, $p = .001$. Measures of general cognitive functioning (MMSE), processing speed as well as as balance and movement coordination explained 73.2 % of the variance in reaction time, $R^2 = .732$, $F(3,12) = 10.92$, $p = .001$.

Conclusions: Preliminary results show that neurological and neuropsychological measures are useful predictors of driving competence in individuals with MCI and could be used for detecting MCI patients at risk for car accidents.

Table 1. Summary of multiple regression analyses for driving speed, number of crashes and reaction time

Predictor	β	t	p	Outcome
TW (Balance/Mov. Coordination)	0.63	3.22	0.007	Driving Speed
UFV_1 (Processing Speed)	0.48	2.58	0.027	Number of crashes
BVMT_Rec. (Visuospatial Memory)	0.40	2.16	0.056	Number of crashes
SDMT (Processing Speed)	0.60	2.87	0.014	Reaction time
TW_RNC (Balance/Mov. Coordination)	0.54	3.21	0.007	Reaction time

TW=Tandem Walking; UFV_1= Useful Field of View Subtest1; BVMT_Rec.= Brief Visuospatial Memory Test Recognition Trial; SDMT = Symbol Digit Modalities Test; TW_RNC = Tandem Walking with Reverse Number Counting.

Disclosure: Nothing to disclose.

OS1108

Structural connectivity in patients with major depression with or without generalized anxiety disorder comorbidity

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Introduction: According to the diagnostic criteria for Major Depressive Disorder (MDD), a common overlap occurs between depression and Generalized Anxiety Disorder (GAD). Aim of this study is to assess white matter (WM) alterations in MDD patients with or without GAD comorbidity (MDD-GAD).

Methods: Fifty-five MDD patients (including 16 MDD-GAD cases) and 21 controls underwent a diffusion tensor (DT) MRI. DT MRI metrics were obtained from the major interhemispheric and long association WM tracts. Between groups comparisons and multiple regressions with the Hamilton depression and anxiety scale sub-scores were performed.

Results: Compared to controls, MDD and MDD-GAD patients showed WM alterations in the corpus callosum (CC) and right superior longitudinal fasciculus (SLF). Compared to controls, MDD patients showed further abnormalities in the right inferior longitudinal fasciculus, while MDD-GAD in the body of CC. The alterations of the body of CC in the MDD-GAD group was positively related to insomnia and gastrointestinal symptoms. When compared to each other, MDD patients showed alterations of the left SLF, while MDD-GAD of the left uncinate fasciculus. Left SLF and uncinate abnormalities were related with patient depression and anxiety symptoms, respectively.

Conclusions: Although MDD and MDD-GAD share a common pattern of WM alterations of the frontoparietal and interhemispheric tracts, they also show different damage involving the fronto-temporal-occipital connections in MDD patients, and the connections to the motor/somatosensory and frontal cortices in the MDD-GAD group. The relationships between WM alterations and the clinical symptoms might increase our understanding of the pathophysiology of these disorders.

Disclosure: Nothing to disclose.

OS1109

Differences in spatial navigation among patients with various neurodegenerative dementias

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Introduction: Spatial navigation impairment may play an important role in loss of self-sufficiency in patients with dementia. Reliable tests that capture possible differences in real-space navigation among patients with different types of dementia are still lacking. The aim was to compare differences in real-space navigation among patients with three common types of neurodegenerative dementias—Alzheimer's disease (AD), frontotemporal lobar degeneration (FTLD), and dementia with Lewy bodies (DLB).

Methods: There were 78 patients (61 with AD, 9 with FTLD [including 5 with behavioral variant and 4 with primary progressive aphasia], and 8 with DLB). All patients were tested in the real-space human analogue of the Morris Water Maze, which allows to measure performance in each of the three spatial navigation components–cued navigation (using a close orientation cue), egocentric navigation (using a position of the body at the starting position) and allocentric navigation (using a distant orientation cue). One-way analysis of variance was used.

Results: In the cued navigation test, the FTLD group performed better than the AD ($p = .030$) and DLB ($p = .006$) groups. In the egocentric navigation test, the DLB group had worse scores than AD ($p = .012$) and FTLD ($p = .012$) groups. Group differences in allocentric navigation were not significant ($p = .069$).

Conclusions: Overall spatial navigation impairment may be least pronounced in FTLD and most pronounced in DLB patients. There are qualitative differences in spatial navigation impairment among patients with AD, FTLD and DLB that can be measured with the real-space human analogue of the Morris Water Maze.

Disclosure: Dr. Laczó has consulted for Pfizer and holds shares of Polyhymnia-TS. Dr. Hort has consulted for Pfizer, Janssen, Merck, Novartis, Elan, Zentiva, Ipsen and holds shares of Polyhymnia-TS.

OS1110

Long-term correlates of future incident AD in prospective population cohorts according to education. Longitudinal neurocognitive data

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Analyzing long-term trajectories of cognitive decline is key to the understanding of the process leading to dementia. Level of education is a major modulator for the occurrence of sporadic Alzheimer's disease (AD).

We compared the pattern and duration of neuro-cognitive trajectories before dementia in elderly subjects with low and high education (LES and HES respectively) followed within the PAQUID cohort over 20 years. There were 442 cases of incident AD (27.2 % men), 171 LES (age = 86.2; SD = 5.3) and 271 HES (age = 86.5; SD = 5.4) and 442 controls matched for age, sex and education. Cases of AD were diagnosed clinically and comprehensive cognitive and clinical measures were repeatedly collected. The evolution of these measures in pre-demented subjects and matched controls was analyzed with a semi-parametric extension of the mixed effects linear model.

In HES a decline in the IST and DSST began 15–16 years before dementia, with no memory or functional complaints during the first 7–8 years. About 7 years before dementia, global cognitive abilities begin to deteriorate, along with difficulties with complex activities of daily living. By contrast, LES presented a single period of decline lasting about 7 years before dementia, with more global cognitive impairment along with alteration in functional abilities.

These data show a latent phase of 7–8 years in HES who will become demented 15–16 years later, objectived on sensitive neuropsychological tests. LLES begin to decline only around 7 years before diagnosis, at the same time when the HES enter a phase of acceleration and broadening of their decline.

Disclosure: Nothing to disclose.

OS1111

Patterns of regional gray matter and white matter atrophy in "cortical multiple sclerosis"

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Introduction: "Cortical" multiple sclerosis (cort-MS) is a rare form of the disease characterized by a severe progressive cognitive impairment, focal cortical syndromes, cortical signs with a relative sparing of motor, sensory and cerebellar functions. We used voxel-based morphometry (VBM) to investigate the patterns of regional gray matter (GM) and white matter (WM) atrophy in patients with cort-MS in comparison to classical MS (c-MS) to elucidate the contribution of GM and WM damage to cognitive and psychiatric symptomatology.

Methods: Eighteen MS patients (9 cort-MS and 9 c-MS) and nine age-matched healthy controls (HC) were enrolled. MS patients underwent neurological and neuropsychological evaluations. All subjects underwent a brain MRI exam, including a fluid attenuation inversion recovery (FLAIR) and a high-resolution T1-weighted scans. VBM was used to assess between group differences of GM and WM volumes (SPM8, $p < 0.001$, uncorrected). T1-lesion probability maps (LPMs) were obtained.

Results: Performance at each neuropsychological test was significantly worst in cort-MS *vs* c-MS patients (p ranging from <0.0001 to 0.01). Compared to HC, MS patients had cortical and subcortical GM atrophy and WM atrophy of the corpus callosum and bilateral corticospinal tracts. No GM/WM area was more atrophied in c-MS vs cort-MS patients. Compared to c-MS, cort-MS patients had GM atrophy of fronto-temporal-parietal areas and cingulum, and WM atrophy of the cingulum, bilateral cerebral peduncles, right inferior and left superior longitudinal fasciculus.

Conclusions: Higher susceptibility to neurodegenerative processes in key brain regions known to be related to cognitive functions could underlie the clinical presentation of cort-MS.

Disclosure: MAR speakers honoraria from Biogen Idec and Serono Symposia International Foundation. MF received compensation for consulting and/or speaking from Bayer, Biogen Idec, Merck Serono, and Teva.

OS1112

Relationship between cognitive impairment and physical disability in MS patients

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Objectives: To investigate cognitive functioning in a Portuguese MS population and to examine its relationship with physical and clinical course characteristics.

Methods: 419 MS patients (266 women; mean age = 40, sd = 13; mean education = 11, sd = 5; mean disease duration = 9.92, sd = 8.47; 332 RRMS, 44 SPMS and 43 PPMS) and 159 healthy comparison subjects (HC; women; mean age = 41 sd = 13; mean education = 12 sd = 5) performed a series of neuropsychological (NP) tests (i.e., Attentive Matrices-AT, Digit Span-DS, Wisconsin Card Sorting Test-WCST, Corsi Block-Tapping Test-CB, Auditory Verbal Learning Test-AVLT, Sentence Repetition-SR, Letter Word Fluency-LWF) and answered the Hospital Anxiety and Depression Scale-HADS. Based on HC group's multiple linear regression coefficients, MS patients' NP scores were adjusted for gender, age and education. Univariate and multivariate logistic regressions were used to compute the odds of deficit among MS subjects.

Results: Among MS patients, deficit on NP measures AT, AVLT, CB, and SR was statistically related ($p < 0.05$) with EDSS, MSSS and SP course. The associations with EDSS and MSSS (separate regression models) remained statistically significant for AT, AVLT and CB, while adjusting for other covariates (gender, age, education, disease duration, disease course, and depression scores). Deficit on AVLT, CB, and SR remain significantly associated with secondary progressive course ($p < 0.05$), even after adjusting for others covariates (gender, age, disease duration, depression scores, and EDSS or MSSS).

Conclusions: These results suggest that the likelihood of cognitive dysfunction in MS increase with higher severity of physical

symptoms and with SP course. These associations appear to be independent of demographic and psychopathological features.

Disclosure: Nothing to disclose.

Multiple sclerosis and related disorders 1

OS1113

Contribution of spinal cord MR to the diagnosis of patients with clinically isolated syndromes suggestive of multiple sclerosis

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Introduction: Spinal cord (SC) topography is used to determine dissemination in space (DIS, 2010 criteria). The added value of SC magnetic resonance (MR) at 3.0 and 1.5T in the diagnosis of multiple sclerosis (MS) was evaluated.

Methods: From a clinically isolated syndrome (CIS) cohort, 100 patients with brain and SC MR at 3.0T and 107 with MR at 1.5T were identified. Baseline characteristics were compared. As there were no significant differences, the 3.0T (N = 76) and 1.5T (N = 67) non-SC CIS groups were merged to identify the proportion of patients fulfilling DIS, first assessing brain MR and then both brain and SC MR, to determine DIS and dissemination in time (DIT) in each case and the number needed to scan (NNS) to diagnose one additional MS case. Hazard ratios were calculated for four CIS subtypes.

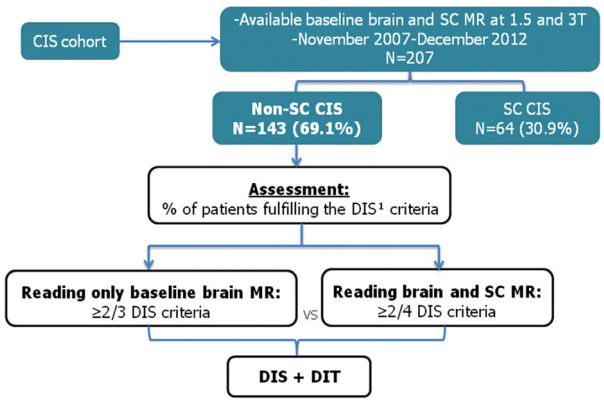

Figure 1. Flowchart depicting the patient selection process (blue cells) and MR analysis (white cells).
Abbreviations: CIS: clinically isolated syndrome; SC: spinal cord; MR: magnetic resonance; DIS: dissemination in space; DIT: dissemination in time.

1. Polman CH et al. Ann Neurol. 2011;69:292-302.

Results: When additionally reading SC MR in non-SC CIS (N = 143), 4 (2.8 %) more patients fulfilled DIS and DIT (NNS = 36). This analysis was repeated for pathological brain MR (N = 90, NNS = 23) and pathological brain MR not fulfilling DIS and DIT (N = 70, NNS = 18).

Table 1. Proportion of additionally diagnosed patients when taking SC MR into account and number needed to scan to diagnose one additional patient.

Groups of patients	Patients fulfilling DIS and DIT: N (%)		ARR	NNS
Non-SC CIS N= 143	Brain MR only	20 (14.0)	2.8	36
	Brain and SC MR	24 (16.8)		
Non-SC CIS and pathological brain MR N=90	Brain MR only	20 (22.2)	4.5	23
	Brain and SC MR	24 (26.7)		
Non-SC CIS and pathological brain MR not fulfilling DIS and DIT N= 70	Brain and SC MR	4 (5.7)	5.7	18

Abbreviations: DIS: dissemination in space; DIT: dissemination in time; ARR: absolute risk reduction; NNS: number needed to scan; SC: spinal cord; CIS: clinically isolated syndrome; MR: magnetic resonance.

Presence of SC lesions posed a higher risk of developing clinically definite MS in: all cases, non-SC CIS, and non-SC CIS with pathological brain MR, whereas a trend was observed in non-SC CIS with pathological brain MR not fulfilling DIS and DIT.

Table 2. Risk of conversion to clinically definite multiple sclerosis according to presence of spinal cord lesions.

	p	HR	95% CI
All cases N=207	<0.0001	3.3	1.8-6.2
Non-SC CIS N=143	<0.0001	4.1	2.0-8.5
Non-SC CIS with pathological brain MR N=90	0.025	2.4	1.1-5.3
Non-SC CIS with pathological brain MR not fulfilling DIS and DIT N=70	0.085	2.1	0.9-5.0

Abbreviations: HR: hazard ratios; 95% CI: 95% confidence interval; SC: spinal cord; CIS: clinically isolated syndrome; MR: magnetic resonance; DIS: dissemination in space; DIT: dissemination in time.

Conclusions: Although the added value of SC MR appears to be modest when analysing MR at 3.0 and 1.5T together, the prognostic impact of SC lesions seems relevant in all CIS subtypes.

Disclosure: G Arrambide: travel expenses for scientific meetings from Merck-Serono. M Tintoré, A Rovira, J Sastre-Garriga, M Comabella, and X Montalban: speaker honoraria from Bayer Schering Pharma, Sanofi-Aventis, Bracco, Merck Serono, Teva Pharmaceuticals, Biogen Idec, Novartis, Sanofi, Genentech, Genzyme, and Almirall. Other authors: no disclosures.

OS1114

Proportion of multiple sclerosis patients with brain volume loss comparable to healthy adults in the phase 3, placebo-controlled fingolimod studies, FREEDOMS and FREEDOMS II

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Introduction: In healthy adults up to age 55, the mean yearly rate of brain volume loss (BVL) reported in the literature is approximately −0.2 % to −0.3 %. The mean annual rate of BVL observed in multiple sclerosis (MS) patients is approximately −0.6 % to −1.0 %. BVL has been correlated with increasing measures of disability progression. Fingolimod significantly reduced BVL vs. active comparator/placebo in all three, pivotal phase 3 studies. We have conducted an analysis of the pooled 2-year FREEDOMS and FREEDOMS II study data in relapsing-remitting MS, to assess the proportion of patients on fingolimod 0.5 mg with annual rates of BVL comparable to that reported in healthy adults.

Methods: Percentage change from baseline in BV was estimated at 6-, 12- and 24-months using the Structural Image Evaluation using Normalisation of Atrophy (SIENA) methodology. We present proportions of patients whose annual rate of BVL did not exceed −0.2 %, an arbitrary cut-off value based on a literature-based mean estimate of BVL in healthy adults. Patients were categorised by

treatment-group during months 0–24 and according to the following age-groups: 17–30, 31–40, 41–50, and 51–60 years, given the known positive correlation of age with BVL.

Results: In all age strata, more fingolimod patients exhibited BVL of less than −0.2 % per annum than patients on placebo.

Table: Proportion of patients by treatment group with BVL of less than -0.2% per annum (Months 0-24)

Age group (years)	Fingolimod 0.5 mg				Placebo			
	N	N'	n	% (n/N')100	N	N'	n	% (n/N')100
17-30	163	125	41	32.8	147	111	24	21.6
31-40	282	225	60	26.7	293	224	41	18.3
41-50	267	224	61	27.2	262	197	42	21.3
51-60	71	49	19	38.8	71	48	9	18.8

N=Total number of patients in the age group (pooled FREEDOMS and FREEDOMS II population)
N'=Number of patients with valid records at the corresponding time point
n=Number of patients whose annual rate of brain volume loss was less than -0.2%

Conclusions: The proportion of patients having the least degree of global BVL, comparable to the reported mean of cohorts of healthy adults, was greater with fingolimod than placebo over 2 years. This result was consistent across the age categories assessed.

Disclosure: Nicola De Stefano has received honoraria from Schering, Biogen-Dompè, Teva and Merck Serono S.A. for consulting services, speaking and travel support. He serves on advisory boards for Merck Serono S.A. He has received research grant support from the Italian MS Society. Ernst-Wilhelm Radue has received research support: Biogen Idec, Merck-Serono, Novartis and Actelion. Till Sprenger has consulted for Mitsubishi Pharma, Eli Lilly, Genzyme, Novartis, ATI, Biogen Idec and Allergan. Ludwig Kappos has received research support through his institution by Actelion, Allozyne, Bayer Health Care Pharmaceuticals, Bayer Schering Pharma, Biogen Idec, CLC Behring, Elan, GeNeuro SA, Genzyme, GlaxoSmithKline, Lilly, Merck Serono, Mitsubishi, Novartis, Sanofiaventis, Santhera, Roche, and Teva. Davorka Tomic, Dieter Haering and Gordon Francis are Novartis employees.

OS1115

How to treat MS patients after the 24th natalizumab administration: the TY-STOP trial

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Introduction: Natalizumab is the most effective drug for relapsing-remitting MS but could be associated with progressive multifocal leukoencephalopathy (PML), whose risk increases after 24 natalizumab administrations.

Methods: Spontaneous, prospective, multicenter, observational study to evaluate disease course after the 24th natalizumab administration. Primary outcome: annualized mean relapse rate. Secondary outcomes: annual MRI activity, mean confirmed EDSS at 1 year. Groups of treatment:

(1) patients who continued natalizumab (CONTINUATORS);

(2) patients who did not received any disease modifying therapy (INTERRUPTERS);

(3) patients switching among different therapeutic options (including natalizumab)(SWITCHERS).

All statistical tests were two-sided, significance level set at 0.05.

Results: 130 patients from 7 Italian centers were observed for 12 months: 47 (36 %) continued natalizumab while 83 (64 %) interrupted it. Both intention-to-treat and "as treated" population (N = 124) analyses showed that annualized mean relapse rate was higher in SWITCHERS (N = 16) (OR: 3.28 [0.99–10.79]; p = 0.05) and in INTERRUPTERS (N = 73) (OR:4.40 [1.721.23]; p = 0.002) compared to CONTINUATORS; annual MRI activity higher in INTERRUPTERS compared to CONTINUATORS (OR:2.81 [1.17–6.74]; p = 0.029); confirmed EDSS at 1 year lower in CONTINUATORS compared to the other groups (p = 0.033). One PML case occurred 3 months after natalizumab discontinuation. He was treated with plasmapheresis and mirtazapine with full remission.

Conclusions: Patients who interrupted natalizumab developed clinical and radiological disease activity more frequently than those who continued it beyond 24 administrations. Therapeutic decision must take into account two types of risk: disease resumption if natalizumab is stopped; PML development if natalizumab is continued. If PML risk is high, natalizumab should be reasonably stopped; otherwise it should be continued carefully monitoring PML subclinical occurrence.

Disclosure: Nothing to disclose.

OS1116

Efficacy of delayed-release dimethyl fumarate for relapsing-remitting multiple sclerosis (RRMS) in "non-responders" to prior treatment with interferon beta

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Introduction: A post hoc analysis of integrated data from the Phase 3 DEFINE and CONFIRM studies was conducted to assess the efficacy of delayed-release dimethyl fumarate (DMF) over 2 years in RRMS patients who were considered "non-responders" to prior treatment with interferon beta (IFNβ) before randomization in DEFINE/CONFIRM.

Methods: Eligibility criteria for DEFINE and CONFIRM included age 18–55 years, RRMS diagnosis (McDonald criteria), and EDSS score 0–5.0. Patients were randomized to receive placebo (n = 771), delayed-release DMF 240 mg twice (BID; n = 769) or three times daily (TID; n = 761), or glatiramer acetate (CONFIRM only; n = 350), for up to 96 weeks. For this analysis, IFNβ "non-responders" were defined as having ≥12 months prior treatment with IFNβ and

(a) 1 relapse while on treatment and radiological activity (≥9 T2-hyperintense or ≥1 gadolinium-enhancing lesions), or

(b) unchanged or increased relapse rate in the 1 year prior to entry into DEFINE/CONFIRM compared with the preceding 2 years.

Results: A total of 475 patients fulfilled IFNβ "non-responder" criteria, including 162, 156, and 157 in the placebo and delayed-release DMF BID and TID groups, respectively. In these patients, at 2 years, the annualized relapse rate was reduced significantly by delayed-release DMF BID (rate ratio [95 % confidence interval]: 0.570 [0.388–0.836]; P = 0.004) and TID (0.471 [0.316–0.701]; P = 0.0002), compared with placebo. Other definitions of IFNβ "non-response" will also be examined.

Conclusions: These results suggest that delayed-release DMF demonstrates significant efficacy in IFNβ "non-responders." The magnitude of the effect is similar to that seen in the overall intent-to-treat population of DEFINE/CONFIRM.

Disclosure: Study supported by: Biogen Idec, Inc.

OS1117

Cortical thickness and cortical surface area relate to specific symptoms in early multiple sclerosis

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Introduction: The relation between the clinical manifestations of early relapsing remitting Multiple Sclerosis (RR MS) and structural cortical changes are poorly characterised. Our objectives were to investigate the difference in cortical structure between recently diagnosed RR MS patients and healthy controls, and to investigate the relation between cortical structure and the different manifestations of the disease.

Methods: Patients diagnosed with RR MS within the last 3 years underwent MRI, neurological and neuropsychological examinations. Cortical surface area, thickness and volumes were estimated based on 3D T1 MRIs from 61 RR MS patients and 61 matched controls. General linear models were used to compare the patients and controls and to study the relation between neurological disability, cognition, fatigue and depressive symptoms and cortical structure within the patient group.

Results: We found widespread differences in cortical thickness and a 6.5 % (p < 0.001) smaller cortical volume, but no difference in cortical surface area, between the groups. Within the patient group we identified large regions, mainly of the frontal lobes, with higher depression scores related to a smaller cortical surface area and volume. Neurological disability was related to regionally reduced cortical thickness, while better verbal memory was associated with regionally larger surface area. Fatigue was associated with regionally smaller cortical volume.

Conclusion: Cortical thickness reduction represents the primary change of cortical morphology in RR MS. We identify specific structural correlates to the main clinicial manifestations in early RR MS, emphasizing the relevance of both cortical thickness and surface area in explaining these symptoms.

Disclosure: Nothing to disclose.

OS1118

A subgroup meta-analysis of multiple sclerosis clinical trials

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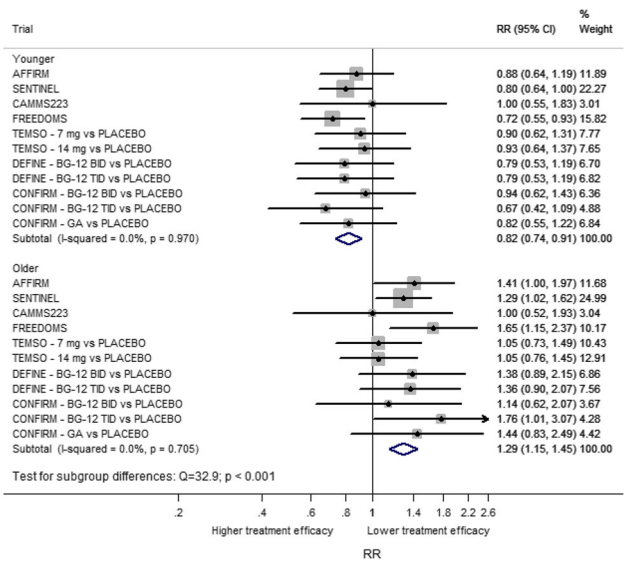
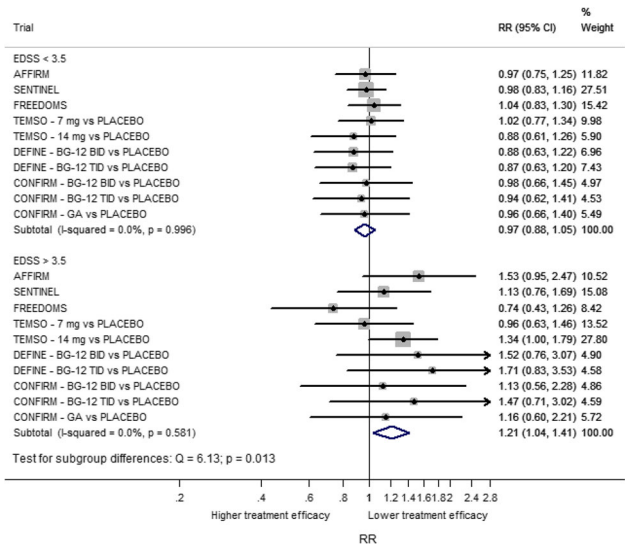
Introduction: The object of this work was to evaluate whether there are subgroups of relapsing-remitting (RR) multiple sclerosis (MS) patients that are more responsive to treatments.

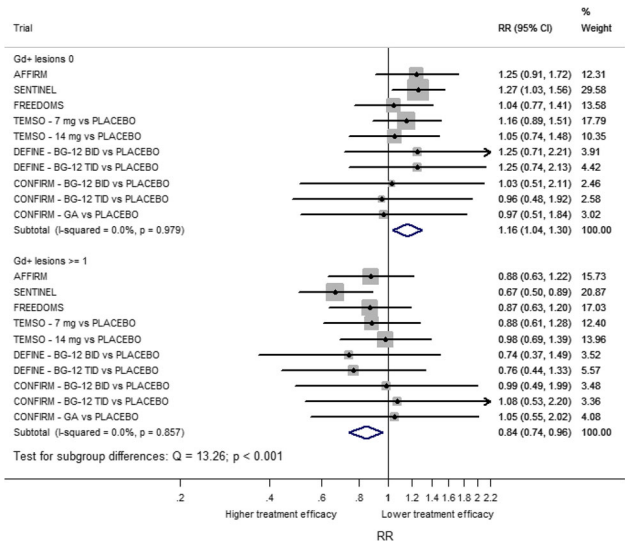
Methods: We collected all published randomized clinical trials in RRMS reporting a subgroup analysis, that is, an assessment of the treatment effect in different subgroups of patients defined according to baseline characteristics (sex, age, baseline Expanded Disability Status Scale (EDSS), relapse history, previous treatments, presence of Gadolinium enhancing lesions and T2 lesion volume on the baseline MRI scan). The primary outcome of the analysis was the treatment effect on the annualized relapse rate (ARR). The treatment effect in each subgroup was rescaled to the overall treatment effect size and reported as a relative contribution to the treatment specific effect. The subgroup specific treatment effects were combined in a meta-analysis weighted by the inverse of variance.

Results: Seven trials including a total of 7037 RRMS patients were included in the meta-analysis. Pooled treatment effects on ARR resulted to be significantly higher in younger subjects (p < 0.0001), in patients with lower baseline EDSS (p = 0.013), in patients with baseline Gd + enhancing activity (p < 0.001) and with high T2 lesion load (p = 0.04). No differences of treatment effect was detected among groups defined by different gender, relapse history or history of previous treatment.

Conclusions: This study shows in a formal way that in RRMS, higher treatment effects are associated to characteristics of an earlier (age and EDSS) and more active (Gd+ and T2 activity) disease.







Disclosure: Nothing to disclose.

Neurorehabilitation 1

OS1119

Brain structural and functional changes after action observation therapy in Parkinson's disease patients with freezing of gait

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Introduction: To assess brain functional and structural changes following action observation therapy (AOT) in Parkinson's disease patients with freezing of gait (PD-FoG).

Methods: 20 PD-FoG patients underwent a 4-week (W4) rehabilitation training. Subjects were randomized into 2 groups: in AOT-group, therapy consisted of AO combined with practicing the observed actions; control-group performed the same training combined with landscape-videos observation. At baseline (T0) and W4, patients underwent: clinical evaluations, 3D-T1-weighted and functional MRI (fMRI tasks: foot simple-movement; observation of videos showing a man in circumstances precipitating FoG; motor imagery as in observation task). Clinical assessments were repeated at week 8 (W8).

Results: At W4, both groups showed reduced FoG severity and walking speed improvement. AOT-group showed additional UPDRSIII, balance, and QoL improvements. At W8, motor improvements were confirmed in both groups, while positive effects on UPDRSIII and QoL were observed in AOT-group only. At W4, AOT was associated with increased cerebellar and parietal grey matter (GM) volumes; in control-group, an increased primary motor cortex (PMC) volume was observed bilaterally. FMRI showed that AOT was associated with increased recruitment of PMC/premotor cortex, mirror neuron system (MNS) and caudate nucleus bilaterally during simple-motor/imagery tasks. At W4, control-group showed reduced PMC recruitment during all tasks. In both groups, structural and functional brain changes correlated with W4 clinical improvements and predicted clinical evolution at W8.

Conclusions: AOT has a positive additional effect on walking ability recovery of PD-FoG patients. In PD, AOT promotes brain structural/functional plasticity of both the primary sensorimotor and MNS.

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OS1120

Post-traumatic Parkinsonism

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Introduction: Amantadine hydrochloride is one of the most commonly used drugs in the pharmacotherapeutic treatment of disorders of consciousness (DOC). Indeed, its actions as a pro-dopaminergic drug and as an N-methyl-D-aspartate antagonist makes amantadine an interesting candidate to improve consciousness and responsiveness in individuals with DOC.

Some patients with DOC following severe Traumatic Brain Injury (TBI) have been reported to have parkinsonian symptoms. We are of the strong opinion that more attention should be given to parkinsonian findings in persons with DOC after severe TBI and would advocate for multicenter, randomized, controlled trials to assess risk factors for parkinsonism following severe TBI.

Methods: Fourteen patients were diagnosed with post-traumatic parkinsonism, according to the Unified Parkinson's Disease Rating Scale. All the enrolled patients had a diagnosis of severe brain injury, a mean coma duration of 30 days and an interval from a coma onset to the enrollment in the study of 26, 9 months.

Results: All the patients were treated with Levo-Dopa + benserazide 100 + 25 three times daily for at least 1 month. The improvement rate of UPDRS was from a minimum of 2 points to a maximum of 8.

Conclusions: Severe TBI and post-traumatic parkinsonism may share a common midbrain network dysfunction. In fact, VS, MCS, akinetic mutism and parkinsonism might represent a recovery continuum following severe TBI. Responsiveness to pro-dopaminergic agents, in some patients and to deep brain stimulation in others, might depend on the integrity, or lack thereof, of the dopaminergic post-synaptic receptors.

Disclosure: Nothing to disclose.

OS1121

Systematic review of the influence of spasticity on quality of life in adults with chronic neurological conditions

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Introduction: Spasticity is a common and often long term symptom in several chronic neurological conditions. Our aim was a systematic review of the published evidence on the relationship between spasticity and quality of life (QOL).

Methods: MEDLINE, Embase, CINAHL and PsycINFO databases were searched using keywords 'spasticity' and 'quality of life'.

Results: 17/551 studies met inclusion criteria for review. These examined the relationship between spasticity and QOL in multiple sclerosis (MS), spinal cord injury (SCI) and stroke. Spasticity was found to be associated with significantly lower scores on health status measures, namely SF-12, SF-36 and EQ-5D, in MS and SCI, but less so in stroke. Spasticity was associated with considerably lower scores on physical components of the health status questionnaires, but with only marginally lower scores on mental components. The studies that employed global QOL measures such as the World Health Organisation Quality of Life—BREF found no significant relationship between spasticity and QOL. Spasticity was often associated with pain, sleep problems, fatigue and urinary dysfunction. A single study in spinal cord injury found spasticity to be an insignificant predictor of HRQOL after accounting for these factors.

Conclusions: Spasticity is associated with worse health status, but not with overall QOL. The relationship between spasticity and QOL is confounded by associated other symptoms. Future studies should account for this, in these conditions and also in the many other spasticity-causing disorders not yet studied.

Disclosure: Nothing to disclose.

OS1122

Comparing unilateral and bilateral computer-supported arm training for the severely affected arm after stroke

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Introduction: Functional recovery after stroke depends on brain plasticity. Ipsilesional and bihemispheric reorganization have been documented. In addition stroke patients experience an increased inhibitory influence from the contralesional to the ipsilesional motor cortex. Yet there is evidence that patients benefit from both bilateral and unilateral arm training. Therefore we compared the effects of bilateral versus unilateral computer-supported arm training on motor recovery in severely affected subacute stroke patients.

Methods: 38 patients with a severe arm paresis (Fugl-Meyer-Score for the arm (FMA) less than 18) were recruited for this randomized single-blinded study. The bilateral arm training entailed a repetitive training on an "arm-bicycle" followed by synchronized bilateral repetitive hand training. The unilateral arm training was identical but performed by the paretic limb only. Both trainings were administered twice daily over 6 weeks and incorporated shaping elements. Main outcome measures included the FMA and biomechanical parameters (hand grip-, hand extension-, elbow flexion- and elbow extension isometric force and rate of force generation), assessed at the beginning, after 6 and 8 weeks.

Results: Both groups improved significantly over time regarding the FMA and all biomechanical parameters. There was a significantly greater improvement following the bilateral training in FMA ($p = 0.04$) and isometric force of hand grip and hand extension ($p = 0.04$) compared to the unilateral training.

Conclusions: Bilateral computer-supported arm training followed by repetitive bilateral hand training leads to greater improvements in motor control and force of the severely paretic upper limb compared to the unilateral version of the same training.

Disclosure: Nothing to disclose.

OS1123

Social-networks and multiple sclerosis: an Italian experience

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Introduction: The aim of blogs and websites on multiple sclerosis (MS) is connecting people and sharing information that acquire assertive importance even not referring to scientific references. Social-network MS users/patients are generally informed about the disease but are also influenced by false hopes arising from wrong information, myths and not scientifically proven therapeutic approaches. Our aim was to create a MS web-community to facilitate the sharing of information, monitored by a doctor and based on scientific rigor.

Methods: http://www.smsocialnetwork.com gives the opportunity to its users to publicly or privately interact using chat, messages and community wall. All the users can even contact doctors, psychologists and, through the streaming page, watch outpatient visits and medical conferences.

Results: Started in March 2012, our web-community includes over 5,500 visitors and over 800 registered users. The total number of pages viewed is 132,937. After 19 months, we can clearly distinguish two macrogroups of users: A (leaders) and B (receivers). In group A there are users who propose innovations and suggestions and in group B there are users who share, partially approve or reject these standpoints.

Conclusions: The aim of the team of smsocialnetwork.com was to monitor and promote interactions between patients, controlling that information sharing was based on current medical science. In line with our aim, we have obtained that Group A is driven by common sense and wise use of the network. In the internet emotions often prevail on rationality, but we have tried not to make them necessarily acquire a clinic value.

Disclosure: Nothing to disclose.

OS1124

Living independently with intensive support (WmI): long-term results of a new housing project for people with severe disabilities in Germany

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Introduction: In 2009 the Fürst-Donnersmarck-Foundation launched a new housing project in Berlin/Germany for people with severe disabilities caused by acquired brain injuries. Residents from a permanent residential living facility (LTC) are offered the opportunity to move into newly built supported living accommodations (SLA) with a 24/7 individual support. The aim of the study is to investigate effects of SLA on residents' social and health-related outcomes.

Methods: In a longitudinal design residents in two SLA and one LTC were surveyed at baseline and follow-up after 6, 12 and 36 months. Considered outcomes are perceived disability (WHODAS II), ADL-functioning (EBI), needs of assistance (Metzler), quality of life (WHOQoL-Bref, EQ-5D), anxiety and depression (HADS-D), sense of mastery (Pearlin Mastery Scale) and social contacts.

Results: 40 residents (average age 46.2 years) were included into the study, 29 of them moved into SLA. During the study perceived disability (WHODAS II) as well as ADL-functioning (EBI) worsened significantly but we could not show differences between groups (mixed model $p > 0.05$). Changes in quality of life (WHOQoL-Bref, EQ-5D) could not be shown in general (mixed models $p > 0.05$). The perceived sense of mastery (Pearlin Mastery Scale) increased significantly and showed more positive developments in SLA. Everyday activities in SLA increased to a large extent.

Conclusions: Some positive but no overall effects of moving into SLA could be shown. The new housing project offers residents of LTC with multiple severe disabilities the chance of a more self-determined life and of active participation in new social networks.

Disclosure: Nothing to disclose.

Sleep disorders

OS1125

The evolution of REM sleep behaviour disorder in Parkinson disease patients with *Parkin* mutations: a report from the DeNoPa cohort

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Objective: We analyzed the occurrence of REM sleep behaviour disorder (RBD) and REM without atonia (RWA) in Parkinson disease (PD) patients with heterozygous *Parkin* mutations at baseline and at follow up after 2 years.

Patients and methods: In 159 de novo PD patients (DeNoPa cohort) we performed multiplex ligation-dependent probe analysis to test for exon rearrangements in various genes frequently associated with PD. In individuals found to carry an exon rearrangement in the *Parkin* gene in the heterozygous state, all 12 *Parkin* exons were sequenced. Video-supported PSG (vPSG) was performed in all patients on two consecutive nights at baseline and after 2 years for identification of RBD and for measuring REM without atonia (RWA).

Results: We identified 6/159 (4 %) de novo PD patients with heterozygous *Parkin* mutations. At baseline, mean age was 63.3 ± 11.5 years. (range 48–76) and Hoehn & Yahr stage was determined at 1.3 ± 0.27 (range 1.0–1.5). At baseline, none of the *Parkin* mutation carriers, but 40 out of 152 (26 %) non-carriers were identified with RBD, RWA values were 5.9 ± 3.9 % (range 0.7–11.1 %). After 2 years, 1/6 *Parkin* PD patients showed mild RBD and one *Parkin* PD patient had developed excessive RWA measured at 55.7 %.

Conclusion: In this small cohort of 6 patients with heterozygous Parkin mutations we identified a possibly smaller proportion of RBD both at baseline and after 2 years compared to the remaining 152 PD patients of the DeNoPa cohort.

Disclosure: Nothing to disclose.

OS1126

Resting muscle sympathetic activity and blood pressure during wake in narcolepsy with cataplexy patients

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Introduction: Conflicting data have been reported on resting autonomic tone in narcolepsy with cataplexy (NC) including both reduced or increased sympathetic activity. If confirmed, increased sympathetic activity may represent an additional cardiovascular risk factor for NC patients usually presenting obesity, diabetes, sleep apnea and metabolic syndrome. In order to settle this important point we aimed to measure the resting sympathetic and cardiovascular activities in NC patients by direct microneurographic monitoring of muscle nerve sympathetic activity (MSNA) during wakefulness.

Methods: We studied 19 untreated patients with established criteria for NC and hypocretin deficiency, and 19 sex and age matched healthy subjects. Subjects underwent resting microneurographic recording of MSNA from peroneal nerve and heart rate (HR) whereas blood pressure (BP) was measured with a sphygmomanometer after the end of microneurographic recording. The awake state was continuously monitored by an ambulatory polygraphic recorder.

Results: NC patients displayed significantly lower resting MSNA, HR and BP values than controls. Pearson regression analysis showed a significant correlation between CSF hypocretin-1 level and MSNA or HR whereas no correlation was found with BP; however patients with virtually absent hypocretin-1 displayed lower BP than patients with the highest hypocretin-1 value.

Conclusions:

1) NC patients displayed decreased resting MSNA, HR and BP during wakefulness lowering their cardiovascular risk profile;

2) a positive correlation supported a direct effect of CSF hypocretin-1 deficiency on MSNA or HR regulation;

3) although hypocretin-1 was not correlated with BP, patients with absent hypocretin-1 had lower BP.

Disclosure: Nothing to disclose.

OS1127

Selective activation of LH GABA→RTN circuit induces rapid arousal

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Introduction: The sleep-wake cycle is a highly conserved physiological process across all vertebrates that result from a complex, yet undefined, inhibitory/excitatory balance between neural circuits distributed throughout the brain. Here, we investigate the role of inhibitory cells from the lateral hypothalamus (LH) on sleep-wake states.

Methods: We targeted the expression channelrhodopsin-2 opsin (ChETA) to the LH-GABA cells in VGAT::Cre mice. Chronic EEG/EMG recordings were use to characterize changes in their sleep/wake cycles in response to bilateral optogenetic stimulation.

Results: First, we identified anatomical and functional connections between LH-GABA neurons and neurons located in the septum, periaqueductal grey area, ventral-tegmental area, locus coeruleus, ventral tegmental area and reticular thalamic nucleus (RTN). We then, using a semi-chronic activation (1–20 Hz, 10 s every minute over 1 h), show that LH-GABA cells at 20 Hz, but not 1 Hz, resulted in a 2-fold increase in wake duration. We further found that a 10 s single stimulation of LH-GABA cells at 1–20 Hz, induces a rapid switch from NREM, but not REM, sleep to wakefulness (<2 s) in ChETA compare to control animals. Local optical activation of LH GABA terminals in the RTN induced $GABA_A$-mediated IPSCs in reticular neurons in vitro, and desynchronisation of cortico-thalamic loops.

Conclusion: Collectively, our results suggest that activation of a subpopulation of LH-GABA neurons induces rapid arousal from sleep, through inhibition of RTN cells and subsequent re-activation of thalamo-cortical loops, revealing a new hypothalamic -thalamic circuit for modulation of arousal, as well as somatosensory inputs during sleep.

Disclosure: Nothing to disclose.

OS1128

Impact of sleep apnea on mean blood pressure and blood pressure variability in patients with acute and chronic ischemic stroke or TIA (SAS-CARE study)

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Introduction: Sleep apnea (SA) is an independent risk factor for both stroke and hypertension. Previous studies have shown a correlation between severe SA and increased blood pressure (BP) after acute stroke in small cohorts. The aim of this multicenter prospective study (SAS-CARE) was to assess the impact of SA on mean BP and BP variability in patients with stroke/TIA.

Methods: We assessed 115 patients with acute (within 96 h) and 115 patients with chronic (after 60–90 days) stroke/TIA from two centers (Bern/Lugano). Polysomnography and 24-hour-BP-monitoring were performed within 7 and after 60–90 days. SA was defined by an apnea-hypopnea-index (AHI) $\geq$ 10/h. Mean, maximum and minimum systolic and diastolic BP readings were assessed. Short-term BP variability was defined as standard deviation (SD) and coefficient of variation (CV). Non-dipping-state (NDS) was defined as ratio >0.9 of mean systolic diurnal/mean systolic nocturnal.

Results: SA was detected in 72 patients (63 %) in the acute and in 69 (59 %) in the chronic phase. NDS was present in 75 patients (65 %) in the acute and in 72 (63 %) in the chronic phase. Mean systolic BP correlated with AHI in the acute phase ($r = 0.191$; $p = 0.042$), mean and maximum systolic BP with AHI in the chronic phase (mean: $r = 0.344$, $p = 0.001$; max: $r = 0.313$, $p = 0.001$). Systolic BP-variability and AHI correlated in the chronic, but not in the acute phase ($r = 0.240$, $p = 0.01$).

Conclusion: There is a correlation of mean systolic BP and BP-variability with AHI in patients with chronic stroke/TIA. This correlation has potential clinical implications on early intervention strategies.

Table 1: Baseline Characteristics

Variable	All patients acute (n=115)	All patients chronic (n=115)
Age	61.3 +/-10.0 (30 to 75)	61.1 +/-9.1 (30 to 75)
Male/female (%)	90/25 (78/22)	91/26 (78/22)
BMI kg/m2	27 +/-5 (18 to 40)	27+/-5 (18 to 41)
Thrombolysis yes/no (%)	22/93 (20/80)	25/90(21/79)
Wake-up Stroke	29 (25)	28 (24)
Hypertension (%)	68 (59)	69 (60)
Anithypertensive treatment (%)	65 (56)	53 (46)
Betablockers (%)	29 (25)	28 (24)
Smoking (%)	31 (27)	34 (30)
Diabetes (%)	10 (9)	13 (11)
Hypercholesterinemia (%)	83 (72)	81 (70)
Positive family history of stroke	31 (27)	29 (25)
Positive family history of coronary artery disease (%)	34 (29)	40 (35)
AHI/h	**20.3+/-18.6 (0 to 87.8)**	**15.9 +/-15.0 (0 to 79.2)**
Obstructive AI/h	6.3+/-10.2 (0 to 43.5)	3.4 +/-5.5 (0 to 36.3)
Central AI/h	3.7 +/-9.0 (0 to 44.4)	2.0 +/-6.0 (0 to 45.0)
Mixed AI/h	0.9 +/-3.3 (0 to 24.0)	0.3 +/-1.0 (0 to 7.5)
ODI/h	14.4 +/-17.1 (0 to 83.0)	12.9 +/-14.7 (0 to 78.9)
NIHSS admission	3.9 +/-4.9 (0 to 25)	3.6 +/-4.4 (0 to 20)
NIHSS after 24 hours	2.5+/-3.4 (0 to 23)	2.1 +/-2.7 (0 to 18)
NIHSS 3 months	0.7 +/-1.3 (0 to 9)	0.7 +/-1.8 (0 to 17)
Barthel dismissal	93.9 +/- 18.9 (0 to 100)	97.6 +/-10.1 (35 to 100)
Barthel Follow-up	99.3 +/-4.4 (60 to 100)	99.8 +/- 0.9 (95 to 100)

Values are mean +/-SD (Range in brackets) unless otherwise indicated

Table 2: Blood pressure values

Variable	All patients acute (n=115)	All patients chronic (N=115)
Systolic BP night mean	120 +/- 15 (92 to 167)	115 +/- 13 (89 to 115)
Systolic BP day mean	128 +/-14 (97 to 172)	125 +/- 13 (93 to 162)
Systolic BP whole period mean	127 +/- 14 (96 to 169)	122 +/- 13 (97 to 156)
Diastolic BP night mean	75 +/-16 (77 to 154)	71 +/- 9 (51 to 95)
Diastolic BP day mean	84 +/- 10 (62 to 112)	82 +/- 10 (53 to 111)
Diastolic BP whole period mean	81 +/- 10 (63 to 109)	79 +/- 9 (57 to 106)
Nondippers (%)	75 (65)	72 (63)

Values are mean +/-SD (Range in brackets) unless otherwise indicated

Table 3: Correlation Blood pressure/AHI

Variable	Acute phase: Correlation coefficient/p	Chronic phase: Correlation coefficient/p
Systolic BP night mean	**0,209*/ 0,026**	**0,290**/ 0,002**
Systolic BP day mean	0,155/ 0,099	**0,276**/ 0,003**
Systolic BP whole period mean	**0,191*/ 0,042**	**0,334**/ 0,000**
Diastolic BP night mean	0,149/ 0,114	**0,184*/ 0,049**
Diastolic BP day mean	0,077/ 0,415	0,147/ 0,114
Diastolic BP whole mean	0,098/ 0,302	0,177/ 0,058
Systolic BP night max	0,138/ 0,144	**0,268**/ 0,004**
Systolic BP day max	0,182/ 0,053	**0,285**/ 0,002**
Systolic BP whole period max	0,172/ 0,067	**0,313**/ 0,001**
Diastolic BP night max	0,158/ 0,094	0,179/ 0,055
Diastolic BP day max	0,163/ 0,082	0,130/ 0,163
Diastolic BP whole period max	0,166/ 0,078	0,123/ 0,190
Systolic BP night min	0,104/ 0,270	**0,253**/ 0,006**
Systolic BP day min	0,092/ 0,333	0,170/ 0,066
Systolic BP whole period min	0,109/ 0,249	0,166/ 0,077
Diastolic BP night min	0,130/ 0,168	0,200*/ 0,032
Diastolic BP day min	0,080/ 0,396	0,082/ 0,378
Diastolic BP night min	0,124/ 0,190	0,158/ 0,092
SD systolic	0.25/0.801	**0,240**/ 0,010**
SD diastolic	-0.15/0.880	0,078/ 0,406

*p<0.05; **p<0.01

Disclosure: Nothing to disclose.

OS1129

Role of DA-ergic therapy on REM sleep behaviour disorder in a large population of Parkinsonians

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Introduction: Patients with Parkinson's disease usually complain of a wide range of parasomnias most of them related to rapid eye movements sleep behaviour disorder (RBD).This study is aimed to investigate clinical features of RBD which allows to report its prevalence in these patients and whether DA-ergic therapy plays a role in its pathophysiology.

Methods: 261 subjects (mean age 68.7±13.4) affected by Parkinsonism were consecutively recruited. Among them, 86 patients were Naive without any DAergic treatment. Clinical sleep scoring was realized by using PDSS, the RBD screening questionnaire, UPDRS and H&Y scores. According to treatment, patients were grouped in non-DAergic therapy (n = 86); only L-dopa (n = 87); exclusively Dopamine-agoniste (n = 30) and combined L-dopa + Da-agonist therapy (n = 58). Non-parametric Kruskal–Wallis test with Dunn's Multiple Comparison post hoc test were computed between the four categories.

Results: Parasomnias were evident in 70.2 % of the total patients and specifically 62.45 % were positive to RBD score. No significant correlation was found between Daergic and non-Daergic therapy in the RBD group, neither significant correlation was found in respect to H&Y score. As expected, RBD is not related to stage of PD. Nonetheless, therapy stratification surprisingly showed direct effect connected with L-dopa therapy, with a significant highest RBD-score in respect to no-therapy subjects ($p = 0.019$).

Conclusions: The role of L-DOPA treatment seems crucial in this observational study with an enhancing/inducing effect; however, Da-agonists seem to modulate and attenuate clinical manifestations of RBD. Further studies, longitudinal follow up monitor and possible investigations on animal models are required for the adequate comprehension of the subtended mechanism.

Disclosure: Nothing to disclose.

OS1130

A novel NREM and REM parasomnia with sleep breathing disorder associated with antibodies against IgLON5: a case series, pathological features, and characterization of the antigen

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Introduction: We describe the clinical, video-polysomnographic and neuropathological features of an unrecognized disorder characterized by prominent sleep symptoms and antibodies against a novel cell-surface protein named IgLON5.

Methods: Eight patients with antibodies showing similar reactivity with neuropil of rat brain underwent PSG and two had brain post-mortem examination. Immunoprecipitation and mass spectrometry identified the novel antigen.

Results: All eight patients (five women; age range: 52–76 years) had abnormal sleep movements and behaviors along with obstructive sleep apnea. Five patients underwent video-polysomnography showing stridor, obstructive sleep apnea, undifferentiated NREM sleep and poorly structured N2 sleep with frequent simple movements and finalistic-purposeful behaviors and REM sleep behavior disorder. Normalization of NREM sleep characteristically occurred in the last part of the night. Clinical course was protracted in 6 (median: 5 years, range 2–12 years); in four the sleep disorder was the initial symptom, and in two it was preceded by progressive gait instability, and subsequently accompanied by dysarthria, dysphagia, and chorea. Two patients had a rapid presentation of the sleep disorder (2–6 months) with disequilibrium, dysarthria, dysphagia, and central hypoventilation. Sudden death occurred in six patients (median time from symptom onset: 3.5 years). Neuropathological examination showed a novel neuronal tauopathy mainly involving the tegmentum of the brainstem and hypothalamus. All patients had serum and CSF antibodies against an extracellular epitope of IgLON5, a cell-adhesion molecule involved in synaptogenesis.

Conclusions: IgLON5-antibodies identify a unique NREM and REM parasomnia with sleep breathing dysfunction and pathological features suggesting a novel tautopathy, linking autoimmunity and neurodegeneration.

Disclosure: Nothing to disclose.

Ageing and dementia 2

OS1201

Selective affection of hippocampal subfields in pre-dementia is related to spinal fluid amyloidbeta and tau

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Introduction: Early etiological diagnosis of cognitive impairment depends on precise characterization of regional neurodegenerative changes. We hypothesize that hippocampal subfields are selectively affected in subjective and mild cognitive impairment (SCI and MCI), and that it's related to established pathological mechanisms in Alzheimer's disease.

Methods: 159 cases, 81 MCI, 32 SCI and 46 controls (NC) were included in this cross-sectional study. MRI volume measures of hippocampal subfields were obtained using FreeSurfer, and patients underwent lumbar puncture for spinal fluid biomarkers (CSF Abeta42, T-tau and P-tau). Cluster analysis was performed on MRI data, and MANOVA-tests used for multiple comparisons. Subsequently, regression analyses were used to predict effects of CSF biomarkers on volumes in the subgroups.

Results: CSF Abeta42 was a significant predictor of presubiculum ($p < 0.005$), subiculum ($p < 0.05$) and hippocampal volumes

($p < 0.05$) in SCI, whereas T-tau was the best predictor for subfield volumes in MCI. Volumes of hippocampus ($p < 0.001$), presubiculum ($p < 0.001$), subiculum ($p < 0.001$), CA2-3 ($p = 0.002$) and CA4-DG ($p = 0.005$) and entorhinal cortex thickness ($p < 0.001$) were significantly different between MCI and NC. CA1 volumes did not differ between groups, and no volumes were significantly different between NC and SCI.

Conclusions: No significant volume loss is observed at the SCI stage (as compared to NC), but hippocampal subfield volumes are best predicted by levels of CSF Abeta42. Volume loss has occurred at the MCI stage and is best predicted by levels of tau. This is in accord with amyloid dysmetabolism as an early event in cognitive impairment and dementia.

Disclosure: Nothing to disclose.

OS1202

The effect of age of onset on the brain functional connectivity in Alzheimer's disease: a graph analysis study

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Introduction: To examine the relation between the topological organization of functional brain networks and the age of onset in patients with Alzheimer's disease (AD) using a network-based approach.

Methods: Graph theoretical analysis was applied to resting state fMRI from 36 late onset AD (LOAD) patients, 23 early onset (EOAD) patients and two groups of old and young healthy individuals. Measures of global and local network organization were obtained.

Results: Small-worldness was verified in controls and patients. Globally, the functional brain networks of LOAD patients were characterized by a significantly lower local and global efficiency, lower clustering coefficient and higher assortativity compared with age-matched controls. In contrast, functional brain networks of EOAD patients were characterized by a significantly higher hierarchy and lower assortativity compared with age-matched controls. Locally, lower nodal degree and local efficiency, and higher betweeness centrality were observed in both AD groups compared to the age-matched controls. However, while LOAD showed local alterations (in terms of decreased nodal degree and increased betweeness centrality) in the medial temporal, parietal and occipital lobes, EOAD patients showed a widespread pattern of damage involving also the frontal regions.

Conclusions: Graph analysis showed that global functional network organization was abnormal in AD patients. Compared to LOAD, the EOAD patients showed a widespread pattern of local network alterations involving also the frontal regions. The topological differences between patient groups may represent the effect of age of onset on functional connections.

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OS1203

Cardiovascular medication burden in dementia disorders: a nationwide study of 19 743 dementia patients included in Swedish Dementia Registry, SveDem

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Introduction: We aimed to investigate whether there are differences in the use of cardiovascular (CV) medication (as a proxy for CV disease) between different dementia disorders.

Methods: Data come from Swedish Dementia Registry (SveDem). Patients were diagnosed with one of following dementia disorders: Alzheimer's disease ($n = 8139$), mixed dementia ($n = 5203$), vascular dementia ($n = 4982$), Lewy body dementia ($n = 605$), frontotemporal dementia ($n = 409$) and Parkinson's disease dementia ($n = 405$). Multivariate logistic regression analysis was performed to investigate the association between dementia disorders and the use of CV medication, after adjustment for age, gender, living condition, MMSE score and total number of drugs (a proxy for overall comorbidity).

Results: Seventy percent of all patients use CV medication. CV drugs are prescribed to more than 50 % of patients diagnosed with each dementia disorder. The use of CV medication has been found related especially to vascular and mixed dementia compared to other dementia disorders. On the other hand, the use of CV drugs lowers the probability of being diagnosed with Alzheimer's disease and Parkinson's disease dementia. Male gender correlated with a higher risk of using CV medication compared to women. Living alone has been found negatively associated with the use of CV drugs.

Conclusions: In clinical reality, the burden of CV disorders in dementia is large in all dementia types, with predominance in vascular and mixed dementia.

Disclosure: Nothing to disclose.

OS1204

Circulating and intrathecal miRNAs as potential biomarkers for Alzheimer's disease

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Introduction: Circulating micro(mi)RNAs have been reported as promising biomarkers with great accuracy for neurodegenerative disorders and processes affecting the central nervous system (CNS), especially in aging, Parkinson's disease and multiple sclerosis. Aim of this study is to identify specific circulating miRNAs in serum as possible biomarkers for Alzheimer's disease (AD).

Methods: A specific PCR array containing 84 common miRNAs was initially used to screen miRNA serum levels in 7 patients with AD and 6 non-inflammatory neurological controls (NINDCs). Best hits were first validated by real time PCR in an independent cohort

consisting of 15 serum samples from AD patients and 12 NINDCs, comparing them also to 10 subjects affected by frontotemporal lobar degeneration (FTLD) and 8 inflammatory neurological controls (INDCs). Finally, the same analysis was conducted also in samples of cerebrospinal fluid (CSF).

Results: Statistically significant decreased levels of miR-125b, miR-223, miR-23a and miR-26b were observed in AD patients compared to NINDCs (−5.5, −4.5, −5.0 and −6.3 fold regulation over NINDCs respectively, $p < 0.050$). MiR-125b, miR-223 and miR-26b were then validated both in serum and CSF ($p < 0.050$), while miR-23a failed to be replicated in CSF. Moreover, miR-223 was also found down-regulated both in serum and CSF from FTLD patients ($p < 0.050$).

Conclusions: Our findings suggest a potential use of circulating miRNAs, along with other markers, as non-invasive, relatively inexpensive and peripheral biomarkers for AD diagnosis.

Disclosure: Nothing to disclose.

OS1205

Beyond visual deficits: motor features and associated atrophy patterns in posterior cortical atrophy

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Introduction: Posterior cortical atrophy (PCA) is a neurodegenerative syndrome which is typically but not exclusively caused by Alzheimer's disease (AD). Clinically, it is characterised by impaired higher visual processing, literacy and numeracy skills, however motor features more commonly associated with corticobasal syndrome (CBS) may also occur. This study investigated the frequency, clinical characteristics and neuroimaging correlates of motor features in a cohort of 44 PCA patients.

Methods: Clinical, neuropsychological, genetic and pathological data from the cohort were reviewed and the presence of prominent limb rigidity used to define a PCA + CBS subgroup. MRI brain scans of the two patient subgroups and 30 healthy controls were compared using voxel-based morphometry, cortical thickness and subcortical region of interest volumetric analyses.

Results: In this PCA cohort, 30 % (13) had PCA + CBS; all demonstrating asymmetrical left upper limb rigidity. Limb apraxia was more frequent and asymmetrical in PCA + CBS, as was myoclonus. Tremor and alien limb phenomena only occurred in this subgroup. The subgroups did not differ in neuropsychological test performance or *Apolipoprotein E4* allele frequency. Greater asymmetry of atrophy occurred in PCA + CBS, particularly involving right frontoparietal and peri-rolandic cortices, putamen and thalamus. The nine patients (including four PCA + CBS) with pathology or CSF all showed evidence of AD.

Conclusions: Our data suggest that PCA patients with motor features have greater atrophy of contralateral sensorimotor areas but are still likely to have underlying AD. Appreciation that PCA presentations of AD may include motor aspects of CBS is important to ensure that these patients receive appropriate treatment options.

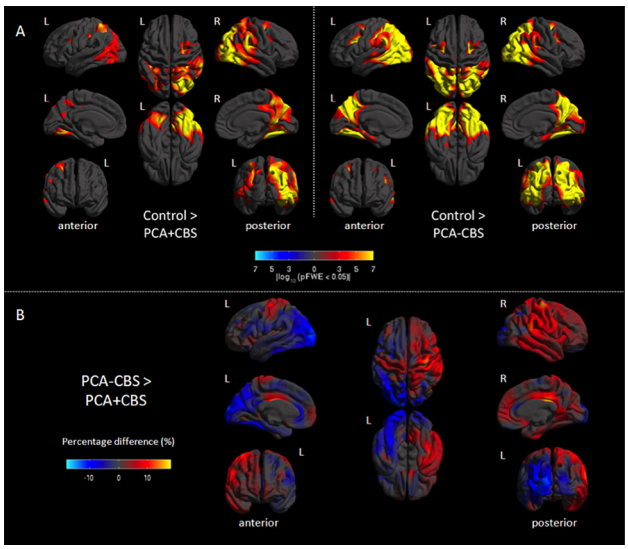
	Controls (N=30)	PCA + CBS (N=13)	PCA –CBS (N=31)	*p*.value
Gender (male, female)	13, 17	7, 6	12, 19	0.71*
Age in years, mean (S.D.)	63.9 (6.2)	63.8 (8.0)	63.4 (6.2)	0.94**
MMSE, mean (S.D.)	29.3 (0.8)	17.4 (6.3)	18.9 (6.4)	0.49~
Disease duration in years, mean (S.D.)	N/A	4.9 (2.1)	5.3 (2.8)	0.66~
Scanner (3.0T, 1.5T)	18, 12	7, 6	18, 13	0.95*
APOE4, no. (percentage) with *E4* allele / no. with DNA sample)	N/A	5/11 (45%)	12/29 (41%)	1.00*
Neurological signs				
Limb rigidity [a,b]	N/A	13 (100%)	0	
Alien limb phenomena [a]	N/A	2 (15%)	0	
Tremor [a]	N/A	3 (23%)	0	
Myoclonus [a] - asymmetrical	N/A	10 (77%) 8 (80%)	14 (45%) 4 (29%)	0.10* 0.04*
Apraxia [a] - asymmetrical	N/A	13 (100%) 12 (92%)	12 (39%) 2 (17%)	<0.001* <0.001*
Limb apraxia subtest (3A) of Apraxia battery for adults (ABA-2A)		**PCA + CBS (N=4)**	**PCA –CBS (N=4)**	***p*.value**
Right upper limb score [c], mean (S.D)	N/A	34.4 (12.3)	42.75 (10)	0.32~
Left upper limb score [c], mean (S.D)	N/A	21.3 (13.3)	42.75 (7.3)	0.05~
Difference between left and right scores, mean (S.D)	N/A	13 (5.9)	2 (2.3)	0.01~
p.value for paired samples t-test comparing left and right upper limb scores		0.02	1.00	

* Fisher's exact test ** one way ANOVA ~ two sample unpaired t-test comparing PCA+CBS against PCA–CBS

(a) Numbers indicate the number (percentage) of patients in each group documented as manifesting the sign on clinical examination. Where indicated, the number (percentage) of these subjects in whom the sign was asymmetrical ie. observed only or more prominently on one side than the other, is recorded on the line below. The remaining signs were asymmetrical in all cases.

(b) Limb rigidity was the feature used to define membership of the PCA+CBS group and affected the left upper limb in all cases

(c) Maximum score 50, with lower scores indicating more severe apraxia



Disclosure: Nothing to disclose.

OS1206

Abstract withdrawn

Movement disorders 1

OS1207

Brain functional connectomics in early Parkinson's disease

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Introduction: To explore the integrity of the functional brain connectome in patients at different stages of Parkinson's disease (PD).

Methods: Graph theoretical analysis was applied to resting state fMRI data from 212 PD patients (100: Hoehn and Yahr score [HY] = 1–1.5; 54: HY = 2–2.5; 44: HY = 3–3.5; 14: HY = 4–5) and 46 controls (HC). Measures of global and regional network properties were obtained. Correlations between UPDRSIII score and network metrics were tested.

Results: Functional brain networks in PD and HC showed the same hub organization, with differences only in the right cingulum, left postcentral gyrus and precuneus bilaterally (hubs only in patients), and right fusiform gyrus (hub only in HC). However, all global network metrics were altered in PD patients. At a regional level, PD patients showed nodal degree reduction and betweeness centrality increase compared with HC. Such local abnormalities were relatively focal in patients with HY = 1–1.5, involving the globus pallidus, putamen, supplementary motor area, cingulum, and gyrus rectus bilaterally, spreading to the frontal, temporal, parietal and occipital cortical regions in the more advanced disease stages. In PD, network metrics showed significant correlations with UPDRS III.

Conclusions: In PD, functional brain networks are characterized by an imbalanced structure, with a loss of efficiency in information exchange between both close and distant brain areas. Abnormal functional network connectivity occurs even at the earliest stages of the disease and is an important factor contributing to PD motor deficits.

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Disclosure: FA funding for travel from Teva and speaker honoraria from Bayer, Biogen, Sanofi Aventis, SSIF. VK reports grants and speaker onoraria from Hemopharm Stada, Pharma Swiss, Boehringer Ingelheim, Novartis, Glaxo, Bayer and Pfizer. MF received compensation for consulting and/or speaking from Bayer, Biogen Idec, Merck Serono, and Teva.

OS1208

The first data on retinal optical coherence tomography parameters in Huntington's disease

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Introduction: Huntington's disease (HD) is a severe progressive neurodegenerative disorder. Optical coherence tomography (OCT) is non-invasive method for retinal structure visualization. The aim of this study was to evaluate the number of retinal OCT parameters in patients with HD.

Methods: We examined 90 participants divided into three groups. The first group consisted of 30 patients with HD clinic expanded, the second group included 30 patients—carriers of the mutant HD gene, the third—control group of 30 healthy patients. The excluding criteria were diabetes mellitus and diagnosed ophthalmological pathology. Three groups of parameters were assessed by the retinal OCT (Cirrus HD-OCT 4000): peripapillary Retinal Nerve Fiber Layer (RNFL) thickness, Ganglion Cell Layer (GCL) characteristics and Macular Thickness.

Results: The healthy control group had no significant pathological changes. Peripapillary RNFL thickness was decreased in 70 % patients from the first group and in 40 % from the second. GCL damage was registered in both groups with equal frequency (30 %). The macular thickness was also decreased in 53 % HD clinic expanded patients and in 57 % gene carriers. All the patients from the first two groups had abnormalities at least in one of the three retinal parameters, mostly symmetrically.

Conclusions: We have identified a number of pathological changes in the retina in both groups—carriers of the mutant HD gene and patients with HD clinic expanded. Thus, retinal OCT can be served as a new biomarker for neurodegenerative diseases in an early stage.

Disclosure: Nothing to disclose.

OS1209

Sensory attenuation in functional movement disorders

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Introduction: Sensory attenuation (SA) is the phenomenon whereby self-produced sensation is perceived as reduced in intensity compared to an identical externally produced sensation. This phenomenon has previously been linked to sense of agency for movement.

Objective: Assessment of SA through measurement of sensory evoked potentials (SEPs) at the onset of movement. We hypothesised that patients with functional movement disorders (FMD) have loss of SEPs suppression at the onset of movement as consequence of loss of SA.

Methods: 17 right-handed patients with FMD and 17 right-handed age-matched healthy participants were studied. SEPs were elicited after electrical stimulation of the median nerve at the wrist. EEGs were recorded over the scalp at three sites on according to the International 10–20 System (F3, C3 and P3). SEPs were recorded in two conditions: at rest and at the onset of movement.

Results: A repeated measures ANOVA with SEPs ELECTRODE (F3, C3 and P3) as within-subjects factors and DIAGNOSIS as between group factor revealed that there was a significant main effect of GROUP ($F(1,21) = 0.8$, $p = 0.000$).Post Hoc exploration of this effect revealed it to be due to an absence of SEPs suppression in patients (ratio > 1 for all the SEP components) compared to controls, who had SEPs gating (ratio < 1 for all the SEP components).

Conclusions: We demonstrate abnormal SEPs suppression at the onset of movement in patients with FMD. We suggest that these results could reflect abnormalities in sensory predictions relating to the expected sensory consequences of voluntary movement, which could be directly related to deficits in sense of agency seen in patients with FMD.

Disclosure: Nothing to disclose.

OS1210

Olfactory assessment for predicting transition to neurodegenerative parkinsonian disorders in subjects with idiopathic rapid-eye-movement sleep behaviour disorder: a prospective cohort study

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Introduction: Olfactory dysfunction is present in approximately 80 % of patients with Parkinson's disease (PD) and may antedate the onset of classical motor symptoms by years. The latter is also true for idiopathic rapid-eye-movement sleep behaviour disorder (iRBD) and the aim of the present study was to determine the predictive value of olfactory dysfunction for conversion into PD or other types of neurodegeneration in subjects with iRBD.

Methods: A total of 35 polysomnography-confirmed iRBD subjects underwent olfactory testing using the Sniffin' Sticks test assessing odour-identification, odour-discrimination and threshold at baseline. Subjects were routinely followed-up including a thorough neurological examination for a mean of 4.4 (±standard deviation 0.7) years. The diagnosis of PD and other neurodegenerative parkinsonian disorders was based on current clinical diagnostic criteria.

Results: Overall, 9 subjects developed a neurodegenerative parkinsonian disorder (6 PD and 3 lewy-body dementia). Receiver operating characteristic curve analysis revealed that baseline olfactory function was predictive for their development with areas under the curve of 0.82 [95 % confidence interval (CI), 0.66–0.99] for the entire Sniffin' Sticks, 0.82 [95 % CI, 0.66–0.97] for odour-identification, 0.77 [95 % CI, 0.56–0.97] for odour-discrimination and 0.65 [95 % CI, 0.39–0.91] for threshold. The relative risk for a neurodegenerative parkinsonian disorder in the lowest tertile of olfactory function was 7.4 [95 % CI, 1.9–29.2] compared with the top two tertiles.

Conclusions: Assessment of olfactory dysfunction may help to predict the development of a neurodegenerative parkinsonian disorder in iRBD patients over a short time period.

Disclosure: Nothing to disclose.

OS1211

On the basis of reflexive saccadic eye (RS) movements responses machine learning (ML) predicts UPDRS in individual Parkinson's disease (PD) patients

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Introduction: L-DOPA as well as DBS has been shown to improve peripheral motor abnormalities in PD measured as UPDRS. We propose to measure RS in order to find if their parameter correlate with UPDRS.

Methods: We conducted horizontal RS measurements in nine patients with Parkinson's disease (PD) in four sessions: S1: MedOffDBSOff, S2: MedOffDBSOn, S3: MedOnDBSOff, S4: MedOnDBSOn. Changes of motor performance, behavioral dysfunction, cognitive impairment and functional disability were evaluated in each session according to the UPDRS. RS were recorded by head-mounted saccadometer (Ober Consulting, Poland). ML method was based on RSES 2.2 (Rough System Exploration Program).

Results: The mean age was 51.1 ± 10.2 (SD) years, mean disease duration was 11.3 ± 3.2 years, mean UPDRS: S1: 66.6 ± 13.8 S2: 30.0 ± 16.3; S3: 58.1 ± 13.5; S4: 22.3 ± 13.6; mean RS latencies: S1: 291.2 ± 93.1 ms, S2: 199.6 ± 39.5 ms, S3: 232.9 ± 82.7 ms; S4: 183.2 ± 30 ms. Differences between latencies: S1–S2, and S1–S4 were stat sig (t test $p < 0.01$), S1–S3—not stat sig., similar to differences between UPDRS: S1-S2, and S1-S4 were stat sig ($t < 0.001$) and S1-S3—not stat sig. Prediction of individual UPDRS values only from RS latencies was not possible (ML). But patient's age, RS: latency, amplitude, duration give global accuracy in UPRDS prediction 83.3 % (ML: cross-validation-method).

Conclusions: ML approach is more precise and powerful than popular statistical methods.

Disclosure: This work was supported by Grant 2011/03/B/ST6/03816 from the National Centre for Research and Development, Poland. No conflict of interest exists.

OS1212

All in the blink of any eye: insights into the pathophysiology of DYT1 and DYT6 dystonia

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Introduction: Traditionally dystonia has been considered a disorder of basal ganglia dysfunction however recent research has advocated a more complex neuroanatomical network. In particular, there is increasing interest in the pathophysiological role of the cerebellum. Patients with cervical and focal hand dystonia have impaired cerebellar associative learning using the paradigm eye blink conditioning. This is perhaps the most direct evidence to date that the cerebellum is implicated in patients.

Methods: We examined eleven patients with DYT1 dystonia and five patients with DYT6 dystonia and compared rates of eye blink conditioning to age-matched controls. In addition we studied brainstem circuit excitability by testing blink reflex recovery in the same groups.

Results: Patients with DYT1 and DYT6 are both able to acquire eyeblink conditioning to the same ability as age-matched controls. There was evidence of enhanced blink reflex recovery excitability in DYT1 but this effect was not seen in DYT6.

Conclusions: If the cerebellum is an important driver in DYT1 and DYT6 dystonia our data suggest that there is specific cerebellar dysfunction such that the circuits essential for conditioning function normally. In addition, these data are contrary to observations in focal dystonia and suggest that the cerebellum may have a more dominant role in focal subgroups of dystonia. We do not find evidence of enhanced blink reflex recovery in all patients with dystonia and recent studies calling for the blink recovery reflex to be used as a diagnostic test for dystonic tremor may require further corroboration, especially in genetically proven dystonia.

Disclosure: Nothing to disclose.

Muscle and neuromuscular junction diseases

OS1213

Myofiber HLA-DR expression: a distinctive biomarker for antisynthetase myositis

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Introduction: Idiopathic autoimmune myopathies (IIM) mainly include dermatomyositis (DM), polymyositis (PM), and necrotizing autoimmune myopathy (NAM). Anti-RNAt-amino-acylsynthetase (anti-synthetase, AS) autoantibodies are characteristics of a subset of IIM associated with extramuscular features and perimysial pathology. Current diagnostic approaches of IIM require histopathological evaluation of immunological parameters including lymphocyte phenotype, myofiber MHC-1 expression and complement activation (C5b9 formation). In routine practice, we observed myofiber HLA-DR expression seems specifically associated with antisythetase myositis. In present work, we evalueted the reliability of HLA -DR expression as a biomarker of antisynthetase myositis.

Methods: We investigated HLA-DR expression in muscle biopsies from 33 patients with AS syndrome (anti-Jo-1: $n = 26$; anti-PL7: $n = 2$; anti-PL12: $n = 4$; anti-EJ: $n = 1$),16 DM, and 10 histologically normal muscle. For each case, we evaluated (i) the percentage of positive fibers on the whole fascicle, and (ii) the percentage of contiguous positive perifascicular fibers.

Results: HLA-DR myofiber expression was found in 84.8 % (28/33) AS patients (anti-Jo1: 88.4 %) and in 4/17 (23.5 %) patients with DM ($p < 0.0001$). No myofiber HLA-DR expression was found in normal muscles. The mean percentage of positive fibers was 36.3 % in AS (40.5 % in anti-Jo1) and 6.8 % in DM (DM vs AS: $p = 0.001$; DM vs Jo1: $p < 0.001$). All DM had less than 10 % DR-positive myofiber. Myofiber HLA-DR expression was observed in perifascicular areas with ribbon-like pattern. The percentage of DR-positive perifascicular contiguous myofibers was 33.4 % in AS and 2 % in DM ($p < 0.001$).

Conclusions: Myofiber HLA-DR expression is specific biomarker of anti-synthetase myopathy suggesting a role for INF-γ in its pathophysiology.

Disclosure: Nothing to disclose.

OS1214

Autologous transplantation of bone marrow-derived CD133 + stem cells in facioscapulohumeral dystrophy

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Introduction: Facioscapulohumeral muscular dystrophy is the third most common muscular dystrophy, exhibits autosomal dominant inheritance and has no cure. FSHD typically arises with a reduction of facial and shoulder girdle muscle mass. The disease may extend to abdominal and pelvic girdle muscles impairing the ability to walk. The aim of this open pilot study was to establish the profile of tolerability and clinical response of autologous bone marrow-derived CD133+ stem cells in a cohort of patients affected by facioscapulohumeral muscular dystrophy (FSHD).

Methods: Thirteen patients between 30 and 56 years of age were included in this study and two of them treated with two serial infusions of autologous bone marrow-derived CD133+ stem cells and followed for 1 year. All patients were longitudinally assessed using the 6 min walking test (6MWT) and isometric/isokinetic quantitative muscle test (QMT) 6 months before treatment started (T0), at baseline (T1) and 6 and 12 months later.

Results: In treated patients there was no significant change in function between T0 and T1 assessments, but the quantitative scores recorded after 6 and 12 months of treatment were significantly higher than those recorded at baseline ($p = 0.006$). Moreover, the treatment is related to a gain of muscle force unobserved in untreated FSHD patients.

Conclusions: Our results suggest that bone marrow-derived CD133+ stem cells may be beneficial to facioscapulohumeral dystrophic patients without producing any major side effect. Larger prospective randomized, double-blind, placebo controlled trials are needed to confirm these preliminary findings.

Disclosure: Nothing to disclose.

OS1215

$CD4^+$ T cell produced IL17 is essential for loss of B cell tolerance in experimental autoimmune myasthenia gravis (EAMG)

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Introduction: An important contribution of CD4+ T cell produced IL-17 to autoantibody mediated autoimmune disorders like Myasthenia Gravis has recently been suggested, but never been directly demonstrated.

Methods: We used Experimental Autoimmune Myasthenia Gravis (EAMG) induced by repetitive immunizations with torpedo AchR (tAChR) as a model for a classical autoantibody mediated disease in order to dissect the role of Th17 cells in disease pathogenesis.

Results: We show that in wildtype (WT) mice significant numbers of IL17-producing *t*AchR-specific CD4+ T cells can be observed after immunization. Interestingly, IL17ko mice develop less or no EAMG symptoms, although frequencies of tAchR-specific CD4+ T cells secreting IL2, IFNγ or IL21 as well as percentage of FoxP3+ Treg cells are similar. On the other hand anti-tAChR antibody levels are equal. while pathogenic anti-murine AChR antibody levels are significantly lower in IL17ko mice. These results were confirmed in a system with IL-17 deficiency restricted to CD4+ T cells, created by the reconstitution of TCR β/δko mice with CD4+ T cells of either WT or IL17ko origin.

Conclusions: Taken together we show here that numbers and differentiation of antigen specific CD4+ T cells as well as the level of immunization antigen specific antibody titers are not affected by IL17-deficiency in the EAMG model. However, breaking of B cell tolerance resulting in pathogenic anti-murine AChR specific antibodies and subsequent disease induction are dependent on IL17 produced by CD4+ T cells.

Disclosure: Nothing to disclose.

OS1216

'Core rod' congenital myopathy with foot-drop associated with nebuline (*NEB*) gene mutations

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Introduction: 'Core rod' myopathy is a rare congenital myopathy presenting with cores and rods as distinctive morphological picture. Up to now, recessive mutations of the nebulin gene *(NEB)* associated with cores and rods lesions have been described in only two patients with early onset distal myopathy.

Objectives: To describe two patients presenting early onset distal muscle weakness with bilateral foot drop associated with never reported recessive *NEB* mutations.

Methods: Clinical, histoenzymological, and ultrastructural analysis of one 15 years old male patient (P1) and another 21 years old female patient (P2). Molecular screening for NEB gene was effectuated combining Exome sequencing coupled with dHPLC/Sanger sequencing.

Results: P1 presented delayed gait acquisition, frequent falls, and mainly lower limb distal weakness with bilateral foot-drop. P2 showed frequent falls from the age of 1 years. She successively developed slowly progressive distal lower limbs weakness with bilateral foot-drop. P1 and P2 muscle biopsy analysis showed a homogenous pathological picture characterized by the association of distinct and separated cores with nemaline bodies (rods). P1 harbored one intron 106 mutation (c.16909–2A > G), and one exon 171 duplication (c.24392_24395dup). P2 harbored one exon 129 mutation (c. 19944G > A), and one exons' 74–144 deletion.

Conclusions: We describe two novel patients presenting a distal 'Core rod' myopathy with foot drop associated with novel *NEB* heterogeneous mutations. Our report suggests that *NEB* gene should be routinely screened in patients presenting early onset 'Core rod' myopathy with foot drop and should be considered in the differential diagnosis of early onset distal neuromuscular conditions.

Disclosure: Nothing to disclose.

OS1217

Bulbar myasthenia gravis: why are treatable patients needing admission to hospital—are neurologists doing something wrong?

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Introduction: Some patients with autoimmune myasthenia gravis (MG) deteriorate despite treatment. We analysed the demographics and management of patients requiring hospitalisation to identify treatable factors associated with clinical deterioration.

Methods: The study included admissions for MG to the regional neuroscience centre in Greater Manchester, England 2002–2012. Records were obtained for 108 admissions of 78 patients, including characteristics of MG using Myasthenia Gravis Foundation of America (MGFA) clinical classification, and details of treatment changes before each hospital admission.

Results: Disease severity increased leading up to hospitalisation. Bulbar weakness increased from 38.46 % at onset, to 82.57 % at diagnosis and 91.67 % at hospital admission. Of patients with bulbar disease at diagnosis, 42 % had class IV-V severity by the time of admission, while only 16.7 % of patients without bulbar involvement at diagnosis developed class IV–V disease. 90 % of patients requiring ICU admission and 84 % of patients with multiple admissions had bulbar involvement at diagnosis.

From the start of deterioration to admission patients were managed with increased Prednisolone of only 0.16 mg/kg on average, with no change in dose in 45 % of cases. Of patients with bulbar involvement at diagnosis, 46 % had not received immunosuppressants by the time of admission and 35 % were receiving drugs but in low doses.

Conclusions: Bulbar symptoms are a marker for severe MG, however, neurologists do not increase treatment despite patient deterioration. Patients would benefit from guidelines based on evidence combined with expert opinion in areas lacking evidence, conformed by trials. The authors will discuss developments in this direction.

Disclosure: Nothing to disclose.

OS1218

Disease-related symptoms and activities of daily living: a novel survey of patients with nonsense mutation Duchenne muscular dystrophy

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Introduction: Health-related quality of life in Duchenne muscular dystrophy (DMD) is not well understood, and there is a need for a sensitive disease-specific questionnaire. A novel survey of symptoms and activities of daily living (ADL) was developed and piloted in an ongoing open-label study of ataluren 40 mg/kg/day in nonsense mutation DMD (nmDMD). We describe the survey design and provide a summary of interim data from 47 patients with nmDMD.

Methods: The survey was administered by site personnel to the same respondent (patient/parent/caregiver) throughout the study. At each 12-week site visit, respondents were asked whether there were any changes in ADL/disease symptoms compared with baseline, within six pre-specified categories. If yes, respondents were asked to self-report specific ADL/disease symptom terms (within the identified categories) and rate the change from baseline on a 5-point Likert scale.

Results: Patients representing various degrees of ambulatory disability were included. The most common improvements during ataluren treatment occurred in the domains of physical functioning (e.g. walking, stair climbing, swimming, upper extremity activity, self-care). Approximately 80 % of reports reflected stability or improvement in physical functioning over time with ataluren 40 mg/kg/day (week 12, 87.2 %; week 24, 82.9 %; week 36, 78.3 %; week 48, 80.0 %).

Conclusions: Survey data describing changes in ADL/disease symptoms may be used to complement functional outcome measures. Given that the natural history of DMD indicates a progressive decline

in physical function, stabilization of this domain may be regarded as a positive effect.

Disclosure: AR, JB, GLE and RS are all employees of PTC Therapeutics, Inc., which has developed ataluren. Medical writing support was provided by Dr Jonathan Morton of Oxford PharmaGenesis™ Ltd and was paid for by PTC Therapeutics, Inc.

Neuroimaging

OS1219

Computation based diagnosis reveals intermediate Alzheimer's disease phenotypes

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Introduction: A definitive diagnosis of Alzheimer's disease (AD) can only be confirmed with pathology. In-vivo clinical criteria alone can lead to 35 % misdiagnosis rate. We present a new diagnostic tool for AD based on in vivo neuroimaging patterns, which predicts pathological proven (PP) AD. We inspected imaging and cognitive patterns from individuals and explored reasons for diagnostic mismatch based on clinical criteria and the results of MR structural neuroimaging based automated classification. We suggest that such individuals have differential patterns of brain atrophy associated with memory loss.

Methods: We trained a Support Vector Machine (SVM) classifier on grey matter volume (GMv) estimations from post-mortem proved AD and healthy controls (HC). Using this classifier, we relabelled ADNI individuals (clinically diagnosed). Training: 15 HC/18 AD T1-weighted ante-mortem MRI from PP individuals (Klöppel et al., 2008) ADNI set: T1-weighted MRI from 359 HC/284 AD patients (defined by MMSE, CDR scores) at baseline time. We normalized all GMv images to MNI space using a template generated from PP individuals using SPM12.

Results: SVM classified the 33 PP individuals with 87 % accuracy (leave-one-out cross-validation). ADNI individuals were classified either AD or HC and then stratified into 4 subgroups: AD_AD, AD_HC, HC_AD, HC_HC (formatted as clinical_SVM, Table 1). Comparisons of GMv and MMSE scores between these groups are shown in Figs. 1, 2.

	SVM Classified	Age	Gender		Number of subjects
		mean (year)	number of male	number of female	
ADNI HC	HC (HC_HC)	74.64	94	88	182
	AD (HC_AD)	75.6	87	90	177
ADNI AD	HC (AD_HC)	72.7	23	23	46
	AD (AD_AD)	75.5	129	109	238
33 Pathologically Proved HC		64.4	9	6	15
33 Pathologically Proved AD		65.89	12	6	18

Table 1. Demographic information of 33 pathologically proved subjects / 4 stratified groups of ADNI AD / HC subjects. The labels of the 4 groups (HC_HC, HC_AD, AD_HC and AD_AD) are formatted as ADNI_SVM. SVM classifier labeled 177 ADNI HC subjects as AD. They are stratified into group HC_AD. SVM classifier labeled 46 ADNI AD subjects as HC. They are stratified into group AD_HC.

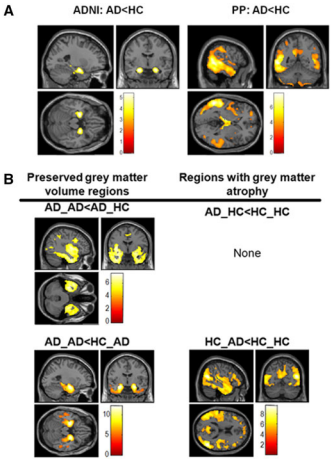

Figure 1.
(A) AD and HC individuals from two cohorts (ADNI and 33 pathologically proven (PP)) were compared separately for grey matter volume (GMv) with voxel-based morphometry in SPM12. GMv was adjusted by age, gender and total brain volume. ADNI labeled AD group has atrophy in amygdale, hippocampus, parahippocampal gyrus and partially temporal lobe and fusiform gyrus compared with HC group (left). PP AD group has atrophy in temporal lobe, amygdale, thalamus, cingulum, cerebellum, frontal lobe, fusiform and insula compared with PP HC group (right). The regions highlighted with color have significantly volume difference between the compared groups (p-value< 0.001). The color bars indicate z statistic.
(B) ADNI / SVM differentially labelled individuals were compared with label matched groups for grey matter volume (GMv) with voxel-based morphometry in SPM12. GMv was adjusted by age, gender and total brain volume. Group AD_HC has preserved GMv in temporal lobe, amygdala, fusiform, parahippocampal gyrus and partially hippocampus compared with AD_AD (top left). Group HC_AD has preserved GMv in amygdale, hippocampus and parahippocampal gyrus (bottom left) but has significant atrophy in temporal lobe, cingulum, thalamus, fusiform and occipital lobe (bottom right). The regions highlighted with color have significantly volume difference between the compared groups (p-value<FWE 0.05). The color bars indicate z statistic.

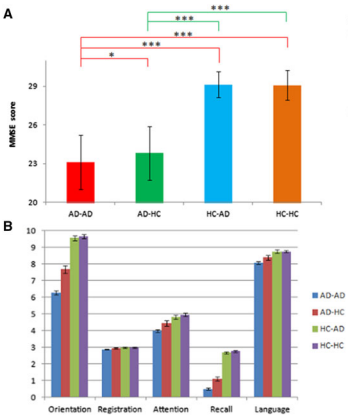

Figure 2.
(A) Total Mini–mental state examination (MMSE) score were compared between the 4 stratified groups. The means and standard deviations are shown in the figure. The stars with bars above the histograms present significant levels (*<0.05, **<0.005, ***<0.0005).
(B) The 5 domains of MMSE score (6 months after baseline time) were compared between the 4 stratified groups. The mean values and confidence intervals are shown in the figure.

Conclusions: Clinical/neuroimaging mismatch labeled individuals (AD_HC and HC_AD) showed intermediate characteristics in both anatomy patterns and memory performance. This result suggests different mechanisms of clinically AD-type dementia syndrome.

Disclosure: Nothing to disclose.

OS1220

Iron deposits in post-mortem brains of patients with neurodegenerative and cerebrovascular diseases: a semi-quantitative 7.0 Tesla magnetic resonance imaging study

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Objectives: Accumulation of iron (Fe) is often detected in brains of people suffering from neurodegenerative diseases. However, no studies have compared the Fe load between these disease entities. The present study investigates on T2*-weighted gradient-echo 7.0 T magnetic resonance imaging (MRI) the Fe content in post-mortem brains with different neurodegenerative and cerebrovascular diseases.

Methods: Hundred-fifty two post-mortem brains, composed of 46 with Alzheimer's disease (AD), 37 with frontotemporal lobar degeneration (FTLD), 11 with amyotrophic lateral sclerosis, 13 with Lewy body disease, 14 with progressive supranuclear palsy, 16 with vascular dementia (VaD) and 15 controls without a brain disease were examined. The Fe load was determined semi-quantitatively on T2*-weighted MRI serial brain sections in the claustrum, caudate nucleus, putamen, globus pallidus, thalamus, subthalamic nucleus, hippocampus, mamillary body, lateral geniculate body, red nucleus, substantia nigra and dentate nucleus. The disease diagnosis was made on subsequent neuropathological examination.

Results: Only in the claustrum, caudate nucleus and putamen of FTLD brains a highly significant Fe load was observed, while also present to a lesser degree in the globus pallidus, thalamus and subthalamic nucleus. In the other neurodegenerative diseases no Fe accumulation was observed, except for a mild increase in the caudate nucleus of AD brains. In VaD brains no Fe increase was detected.

Conclusions: Only FTLD displays a significant Fe load, suggesting that impaired Fe homeostasis plays an important role in the pathogenesis of this heterogenous disease entity while cerebrovascular lesions are not implied.

Disclosure: Nothing to disclose.

OS1221

Diagnostic performance of ioflupane I123 injection (DaTSCAN^{TM}) in patients with movement disorders and dementia

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Introduction: Early and accurate diagnosis of movement disorders and dementia is critical to ensuring optimal clinical management. Ioflupane I 123 Injection (DaTSCAN^{TM} or ioflupane (^{123}I)) is approved to visualize loss of striatal dopamine transporter in a subset of patients with dementia and movement disorders.

Methods: Four clinical trials were pooled to determine the overall sensitivity and specificity of ioflupane (^{123}I) images in detecting or excluding a striatal dopaminergic deficit (SDD), which is associated with Parkinsonian syndrome and dementia with Lewy bodies. Patients with either a movement disorder or dementia, and healthy volunteers were administered ioflupane (^{123}I). Images were assessed by panels of 3–5 blinded experts and/or on-site nuclear medicine physicians, classified as normal or abnormal, and compared with clinical diagnosis (reference standard) to determine sensitivity and specificity.

Results: Pooling the four studies, 928 subjects were enrolled, 849 were dosed, and 764 completed their study. Across all studies, when images were assessed by on-site readers, ioflupane (^{123}I) diagnostic effectiveness had an overall (95 % CI) sensitivity of 91.9 % (88.7–94.5) and specificity of 83.6 % (78.7–87.9). When reads were conducted blindly by a panel of independent experts, the overall sensitivity was 88.7 % (86.8–90.4) and specificity was 91.2 % (89.0–93.0).

Conclusions: In this pooled analysis, the visual assessment of ioflupane (^{123}I) images provided high levels of sensitivity and specificity in detecting the presence/absence of an SDD. Ioflupane (^{123}I) imaging has the potential to improve diagnostic accuracy in patients with signs and symptoms of a movement disorder and/or dementia.

Disclosure: Drs. Sherwin and Grachev are employees of GE Healthcare.

OS1222

DWI intensity values for the prediction of time from stroke onset in acute stroke

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Introduction: In acute stroke, the DWI-FLAIR mismatch allows for the identification of patients eligible for thrombolysis. FLAIR-lesions, however, are difficult to analyze. In comparison, DWI alone may be a suitable bio-marker. We analyzed whether a relative DWI intensity threshold (rSI) can identify stroke patients imaged within the thrombolysis time-window.

Methods: We retrospectively included patients according to the following criteria:

1) proven stroke,
2) symptom-onset < 12 h,
3) confirmed lesion in DW-imaging.

Patients were dichotomized into two groups (stroke-onset-time [SOT] < 4.5 h/> 4.5 h). MR-imaging hardware: 1.5T Intera Master (Philips Medical Systems). A DWI lesion-volume was created and

a) mean (DWmean),
b) minimum (DWmin) and
c) maximum voxel-values (DWmax) of the volume was calculated.

Values were normalized: [value/mean value of a representative slice from the unaffected hemisphere] %. DWI-rSIs were correlated with SOT. The ability of DWmin-, DWmean- and DWmax-rSI values to allocate patients to the thrombolysis window was analyzed using receiver operating characteristics (ROC) curve analysis.

Results: 44 patients were included (in median: stroke-onset-time = 2.3 h; age = 62 a; NIHSS = 8 points; lesion volume = 23 ml). 31 patients were imaged within 4.5 h after stroke-onset. Correlation of SOT with DWmin, DWmean and DWmax was 0.05, 0.46 and 0.43. Area under the curve (AUC) for DWmean and DWmax was 0.75 and 0.81. DWmin performed poorly (AUC: 0.53). Optimal rSI-thresholds with sensitivity/specificity were: for DWmean 162 % with 58 %/85 %; for DWmax 239 % with 71 %/93 %.

Conclusion: DWI-rSIs identified patients within the 4,5 h time-window with high specificity. This finding is promising for the use of DW-rSI in acute stroke.

Disclosure: Nothing to disclose.

OS1223

Thalamic dysfunction is associated with fatigue in patients with multiple sclerosis: a graph theory study

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Introduction: To explore abnormalities of large-scale brain networks (connectome) in MS patients with fatigue.

Methods: Graph theoretical analysis was applied to RS fMRI data from 64 MS patients with fatigue (F) according to the Fatigue Severity Scale. As control groups, 60 MS patients without fatigue (NF) matched for disease duration and brain T2 lesion volume with F-MS patients and 59 gender and age-matched healthy controls (HC) were included. Functional connectivity between 116 cortical and subcortical brain regions was estimated using a bivariate correlation analysis. Small-worldness properties were tested by comparison with matched random networks. Between-group differences of global and local network metrics were investigated using ANOVA models.

Results: Small-worldness was verified in all study groups. All global network parameters were significantly altered in F-MS patients and NF-MS patients compared with HC, with no significant differences between F- and NF-MS patients. The cerebellum (right lobule VI and bilateral crus I), and bilateral middle and inferior temporal gyri were hubs in all study groups. F- and NF-MS patients lost hubs in the bilateral anterior cingulate cortex and cerebellar regions (lobule VII-VIII, crus II). F-MS patients also lost hubs in the thalami and middle cingulate cortex. Compared to HC, F- and NF-MS patients had a decreased degree in the bilateral caudate nucleus. F-MS patients also experienced a decreased degree in the bilateral thalamus.

Conclusions: Fatigue in MS is related to a functional disruption of the thalamic connector, which should be the target of potential therapeutic interventions.

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OS1224

Preoperative memory fMRI predicts verbal memory decline after left anterior temporal lobe resection

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Introduction: Anterior temporal lobe resection brings remission in up to 80 % of patients but up to 30 % of temporal lobe resections in the speech dominant hemisphere cause significant verbal memory decline. The purpose of this study was to develop a robust memory fMRI method as a clinically applicable tool for predicting post surgical memory outcome in individual patients.

Methods: 23 patients with left TLE and 26 controls performed an explicit fMRI memory encoding paradigm of words with a subsequent out of scanner recognition assessment. Neuropsychological assessment was performed pre-operatively and 4 months after anterior temporal lobe resection, and at equal time-intervals in controls. An event related analysis was used to explore brain activations for words remembered and change in verbal memory scores 4 months post-operatively was correlated with pre-operative activations. Individual lateralisation indices were calculated within a medial temporal and frontal region and compared with other clinical parameters (hippocampal volume, pre-operative verbal memory, age at onset and duration of epilepsy) as a predictor of verbal memory outcome.

Results: Greater left than right anterior medial temporal and frontal activations on remembering words correlated significantly with greater verbal memory decline post-operatively. In a step wise regression model, left lateralised memory lateralisation index (>0.5) within a medial temporal and frontal mask was the best predictor of verbal memory outcome after surgery.

Conclusion: We propose a robust, clinically applicable memory fMRI method where both temporal and extra-temporal activations predict post-operative verbal memory decline in individual patients.

Disclosure: Nothing to disclose.

Neurotraumatology and Neuro-oncology

OS1225

Identification and quantification of CSF malignant cells by the CellSearch® technology in patients with lung leptomeningeal metastasis

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Introduction: Diagnosis of lung leptomeningeal metastasis (LM) remains difficult. The usual diagnostic methods of cytomorphological assessment of cerebro-spinal fluid (CSF) and gadolinium-enhanced MRI lack both specificity and sensitivity. The Veridex CellSearch® technology is validated in detection of circulating tumor cells (CTC) in blood and in the follow-up of breast, prostate and colorectal cancer. Our aim was to adapt this technology for detection and quantification of tumor cells in the CSF of lung cancer patients with LM.

Methods: Patients with suspected lung LM from a French neuro-oncological center (Nancy) were prospectively included. The CSF samples were collected on traditional cytology tubes (1 mL) and on CellSave® Preservative tubes (4 mL).

Results: 11 patients with clinical symptoms and/or radiological criteria suggestive of lung LM (5 at diagnosis/6 at recurrence) underwent CSF analysis with conventional cytology and with Veridex CellSearch® technology. Conventional CSF cytomorphological analysis was positive in 5 patients (with a median of 13 tumor cells/mm3; range 10–25 tumor cells/mm3) whereas the assessment with Veridex CellSearch® technology was positive in 11 patients. Quantitative analysis with the Veridex CellSearch® technology showed a median of 203 tumor cells/5 mL of CSF (from 1 to 1500 tumor cells per 5 ml CSF).

Conclusions: In contrast to the current gold standard cytomorphological analysis, this new approach seems more sensitive and allowed a quantification of CSF tumor cells in lung LM.

This methodology could be useful for earlier diagnosis of lung LM and for follow-up.

A large prospective study is required.

Disclosure: Nothing to disclose.

OS1226

Long-term survival in patients with brain metastsis (BM): frequency and accompanying neurological status

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Introduction: BM patients die within an average of 8 months following treatment. Little is known about long-term survivors and their neurological status.

Methods: 2170 patients treated with resection or radiosurgery at M.D. Anderson Cancer Center between 1993 and 2008 for a newly-diagnosed BM were grouped according to their survival status 5 years from BM diagnosis date. Factors impacting long-term survival (LTS; $\geq$5 years) and neurological status were reviewed under an IRB-approved protocol.

Results: The median age of the 163 patients with LTS was 53 years. 47 % were males. The primary cancer was lung in 30 %, melanoma in 20 %, breast in 18 % and renal in 11 %. The interval from primary to BM diagnosis was 14.3 months. 77 % had a stable primary or no evidence of disease at treatment time. 72 % of BM were in or near eloquent brain; 80 % were single. The median largest tumor volume was 4.5 cm^3. 71 % were treated with a resection. In the multivariate analysis comparing the 163 patients with the 2094 patients who were known to have died before 5 years, a KPS $\geq$ 70 and a non-progressing primary had the strongest associations with LTS. The effect of treatment type and adjuvant radiation within different patient subgroups and data on neurological status will be presented.

Conclusions: LTS was observed in all typically unfavorable categories. However, good functional status and non-progressing primary most strongly impacted survival duration. Modern treatments may have enabled BM patients with good functional status and a controlled primary to survive for prolonged periods.

Disclosure: Nothing to disclose.

OS1227

Optogenetic inhibition of primary human malignant glioma

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Introduction: Glioblastoma are aggressive cancers with low survival and poor prognosis because of their highly proliferative and invasive capacity. It is not clear whether precise regulation of membrane depolarization and ion channels can inhibit glioma growth.

Methods: In the current study, we used optogenetics, an ideal tool to precisely control membrane depolarization and neural circuits, to inhibit the in vitro and in vivo growth of human malignant glioma.

Results: We showed that the engineered opsin gene (ChETA) expression in primary human glioma cells and light stimulation could reduce the viability of glioma cells. We further demonstrated that light illumination inhibited subcutaneous/intracranial glioma growth in vivo.

Conclusions: We demonstrated for the first time that precise regulation of membrane depolarization using optogenetics inhibited the proliferation and growth of glioma, thus providing new insights into glioma biology and the regulation of the proliferative capacity of malignant human glioma.

Disclosure: Nothing to disclose.

OS1228

Autologous skin derived stem cells and platelet-rich plasma as treatment for traumatic spinal cord injury

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Introduction: Traumatic spinal cord injury (SCI) results in a devastating loss of neurological function and in psychologically shattering condition that affects young healthy people that are in their most productive years. Currently, there are over 2 million SCI patients worldwide and at present, there are no universally accepted treatments for this neurological disorder. Recently, particular attention is paid to the potential of stem cells in treating SCI, but there are only few clinical studies and insufficient data.This clinical study explored the feasibility and efficacy of autologous skin derived stem cells (SDSCs) transplantation in two patients with complete and chronic spinal cord injury.

Methods: We hypothesized that the combination of autologous SDSCs as accessible sources of stem cells combining with platelet-rich plasma (PRP), rich of growth factors, was a possible treatment of SCI. PRP behave as natural scaffold and is able to improve stem cells survival, proliferation and axon regeneration and remyelination.

Results: Preoperative and postoperative neurological functions were evaluated with neurological clinical examination, MRI, and electrophysiological studies every 2 months after the treatment for 1 years.

Conclusions: Results showed that in the treated patients had a clinical improvement in terms of pin prick sensory and sphincter control. No signs of adverse events such as wound infection, and no sign of tumor were evident until 6 months postoperatively.

Disclosure: Nothing to disclose.

OS1229

Abnormalities of the attentional network following traumatic brain injury in pediatric patients: a fMRI study

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Introduction: To assess abnormalities of fMRI activity during a sustained attention task in pediatric patients with traumatic brain injury (TBI).

Methods: FMRI scans were acquired from 22 pediatric TBI patients (mean age = 14.3 years; mean time from TBI = 1.96 years) and 7 healthy controls (mean age = 10.8 years) during the administration of the Conners' CPT. Patients underwent the Wechsler Intelligence Scale for Children (WISC-IV) and the Functional Independence Measure (FIM) evaluation.

Results: In both groups, significant activations during the different conditions of the CPT task were found in the right somatosensory cortex, supplementary motor area, middle cingulate cortex, inferior frontal gyrus (pars opercularis) and left cerebellum. With increasing task difficulty ("load effect") both groups had increased fMRI activity in the bilateral middle occipital gyrus. During this condition, compared to TBI patients, controls also had an increased recruitment of the middle occipital gyrus as well as temporal and parietal regions. Patients having better performances at the CPT, better scores at WISC-IV and FIM scales and a longer time from TBI showed a reduced activity of the anterior cingulate cortex, superior frontal and middle frontal gyri during the CPT task. Patients having better scores at WISC-IV and a longer time from TBI showed also higher activity of frontal and temporal regions during the "load" condition.

Conclusions: Pediatric TBI patients experience an inability to optimize the recruitment of the attentional network, which might contribute to explain the attentional deficits frequently observed in this condition.

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OS1230

Decreased apparent diffusion coefficient in pituitary is correlated with hypopituitarism in patients with traumatic brain injury

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Introduction: To identify the role of the apparent diffusion coefficient (ADC) using a diffusion-weighted imaging technique and to evaluate the association of such changes with hypopituitarism (HPT) in TBI patients.

Methods: Diffusion weighted images were performed in 164 consecutive patients with TBI within 2 weeks after onset to generate the pituitary ADC as a measure of microstructural change. Patients with TBI were further grouped with or without HPT based on the secretion status of pituitary hormones at 6 months post injury. MRI data and laboratory findings were analyzed blindly. 30 healthy controls were enrolled. Mean ADC values were compared among the control, TBI with and without hypopituitarism group, and correlational studies were also performed. The neurological outcome was assessed with the Glasgow outcome scale (GOS) scores at 6 months post injury as well.

Results: Our study included 84 TBI patients with HPT and 80 TBI patients with normal pituitary function. The pituitary ADC in TBI patients was significantly less than that in controls (1.83 ± 0.16 vs. 4.13 ± 0.33, $P < 0.01$). Furthermore, the mean ADC was much less in TBI patients with pituitary dysfunction compared to those without HPT (1.32 ± 0.09 vs. 2.28 ± 0.17, $P < 0.05$). In addition, the ADC value was positively correlated with the neurological outcome at 6 months following TBI ($r = 0.602$, $P < 0.05$).

Conclusions: We confirm that the ADC in pituitary is correlated with the hormone-secreting status in TBI patients. We also demonstrate that the pituitary ADC may become a novel biomarker to predict the pituitary function in patients with TBI.

Disclosure: Nothing to disclose.

Clinical neurophysiology

OS2101

The significance of dorsal sural nerve recordings in early detecting oxaliplatin-induced peripheral neuropathy

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Introduction: Thus far, there is no gold standard for the accurate monitoring of Oxaliplatin-induced peripheral neuropathy (OXAIPN). For anatomical reasons, Dorsal Sural Nerve (DSN) conduction study might be able to predict the neurological outcome at end of chemotherapy. Our objective was to assess its ability to early detect OXAIPN.

Methods: A total of 116 colorectal cancer patients [75 (64.6 %) male, 41 (35.4 %) female, median age of 64 years; range: 38–77 y.o.] were evaluated before, at middle-point and at the end of chemotherapy. Standard nerve conduction studies plus DSN were performed. The Total Neuropathy Score-clinical version (TNSc) was used to assess OXAIPN. Elaborating a tree regression, cut-offs for z-score of DSN amplitude were individuated to subdivide at mid-treatment subjects at high versus low risk to develop neurotoxicity at the end of chemotherapy.

Results: At baseline all patients had no preexisting neuropathy. At mid-treatment, 11 (9.5 %) patients had abnormal sural nerve amplitudes and 24 (20.7 %) abnormal DSN amplitudes. At the end of treatment, 37 (32 %) patients had grade I neuropathy and 37 (32 %) had grade II/III. Forty-four (38 %) patients had abnormal sural nerve amplitudes and 55 (47.4 %) had abnormal DSN amplitudes. The -0.815 cut-off for the z-score of DSN amplitude was able to individuate the probability of patients to develop OXAIPN, better than sensory nerves conventionally studied, e.g., sural nerve.

Conclusions: DSN recording might be a useful objective outcome measure to individuate patients at higher risk to develop neurotoxicity during chemotherapy. It might also be a significant end-point in neuroprotection trials.

Disclosure: Nothing to disclose.

OS2102

Defective inhibition of exteroceptive cutaneo-muscular reflexes during focal ballistic movement execution in multiple sclerosis

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Introduction: Cutaneous reflexes may be enhanced in patients with multiple sclerosis (MS) reflecting lack of supraspinal inhibitory

control over spinal motoneurons. Cutaneo-muscular reflexes (CMR) to exteroceptive stimuli are usually recorded on pre-activated muscles. In the context of a unilateral simple reaction time paradigm (sRT), the execution of ballistic movements requires focusing excitatory inputs to motoneurons involved in execution of the task and inhibitory inputs to avoid unwanted activity. We hypothesized that CMR may be abnormally present in MS patients during sRT.

Methods: In 13 healthy subjects (HS) and 21 mildly disabled relapsing-remitting MS patients, we recorded bilaterally wrist-extensors activity using surface EMG. The sRT consisted on performing ballistic wrist-extension movements at perception of an electrical somatosensory low-intensity imperative stimulus (IS) given to either ipsilateral or contralateral index fingers. CMR were identified when a response was consistently obtained in the wrist-extensors of the side receiving the IS at a latency of 50–70 ms.

Results: In HS, CMR were present in 4 (31 %) during ipsilateral trials but never during contralateral trials. In patients, ipsilateral CMR was present in 13 (62 %; χ^2, $p = 0.077$) and most of them were larger than in HS. In contralateral trials, CMR were consistently seen in 5 patients (24 %; χ^2, $p = 0.056$ vs HS). All of them had also CMR in ispilateral trials.

Conclusions: Unwanted release of reflex responses to cutaneous inputs occurs more frequently in patients with MS than in healthy volunteers. This may be related to a defective supraspinal control of inhibitory commands during sRT paradigms.

Disclosure: Nothing to disclose.

OS2103

Tafamidis meglumine and nerve fiber function in Portuguese patients with transthyretin familial amyloid neuropathy

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Introduction: Transthyretin familial amyloid polyneuropathy (TTR-FAP) is an inherited amyloidosis that presents as a progressive sensorimotor and autonomic polyneuropathy. Class II evidence suggests that Tafamidis dampens clinical progression and preserves nerve function. Neurophysiologic parameters, including sensory and motor nerve amplitudes and motor nerve velocities, have been used to assess TTR-FAP nerve function.

Objectives: To describe the effect of one year of Tafamidis treatment on nerve conduction studies of TTR-FAP patients.

Methods: Nerve conduction data from patients on Tafamidis for 12 months was analyzed retrospectively, in the two major centers of TTR-FAP in Portugal. Sympathetic skin response, as well as motor and sensory composed scores were obtained after summing the respective nerve amplitudes. Patients were also evaluated with clinical scales, namely Neuropathy Impairment Score (NIS), Karnofsky index and Norfolk Quality of Life-Diabetic Neuropathy total score (TQOL). Paired-samples t-tests were used; a p value <0.01 was considered significant.

Results: We collected data from 118 patients (54 female) with a mean age of 38.4 ± 10.0 years. The sensory score was the only neurophysiological parameter that changed significantly over time from 44.9 to 40.9. Clinical scores showed no significant change in the same period of time.

Conclusions: A significant decrease of the sensory score over time is consistent with subclinical progression of axonal sensory nerve fiber dysfunction. Stabilization of motor nerve fiber function on nerve conduction studies correlates with clinical stabilization of patients assessed by NIS score. Further studies on nerve fiber function comparing different forms of treatment need to be conducted.

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OS2104

Deep repetitive transcranial magnetic stimulation with H-Coil in Parkinson's disease: a randomized, double blind, placebo-controlled study

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Introduction: Parkinson's disease-PD is characterized by a widespread alteration of cortico-subcortical circuits. The H-coil allows a wider and deeper stimulation field compared with traditional coils. We evaluated safety and efficacy of deep repetitive transcranial magnetic stimulation (rDTMS) with H-Coil as add-on treatment for motor symptoms in PD in a double-blind, randomized placebo-controlled study.

Methods: Sixty patients underwent 12 sessions (3 sessions/week) of 10 Hz rDTMS, after randomization into 3 groups: Group 1 (real rDTMS on primary motor-M1 and prefrontal-PF areas); Group 2 (M1-real/PF-sham), Group 3 (M1-sham/PF-sham). Primary outcome was percent reduction of Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III, OFF therapy. Secondary outcomes were: changes in UPDRSIII sub-scores; improvement in timed tests (Hand Tapping-HT, Foot Tapping-FT, Walking Time-WT, Nine Hole Peg Test-NHPT). Statistical analysis was performed using Mann–Whitney or t-test. Outcomes were tested in hierarchical order, by comparing the two real groups (1–2) only if their pooled data significantly differed from sham.

Results: No drop-outs or serious adverse effects were recorded. Both real groups improved significantly more than sham in UPDRSIII (p.010 and p.045 respectively), while they did not significantly differ between them. Pooled real groups showed a significant improvement vs sham in UPDRSIII ($p = .007$), tremor ($p = .011$) and lateralized sub-scores ($p = .042$ and p.012 for worse and better side respectively). Timed tests significantly improved more in the real group vs sham on the worse side (HT $p = .041$, FT $p = .012$, NHPT $p = .003$).

Conclusion: rDTMS with H-Coil appeared safe and effective on motor symptoms as add-on treatment in PD.

Disclosure: Nothing to disclose.

OS2105

Visual evoked potentials and optic coherence tomography in monitoring multiple sclerosis

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Introduction: In the assessment the involvement of visual pathways in Multiple Sclerosis-MS, optical coherence tomography-OCT and visual evoked potentials-VEPs are mainly used. The aim of our study was to investigate their value in longitudinal monitoring of the disease.

Methods: Eighty people with MS patients (13 clinically isolated syndrome-CIS, 55 relapsing-remitting-RR, 9 secondary progressive-SP, 3 primary progressive-PP) underwent neurological and neurophysiological evaluation with OCT and VEPs, with repeated clinical assessment after a mean follow-up of one year, when 50 patients also repeated OCT-VEPs.

Results: VEPs were more sensitive vs OCT in eyes with recent (<3 months) optic neuritis-ON at baseline (80.0 % vs 6.7 %, $p = 0.001$), the two sensitivities were similar in chronic ON eyes (78.4 %). Comparing eyes with and without previous ON, VEP latency and RNFL thickness were respectively significantly higher (131.2 ms Vs 118.8 ms, $p = 0.008$) and lower (78.15 μm vs 90.00 μm, $p < 0.001$) in the first subgroup. Significant longitudinal changes at follow-up, consisting in improved VEPs (−15.3 ms) and worsened RNFL thickness (−7.7 μm), were found only in eyes with baseline recent ON. No significant correlation was found between OCT-VEPs parameters and disease activity. Similar results were found when considering only RR and CIS patients.

Conclusions: These results would exclude recommending OCT and VEPs as surrogate biomarkers in short-medium term monitoring as in Phase II studies, with the exception of acute ON. However, these findings cannot exclude the usefulness of these techniques for longer follow-ups and/or large phase III studies.

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OS2106

Contact heat evoked potentials and quantitative thermal testing in a patient with Hansen's disease

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Introduction: Leprosy is one of the most common causes of non-traumatic peripheral neuropathy in the developing world, rarely diagnosed in Europe. We had the opportunity to study a full blown case of multifocal sensory neuropathy with small fiber involvement in a 38 year old Colombian woman in our center.

Methods: The patient was first seen after a 6 years history of slowly progressive distal thermoalgesic hypoesthesia on all four limbs, with a lower limb predominance as well as pain related to distal skin lesions (ulcers) in fingers and toes. Physical examination showed distal lesions with nail loss and toes deformities, eyebrow and eyelash alopecia, normal tendon jerks and normal motor balance. We performed motor, sensory and mixed nerve conduction studies on all 4 limbs, recorded long latency evoked potentials to contact heat (CHEPs) and electrical stimuli with simultaneous recording of the SSR and assessed quantitative thermal testing (QTT).

Results: A skin biopsy showed histiocytic cell accumulates in dermis with normal epidermis and was positive for Hansen's disease. Nerve conduction studies showed a severe asymmetric sensory neuropathy. Evoked potentials were normal to electrical stimuli but CHEPs were absent. QTT showed misperception of heat and cold with increased thresholds to all thermoalgesic sensations in all 4 limbs.

Conclusions: The absence of CHEPs to stimuli in an area where electrical stimuli induced normal evoked potentials documents the clinically suspected involvement of the small fibers conveying thermoalgesic sensations in sensory neuropathy of Hansen's disease.

Disclosure: Nothing to disclose.

Headache and pain

OS2107

Correlation between habituation of visual evoked potentials and magnetophosphene thresholds in migraine

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Introduction: An interictal habituation deficit of visual evoked potentials (VEP) and a reduced threshold (PT) of magnetophosphenes have been reported in migraine in separate studies. While the habituation deficit was attributed to reduced preactivation level of the visual coretx, the reduced PT likely indicates cortical hyperexcitability. Both phenomena have not yet been explored in the same patients.

Methods: We assessed PT by transcranial magnetic stimulation (TMS) in 15 healthy volunteers (HV) and in 13 episodic migraineurs without aura between attacks (MO), whereafter we recorded pattern-reversal VEP (6 blocks of 100 responses) and measured habituation. Results were compared using Mann–Whitney U test. Interrelationships were examined using Spearman's correlation.

Results: Phosphene thresholds was not significantly different between HV and MO. By contrast, MO patients had a reduced VEP habituation compared to HV ($p = 0.001$). There was no correlation between PT and habituation in neither group of subjects.

Conclusions: This study confirmed that migraineurs present interictally a deficit of VEP habituation, but failed to find decreased PT in these patients. VEP habituation and phosphene threshold values are not reciprocally correlated in healthy volunteers or in migraine patients, which suggest that they index different aspects of cortical excitability, i.e. a punctual measure of cortical activation threshold for PT, as opposed to a dynamic response pattern to repeated stimuli for VEP habituation.

Disclosure: Nothing to disclose.

OS2108

White matter abnormalities in chronic migraine patients are located in anterior corpus callosum: study using a new automatic tractography selection method

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Introduction: Diffusion tensor imaging techniques may detect white matter abnormalities in migraine patients. We analyzed

microstructural changes in some tracts using a new automatic selection method and compared them between episodic and chronic migraineurs.

Methods: 30 patients (3 male, 27 females) were selected. We gathered demographic and nosological characteristics. Episodic (Group A) and Chronic migraine (Group B) was diagnosed accordingly to ICHD III edition. Streamline tractography was performed on the tensor data; we automatically extracted six major fiber tracts using geometrical constraints specific for each fiber bundle: corpus callosum (CC), cingulate gyrus, corticospinal tract, inferior frontoccipital fasciculus, inferior longitudinal fasciculus and uncinate fasciculus. Tracts belonging to CC were also separated into five sectors according to Hofer criteria and a volumetric segmentation of CC and its five sectors was automatically performed. We analyzed Fractional Anisotrophy (FA), Mean Diffusivity (MD), Tensor Mode (TM) and Linear Measure (LM).

Results: 11 patients (2 male, 9 females, 33.2 ± 7.3 years) in Group A, and 19 (1 male, 18 females, 38 ± 13.4 years) in Group B. Chronic migraine patients showed significantly lower values of FA (0.6855 ± 0.0229 vs 0.7051 ± 0.0171, p: 0.02), TM (0.8407 ± 0.0138 vs 0.8558 ± 0.0254, p: 0.04) and LM (0.6621 ± 0.0172 vs 0.6809 ± 0.0184, p: 0.008) in the anterior CC (Hofer first sector). No significant differences were found in the rest of CC sectors or the other tracts studied.

Conclusions: Results indicate that white matter alterations in chronic migraine are concentrated on the anterior CC.

Disclosure: Nothing to disclose.

OS2109

Greater occipital nerve blocks with bupivacaine in the treatment of chronic migraine: randomized, multicenter, double-blind, parallel, placebo-controlled study

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Introduction: Background Our aim was to assess the efficacy of greater occipital nerve (GON) blocks at chronic migraine (CM). There is not randomized, multicenter, double-blind, parallel, and placebo-controlled study with GON blocks; headache days, headache duration and VAS scores were evaluated.

Methods: 72 patients who have CM according to IHS Criteria 2004 were enrolled from 6 clinics. After 4 weeks pretreatment headache diary. Patients were divided in two groups randomly as "A" (placebo) and "B" bupivacaine). 33 patients as "A" and 39 patients as "B" completed the study. Blocks were applied 4 times with saline or bupivacaine 1 week intervally. After 4 weeks blindness is opened; in "A", GON were blocked by bupivacaine as "B", then blocks were done monthly and followed for 2 months, "B" for 3 months. The primary endpoint was the difference in headache days, headache duration and, VAS scores during bupivacine blocks.

Results: 72 patients completed the study. Headache days decreased from 16.9 ± 5.7 to 13.2 ± 6.7 in "A" (0.035); 18.1 ± 5.3 to 8.8 ± 4.8 (<0.001) in "B"; headache duration is decreased from 24.2 ± 13.7 to 21.2 ± 13.4 (0.223) in "A"; 25.9 ± 16.3 to 19.3 ± 11.5 in"B"(<0.001) and VAS decreased from 8.1 ± 0.9 to 6.7 ± 1.6 in "A" (0.002); 8.4 ± 1.5 to 5.3 ± 2.1 in "B"(<0.001) in the first month. After blindness is opened, Group "A" showed similar results as "B" after bupivacaine blocks. No severe adverse effects were reported only local pain, vertigo and nausea to stop treatment.

Conclusions: GON blocks with bupivacaine can be effective treatment in CM.

Disclosure: Nothing to disclose.

OS2110

Anodal transcranial direct current stimulation alleviates pain in trigeminal neuralgia

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Introduction and objective: To investigate the efficacy of transcranial direct current stimulation (tDCS) of the primary motor cortex on pain and trigeminal nociceptive processing in subjects with classical trigeminal neuralgia (TN).

Methods: Seventeen subjects with TN were recruited in the study. Patients stimulated daily for 20 min over 2 weeks using anodal (1 mA) or sham tDCS in a randomized cross-over design. Primary outcome variable was pain intensity on a verbal rating scale (VRS). VRS and attack frequency were assessed daily for 1 month before and after tDCS using an individual patient diary. The impact on trigeminal pain processing was assessed with pain-related evoked potentials (PREP) and the nociceptive blink reflex (nBR) following electrical stimulation on both sides of the forehead (V1) before and after tDCS.

Results: Anodal tDCS reduced pain intensity more effectively than sham stimulation after 2 weeks of treatment. The attack frequency reduction was not significant. PREP showed an increased N2 latency and decreased peak-to-peak amplitude after anodal tDCS. No severe adverse events were reported. Patients with concomitant chronic background pain do not seem to benefit from tDCS as described previously for medical therapy and surgical intervention.

Conclusions: Daily anodal tDCS over 2 weeks ameliorates trigeminal pain in TN. It may become a valuable treatment option for patients unresponsive to conventional medical treatment or on wait for surgical procedures. International, multicenter, randomized controlled trials are needed with higher patient numbers before a definite recommendation can be proposed.

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OS2111

Visual induced analgesia in the face in healthy subjects and migraineurs

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Introduction: Visually induced analgesia (VIA) is the reduction of pain perception when seeing the stimulated body site, due to interplay between the brain's pain network and a posterior visual network. VIA was not demonstrated in the face and migraine is associated with abnormal connectivity in visual areas. We performed a comparative study of facial VIA in healthy subjects (HS) and migraine without aura patients (MO).

Methods: CHEPs were analyzed in 10 HS and 12 MO (interictal) with a stimuli of 53 °C applied to the right forehead with or without observation of the face with a mirror. For comparison, we recorded CHEPs by stimulating the right wrist. Twenty averaged sweeps were partitioned in 5 blocks of 4 responses to measure latency, amplitude and habituation of the cortical response. Pain was rated with a visual analog scale (VAS).

Results: Seeing the face decreased latency of N2 ($p = 0.04$) and amplitude of P1-N2 ($p = 0.03$) and N2-P2 ($p = 0.006$) in HS; P1-N2 habituation increased in HS ($p = 0.02$), but decreased in MO ($p = 0.002$). There was no effect of the mirror CHEPs at wrist, on facial or wrist pain perception, nor in pain perception between HS and MO.

Conclusion: Seeing the stimulated face attenuates thermonociceptive potentials but leaves pain ratings unchanged in healthy subjects, which contrasts with extarcephalic sites where both pain perception and cortical potentials are reduced. We found no visually induced effect on heat pain evoked in migraineurs between attacks, possibly because of changes in connectivity of visual areas with the pain network.

Disclosure: Nothing to disclose.

OS2112

Headache yesterday: analysing a new approach for estimating the burden of headache in children and adolescents

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Introduction: Within our process of developing a questionnaire for a global study on burden of headache in children and adolescents we focus here on headache yesterday as a new approach for estimating the impact of headache (IoH) and quality of life (QoL) in headache sufferers.

Methods: In this pilot study, we administered a structured questionnaire (1) to pupils in Vienna (age 6–11 year) and Istanbul (age 14–18 year). The questionnaire included 45 questions, 14 on IoH and 13 on QoL. Six IoH questions and all QoL questions were rated on a 4-point Likert scale.

Results: We analyzed 491 questionnaires: 122 from Vienna (49 % girls, age 8.7 ± 1.3 year) and 369 from Istanbul (53 % girls; age 15.8 ± 0.9 year). Headache yesterday was recorded by 27 % of the children and by 30 % of the adolescents and was associated with statistically significant differences from headache sufferers without headache yesterday: headache frequency was higher, duration longer, intensity more severe and use of abortive headache medication more common. Children and adolescents with headache yesterday recorded more days with loss of own activities and with parental work loss. The IoH sum score was significantly higher in adolescents but not in children with headache yesterday compared to other headache sufferers. QoL was poorest in children and adolescents with headache yesterday, intermediate in other subjects with headache and best in headache-free controls.

Conclusions: This pilot study suggests that headache yesterday is a frequent problem and a useful predictor for the burden of headache in children and adolescents.

Disclosure: Nothing to disclose.

Movement disorders 2

OS2113

Clinical and genetical analysis of Wilson's disease families with pseudo-dominant inheritance

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Introduction: Wilson's disease (WD) is an autosomal recessive inherited disorder of copper metabolism caused by mutation of the ATP7B gene, which leads to copper accumulation and presents with hepatic, neurological symptoms. The prevalence of WD in most populations in previous studies is calculated as 1 in 30,000, the carrier frequency 1 per 90, so the risk of the offspring is 0.5 %. The aim of the study was to establish frequency of pseudo-dominant inheritance among our WD patients. We also performed clinical and genetic analysis of affected members in families with pseudo-dominant inheritance.

Materials and methods: In our registry by the end of October 2013 we had 742 WD confirmed cases. For the present analysis, we selected families where WD was diagnosed through consecutive generations. Diagnosis of WD was based on copper metabolism tests results, genetic testing and in uncertain cases radiocopper study was used.

Results: Between 1957 and October 2013, 1043 (623 siblings, 288 offspring, 103 parents) relatives of affected members were examined by family screening. Pseudo-dominant inheritance was observed in 8 non-consanguineous families. We identified 9 affected offspring of 7 probands. Eight of 9 diagnosed offspring were presymptomatic, 1 presented hepatic symptoms.

Conclusion: Our study showed higher (3.1 %) than expected (0.5 %) incidence of WD among offspring. This is in accordance with some recent studies which suggested higher WD gene prevalence in European population. Because WD is a treatable disorder, family screening should also be performed among probands' offspring.

Disclosure: Nothing to disclose.

OS2114

A large Turkish Parkinson pedigree with alpha-synuclein duplication: blood expression biomarker profile for predictive diagnostics

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Introduction: Parkinson's disease (PD) is the second most common neurodegenerative disorder, affecting 2 % of the aged population. Most cases are sporadic, monogenic variants are found particularly in the early-onset group. Alpha-synuclein (SNCA) was the first PD gene identified; missense mutations and increased gene dosage were shown to cause monogenic PD with complete penetrance, while polymorphisms in the promoter and the mRNA-3′UTR enhance risk through elevated expression levels. SNCA variants are the most evident genetic risk among sporadic PD patients in genome-wide-association studies. The alpha-synuclein protein was also found to aggregate in degenerating neurons, forming the cytoplasmic "Lewy bodies", the diagnostic hallmark of PD.

Methods: We have identified a large Turkish Parkinson pedigree with SNCA duplication, including two patients, 12 pre-symptomatic and eight unaffected individuals. Genotyping studies and expression level quantification of several downstream genes were performed by qRT-PCR. Protein levels were detected using Western blot analysis.

Results: To study the effects of the alpha-synuclein gain-of-function in whole blood, first the 1.5-fold increase in transcript and monomeric protein levels were documented in blood. Secondly, although the SNCA transcript levels showed high variance in blood and their correlation with the genotypes did not attain statistical significance, mutation effects on the expression of several downstream genes were detectable, partially in significant association or statistical trends. The combined profile of these mRNA biomarkers upon ROC (receiver operating characteristic) curve analysis showed predictive diagnostic value with high sensitivity and specificity.

Conclusions: This study suggests promising predictive diagnostics, which is a prerequisite for neuroprotective therapy.

Disclosure: Nothing to disclose.

OS2115

Skin nerve α-synuclein deposits: a biomarker for idiopathic Parkinson's disease

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Introduction: To investigate

1) whether phosphorylated α-synuclein deposits in skin nerve fibers might represent a useful biomarker for idiopathic Parkinson's disease (IPD);

2) the underlying pathogenesis of peripheral neuropathy associated with IPD.

Methods: 21 well-characterized IPD patients were studied together with 20 patients with parkinsonisms assumed not to have α-synuclein deposits (PAR: 10 patients fulfilling clinical criteria for vascular parkinsonism, 6 for taupathies and 4 with parkin mutations) and 30 controls. Subjects underwent: nerve conduction velocities from the leg to evaluate large nerve fibers; skin biopsy from proximal (i.e. cervical) and distal (i.e. thigh and distal leg) sites to study small nerve fibers and deposits of phosphorylated α-synuclein, considered the pathological form of α-synuclein.

Results: IPD patients showed a small nerve fiber neuropathy prevalent in the leg with preserved large nerve fibers. PAR patients showed normal large and small nerve fibers. Phosphorylated α-synuclein was not found in any skin sample in PAR patients and controls but it was found in all IPD patients in the cervical skin site. Abnormal deposits were correlated with leg epidermal denervation.

Conclusions: The search for phosphorylated α-synuclein in proximal peripheral nerves is a sensitive biomarker for IPD diagnosis helping to differentiate IPD from other parkinsonisms. Neuritic inclusions of α-synuclein were correlated with a small fiber neuropathy suggesting their direct role in peripheral nerve fiber damage.

Disclosure: Nothing to disclose.

OS2116

Abnormal tactile and proprioceptive temporal discrimination in psychogenic tremor

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Objectives: Tactile (TDT) and proprioceptive (TDMT) temporal discrimination thresholds, defined as the shortest interval at which two tactile stimuli and two passive movements are perceived as temporally separate, are reliable measures of somatosensory processing. We recently reported abnormal TDMT and normal TDT in patients with essential tremor of the upper limbs and the opposite pattern in patients with tremor associated with dystonia.

Methods: In the present study we assessed TDT and TDMT in 11 patients with psychogenic tremor of the upper limbs (Psy-T) and compared the results with those assessed in 11 patients with essential tremor (ET) and in 13 healthy subjects matched for age and sex.

Results: We found that Psy-T had significantly higher TDT values compared to ET and control subjects, while TDMT was significantly higher in both Psy-T and ET than in control subjects.

Conclusion: Our study, demonstrating a more widespread impairment of temporal processing of somatosensory (both tactile and proprioceptive) inputs in psychogenic than in essential tremor, highlights the involvement of different mechanisms in the two diseases.

Disclosure: Nothing to disclose.

OS2117

Validation of "laboratory-supported" criteria for functional tremor

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Introduction: In a small group of patients, we have previously shown that a combination of electrophysiological tests was able to distinguish functional (FT) and organic tremor (OT) with excellent sensitivity and specificity. Here we aimed to validate this electrophysiological test battery as a tool to diagnose patients with FT based on a "laboratory-supported" level of certainty.

Methods: We prospectively recruited 40 patients with FT (mean age 37.3 ± 24.7 years; mean disease duration 5.7 ± 8.9 years) and 72 patients with OT (mean age 56.1 ± 24.7 years; mean disease duration 16.1 ± 17.8 years). Tremor was recorded at rest, posture (±loading), and action, while performing three tapping tasks, and while performing ballistic movements with the less affected hand. Analyses were performed as previously described (Schwingenschuh et al. Mov Disord 2011) by raters blinded to the clinical diagnosis. A subset of recordings was analyzed by three blinded raters and another subgroup of patients was tested twice on different days.

Results: Patients with FT had a higher average score on the test battery, compared to patients with OT (3.5 ± 1.5 points versus 1.0 ± 0.8 points; $P < 0.001$). The predefined cut-off score for a diagnosis of laboratory-supported FT with 3 out of 10 points yielded a test sensitivity of 85.0 % and a specificity of 95.8 %; $P < 0.001$. We demonstrated good interrater-reliability and test-retest-reliability.

Conclusions: We propose this test battery as the basis of laboratory-supported criteria for the diagnosis of functional tremor and we now encourage its use in the work-up of patients with presumed FT.

Disclosure: Nothing to disclose.

OS2118

Phenotypic spectrum of SNCA G209A mutation carriers for familial Parkinson's disease in Greece

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Introduction: The G209A mutation in the SNCA gene encoding for alpha-synuclein was the first Mendelian genetic defect identified in Parkinson's Disease. The mutation occurred in families of Italian and Greek origin with an autosomal dominant pattern of inheritance.

Methods: As part of the FP7 Project MEFOPA, we are attempting to

1) identify living carriers of the G209A SNCA mutation in Greece,
2) register demographic and clinical information,
3) perform relevant questionnaires and scales,
4) obtain biological samples in order to establish the phenotype of the disease, and to examine questions regarding its biological underpinnings.

Results: We have so far registered 30 mutation carriers and we have followed them for at least 2 years. Of the 30 carriers, 8 are asymptomatic. 7 probands belong to new families, apparently unrelated to those already known to carry the G209A SNCA mutation. Mean age of disease onset is 44.8 ± 10.3 years (range 30–65), and mean disease duration is 7.1 ± 4.3 years (range 0.5–18). There is a large variability in the clinical phenotype ranging from a still asymptomatic carrier at age 90 to subjects presenting with early disease onset and either a relatively benign clinical course or rapid progression to dementia. There is also a varied range of presentation of Non-Motor symptoms such as depression, psychosis and dementia.

Conclusions: G209A SNCA carriers demonstrate a wide clinical phenotypic spectrum. Greek PD patients with a compatible inheritance pattern should be screened for this mutation. The biggest challenge now is to identify the biological basis of this variability providing a foundation for novel therapeutics.

Disclosure: Nothing to disclose.

Multiple sclerosis and related disorders 2

OS2119

Are GABA levels abnormal in progressive MS?

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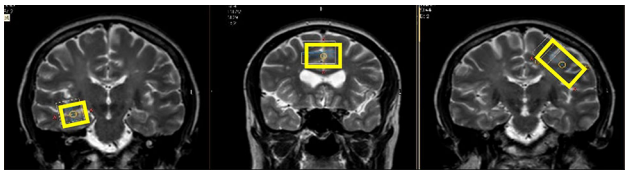
Introduction: Gamma-aminobutyric acid (GABA) is the main inhibitory neurotransmitter in the human brain. Given the possible involvement of GABA in motor impairment and cognitive problems in MS, we sought to develop ^{1}H Magnetic Resonance Spectroscopy (MRS) at 3T to measure GABA in the sensorimotor cortex (SMC), pre-frontal cortex (PFC) and, for the first time in MS, in the hippocampus (HPC). These have been identified as key areas in cognitive and motor function and correlate with performance on clinical tests. We looked at secondary progressive MS patients, as it is crucial to understand the mechanism underlying progressive disease.

Methods: Written informed consent was obtained from 21 patients with SPMS (15F, 6 M), mean age 50.42 years (SD 8.80), and 16 healthy controls (9F, 7 M), mean age 43.80 (SD 12.5).

Results: Patients showed reduced [$GABA^+$] in the HPC (mean = 0.99 mM (patients) vs. 1.44 mM (controls), $p = 0.044$) and a trend towards reduced [$GABA^+$] in the SMC (mean = 1.30 mM (patients) vs. 1.52 mM (controls), $p = 0.068$) compared to healthy controls. No statistical difference in [$GABA^+$] in the PFC was seen between groups. In patients, reduced right upper and lower limb power measured

using the MRC (Medical Research Council) scoring system, was associated with lower [$GABA^+$] levels in the left SMC ($r_s = 0.45, p = 0.013$).



Conclusions: Using the MEGA-PRESS ^1H MRS at 3T, this study provides the first evidence that [$GABA^+$] is reduced in the hippocampus and sensorimotor cortex in secondary progressive MS patients when compared to healthy controls. In patients, reduced [$GABA^+$] in the sensorimotor cortex correlates with motor dysfunction.

Disclosure: Nothing to disclose.

OS2120

Serum biomarkers predict IFNb treatment response in patients with multiple sclerosis

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Introduction: A considerable proportion of multiple sclerosis (MS) patients do not respond to interferon-beta (IFNb) treatment. Apart from neutralizing antibodies there are no biomarkers that predict IFNb treatment response.

Objective: To investigate whether serum markers can predict IFNb treatment response.

Methods: Patients with MS or clinically isolated syndrome receiving de novo IFNb treatment were included in this prospective multicenter study. Number of relapses 2 years prior to and 2 years after IFNb initiation were monitored. Serum samples were collected at baseline and after 3 months on therapy. Cytokines were assessed by Luminex multiplex assay. Baseline samples were grouped using Gene Cluster software. Clinical outcome in these groups were assessed by relapses pre- and post-initiation of therapy.

Results: Baseline cytokine profiles of patients were clustered into three groups. Group 1 had elevated IL-8, CXCL1/Gro-α, CD40L and Eotaxin concentrations. Group 2 showed elevated CD40L and Eotaxin but low IL-8 and CXCL1/Gro-α levels. Group 3 were low for all cytokines. 24 months after therapy, 34.8 % of patients in group 1 were relapse free, whereas 70.3 % and 50.8 % of patients in group 2 and group 3, respectively, remained relapse free. Patients in group 2 and group 3 had reduced relapses after IFNb treatment. Group 1 had no difference in relapses pre and post treatment.

Conclusions: Patients with elevated baseline serum CD40L and Eotaxin, but low IL-8 and CXCL1 are more likely to respond to IFNb treatment compared to patients with high IL-8 and CXCL1/Gro-α.

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OS2121

Dynamics of brain iron accumulation differ between clinically isolated syndrome and multiple sclerosis: a longitudinal 3T MRI study

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Introduction: Increased iron concentration in cerebral deep grey matter is a consistent finding in multiple sclerosis (MS) while respective results have been controversial in patients with a clinically isolated syndrome (CIS). This suggests a temporal dynamic of iron accumulation.

Methods: We studied 76 CIS and 67 MS patients with baseline and follow-up 3T MRI (median follow-up CIS 2.6 years, MS 3.0 years; p = n.s.). Iron deposition in caudate nucleus, globus pallidus, putamen and the thalamus was assessed by automated, regional calculation of R2* rates. We further determined T2 lesion load and percentage of brain volume change (PBVC).

Results: In CIS, R2* relaxation rates significantly increased over time in the globus pallidus ($p < 0.001$), putamen ($p < 0.001$) and the caudate nucleus ($p < 0.005$), whereas R2* rates within the thalamus decreased ($p < 0.05$). In contrast in MS, R2* rates only slightly increased in the putamen ($p < 0.05$), remained stable in the globus pallidus and caudate nucleus and significantly decreased in the thalamus ($p < 0.01$).

Using a hierarchical regression analysis, the change of R2* rates within the globus pallidus independently predicted PBVC in CIS ($\beta = -0.4$, $p < 0.05$) but not in MS. There were no correlations with the change in other morphologic variables.

Conclusions: Iron accumulation is an early phenomenon of the disease, which parallels brain volume loss and appears to plateau over time. These dynamics suggest that higher iron concentration in MS is a consequence of ongoing morphologic damage. Whether increased iron concentration exerts detrimental effects of its own deserves separate investigation.

Disclosure: Nothing to disclose.

OS2122

Brain atrophy in Relapsing-remitting multiple sclerosis patients treated with interferon-beta and atorvastatin (The ARIANNA study)

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Introduction: Statin effects on brain atrophy in multiple sclerosis (MS) is still poorly investigated, although a neuroprotective effect has been suggested.

Methods: This multi-center, double-blind, randomized, placebo-controlled, study in 154 RRMS patients in treatment with IFN-beta 1b, compared for 24 months the add-on of atorvastatin 40 mg p.o.daily to placebo, to evaluate efficacy on cerebral atrophy. MSFC score, Rao battery and brain MRI were obtained at baseline and yearly since then. The MRI scans were analysed centrally in a blinded fashion by a core lab. MRI volumes were segmented into Grey Matter, normal and abnormal White Matter, and cerebrospinal fluid using a fully automated relaxometric method.

Results: Intent to treat (ITT) patients were 75 in the atorvastatin arm and 79 in the placebo. Month 24 was reached by 97 patients (63 %). Patients clinical and demographic characteristics were not different in the two groups. Brain atrophy over 2 years was not different in the two groups, even when analyzing the 2 years separately (-0.367 % and -0.382 for the atorvastatin and -0.302 % and -0.545 % for the placebo groups respectively). Stratification of patients for the presence of gadolinium enhancement at baseline MRI did not reveal significant differences in brain atrophy. No differences in secondary endpoints were found between the two groups.

Conclusions: Our data indicate Class I evidence that atorvastatin 40 mg daily as an add-on therapy with IFN-beta 1b, despite being safe, has no effect on brain atrophy changes or on other disease activity and progression parameters.

Disclosure: Nothing to disclose.

OS2123

Longitudinal changes of global and compartmental brain atrophy in patients with clinically isolated syndrome and clinically definite multiple sclerosis using 3-Tesla magnetic resonance imaging

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Background: Brain atrophy is an important element in the course of multiple sclerosis (MS) but its association with different phases of the disease is still under discussion.

Aim: To determine the rate and clinical association of global and compartmental brain atrophy in patients with a clinically isolated syndrome (CIS) compared to patients with clinically definite MS (CDMS) by long-term follow-up.

Methods: We investigated 63 CIS and 57 CDMS patients at baseline and after 3–4 years with detailed clinical examination and a comprehensive MR imaging protocol at 3T. Imaging assessment consisted of the annual change of brain parenchymal fraction (BPF), grey matter (GMF) and white matter (WMF) fractions, the percentage of brain volume change (PBVC) and change of T2 lesion load (T2-LL).

Results: The age at baseline and mean follow-up time were comparable between CIS and CDMS. During follow-up 33 CIS patients (52.4 %) converted to CDMS.

While BPF ($p = 0.018$) and WMF ($p = 0.008$) were significantly lower in CDMS patients at baseline, the T2-LL in CDMS was significantly higher ($p = 0.003$).

CIS and CDMS patients had comparable rates of GMF, WMF and BPF changes over time but the PBVC was significantly higher in CDMS ($p = 0.001$). Converters from CIS to CDMS showed a significantly higher PBVC than non-converters ($p = 0.029$).

Conclusion: The rate of global and compartmental brain atrophy is comparable between CIS and CDMS and especially pronounced in CIS converters, with PBVC being the most sensitive marker. This confirms the importance of brain volume changes to monitor the evolution of MS already early on.

Disclosure: Nothing to disclose.

OS2124

The CSF JCV antibody index for diagnosis of natalizumab-associated PML

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Introduction: Progressive multifocal leukoencephalopathy (PML), caused by JC virus (JCV), can occur in patients receiving natalizumab for multiple sclerosis (MS). JCV detection by quantitative polymerase chain reaction (qPCR) in cerebrospinal fluid (CSF), or brain biopsy is required for probable or definite diagnosis of PML. However, in some patients only low levels of JCV-DNA (< 100 copies/ml) are present in CSF, making the diagnosis challenging.

Objective: To assess the complementary value of a CSF JCV antibody index (AI_{JCV}) in the diagnosis of natalizumab-associated PML.

Methods: In 37 cases of natalizumab-associated PML and 89 MS-patients treated with natalizumab without PML AI_{JCV} was assessed. Sera and CSF were tested in a capture ELISA, using JCV-VP1 fused to glutathione S-transferase (GST) as antigen. Albumin levels and total IgG concentration were determined by immunonephelometry, and the AI_{JCV} was calculated as published.

Results: Twenty-six of 37 (70 %) patients with natalizumab-associated PML exhibited an $AI_{JCV} > 1.5$, while this was seen in none of the controls ($p < 0.0001$). At time of the first positive qPCR for JCV-DNA, 11/20 (55 %) of patients with natalizumab-associated PML had an $AI_{JCV} > 1.5$. JCV-DNA levels of < 100 copies/ml were seen in 14/20 (70 %) of these patients of which 8 (57 %) demonstrated an $AI_{JCV} > 1.5$.

Conclusions: Determination of the AI_{JCV} could be an added tool in the diagnostic workup for PML and should be included in the case definition of natalizumab-associated PML.

Disclosure: Dr. Warnke reports grants and personal fees from European Commitee for Treatment and Research in Multiple Sclerosis (ECTRIMS), during the conduct of the study.

Epilepsy

1OS2201

Interictal epileptic networks and postsurgical outcome using intracranial EEG-fMRI

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Introduction: Most advanced localization techniques may fail to reveal the full extent of the epileptogenic zone (EZ), as 30 % of patients with refractory focal epilepsy continue having seizures after surgery. In 14 patients with refractory focal epilepsy undergoing invasive presurgical evaluation, we compared the distribution of interictal epileptiform discharges (IED)-related blood-oxygen-level-dependent (BOLD)-changes with the invasively-defined epileptogenic zone (EZ) and postsurgical-outcome, using simultaneous intracranial EEG-fMRI (icEEG-fMRI).

Methods: IEDs were classified according to their field distribution in 13 patients. BOLD changes were assessed using statistical-parametric-mapping (SPM8). SPM[F]-maps were generated for individual IED-types and for all IEDs originating in the EZ (*'combined-EZ-interictal-BOLD-map'*) for each patient. The degree-of-concordance of the BOLD-maps was based on the localization of clusters in relation to the EZ. We evaluated the association between BOLD-changes in deep brain structures, degree-of-concordance and postsurgical-outcome.

Results: Fifty three different IED-types, identified across the group, revealed significant BOLD-changes in the EZ, healthy neocortex and deep brain structures. BOLD-changes in deep brain structures were associated with discordant maps. 10 patients who underwent surgery revealed 44 different IED-types and 33/44 IED-types originated in the EZ. BOLD-maps for 21/33 had a degree-of-concordance with the EZ. '*Combined-EZ-interictal-BOLD-map*' had a degree-of-concordance with the EZ in 7/10 patients (postsurgical-outcome: ILAE-class-1 = 6, ILAE-class-3 = 1). Three patients had discordant '*combined-EZ-interictal-BOLD-map*' and ILAE class 4 and 5 postsurgical-outcome. The higher level of concordance of '*combined-EZ-interictal-BOLD-maps*' was significantly associated ($r_s = 0.8$; $p < 0.05$) with ILAE-class-1 outcome.

Conclusions: Intracranial-EEG-fMRI can map IED-related BOLD-changes across the whole brain, and their degree-of-concordance with the EZ may help to understand postsurgical-outcome.

Disclosure: Nothing to disclose.

OS2202

White matter development in children with benign childhood epilepsy with centro-temporal spikes

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Introduction: Benign childhood epilepsy with centro-temporal spikes (BCECTS) is an age-dependent epilepsy with rare seizures, focal EEG abnormalities, and moderate cognitive dysfunctions. It is hypothesized that interictal EEG discharges might interfere with local brain maturation, resulting in altered cognition. Diffusion tensor imaging (DTI) allows testing this hypothesis by investigating the white matter microstructure.

Methods: We investigated 25 children suffering from BCECTS and 25 age-matched controls and explored changes in white matter (fractional anisotropy (FA) and diffusivity). We used a voxel-based analysis (FSL, SPM8) to detect abnormalities at both the group and individual levels, contrasting patients and controls. FA and diffusivity images were further correlated to neuropsychological and clinical variables.

Results: Group analysis showed significantly reduced FA and increased diffusivity in patients compared with controls, predominantly over the left pre- and postcentral gyri and ipsilateral to the EEG focus. At the individual level, regions of significant differences were observed in 10 patients (40 %) for anisotropy, and 17 (56 %) for diffusivity. There were significant negative correlations between FA maps and duration of epilepsy in the precentral gyri, bilaterally, and in the left postcentral gyrus.

Conclusions: Children with BCECTS demonstrate alterations in the microstructure of the white matter, undetectable with conventional MRI, predominating over the regions displaying chronic interictal epileptiform discharges. The association observed between DTI changes, duration of epilepsy and cognitive performance appears compatible with the hypothesis that interictal epileptic activity alters brain maturation, which could in turn lead to cognitive dysfunction.

Disclosure: Nothing to disclose.

OS2203

Surface EEG markers of underlying focal cortical dysplasia: a blinded analysis comparing epilepsy patients with dysplasia and other etiologies

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Introduction: Focal cortical dysplasia (FCD) is among the most frequent cortical alterations underlying pharmacoresistant epilepsy. High diagnostic effort is necessary to identify dysplastic cortical changes in many patients. Here surface EEG recordings were analyzed in patients with FCD with other etiologies to analyze if specific patterns distinguish dysplastic brain areas.

Methods: Surface EEG recordings from 103 patients with pharmacoresistant focal epilepsy, recorded during wakefulness and sleep, were analyzed retrospectively in a blinded fashion by three certified electrophysiologists. 66 patients had histologically ascertained FCD,

37 patients other etiologies. Surface EEG patterns reported in the literature as well as other visually identified patterns were classified as either present or not in each patient. Statistical analysis was performed using Fisher's exact test to analyze whether the presence of a specific pattern was associated with an underlying dysplastic brain lesion. Results were considered statistically significant when $p < 0.01$.

Results: Beta bursts, frequent bursting rhythmic epileptiform activity and continuous rhythmic slowing were significantly more frequent in regions overlying cortical dysplasia, whereas other markers were found to be present, but not specific for dysplasia.

Conclusions: Three surface EEG markers were identified which, when present, point to an underlying dysplastic lesion in the patients studied here. Other markers previously reported were not specific for this etiology, showing the need for control groups in the interpretation. Surface EEG may assist to identify not only the region but also the etiology of patients with cortical dysplasia, and may steer specific high resolution imaging in patients with pharmacoresistant focal epilepsy.

Disclosure: This study was supported by EFNS educational grant.

OS2204

Efficacy of antiepileptic drugs on secondary generalized tonic–clonic seizures in patients with drug-resistant partial epilepsy: a meta-analysis

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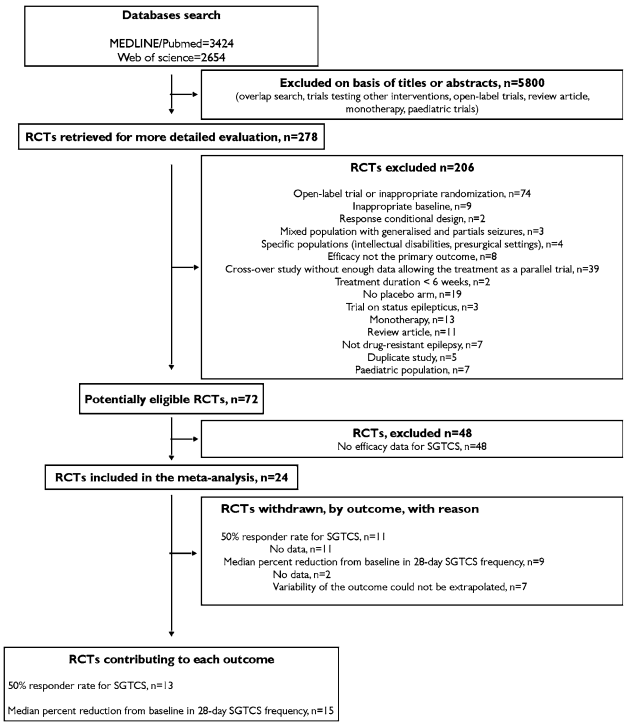
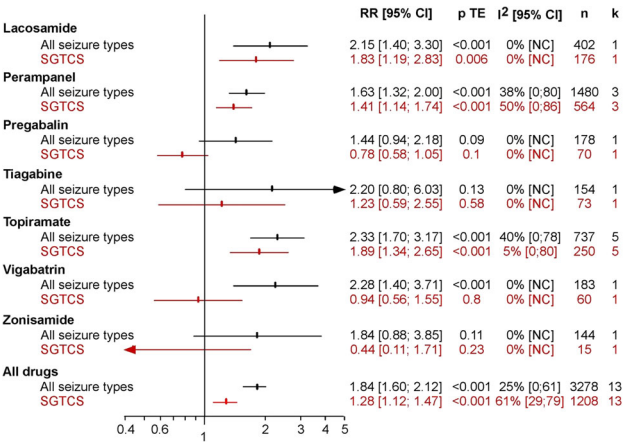
Introduction: There is currently no effective treatment to prevent Sudden Unexpected Death in Epilepsy (SUDEP), apart from optimising antiepileptic drugs (AEDs). In patients with drug-resistant partial epilepsy, secondary generalised tonic–clonic seizures (SGTCS) represent the main risk factor of SUDEP and their prevention might therefore be an important parameter for treatment choice. However, whether or not some AEDs might be more efficacious than other on SGCTS remains unknown.

Methods: We performed a meta-analysis of randomised placebo-controlled trials of adjunctive AED in which information on efficacy outcomes (i.e. responder rate and/or frequency per 28 days relative to baseline) were available both for all seizure types and for SGTCS. The primary analysis evaluated the efficacy of AEDs on all types of seizure and on SGTCS by comparing the responder rate in the AED treatment group with that observed in the placebo group.

Results: Responder rate was available both for all seizure types and for SGTCS in 13 of the 72 eligible trials, evaluating seven AEDs. Only three AEDs, lacosamide, perampanel and topiramate, showed significant greater efficacy than placebo on SGTCS. However, confidence intervals of relative risks overlapped for all AEDs. Moreover, there was a non-significant trend toward a lower relative risk of responder rate for SGTCS than for all seizure types, which appeared related to a greater response to placebo for this outcome.





Conclusion: These data did not support robust differences between AEDs to prevent SGTCS. Alternative designs for evaluation of therapeutic interventions in patients at risk of SGTCS-related complications are required.

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OS2205

Clinical- and cost-effectiveness of a nurse led self-management intervention to reduce emergency visits by people with epilepsy

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Introduction: Some people with chronic epilepsy (PWE) make frequent, costly, and clinically unnecessary emergency department (ED) visits. No studies have examined interventions to reduce them. An intervention delivered by an epilepsy nurse specialist (ENS) might reduce visits. We examined such an intervention's clinical- and cost-effectiveness.

Methods: Eighty-five adults with epilepsy were recruited from three London EDs. Forty-one PWE recruited from two EDs received treatment-as-usual (TAU). The remaining 44 PWE were recruited from the ED of a hospital that had developed an ENS service for PWE attending ED. They were offered 2 one-to-one sessions with an ENS, plus TAU. Participants completed questionnaires on health service use and psychosocial well-being at baseline, 6- and 12-month follow-up.

Results: Sixty-nine (81 %) participants completed follow-up. There was no significant effect on ED visits at 12 months. However, due to less time as inpatients, the average service cost for intervention participants over follow-up was less than for TAU participants' (adjusted difference £558, 95 % CI, -£2409, £648). Covariates most predictive of subsequent ED visits were patients' baseline feelings of stigmatization due to epilepsy and low confidence in managing epilepsy.

Conclusions: The intervention did not lead to a reduction in ED use, but did not cost more, partly because those receiving the intervention had shorter hospital admissions. Our findings on long-term ED predictors clarifies what causes ED use, and suggests that future interventions might focus more on patients' perceptions of stigma, and on their confidence in managing epilepsy. If addressed, ED visits might be reduced and efficiency-savings generated.

Disclosure: Nothing to disclose.

OS2206

Abstract withdrawn

Motor neurone diseases

OS2207

The distinct genetic pattern of ALS in Turkey

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Introduction: Recently the frequency of ALS mutations has been extensively investigated in several populations, however a systematic analysis has not been reported in Turkey so far.

Methods: A total of 411 Turkish ALS patients, 96 fALS, belonging to 66 families, and 315 sALS cases were screened for mutations in common ALS genes. Patients were genotyped for SOD1 and UBQLN2 gene mutations via conventional PCR; for *C9orf72* RP-PCR and Southern blotting were performed. A subset of patients was also subjected to exome sequencing. Haplotype analysis was applied to patients carrying the SOD1-D90A mutation.

Results: SOD1 (12 %), *C9orf72* (13.5 %) and UBQLN2 (6 %) gene mutations were found to account for approximately 30 % of fALS in Turkey. While no SOD1 mutations were shown so far in Turkish sALS patients; *C9orf72* (3.5 %) and UBQLN2 (0.7 %) explained 4.2 % of sALS in the cohort under study. Exomic sequencing revealed FUS, OPTN, SPG11 and PLEKHG5 mutations in four families. SOD1-D90A, known to occur in dominant and recessive pedigrees, behaved as a recessive trait in all three Turkish families in this study with the common Scandinavian founder haplotype.

Conclusions: In the framework of this study we report a systematic screening of Turkish ALS patients for disease-causing mutations. Our results indicate that SOD1, C9Orf72 and UBQLN2 mutations are important genetic causes of ALS in the Turkish population. The frequency of SOD1 is consistent with other Mediterranean countries. The spectrum of mutations reflects both the different genetic background and the more heterogeneous nature of the Turkish population.

Disclosure: Nothing to disclose.

OS2208

Analysis of patients with amyotrophic lateral sclerosis (ALS) treated with autologous differentiated mesenchymal stem cells: a phase I/II and IIa clinical trial

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Aim: To evaluate the safety and tolerability of treatment with autologous mesenchymal stem cells differentiated to secrete neurotrophic factors ("MSC-NTF") in ALS patients.

Background: Previous study from our group has shown the safety of IV/IT administration of unmodified MSC in ALS patients. The neuroprotective effects of MSC-NTF have been demonstrated in various animal models of neurodegenerative diseases, including ALS. We are currently conducting the second part of two sequential clinical trials to evaluate the safety and tolerability of autologous MSC-NTF cells in ALS patients.

Methods: MSC were isolated from the bone marrow of 12 ALS patients, expanded ex vivo and induced to secrete neurotrophic factors

such as GDNF and BDNF using BrainStorm's NurOwn™ technology. These autologous MSC-NTF cells were transplanted by IM or IT injections to ALS patients. All patients were followed up on a monthly basis for a pre-treatment period of 3 months and for 6 months post-transplantation.

Results: During the 6-month follow-up of the 12 transplanted patients, no serious treatment-related adverse events were observed. The clinical follow-up revealed a change in the rate of clinical progression (ALSFRS) and respiratory function (FVC) in favor of the IT-treated patients during the 6 months following treatment.

Conclusions: This trial showed that intrathecal or intramuscular injection of MSC-NTF is safe and revealed some indications of clinical beneficial effects. In the second part of the ongoing Phase IIa, 12 additional ALS patients are currently receiving combined IM and IT treatment with escalating doses of MSC-NTF cells. More detailed and updated data from this trial will be presented.

Disclosure: Nothing to disclose.

OS2209

Development of a gene therapy for sporadic ALS by normalizing ADAR2 activity in the motor neurons using a vascular type AAV vector

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Introduction: Amyotrophic lateral sclerosis (ALS) develops in the middle-aged and elderly and is a fatal disease characterized by progressive muscular weakness resuting from degeneration of motor neurons. There is no known cure preventing patients from death. Downregulation of the RNA editing enzyme ADAR2 is involved in the death of motor neuorns of sporadic ALS, which accounts for the great majority of cases of the disease. Therefore, normalization of ADAR2 activity in motor neuorns is likely a therapeutic strategy for ALS.

Methods: We developed an adeno-associated virus serotype serotype 9 (AAV9) vector that provides gene delivery to a wide array of central neurons after peripheral administration. Using conditional ADAR2 knockout mice (AR2), which comprise a mechanistic mouse model of sporadic ALS, we investigated whether the delivery of the human ADAR2 gene by the AAV9 vector enabled to enhance ADAR2 activity in the motor neurons to a level sufficient to stop the disease progression.

Results: A single intravenous injection of AAV9-ADAR2 in AR2 mice caused expression of exogenous ADAR2 in the central neurons and effectively prevented progressive motor dysfunction. Notably, AAV9-ADAR2 rescued the motor neurons of AR2 mice from death by normalizing TDP-43 expression. There was no detectable glial reaction in the brans or spinal cords of AAV-treated AR2 mice.

Conclusions: One intravenous injection alone was sufficient to safely bring about long-lasting expression of an effective quantity of the ADAR2 gene in the mouse motor neurons. This AAV9-mediated ADAR2 gene delivery may therefore enable the development of a gene therapy for ALS.

Disclosure: Nothing to disclose.

OS2210

Cognitive changes and white matter tract damage in the motor neuron disease spectrum

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Introduction: To assess the relationship between white matter (WM) tract abnormalities and cognitive changes in patients within the motor neuron disease (MND) spectrum using diffusion tensor (DT) MRI tractography.

Methods: Eighty-one MND patients (including 40 amyotrophic lateral sclerosis [ALS], 31 primary lateral sclerosis/pure upper motor neuron, and 10 progressive muscular atrophy [PMA]) and 35 controls were studied. All patients underwent clinical evaluation, neuropsychological assessment, and DT MRI. To fulfill criteria for cognitive impairment, patients had to demonstrate impairment in at least 2 validated executive tasks. The presence of non-executive cognitive impairment was also considered. DT MRI metrics were obtained from corpus callosum (CC), corticospinal tract and extra-motor tracts. Group comparisons were assessed using age-adjusted linear regression models. WM damage contribution to cognitive deficits was assessed using Spearman correlation coefficients adjusted for age and ALSFRS-r.

Results: No PMA patients had cognitive impairment. In the remaining group, seven patients (9.7 %) had frontotemporal dementia, six patients (8.6 %) had an executive cognitive impairment, and non-executive deficits were found in two patients (2.8 %). Relative to controls, ALS patients showed damage to motor and extra-motor tracts ($p < 0.001$–0.49). PMA patients did not show tract damage. In the whole MND group, verbal fluency, attention and executive function performances correlated with DT MRI measures of the CC, cingulum, inferior and superior longitudinal fasciculi, and uncinate bilaterally (R from −0.47 to 0.47; $p < 0.001$–0.049). Correlations remained significant adjusting for ALSFRS-r.

Conclusions: Interhemispheric, limbic and associative WM tract degeneration is associated with neuropsychological deficits in patients with MND.

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OS2211

Genetic epidemiology of ALS in Italy

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Introduction: ALS is a genetically heterogeneous disease and causative mutations have been described in ~20 genes. Here we aim to determine the prevalence of mutations in ALS-associated genes in Italian patients with sporadic (SALS) and familial ALS (FALS), and to attempt a genotype-phenotype correlation.

Methods: We screened 925 patients (208 FALS and 717 SALS) for mutations in the *C9orf72*, *SOD1*, *TARDBP*, *FUS*, and *ATXN2* genes. FALS cases were also screened for *ANG*, *PFN1*, *OPTN*, *VCP*, *UBQLN2*, *SETX*, and *hnRNPA1-A2/B1*.

Results: Pathogenic mutations were identified in 175 individuals (110 FALS and 65 SALS). The most common mutated gene in FALS was *C9orf72* (24.5 %), followed by *SOD1* (8.5 %), *FUS* (5.2 %), and *TARDBP* (4.1 %). In SALS patients, *C9orf72* repeat expansions accounted for 4.9 % and *TARDBP* mutations for 3.1 % of cases. All other genes represented less than 3 % of our cohort.

Conclusions: Clinical comparison among mutated patients revealed differences in site of onset (predominantly lower limbs for *SOD1*, bulbar for *C9orf72*), phenotype (predominant LMN signs for *SOD1* and *TARDBP*; predominant UMN signs for *ANG*, *OPTN* and *UBQLN2*), age of onset and disease duration (reduced for *C9orf72* and *FUS*), and concurrence of dementia (in *C9orf72*, *TARDBP* and *FUS*). For the most common mutations (*C9orf72* repeat expansion; p.A4V, p.L84F, p.F45C, p.G93D, and p.L144F in *SOD1*; p.A382T in *TARDBP*; p.R521C in *FUS*) we could also observe distinct clinical phenotypes. Lastly, we observed a geographical clustering for some mutations, suggesting a founder effect. Our study thus represents a comprehensive survey on genetic epidemiology of ALS in Italy.

Disclosure: Nothing to disclose.

OS2212

New data from BENEFIT-ALS: blinded evaluation of neuromuscular effects and functional improvement with *tirasemtiv* in ALS

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Introduction: *Tirasemtiv* is a fast skeletal muscle activator that sensitizes the sarcomere to calcium and increases the force of muscle contraction at submaximal contraction rates. In previous studies, it was well tolerated in ALS patients, and dose dependent improvements on measures of muscle strength and patient function were noted.

Methods: ALS patients (N = 711) were recruited from 73 centers in North America and Europe. Slow vital capacity was >50 % of predicted, at least one handgrip was moderately weak, and ≥4 ALSFRS-R items scored 2 or 3. Before randomization, patients received 1 week of open-label *tirasemtiv* 125 mg BID to ensure this dose was tolerated. Patients who tolerated open-label *tirasemtiv* were randomized 1:1 to double-blind placebo or *tirasemtiv* beginning at 125 mg BID and escalating weekly based on tolerability to a maximum of 250 mg BID for a total of 12 weeks of treatment. ALSFRS-R and quantitative measures of respiratory and extremity muscle strength and endurance were assessed at baseline, after 4, 8, and 12 weeks of treatment, and 1 and 4 weeks after the last dose. Plasma concentrations of *tirasemtiv* were measured during double-blind treatment.

Results: The last patient was enrolled on November 27, 2013; the last visit will occur in late March, 2014. Safety and efficacy results related to the dose and plasma concentration of *tirasemtiv,* and the effects of withdrawing *tirasemtiv* after 12 weeks of treatment, will be presented.

Conclusions: BENEFIT-ALS tests the hypothesis that *tirasemtiv* increases skeletal muscle performance to improve function in ALS patients.

Disclosure: Dr. Shefner is a consultant to the sponsor, Cytokinetics, Inc. Drs. Andrews, Meng, James and Wolff and Ms. Lee are employees of the sponsor.

Movement disorders 3

OS2213

Cerebellar continuous theta burst stimulation in essential tremor

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Introduction: An abnormal cerebello-thalamo-cortical connectivity is thought to be involved in the pathophysiology of essential tremor (ET). In the present study we aimed to investigate whether the severity of postural tremor can be improved by non-invasive stimulation of cerebellum using the continuous theta-burst stimulation (cTBS) protocol. We also aimed to examine whether cTBS-related changes of postural tremor severity are reflected in excitability changes in the contralateral primary motor cortex (M1).

Methods: Fourteen patients with ET and 10 healthy subjects underwent two experimental sessions: (i) cTBS of the right cerebellar hemisphere (real cerebellar cTBS) and (ii) cTBS over the neck muscles (sham cerebellar cTBS). The two sessions were performed at least 1 week apart. Postural tremor was rated clinically and objectively measured using kinematic techniques, before and after cerebellar cTBS. The M1 excitability was assessed by recording the input/output curve of the motor evoked potentials from the right first dorsal interosseous muscle.

Results: There were no significant changes in clinical tremor rating after real and sham cerebellar cTBS in patients with ET. Again, cerebellar cTBS did not modify the postural tremor total power assessed with kinematic techniques in patients. Real cerebellar cTBS, but not sham cerebellar cTBS, reduced the excitability in the controlateral M1 only in healthy subjects but not in patients with ET ($p < 0.05$).

Conclusions: The results suggest that the cerebello-thalamo-cortical connectivity is abnormal in ET and as a consequence cerebellar cTBS does not modify the severity of postural tremor and the M1 excitability in this condition.

Disclosure: Nothing to disclose.

OS2214

OPTIPUMP study: impact of apomorphine pump therapy at 6 months on 145 parkinsonian patients quality of life. A multicentric french observational prospective study

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Introduction: Apomorphine pump is used in patients suffering from Parkinson's disease with motor fluctuations and/or dyskinesia. However the efficacy and tolerance of apomorphine pump and the strategies used remain not well known.

Methods: Inclusion criterias were parkinsonian patients $\geq$18 years with refractory motor fluctuations and/or levodopa-induced dyskinesia. Patient characteristic, dose and duration of all treatment are described. Primary endpoints are PDQ 39 and CGI-Improvement (evaluated both by patient and physician). Secondary endpoints are UPDRS and Ardouin behavioural scale. Endpoints are recorded at baseline, 3 months and 6 months.

Results: 145 patients with apomorphine pump were included (59 % female). The average age of patients was 66.8 $\pm$ 10.8 years. The average disease duration was 11.6 $\pm$ 5.4 years. 97 % of patients had motor fluctuations and 86 % had dyskinesias. At hospital discharge, 10 % of patients were treated without dopamine agonists nor L-dopa (apomorphine pump monotherapy), 57 % with L-dopa, 32 % with L-dopa and a dopamine agonist.

At 6 months, 73 % of patients according to neurologist and 70 % according to the patient themselves were very much improved, much improved or minimally improved on the CGI-I. According to Ardouin behavioural scale, no more hyperdopaminergic side effects were observed with apomorphine pump. Anxiety, depressive mood, hyperemotivity and non-motor fluctuations (On/Off) were slightly improved. At 6 months, dropout rate was 28 %.

Conclusions: Globally, the different treatment strategies used at the apomorphine pump introduction appear to be effective and well tolerated in accordance to previous data. Apomorphine pump presents a good benefit/risk ratio.

Disclosure: Nothing to disclose.

OS2215

Prevalence of hypo- and hyperdopaminergic behaviors in PD patients and impact on quality of life

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Objectives: To assess the prevalence of behavioral disorders in PD and their impact on quality of life.

Methods: 136 (62 % male) patients were assessed with the Ardouin scale and PDQ-39. The Ardouin scale is a new instrument that uses a structured, standardized interview to detect and quantify all the hypo- and hyperdopaminergic symptoms, and the non-motor fluctuations (NMF) in PD.

Results: 97 % of PD patients had at least one symptom listed from the Ardouin scale. The prevalence of depressive mood was 42.3 %, apathy 31.2 %, anxiety 45.0 %, compulsive shopping 15.0 %, pathological gambling 10.0 %, hypersexuality 16.9 %, eating behavior 36.5 %, dopaminergic addiction 2.7 %. Hypodopaminergic disorders (depression, anxiety, irritability, apathy, hyperemotivity) were correlated to the following dimensions of the PDQ-39 (emotional well-being, $r = 0.55$, $p < 0.01$; stigma, $r = 0.23$, $p < 0.05$; social support, $r = 0.25$, $p < 0.05$; cognition, $r = 0.29$, $p < 0.01$ and bodily discomfort, $r = 0.22$, $p < 0.05$). NMF were correlated to dimensions mobility, $r = 0.25$, $p < 0.05$; activities of daily living, $r = 0.27$, $p < 0.01$; emotional well-being, $r = 0.23$, $p < 0.05$; stigma, $r = 0.31$, $p < 0.01$ and communication, $r = 0.24$, $p < 0.05$. No correlation was observed between PDQ-39 and hyperdopaminergic symptoms (behavioral addictions, dopaminergic addiction, nocturnal hyperactivity…).

Conclusions: This study shows the high frequency of behavioral disorders in PD and the main impact of hypodopaminergic symptoms and NMF on quality of life in PD.

Disclosure: Nothing to disclose.

OS2216

Microelectrode recording in subthalamic deep brain stimulation for advanced Parkinson's disease

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Introduction: Microelectrode recording (MER) is used to optimize accuracy of electrode placement during deep brain stimulation surgery (DBS). However, direct advantages of MER for clinical improvement in patients with advanced Parkinson's disease (PD) are not defined. Our study aimed to reveal the impact of MER on motor and functional outcome in subthalamic DBS.

Methods: We analyzed PD patients operated in the last years using uniform stereotactic procedure. In 40 patients, intraoperative MER was performed for implantation of electrodes into sensorimotor STN. 49 patients were operated without MER. Both groups did not differ significantly in disease duration, severity, age at surgery, and medication dosage. Data available at follow-up of 6–12 months were assessed (surgical tactics, complications, UPDRS, PDQ-39).

Results: MRI-calculated trajectory matched the best neurophysiologically defined track only in 65 % of cases with MER; medial track was chosen in 24 %, lateral—in 7.5 %. Intracranial hemorrhage occurred in 1 case. Without MER, central trajectory was used in 95.1 %. In patients with MER, in off-medication state, alleviation of motor disability as well as improvement in activity of daily living appeared to be better (65.4 % versus 46.0 %, $p = 0.000355$, UPDRS-3, and 61.4 % versus 48.6 %, $p = 0.012325$, UPDRS-2, respectively). Reduction in levodopa equivalent daily dose was more substantial in group with MER (63.1 % versus 45.4 %, $p = 0.009288$). Stimulation-related dysarthria and necessity for postoperative electrode correction were higher without MER.

Conclusion: In STN-DBS for PD, MER seems not only to precise electrode placement, but also to improve clinical outcome, and to diminish potential side effects at short-term follow-up.

Disclosure: Nothing to disclose.

OS2217

Treatment-induced changes of sensorimotor networks in cervical dystonia: fMRI study of first-time botulinum toxin effect

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Introduction: Intramuscular botulinum neurotoxin type A (BoNT-A) application has a proven clinical effect on pathological muscle activation in CD but has also been shown to modulate sensorimotor networks. We used functional MRI of sensorimotor networks to describe changes associated with first-time botulinum toxin treatment of CD.

Methods: We studied 12 BoNT-A naïve CD patients using whole-brain functional MRI at 1.5 Tesla during a finger opposition task, before the first BoNT-A application and 4 weeks after application. Clinical treatment response was evaluated with the Tsui score. Functional MRI data were analyzed with FSL. Group mean maps were used to describe task-related activation, BoNT-A treatment effects were tested in linear contrasts (Pre > Post and Post > Pre).

Results: Group maps demonstrated activation of the bilateral sensorimotor network, with lesser extent before BoNT-A therapy. Comparing activations before and after BoNT-A demonstrated bilateral treatment-related increases in local BOLD response in several bilateral frontoparietal areas (primary and association motor and somatosensory cortices), ipsilateral insula and thalamus.

Conclusions: Considering the previously described sensorimotor network hypoactivation during non-dystonic motor task performance in CD (e.g., Oga 2002, also our previous studies, Opavsky et al. 2011, 2012), our observed effect of activation increase after first BoNT-A application may be interpreted as approaching the physiological state. The central effect of repeated BoNT-A applications (Opavsky et al. 2011, 2012) is somewhat different from ours, which likely corresponds to the gradual evolution of the clinical responses to repeated BoNT-A treatment in cervical dystonia.

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Disclosure: Nothing to disclose.

OS2218

Apomorphine improves morning akinesia in Parkinson's disease: interim analysis of the AM-IMPAKT trial

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Introduction: Motor fluctuations are common with L-dopa treatment in PD and include delayed and/or inconsistent onset of L-dopa effect (delayed-ON). Delayed-ON of the first morning dose of L-dopa manifests as morning akinesia, which may be prolonged and is known to significantly impact patient quality of life.

Methods: In this multicenter open-label study, subjects completed a Baseline Period recording daily time-to-ON (TTO) every 5-min following their morning dose of L-dopa for 7 days. After starting trimethobenzamide antiemetic therapy, they were injected with 0.2 mg of apomorphine and titrated to an optimal dose, defined as achieving within 15 min at least 90 % of post-L-dopa UPDRS. Patients then self-injected apomorphine each morning on awakening for a 7-day Treatment Period and recorded TTO following each injection. Efficacy was assessed by comparing baseline vs. apomorphine TTO (primary endpoint), EQ-5D-3L, CGI-S, and PGI-S scales. Safety/tolerability was also assessed.

Results: Fifty subjects meeting the "Completer" definition are evaluated in this interim analysis. Change from baseline in TTO and all secondary efficacy measures showed significant improvement ($p < 0.0001$). 94 % of patients experienced a reduction in TTO of at least 15 min; 84 % experienced a 20-min reduction from baseline. The most common adverse event was nausea (22.0 %, not dose-related). Hypotension and orthostatic hypotension were not observed in the 50 Completers included in this interim analysis, but led to 8 discontinuations in the Safety population.

Conclusions: Apomorphine subcutaneous injection significantly reduced TTO in PD patients experiencing delayed onset of their morning L-dopa dose, and was generally well tolerated.

Disclosure: Authors report consulting fees for US WorldMeds, LLC.

Neuroimmunology

OS2219

Cerebellar ataxia associated with glutamic acid decarboxylase 65 autoantibodies (GAD65-ab). Long-term impact of immunotherapy

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Introduction: Current clinical and immunological knowledge on cerebellar ataxia (CA) associated with GAD65-ab is based on case reports and small series with short-term follow-up. We aimed to describe the clinical profile, presence of additional antibodies, and long-term outcome in a series of 34 patients with CA and GAD65-ab.

Methods: We retrospectively reviewed the clinical features of 34 patients with CA and GAD65-ab, including the long-term (median 5.4 years, IQR 3.1–10.3) outcome of 25. Immunochemistry on rat brain sections, neurones in culture, and HEK cells transfected with the alpha-1 subunit of the glycine receptor (GlyR) or GAD67 were used to identify additional antibodies. Patients with stiff-person syndrome and GAD65-ab (SPS, $n = 28$) served as controls.

Results: Patients' median age was 58 years (range 33–80); 82 % were women. Clinical onset was subacute (weeks) in 13 patients. Five patients were not treated and only one deteriorated. Twenty patients received immunotherapy (11 IVIg, and 9 IVIg and steroids) and 7/20 improved. The only predictor of improvement was the subacute onset of symptoms (OR = 13.8, 95 %CI 1.5–127.5; $p = 0.02$). The titers of GAD65-ab, predominantly IgG subtype (IgG1), reactivity with linear epitopes, and occurrence of GAD67-ab (in 72 % of patients) was similar in patients with CA and SPS. GlyR-ab were identified in 4 patients with CA but in none with SPS. No other cell-surface autoantibodies were detected.

Conclusions: Among patients with CA and GAD65-abs, immunotherapy is more likely to benefit those with a subacute presentation

of symptoms. The immunological profile is similar to that of patients with SPS.

Disclosure: Nothing to disclose.

OS2220

Charcot-Marie-Tooth neuropathy type 1A associated with chronic inflammatory demyelinating polyneuropathy: coincidence or immune response to post-translationaly modified proteins in inherited neuromuscular disease? Case report

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Introduction: Inherited neuromuscular disorders may be associated with an immune mediated superimposed affection of the same target tissue. If not recognized, this association presents as a deterioration of the primary, inherited, disease.

Methods: We present patient with Charcot-Marie-Tooth neuropathy type 1A (CMT1A) who developed 15 years after CMT1A diagnose establishment stepwise worsening of the initial neurologic deficit.

Results: Control neurographic analyses showed multiple conduction blocks and prolonged F-wave latencies. The antiganglioside antibodies were positive. The diagnosis of chronic inflammatory demyelinating polyneuropathy (CIDP) was established. After 6 months of prednisone treatment (60 mg per day) the recovery occurred and the patient became ambulatory. The inherited polyneuropathy may expose myelin antigens or the gene duplication may contain genes that modify the immune response. The subgroup with stepwise progression of CMT1A may represent patients in whom a heightened humoral immune response occurs, directed against myelin proteins.

Conclusion: There are times when the presence or absence of post-translational alterations in self-proteins can profoundly affect antigen recognition in immune functions. This is of special interest in the field of inherited neuromuscular diseases in which the congenital change in various proteins may lead to the additional susceptibility to the immune response to the same target tissue. The pathways that control post-translational modifications may become targets of immunotherapeutic strategies to alter the states of autoimmunity versus immune tolerance. In the patients with inherited neuromuscular disorders the stepwise worsening may be representation of additional underlying autoimmune process and immunosuppressive/immunomodulatory therapy may be the valuable treatment option.

Disclosure: Nothing to disclose.

OS2221

total plasma exchange in neuromyelitis optica patients: single centre experiences

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Introduction: Neuro Myelitis Optica (NMO) is an autoimmun demiyelinating central nervous system disorder thought to be caused by auto antibodies against Aquaporin-4 that mainly attacks the optic nerves and spinal cord. The most common treatment option against NMO attacks is high dose steroids.However, TPE is used effectively in steroid refractory patients. Here we report our patients with NMO, treated with total plasma exchange between 2011 and 2013 in Ege University School of Medicine, Neurology Department and Apharesis Centre. Our goal was to analyze indications, adverse events, responses, and outcome of TPE in NMO.

Methods: We retrospectively reviewed the medical records of 12 patients who were diagnosed as NMO and recieved TPE. The patients were evaluated and compared regarding their age, number of attacks, mean duration between attacks and TPE, number of TPE sessions, baseline EDSS, EDSS on first and third months follow up and responces to TPE.

Results: 12 NMO patients were treated with TPE for 14 acute attacks. 9 patients tested positive for NMO antibody. The total number of TPE sessions was 70. The mean number of TPE sessions was 5. 6 patients recieved TPE on their first attacks. In 1 patient TPE was chosen as first line treatment. The mean baseline EDSS was 3 (0–9). Mean EDSS at acute attacks was 8.5 (7–9.5). In 10 patients TPE was chosen as second line treatment option after high dose intravenous corticosteroids.

Conclusions: In steroid refractory NMO patients TPE was found to be beneficial in small studies.

Disclosure: Nothing to disclose.

OS2222

Blood brain barrier permeability in limbic encephalitis and neuromyelitis optica

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Limbic encephalitis (LE) is characterized by an acute or subacute onset, memory loss, psychiatric features and often seizure. Neuromyelitis optica (NMO), also known as Devic's disease or Devic's syndrome, is an heterogeneous condition consisting of simultaneous inflammation and demyelination of the optic nerve (optic neuritis) and the spinal cord (myelitis).It is well documented blood brain barrier (BBB) rupture in limbic encephalitis (LE) and neuromyelitis optica (NMO) both neuroinflammatory brain diseases with autoimmune component, which characterized by autoantibodies (AAB) against membrane-bound, intracellular or secreted proteins (e.g., voltage gated potassium channels VGPC). Little is known regarding autoantibodies targeting such nuclear antigen as antineuronal nuclear AAB type 2 (anti-Ri) and VGPC AAB directed against Aquaporin 4 (AQP4). The aim of our study was comparison between AAB levels against membrane-bound and intracellular proteins targeting nuclear antigen in patients with LE and NMO. We observed 42 LE patients and 37 NMO patients, men aging from 17 to 64 years old. We used ELSA and Western blot analysis for evaluation of AQP4 and anti-Ri AAB in CSF and serum. Control group comprised of 68 relatively healthy donors of same age groups. It was revealed that NMO the level of AQP4 were increased both in CSF and serum. In LE concentration of anti-Ri AAB was higher in CSF than in serum. On the other hand, levels of AQP4 weren't increased in NMO. The difference on concentration of AAB against various neuro-antigen revealed uneven rupture of BBB, which is especially important for developing of future therapeutic approaches.

Disclosure: Nothing to disclose.

OS2223

The choroid plexus as a depository for the innate and humoural adaptive immune systems

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Introduction: Inflammatory cellular infiltrates in the choroid plexus (CP) have been described in a variety of circumstances (Engelhardt et al. *Microsci Res Tech* 52: 112–129, 2001), including multiple sclerosis (MS) where CP T-cell infiltrates are only modest (Vercellino et al. *J Neuroimmunol* 199:133–141, 2008). To our knowledge the roles of the innate and humoural immune systems in the CP have received little attention, aside from a report describing complement receptors (Singhrao et al. *Lab Invest* 79: 1247–1259, 1999). Thus, the purpose of this study was to examine these systems in the CP in situ.

Methods: Formalin-fixed paraffin-embedded sections of CP from an autopsy series comprising 12 MS cases, 24 cases with other neurological conditions, and 11 cases without neurological involvement were examined for the presence of components of the complement cascade and immunoglobulins (Ig) in an immunofluorescence and confocal microscopy study.

Results: Complement was deposited in the form of C3d, C9 and C9 neo-antigen in focal areas of sclerosis and/or calcification ("concretions") in the CP stroma. IgM was variably present in the concretions, while IgG and IgA tended to localize in CP epithelial cells or showed a diffuse staining pattern in the stroma.

Conclusions: Complement and immunoglobulins are deposited in the CP in a variety of circumstances; there is no MS-specific pattern. CP concretions appear to be important in trapping immune molecules involved in the early phases of immune responses (complement and IgM), whereas epithelial cells appear important in the CP's management of IgG and IgA.

Disclosure: Nothing to disclose.

OS2224

Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS): insights from the first autopsy case description

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Introduction: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is a recently defined inflammatory entity, prominently involving the pons.

Case report: A 76yo, diabetic, hypertensive and dyslipidemic woman, developed during 3 weeks headache, VI right and VII left nerves paresis and a cerebellar syndrome. Partially recovered within 3 weeks without treatment. 1 month later started incoherent speech, visual hallucinations, ophthalmoplegia, left facial and palate paresis, left pyramidal hemiparesis, cerebellar syndrome and depression of consciousness progressing to coma. Brain MRI showed contrast enhancing linear lesions in brainstem, middle cerebellar peduncle and cerebellar deep white matter. Electroencephalogram/electromyography: normal. CSF: 37 monocytes, 0,94 g/l proteins, normal glucose; no oligoclonal bands; 14.3.3 protein weakly positive. Infections (including tuberculosis, syphilis, Whipple's disease), autoimmune disorders (including sarcoidosis, Devic and Behçet diseases), neoplastic and paraneoplastic disorders were excluded. With 1 g methylprednisolone/day during 5 days followed by prednisolone 60 mg/day she improved consciousness, keeping left eye abduction limitation, cerebellar syndrome and pyramidal tetraparesis. Due to side-effects prednisolone was reduced and immunoglobulins attempted without further improvement. Remained stable during 2 years. Died from an aspiration pneumonia. Neuropathological study revealed predominantly brainstem white matter perivascular lymphocytic infiltrates, particularly the in pons, accompanied by CD68 positive histiocytes and activated microglia. Involvement was striking localized to superior cerebellar peduncles decussation and white matter surrounding red nucleus.

Conclusions: Clinical, imaging and pathological criteria for CLIPPERS were met. Partial therapeutic response could be attributed to clinical severity, late onset of treatment or low corticosteroid dose. This is the first autopsy case described.

Disclosure: Nothing to disclose.

Neuro-ophthalmology

OS2225

Impaired cortical inhibitory activity: a pathophysiological mechanism of vestibular migraine?

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Introduction: In vestibular migraine (VM), episodic vertigo is accompanied by typical migraine symptoms. The aim of this fMRI study was to investigate the activity of excitatory and inhibitory cortical circuits in VM patients and healthy controls (HC) during visual (optokinetic) stimulation. As a neurophysiological correlate the postural consequences of visual-vestibular interaction were examined by posturography.

Methods: 10 VM patients and 14 matched HC were examined by fMRI during two different visual optokinetic stimulations (6°/s vertical black and white stripes horizontally slowly moving rightward (OKN-L) or leftward (OKN-R)) and a rest condition. Statistical analyses were performed with SPM5. Body sway during visual motion stimulation was examined with static posturography (Kistler, Switzerland).

Results: Compared to HC, in VM patients OKN-L induced significantly increased responses bilaterally within visual and somatosensory areas and the cerebellum. During OKN-R there were significantly reduced activations. The deactivation pattern, in HC

typically occurring within the posterior insular cortex, the anterior cingulate cortex, or the superior temporal gyrus, was absent in VM patients: Deactivations were overall significantly reduced. Comparison of OKN-R vs. OKN-L revealed significantly asymmetrical activations, which was not the case in HC. Applying visual motion stimulation during static posturography VM patients showed significantly more instability than HC.

Conclusions: These results confirm the hypothesis of a reduced intracortical inhibition (1, 2) while excitatory activity is increased in VM patients. Moreover, the disturbed visual-vestibular cortical interaction appears to result in an enhanced postural body sway in VM.

Reference:
1: Aurora et al., 2007; 2: Antal et al., 2011

Disclosure: Nothing to disclose.

OS2226

Head jolting vertigo and nystagmus: a new vestibular syndrome?

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Introduction: Two patients are reported in whom violent horizontal shaking of the head (head jolting) induced vertigo and nystagmus. The condition cannot be explained as positional vertigo or head-shaking nystagmus.

Methods: Patient 1 was a 58 year old man and Patient 2 was a 62 year old man, with no relevant medical history. The main symptom was rotational vertigo after violent and brief oscillations of the head. This triggered violent horizontal nystagmus, with peak eye velocities above 100 deg/s, lasting for approximately 45 s. Horizontal angular velocities of the head required to induce these episodes could only be achieved by the patients themselves—approximately 700 deg/s. Positional manoeuvres for horizontal/vertical canals were negative. Imaging was unrevealing.

Results: On the basis that this syndrome resulted from mechanical excitation of the horizontal canal on the side of the nystagmus beat, Patient 1 underwent canal plugging and his symptoms disappeared immediately. Patient 2 was followed up conservatively and gradually, over a period of 6 years, the episodes disappeared. Tiggering an attack became impossible. Videorecordings will be shown at the meeting.

Conclusions: The 'head jolting' nystagmus in these two patients illustrate a hitherto undescribed vestibular syndrome that we attribute to mechanically dislodged material within the horizontal semicircular canal causing cupular deflection and excitation. The underlying pathology is unknown but vestibular athelectasis should be considered. Clinical examination, rather than imaging or vestibular testing established the diagnosis. Surgical or conservative treatment appears successful long term but canal plugging can resolve the problem rapidly.

Disclosure: Nothing to disclose.

OS2227

Beyond the EYE: behavioral and cortical assessment in posterior cortical atrophy (PCA)

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Introduction: Posterior cortical atrophy (PCA) is a dementing syndrome in which the most pronounced pathologic involvement is in occipito-parietal visual regions. Even though the syndrome has been recognized for more than two decades, PCA is relatively neglected by clinicians and researchers, and the patients are often referred to recurrent ophthalmic evaluation and face considerable delay in diagnosis.

Methods: 6 patients with PCA and 5 age matched controls underwent a comprehensive set of visual and neuropsychological tests, aimed to differentiate between lower and higher visual functions as well as between dorsal and ventral-related cortical functions affected in the syndrome. Functional MRI (fMRI) was performed on 3 patients addressing the neuronal substrate of the visual dysfunctions.

Results: Higher visual functions deficits were mainly seen within dorsal-related functions including simulant perception, image orientation, figure from ground, closure and spatial orientation. In addition, fine details discrimination was impaired in some patients. Face perception, letter reading and color naming were intact. In accordance with the behavioral findings, fMRI revealed intact activation in ventral visual regions of face and objects perception. Comparing cortical activation during local and global analysis (Navon letters) revealed greater activation for local processing in the Temporo-parietal junction which is usually involved in Gestalt perception.

Conclusions: A myriad of both higher and lower visual functions' deficits were evident both behavioraly and cortically. Greater awareness of the syndrome is needed to improve diagnostic accuracy, clinical management and design of research studies.

Disclosure: Nothing to disclose.

OS2228

White matter microstructure abnormalities in patients with dominant optic atrophy and OPA1 mutations

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Introduction: Aim of this study was to assess abnormalities of white matter (WM) microstructure in patients affected by dominant optic atrophy (DOA) linked to OPA1 gene mutations, using tract-based spatial statistics (TBSS) analysis.

Methods: Using a 3.0 Tesla scanner, dual-echo and diffusion tensor (DT) MRI images were derived from 19 patients with DOA (10 females, mean age = 43 years, range = 22–64) and 20 sex- and age-matched controls. A complete neurological and neuro-ophthalmologic examination was obtained in all patients. TBSS analysis was performed using FMRIB's Diffusion Toolbox.

Results: Visual acuity was reduced in almost all patients, whereas none of the patients had extra-ocular neurological complications. Focal lesions in the brain WM were identified in ten patients. Three patients presented hyperintense optic nerve lesions on T2 weighted scans. Optic nerve and chiasm atrophy were detected in twelve patients. TBSS analysis showed that compared to controls, patients with DOA had significant lower mean diffusivity, axial and radial diffusivity in WM of the cerebellum, brainstem, thalamus, fronto-occipital-temporal lobes, including the cingulum, corpus callosum, corticospinal tract and optic radiation bilaterally. No abnormalities of fractional anisotropy were detected. DT MRI measures were correlate with ganglion cell complex thickness.

Conclusions: Patients with DOA linked to OPA1 gene mutations present diffuse WM microstructural abnormalities. Clinical

expression of DOA could be influenced by the level of mithocondrial impairment and potential compensatory mechanisms, such as increased protein expression. Restricted water diffusion might be explained by a higher macromolecular water binding, due to increased molecular crowding and microviscosity.

Disclosure: MAR speakers honoraria from Biogen Idec and Serono Symposia International Foundation. CG received compensation for consulting and/or speaking from Novartis, Teva, Sanofi, Genzyme, Merck Serono, Biogen, Bayer, Actelion, SSIF. MF received compensation for consulting and/or speaking from Bayer, Biogen Idec, Merck Serono, and Teva.

OS2229

The effect of demyelinative damage on neighboring white matter integrity: an optic neuritis study

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Introduction: Neuronal loss following damage is often greater than expected from the severity of the injury to the nerve itself. The visual pathways which comprise a well-defined system, and optic neuritis (ON), which is usually a discrete event, make a fine model to study this phenomenon. This study was aimed to understand the effect of focal optic nerve demyelination on neighboring white matter; in distal segments of the same fiber bundle (optic tract) and in the successive trans-synaptic bundle (optic radiation).

Methods: Diffusion Tensor Imaging and probabilistic tractography were used to identify and characterize the optic tracts and radiations of 17 ON and matched controls. Data were correlated with Retinal Nerve Fiber Layer (RNFL) thickness.

Results: Patients' optic tracts exhibited reduced axial diffusivity, which correlated with RNFL thickness values. Patients' optic radiations demonstrated intact axial diffusivity but reduced fractional anisotropy and elevated radial diffusivity, which could be explained by intra-bundle lesions. No correlations were found between diffusivity measurements in patients' optic tracts and radiations; or between RNFL thickness and optic radiations' diffusivity.

Conclusions: Following ON, chronic axonal loss develops distally in the optic tracts, demonstrating Wallerian degeneration. Degeneration did not proceed to the optic radiations, opposing anterograde trans-neuronal changes. DTI in ON provides fine in vivo human model for studying histological abnormalities in normal appearing white matter, localized in close proximity to damaged bundle.

Disclosure: Nothing to disclose.

OS2230

The cortical mechanisms of oscillopsia and its suppression in asymptomatic infantile nystagmus and symptomatic nystagmus in neurological patients

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Introduction: Patients with acquired nystagmus complain of perceived visual world motion (oscillopsia) concomitant with retinal slip of the visual world. In contrast humans with early onset infantile nystagmus typically report no oscillopsia. Human studies into the mechanisms of oscillopsia have thus far have been purely psychophysical.

Methods: We combined psychophysics, eye movement recording and neurophysiology in six healthy volunteers with normal eye movements and four healthy individuals with infantile nystagmus without oscillopsia. We measured visual cortical spatial updating by applying transcranial magnetic stimulation (TMS) to area V5/MT during gaze fixation. Visual cortex TMS-evoked phosphenes phosphenes are retinotopic moving with voluntary gaze.

Results: During a caloric-evoked vestibular nystagmus causing oscillopsia in healthy individuals, there was no updating of phosphene location with eye position ($r^2 = 0.048$; $P > 0.05$ for horizontal eye vs. phosphene position). In contrast in infantile nystagmus subjects fixating upon a perceptually stable target, eye and phosphene position were correlated ($r^2 = 0.43$; $P = 0.006$). When we probed V5/MT excitability (with TMS), we found a continuous modulation of brain excitability across the nystagmus cycle in 3 infantile nystagmus. No such excitability modulation was seen during acute vestibular-nystagmus with oscillopsia.

Conclusions: In summary, both visual spatial updating and a phasic modulation of area V5/MT excitability may contribute to vissual perceptual stability during involuntary nystagmus in humans. We are currently extending this work to patients with pendular nystagmus from multiple sclerosis and cerebellar downbeat nystagmus.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 1

OS3101

Cerebral amyloid angiopathy-related inflammation. A systematic review of individual reported cases

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Introduction: Cerebral amyloid angiopathy related inflammation (CAA-I) is a rare potentially treatable encephalopathy, characterized by an inflammatory response to vascular deposits of β-amyloid. We aimed to perform a systematic review of all neuropathological-proven CAA-I case reports in order to describe its clinical and pathological features, outcome and effect of different treatment.

Methods: We searched PubMed and Cochrane Library and screened references of included studies and review articles for additional citations. Search results and data extraction were performed independently by 2 reviewers. Outcome was classified at last available follow-up by the modified Rankin Scale (mRS).

Results: A total of 54 publications, reporting on 137 patients, were included. Mean age was 66.9 years, 51.8 % were males. The most common clinical presentation was cognitive dysfunction (56.1 %) followed by headaches (38.6 %), pyramidal signs (18.9 %) and confusional syndrome (18,9 %). Vasculitis was the most common pathologic pattern (84.8 %); granuloma was found in 65.6 %. Therapeutic intervention was available in 84.7 % of cases: 85.3 % were treated with corticosteroids and 28.5 % with cyclophosphamide; 31 patients (39.7 %) regained independence (mRS 0-2), while 19 patients (24.4 %) were left with a severe handicap (mRS 3-5) and 28 (35.9 %) died. There were no statistically significant differences ($chi2 = 0.75$; $p = 0.19$), between patients treated with corticotherapy alone comparing to those treated with cytostatic agents alone or in combination with corticotherapy.

Conclusions: In our review, the most common clinical manifestation of CAA-I was cognitive dysfunction. The outcome was unfavourable in the majority of the patients, with death in more than 1/3, despite current treatments, mostly steroids.

Disclosure: Nothing to disclose.

OS3102

Intravenous thrombolysis for cerebral ischaemia in the North of France region. Impact of the regional health policy at the community level

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Introduction: The proportion of patients with ischaemic stroke who are treated by intravenous (i.v.) recombinant-tissue plasminogen activator (rt-PA) is an indicator of quality of stroke care at the hospital level. Little is known about this proportion at the community level, and its evolution over time according to health policies.The objective was to evaluate the impact of a regional health policy on the rate of i.v. thrombolysis in the 13 districts of the North of France region.

Methods: We determined the proportion of residents of the North of France region with ischaemic stroke who were treated by i.v. rt-PA in 2009–2010 (period A; 8 stroke units; no telemedicine) in the region and in each of its 13 districts, and we compared with the same proportions in 2012 (period B; 12 stroke units; telemedicine network between 5 hospitals).

Results: During the study period, 1,563 patients meeting inclusion criteria (period A 835, period B 728) received i.v. rt-PA. For the whole region, the annual rate of thrombolysis per million inhabitants increased from 103 (95 % confidence interval [CI] 85–125) up to 181 (95 %CI 157–209) between the 2 periods (relative increase +76 %, 95 %CI 67 % to 83 %). This proportion increased in 12 of the 13 districts, and was greater in districts where new stroke units, telemedicine, or both, were implemented.

Conclusions: In a region where the proportion of patients with ischaemic strokes who received i.v. rt-PA was one of the highest ever reported, there was still a possibility of improvement.

Disclosure: Nothing to disclose.

OS3103

Stiffer carotids in intracranial atherosclerosis: heart at risk

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Introduction: Arterial stiffness has been proposed as a surrogate marker of cardiovascular risk, independent of conventional risk factors. Intima-media thickening and carotid plaques are associated with an increased risk of cardiovascular events.The aim of our study was to investigate carotid artery wall dynamics in patients with intracranial atherosclerosis comparing them to subjects with carotid atherosclerosis.

Methods: We enrolled 20 consecutive patients (16 males, 4 females, mean age 74.0 ± 7.4years) with a >50 % intracranial symptomatic atherosclerotic stenosis detected by TCCD and confirmed by MRA/CTA/DSA.Twenty gender- and age-matched patients with atherosclerotic disease of the cervical arteries but no TCCD evidence of intracranial vessel disease constituted our control group.Every patient underwent a complete bilateral assessment of common carotid artery wall dynamics parameters and IMT. During the follow up period (2009–2013) any vascular event was recorded.

Results: Mean carotid wall stiffness was significantly higher ($p < 0.01$; 6.38 ± 0.30 vs 5.89 ± 0.27) and mean carotid distensibility was significantly lower ($p < 0.03$; 11.52 ± 1.32 vs 13.03 ± 0.98) in study group compared to controls.No significant differences were found in common vascular risk factors, statin use, antithrombotic treatment and mean IMT values between the two groups.There was a significantly higher rate of cardiovascular events in the study group ($p < 0.05$).

Conclusions: According to our data, carotid wall dynamics is significantly more compromised in patients with intracranial atherosclerotic stenoses compared to patients with carotid atherosclerotic disease. This was associated with a higher cardiovascular event rate. Carotid artery wall dynamics is a useful tool to select those patients at a higher cardiovascular risk who might benefit from a more intensive prevention program.

Disclosure: Nothing to disclose.

OS3104

Gender aspects of acute stroke care: results from the Austrian Stroke Unit Registry

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Introduction: Gender differences in quality of acute stroke care are an important concern with limited data available, specifically regarding the stroke unit (SU) setting. We used the prospective nationwide Austrian SU registry to address this issue.

Methods: Our analysis covered an 8-year time period (January 2005 to December 2012) during which all patients with TIA or ischemic stroke admitted to one of 35 Austrian SU had been captured in the registry. These data were analyzed for age-adjusted preclinical and clinical characteristics and quality of acute stroke care in men and women. In addition we assessed the outcome at 3 months in multivariate analysis.

Results: 47209 individuals (47 % females) had received SU care. Women were significantly older (median age: 77.9 vs. 70.3 years), had higher preexisting disability and more severe strokes. Correcting for age, no significant gender differences in quality of care were identified with comparable onset-to-door times, times to and rates of neuroimaging, as well as door-to needle times and rates of intravenous thrombolysis (14.5 % for both genders). Despite equal acute stroke care and a comparable rate of neurorehabilitation, women had a worse functional outcome at 3-months-follow-up (modified Rankin scale 3–5: OR 1.26 (95 % CI, 1.17–1.36)), but a lower mortality (OR 0.70 (95 % CI, 0.78–0.88)) after correcting for confounders.

Conclusions: We identified no significant differences in quality of care in the acute SU setting between males and females. Further studies on the post-stroke period including socio-economic aspects are needed to get more insights in gender specific prognosis.

Disclosure: Nothing to disclose.

OS3105

Combined use of coronary artery calcification, carotid intima-media thickness and ankle-brachial index for stroke prediction in the general population

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Introduction: The subclinical atherosclerosis markers coronary artery calcification (CAC), carotid intima-media thickness (CIMT) and

ankle-brachial index (ABI) predict stroke in addition to established risk factors in the general population. Whether these markers are surrogates of the same atherosclerotic risk or whether they may be used in combination was unknown.

Methods: 3289 subjects from the population-based Heinz-Nixdorf-Recall study (45–75 years; 48.8 % men) without previous stroke and coronary heart disease were evaluated for incident strokes over 9.0 ± 1.9 years. Cox proportional hazard regressions were used to examine CAC, CIMT and ABI as stroke predictors in addition to established risk factors (age, gender, systolic blood pressure, LDL, HDL, diabetes, smoking).

Results: Eighty-four strokes occurred during the follow-up. In multivariable regressions, CAC (hazard ratio [HR] = 1.40 [95 %-confidence interval = 1.08–1.81]; p = 0.011 per 1-standard deviation (SD) increase in $\log_{10}$ (CAC + 1); SD = 1.04), CIMT (1.31 [1.07–1.62]; p = 0.010 per 1-SD increase; SD = 0.127 mm) and ABI (1.56 [1.32–1.82]; p < 0.001 per 1-SD decrease; SD = 0.148) predicted stroke when adjusted for established risk factors. When combined with each other, the HR of CAC remained similar when CIMT was also inserted (1.37 [1.06–1.77]), but slightly decreased when ABI was inserted (1.28 [0.98–1.66]) into the multivariable model. By contrast, the HR of CIMT hardly changed both when combined with CAC (1.29 [1.05–1.59]) and ABI (1.28 [1.04–1.58]), nor did the HR of ABI when combined with CAC (1.52 [1.28–1.79]) and CIMT (1.52 [1.30–1.79]).

Conclusions: Despite limitations related to by chance variation of HR in multivariable regression analyses, our observations suggest that CAC, CIMT and ABI preserve their values as stroke predictors in the general population even when combined with each other.

Disclosure: Nothing to disclose.

OS3106

Visual hallucinations in acute stroke: a prospective study in 78 patients

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Introduction: Patients with stroke may present visual hallucinations (VH). However the incidence of VH, their clinical characteristics, topographic correlation, underlying physiopathology and prognostic value remain unclear.

Methods: We prospectively recruited 78 patients (mean age 71.09 ± 12.02; 57 % were men) with a diagnosis of acute stroke (ischemic/hemorrhagic, any vascular territory). All subjects were admitted within 24 h after the onset of symptoms. We excluded patients with previous neurodegenerative/psychiatric disease or previous hallucinations. We collected demographic and clinical data. All subjects had an initial neuroimage study (MRI/CT), and answered (the patient/relatives) a structured hallucination and sleep questionnaire at admission and within the first 15 days. A subgroup of patients had also a neuropsychological evaluation (N = 50) and an EEG (N = 34). Functional outcome was assessed with the Rankin scale.

Results: The incidence of VH was 16.7 %. These hallucinations were often complex, began within the first 15 days (76.9 % within the first 3 days) and resolved without medication. VH were associated with lesions in the occipital cortex (4/13 vs. 5/65, p = 0.038), initial visual field defect (6/13 vs. 8/65; p = 0.01), cortical atrophy in neuroimage (7/13 vs. 15/65; p = 0.04) and sleep disturbances during admission (6/12 vs. 6/58; p < 0.01). VH were not related with Rankin scale score at discharge. There were no differences between patients with and without VH in the NIHSS score at admission and discharge, EEG activity, ischemic vs. hemorrhagic etiology, infectious complications or drug/alcohol abuse.

Conclusions: VH are frequent in stroke patients (16.7 %). The visualized images are usually complex, appear early in the evolution and are self-limited. VH are more frequent in occipital cortical lesions, and are not associated with functional prognosis.

Disclosure: Nothing to disclose.

Neurorehabilitation 2

OS3107

Bilateral deep repetitive transcranial magnetic stimulation (rTMS) on lower limb motor function after stroke: a pilot study with H-coil

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Introduction: Repetitive transcranial magnetic stimulation (rTMS) has been recognized as a promising intervention for treatment of stroke patients. The purpose of this double-blind placebo-controlled cross-over study was to assess the efficacy of high frequency (20 Hz) brain stimulation on lower limb motor function in patients with chronic (>6 months) subcortical stroke.

Method: Repetitive TMS (rTMS) was delivered with the H-coil, specifically designed to target deeper and larger brains regions than the figure-of-eight coil. A total of 9 patients received both real and sham rTMS in a random sequence. rTMS treatments (real or sham) were composed of 11 sessions (administered over 3 weeks) and were separated by a 4-week wash-out period. Lower limb functions were assessed by the Fugl–Meyer lower limb scale (FM-LL), the 10-m walking test (10-MT) and the 6 min walking test (6-MWT), before and 1 day after the end of each treatment period, as well as at a 4-week follow-up.

Result: Real rTMS treatment was associated with a significant improvement in FM-LL scores. This effect persisted over time (follow-up) and was significantly greater than that observed with sham stimulation. A significant increase in walking speed was also found after real rTMS but this effect did not reach statistical significance in comparison with the sham stimulation.

Conclusions: These data demonstrated that 3 weeks of high-frequency deep rTMS could induce long-term improvements in lower limb functions in the chronic post-stroke period.

Disclosure: A Zangen is a key inventor of the H-coil and acts as a consultant for Brainsway LTD. The other authors declare no conflicts of interest related to the present study.

OS3108

Stem cell salvage of injured peripheral nerve

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Introduction: We previously have developed a polyglycolic acid (PGA)-collagen tube filled with autologous skin-derived stem cells (SDSCs) for bridge long rat sciatic nerves gaps. Here we describe a case report of this graft for repairing poly-injured motor and sensory nerves of upper arms of a human patient.

Methods: During the 3-year follow-up period, functional recovery of the injured median and ulnar nerve was assessed by pinch gauge test, static two-point discrimination and touch test with monofilaments, in couple with electrophysiological and MRI examinations.

Results: The motor and sensory function of the median nerve demonstrated an ongoing recovery post-implantation during the follow-up period.

Conclusions: The results indicate that the PGA-collagen/SDSCs artificial nerve graft could be used for surgical repair of larger defects in major lesions of peripheral nerves increasing the quality of life of treated patient by salvage the upper arms from amputation.

Disclosure: Nothing to disclose.

OS3109

Voices of patients and physicians in spinal cord pain care: what's needed!

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Introduction: In our previous study *Patients' perspectives on pain (2012),* 18 informants with spinal cord injury (SCI) and neuropathic pain were interviewed. One aim was to explore ideas about how to improve pain treatment for this patient group. The analysis showed that more data was needed on this topic. The present follow-up study sought to deepen our knowledge about how to design future health care for individuals with SCI and neuropathic pain. Sixteen of the former 18 informants participated. Nine physicians working with SCI neuropathic pain rehabilitation from university and regional hospitals were also included as informants.

Methods: The study used focus-group and individual interviews for data collection. Data was analyzed according to content analysis.

Results: Four categories emerged in the preliminary analysis: Structure of SCI pain care, Knowledge, competence and learning to live with pain, Relations between patients and pain care staff, and What's needed. All four categories included both patients' and physicians' perspectives. The patients want to be met by multiprofessional teams specializing in pain with a systematic approach mapping the pain and its consequences. Further, the patients want help and support from health care when learning to live with pain, and also complementary treatments as part of the treatment strategies.

The physicians stressed more competence in cognitive behavioural therapy for conducting individual and group activities.

Conclusions: Rehabilitation needs improvements in order to meet the needs both of individuals with SCI and neuropathic pain and of the physicans treating them.

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Disclosure: Nothing to disclose.

OS3110

Action observation therapy modifies structural brain plasticity in healthy adult individuals

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Introduction: To assess brain gray (GM) volume changes following action observation therapy (AOT) in healthy controls (HC), and their correlations with improvement of motor performance.

Methods: Thirty-six right (R)-handed HC, without particular manual ability, performed a motor training, consisting in 10 sessions of 10-minute passive mobilization of the R hand, vision of three videos lasting 5 min and execution, with the R hand, of three daily-life actions. Subjects were randomized into 2 groups: AOT-group watched videos representing daily-life actions, enviromental-group watched videos of landscapes. At baseline (T0) and after a 2-week of training (W2), dexterity and strength measures were assessed and 3D T1-weighted MRI sequences were acquired. Longitudinal GM volume changes were evaluated using Tensor-Based Morphometry.

Results: At W2, both groups showed GM volume increase of the bilateral paracentral lobule, anterior and posterior cingulum, calcarine cortex, and R cerebellum. The AOT-group showed also an increased GM volume of the R cuneus, and R insula. The AOT-group had a reduced GM volume of the R supplementary motor area, while the enviromental-group had a decreased GM volume of several fronto-patieto-occipital regions, R middle and anterior cingulum and R cerebellum. Compared to enviromental-group, AOT-group had an increased GM volume of the R cerebellum and left insula. In both groups, improvement at motor performance was correlated with GM volumetric changes.

Conclusions: A 10-day manual dexterity training with AOT influences structural reorganization of GM WM volumes in HC, facilitating motor skill improvement and promoting structural brain plasticity.

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OS3111

An analysis of sensitivity to change and reproducibility of a functional scale of the upper limb: UL-ADL

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Introduction: The upper limb assessment in daily living (UL-ADL) scale analyzes the difficulties of hemiplegic patients in active and passive functions of the upper limb in daily life (questionnaire) and test situations. We analyzed its sensitivity to change and reproducibility.

Methods: In this multicenter study, 92 patients were included for 2 years. The 15-item UL-ADL scale follows a proximal-distal progression and includes passive and active functions. Each activity is quoted between 0 (cannot perform) and 10 (perform with no difficulty).The scale was presented twice before the 8th week after stroke and after a time of 4–12 weeks. The change was analyzed by classical indexes of change and the sensitivity/specificity with respect to a predefined criterion (an increase in the Motor Index (MI) $> 20/100$).

Results: The standardized response mean (questionnaire: 0.86; test: 0.71) showed a moderate to good sensitivity, greater than the effect size (0.66, 0.49). These indexes were comparable to those of the Rivermead scale (0.91; 0.63). The area under the ROC curve (sensitivity/specificity) was relatively large, but comparable to that of the Rivermead scale. Correlations were strong ($p < 0.0001$) between changes in the UL -ADL and MI scores. In addition, the intra-observer and interobserver reliability was fair for the questionnaire and the test, as assessed by the intraclass correlation coefficients (> 0.80) and the Bland and Altman method.

Conclusions: The UL-ADL scale showed an overall sensitivity similar to that of the reference tests. Reproducibility was fair.

Disclosure: Nothing to disclose.

OS3112

Trephined syndrome

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Introduction: Decompressive craniectomy (DC) is frequently used to treat increased intracranial pressure or an intracranial mass effect. Trephined Syndrome (TS) describes a neurologic deterioration, which is attributed to a large craniectomy. It often has an orthostatic component. The incidence of TS has been reported between 7 % and 26 %. However, it might be underestimated if the course of cognitive functions before and after cranioplasty (CP) were insufficiently documented.

Methods: We evaluated 20 subsequent patients who underwent DC. Neurological and neuropsychological examination and brain CT scan were performed at admission to neurorehabilitation, when TS was suspected, and 1–4 days before and 1–4 days after cranioplasty.

Results: Eight (40 %) patients had a clinical course compatible with TS. They had an aggravation of their hemisyndrome or stagnation of clinical evolution, which improved after CP. Five of them also had hemineglect and 1 had severe executive dysfunction, all of which improved rapidly after CP. One patient, who had been in vegetative state for 3 months, started to communicate by writing after CP. Five patients had postoperative complications (4 hematomas, 1 abscess), which may have masked a potential effect of the CP.

Conclusions: Neurologists should consider the presence of a Trephined Syndrome (TS) in patients with DC who worsen or fail to progress. The optimal delay to CP is to be determined.

Disclosure: Nothing to disclose.

Peripheral nerve disorders

OS3113

Intra epidermal fiber nerve density (IEFND) in symptomatic transthyretin familial amyloid polyneuropathy (TTR-FAP): patterns of fiber loss and high incidence of amyloid deposit

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Introduction: TTR-FAP are severe and disabling hereditary neuropathy due to a point mutation of TTR gene. Diagnosis is usually difficult and delayed. Main diagnostic tools are nerve biopsy and TTR gene analysis. TTR-FAP present usually as a small fiber polyneuropathy and NCS may be initially normal. Place of skin biopsy by punch in diagnosis procedure is unknown.

Methods: We studied distal and proximal lower limb skin biopsies in 58 patients, with symptomatic and genetic proven familial transthyretin (TTR) amyloid neuropathy. They were associated with 16 varied TTR mutations including Val30Met in 55 %. The mean age was 58.7 yo (20–86); 17 with early onset EO (< 50y)(29 %). 3 mm punch skin biopsies were done 10 cm above the lateral malleolus and 20 cm below the anterior iliac spine under local anesthesiae. IEFND was calculated on bright-field PGP-immunofluorescence along EFNS guidelines. In addition, Congo red staining was done on each skin biopsy to detect amyloid deposition (AD).

Results: Mean delay between the the first symptom and skin biopsy was 3.81 year (0.5–10.3). Decreased IEFND was observed in all patients. 23 pts had complete distal LL IEFN loss (40 %); including 7 with complete proximal loss. A non length dependent pattern was seen in 23 pts (40 %) including 78 % with Late onset (LO), 65 % in non met30. Congo positive AD were present in 44/58 (76 %) patients; in 100 % of EO vs 65 % of LO.

Conclusion: Symptomatic TTR-FAP are characterized by a severe decreased IEFND or non length dependent pattern with frequent amyloid deposits.

Disclosure: Nothing to disclose.

OS3114

Long term effects of tafamidis treatment on transthyretin familial amyloid polyneuropathy (TTR-FAP): interim results from the Fx1A-303 study

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Introduction: Transthyretin familial amyloid polyneuropathy (TTR-FAP) is a progressive disorder associated with both V30M and nonV30M *TTR* mutations. Tafamidis stabilizes TTR, inhibiting amyloid formation, and delays neurologic impairment in patients with TTR-FAP. This is a preliminary evaluation of safety and efficacy of long-term tafamidis treatment.

Methods: Patients were from an ongoing, open-label trial (Study Fx1A-303) and had either received tafamidis in the single-treatment arm Study Fx1A-201 (all nonV30 M), or completed an 18-month placebo-controlled trial (Study Fx-005) and then received tafamidis in a 12-month extension (Study Fx-006; all V30 M).

Results: Tafamidis was generally well-tolerated with no unexpected adverse events. Adverse events possibly related to study medication occurred in 24 (25.8 %) patients; most common were headache and fall, each in 2 (2.2 %) patients. All patient groups experienced some disease progression (Table). Those with V30M in the tafamidis–tafamidis arm had numerically smaller increases in Neuropathy Impairment Score-Lower Limb (NIS-LL) and Norfolk Quality of Life-Diabetic Neuropathy (QOL-DN) scores than those in the placebo-tafamidis arm at 66 months. Furthermore, once patients in the placebo-tafamidis arm began treatment with tafamidis, their apparent rate of increase in NIS-LL scores was similar to those in the tafamidis–tafamidis arm. NonV30M patients had higher disease burden at baseline and increases in NIS-LL scores at 48 months roughly similar to those seen in the V30M patients at 66 months.

	V30M (Fx-005/Fx-006)		nonV30M (Fx1a-201)
	P-T	T-T	
Baseline	n=61	n=64	n=21
NIS-LL total, mean (SD)	11.45 (13.54)	8.36 (11.40)	27.64 (24.67)
NIS-LL muscle weakness, mean (SD)	4.19 (9.28)	2.87 (7.39)	14.41 (16.65)
NIS-LL reflexes, mean (SD)	1.69 (2.22)	1.19 (2.03)	5.20 (3.67)
NIS-LL sensory, mean (SD)	5.57 (3.80)	4.31 (3.39)	8.12 (5.78)
QOL-DN, mean (SD)	30.84 (26.72)	27.31 (24.17)	47.81 (35.14)
Change from Baseline	**at 66 months** n=12	**at 66 months** n=17	**at 48 Months** n=9
NIS-LL total, LS mean (SE)	15.48 (2.50)	9.15 (2.38)	14.71 (2.87)
NIS-LL muscle weakness, LS mean (SE)	9.30 (2.01)	4.24 (1.96)	9.66 (2.35)
NIS-LL reflexes, LS mean (SE)	2.90 (0.50)	1.78 (0.45)	1.06 (0.79)
NIS-LL sensory, LS mean (SE)	3.76 (0.74)	3.20 (0.68)	2.38 (0.73)
QOL-DN, LS mean (SE)	10.25 (3.87) n=29	8.20 (3.82) n=29	23.53 (7.85) n=7

P-T, placebo-tafamidis arm; T-T, tafamidis-tafamidis arm.

Conclusions: Longer-term use of tafamidis in V30M patients was associated with less advancement in polyneuropathy impairment; the lack of a placebo control group hampers interpretation of efficacy results in nonV30M patients.

Disclosure: These studies were sponsored by FoldRx Pharmaceuticals, which was acquired by Pfizer Inc in October 2010.

OS3115

Clinical spectrum, causes and evolution of disabling neuropathies in patients with hematopoietic stem cell transplantation on a 20 years period

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Introduction: Reports concerning neuropathies following hematopoietic stem cell transplantation (HSCT) are scarce in the literature.

Methods: We retrospectively recruited patients who presented disabling neuropathy after HSCT between 1990 and 2012 in our academic hospital.

Results: We report 17 patients, median age 48.5 years [10–66], 12 allografts and 5 autografts. The average delay between HSCT and onset of neuropathy was 10.8 months [pre-existing–35 months]. We describe different patterns and causes of neuropathy: acute polyradiculoneuropathy or Guillain–Barre syndrom (GBS, n = 3), chronic inflammatory demyelinating polyradiculo-neuropathy (CIDP, n = 3), neuropathy due to graft versus host disease (Np-GVHD, n = 4), vasculaitis (n = 3), toxic neuropathy (n = 3), neuropathy revealing hematologic relapse (n = 2) and neuropathy of undetermined cause (n = 1). Over 50 % improved after treatment (n = 10). Particular features existed. GBS occurs prematurely after HSCT (average delay m = 4.9 months) whereas CIDP or Np-GVHD occur later (respectively m = 15.2 and m = 14.2 months). Np-GVHD has different characteristics:

i) a polymorphic clinical presentation, non-length-dependent (62.5 %), with motor symptoms (87.5 %) mimicking CIDP with axonal features;

ii) Neuropathic symptoms often revealing the GVHD, although positive diagnosis was challenging in the absence of other affected organs and

iii) a good response to treatments used in chronic GVHD (steroids and immunosuppressive therapies).

Conclusions: Clinical presentations and causes of disabling neuropathies following HSCT are various. Polyradiculoneuropathies are not rare and GVHD is often implicated. Systematic and large explorations are necessary in order to introduce appropriate treatment associated in our study with good prognosis.

Disclosure: Nothing to disclose.

OS3116

Gene expression changes in chronic inflammatory demyelinating polyneuropathy skin biopsies

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Introduction: To determine molecular changes occurring in the skin biopsies of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) patients and to identify biomarkers for the disease.

Methods: We performed transcriptional profiling microarray analysis on lower leg skin punch biopsies from 20 CIDP patients and 17 healthy controls to identify disease-associated expression changes. The differential expression of genes with a possible role in the pathogenesis of CIDP from ontological studies was validated by quantitative PCR (qPCR) analysis.

Results: Most of the 190 differentially regulated genes were involved in immune and inflammatory responses, nervous system development, cell adhesion, wound response, angiogenesis and apoptotic processes. The differential expression of 26 genes with a putative role in CIDP pathogenesis was confirmed by qPCR. Four downregulated genes encoded members of the MHC class II family, while 22 upregulated genes were involved in cell proliferation and tissue repair such as PDGF1, VEGFR or KDR, A2M, CAV2 and NOSTRIN. The combined upregulation of KDR/DDR2 was found in 95 % of patients.

Conclusions: These findings indicate that gene expression is modified in skin biopsies of CIDP patients, with prominent changes in inflammatory pathway markers. Several repair and protective factors are also activated. The downregulation of HLA II genes may be indirect evidence of activation of dormant multiple sclerosis retrovirus (MSRV) viral particles. Importantly, this study provides a new set of prospective CIDP biomarkers.

Disclosure: Nothing to disclose.

OS3117

Antibodies against neurofascin-155 (NF155) in CIDP associate with disabling tremor, distal weakness and poor response to IVIg

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Introduction: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a heterogeneous disorder with autoimmune origin. The target antigens of the immune response remain largely unknown. Recent studies found antibodies against node of Ranvier proteins, such as contactin and neurofascin in a subset of CIDP patients. The clinical features associated to neurofascin antibodies have not been described. Our study describes the frequency and clinical features of CIDP patients with antibodies against NF155.

Methods: A cell-based assay with NF155-transfected HEK cells was used to screen for the presence of antibodies. Anti-NF155 titers and IgG isotype were determined by ELISA. Serum reactivity against nerve and brain structures was analyzed by teased-nerve fiber and rat brain immunohistochemistry. Clinical features were retrospectively reviewed.

Results: Two of 53 CIDP patients from our unit but none of 204 controls had antibodies against NF155 ($p = 0.041$). Both patients shared an aggresive polyneuropathy with predominantly distal weakness and absence of response to IVIg. Eight additional patients classified as refractory for IVIg treatment were obtained from the CIBERNED national database. Two of these patients were anti-NF155 positive and shared the clinical phenotype with the ones from our unit. Three of the 4 anti-NF155 positive patients presented a prominent, disabling, action tremor with cerebellar features. Anti-NF155 antibodies were predominantly IgG4 in all four patients and their sera bound to paranodal structures and to the neuropil of brainstem, cerebellum and brain.

Conclusions: Anti-NF155 antibodies in CIDP associate with a specific phenotype characterized by aggressive onset, distal weakness, disabling tremor and no response to IVIg.

Disclosure: Consulting honoraria from Bayer-Shering.

OS3118

Fourteen-year catamnesis of patients with vasculitic neuropathy

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Introduction: Vasculitic neuropathies may lead to severe sensory-motor impairment and pain. We retrospectively assessed long-term disease outcome.

Methods: We analyzed medical records of 62 patients with vasculitic neuropathy who reported to our Department for diagnostics and treatment between 1999 and 2008. Outcome was followed up until 2013.

Results: The cohort consisted of 12 patients with systemic vasculitis and polyneuropathy and 50 patients with non-systemic vasculitic neuropathy. The neuropathy was sensory-motor in 46/62 (74 %), pure sensory in 14/62 (23 %), pure motor in 2/62 (3 %), and painful in 37/62 (60 %) cases. No action potential was recordable in the later biopsied sural nerve of 30/62 patients (48 %). Although 12/62 (19 %) patients had received immunosuppressive treatment before biopsy, histology revealed unequivocal signs of vasculitis in all cases. 56/62 patients (90 %) were treated with immunosuppressants after histological confirmation of diagnosis. The major treatment regimes were an initial pulse of i.v. methylprednisolone followed by oral methylprednisolone only (10/56 cases, 18 %) or a combination with azathioprine (22/56 cases, 39 %). All patients had at least a short term response to steroids. Shorter disease duration and younger age were associated with better long-term outcome. In the majority of patients, however, long-term treatment with immunosuppressants did not lead to further improvement of residual sensory-motor symptoms; several patients remained stable even after treatment cessation. Notably, neurophysiology worsened in some patients with clinically stable disease.

Conclusion: Early and high dose i.v. steroid treatment was effective in this cohort of patients with vasculitic neuropathy. Remission with residual symptoms was the most frequent outcome.

Disclosure: Nothing to disclose.

Autonomic nervous system disorders

OS3201

Effect of osteopathic manipulative treatment on variations of HF parameter of HRV in healthy subjects compared to sham therapy and control group: RCT

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Introduction: The effects of osteopathic manipulative treatment (OMT) on autonomic nervous system (ANS) are still under debate. Heart Rate Variability (HRV) is linked to health status and it is an indirect marker of the ANS activity. This randomized placebo controlled within subject cross-over single blinded study investigated the influence of OMT on HRV measures in healthy subjects while at rest. OMT was hypothesised to increase HRV, compared to sham and control, and that the effects would be greatest for a non-linear measure of HRV (the detrended fluctuation scaling exponent).

Methods: 66 subjects were randomized into groups OMT, Sham and Control. Subjects allocated into OMT and Sham groups received 2 weekly treatments. Control group received no intervention. Participants were not on any medications and reported no history of psychiatric illness, neurological disorder, or any other serious medical condition (e.g. diabetes, cardiovascular disease).

Results: OMT engenders a statistically significant increase of parasympathetic activity, as shown by HF rate ($p < 0.001$), and decrease of sympathetic activity, as revealed by Low Frequency (LF) rate ($p < 0.001$); results also show a reduction of LF/HF ($p < 0.001$). These effects were largest using the detrended fluctuation scaling exponent, a non-linear measure. Importantly, participants were unable to correctly guess which treatment they had been assigned at either of the two assessments.

Conclusions: Findings suggest that OMT can influence ANS activity increasing parasympathetic function and decreasing sympathetic activity, in comparison with sham therapy and control.

Disclosure: Nothing to disclose.

OS3202

Composite Autonomic Symptom Scale 31 reveals autonomic pupillary and bladder dysfunction in relapsing remitting multiple sclerosis patients

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Introduction: Autonomic nervous dysfunction (AND) is frequent in Multiple Sclerosis (MS). Yet, little is known whether MS severity influences type and degree of ANDs. Therefore, we assessed severity and type of ANDs and compared ANDs with disease severity in patients with relapsing remitting MS patients (RRMS).

Methods: In 41 RRMS patients (mean age 35.05 ± 9.88 years, 31 women) and 12 healthy controls (mean age 29.27 ± 9.06 years, 7 women), we determined ANDs using the COMPASS-31, a 31-item questionnaire assigning scores from 0–100 to ANDs in the domains orthostatic intolerance, vasomotor, secretomotor, gastrointestinal, bladder and pupillomotor function. Clinical MS severity was assessed with the Expanded Disability Status Scale (EDSS) and the Multiple Sclerosis Functional Composite (MSFC).

The Mann–Whitney-U test compared patient and control values. Spearman signed rank test correlated COMPASS-31 scores with EDSS and MSFC values. Significance was assumed for $p < 0.05$.

Results: The COMPASS-31 total score did not differ between MS patients and controls [median 18.78; lower and upper quartile: 7.18–18.79) vs. 12.20; 3.26–21.32; $p = 0.161$]. However, COMPASS-31 subdomain scores were higher in MS patients than in controls for bladder ANDs [1.11; 0.00–3.33 vs. 0.00; 0.00–0-00, $p < 0.05$] and pupillomotor ANDs [1.67; 1.00–2.67 vs. 0.33; 0.00–0.92, $p < 0.001$]. Only COMPASS-31 bladder scores correlated with EDSS values (Spearman-Rho: 0.420; $p < 0.05$). AND scores did not correlate with MSFC values.

Conclusions: Total COMPASS-31 scores do not suggest increased AND prevalence in our 41 RRMS patients while subscores unveil prominent pupillomotor and bladder dysfunction. Increasing MS severity bears an increasing risk of bladder dysfunction.

Disclosure: Nothing to disclose.

OS3203

Diagnosing PoTS: additional investigations beyond the HUT and standing tests

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Introduction: Diagnosing PoTS remains a challenge, and patients are often encountered with orthostatic intolerance and palpitations highly suggestive of PoTS, who do not meet the arbitrary criteria of excessive tachycardia on head-up tilt (HUT) or standing. Additional factors in daily life, such as food ingestion, physical exercise and heat, that cause vasodilatation, are known to exacerbate the postural tachycardia in PoTS. The aim of this study was to objectively evaluate the cardiovascular autonomic responses to food, exercise and heat stimuli in PoTS.

Methods: Patients with a history of orthostatic intolerance and postural tachycardia underwent HUT and standing tests and liquid meal, modified exercise and whole-body heating tests.

Results: We studied 95 patients with PoTS. 39/95 (41 %) patients met the criteria for PoTS on HUT whereas 51/95 (54 %) patients fulfilled the criteria on standing. There was a significant exacerbation of postural tachycardia on HUT post-meal ($P < 0.001$) and on standing post exercise ($P < 0.001$). There was also an unmasking of postural tachycardia on standing post-heating in 10/20 patients (50 %). Food challenge and modified exercise were complementary tests revealing the diagnosis of PoTS in 91 % and 84 % of patients, respectively, compared with 70 % if only the HUT and standing tests were used.

Conclusions: This study emphasises the use of additional and relevant complementary autonomic function tests in confirming diagnosis of PoTS. Furthermore they provide valuable information for patients and their physicians, in the objective evaluation and in tailoring individually targeted management of symptoms exacerbated by key factors in daily life.

Disclosure: Nothing to disclose.

OS3204

Abstract withdrawn

OS3205

Autonomic dysfunction is a major features of the cerebellar ataxia, neuropathy and vestibular areflexia "CANVAS" syndrome which can mimic multiple system atrophy

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Introduction: Cerebellar ataxia, neuropathy and vestibular areflexia syndrome (CANVAS) is a recently recognised neuro-degenerative disorder. Prompted by the presence of symptomatic postural hypotension in two patients previously diagnosed with CANVAS, we hypothesised that autonomic dysfunction may be a common feature of other CANVAS patients.

Methods: In a cohort of 27 patients from New Zealand with CANVAS, we performed autonomic nervous system testing based on Ewing and Clarke's battery of autonomic tests and assessed symptoms of autonomic dysfunction using the Survey of Autonomic Symptoms and Total Impact Score questionnaires.

Results: 42 % of patients had definite parasympathetic dysfunction and 79 % of patients had definite sympathetic dysfunction according to the pre-specified criteria. In total, 83 % of our patients had

evidence of sympathetic or parasympathetic dysfunction. Two had previously, incorrectly, been diagnosed with multiple system atrophy. All patients had at least one symptom of autonomic disease and 92 % had more than two symptoms.

Conclusions: Our results support the hypothesis that autonomic dysfunction is a major feature of CANVAS. This has implications for the management of patients diagnosed with CANVAS as they are likely to have treatable autonomic symptoms. The findings also provide an important differential diagnosis from multiple system atrophy (MSA) for patients who present with ataxia and autonomic failure. Autonomic failure in MSA is preganglionic whereas evidence points to the autonomic failure of CANVAS as being "post ganglionic". We suspect that, in keeping with the postmortem proven sensory and vestibular ganglionopathies, it is the autonomic ganglia themselves that are affected by the condition.

Disclosure: Nothing to disclose.

OS3206

The usefulness of 24 h ambulatory blood pressure and heart rate monitoring (24 h-ABPM) in diagnosing orthostatic hypotension (OH) in patients with parkinsonian disorders

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Introduction: Orthostatic hypotension (OH) is a common non-motor feature in Parkinson's disease (PD) and a diagnostic criteria of MSA patients. 24 h ambulatory blood pressure monitoring (24 h-ABPM) can be used to assess circadian BP pattern and OH during daily activities. The aim of this study was to determine the effectiveness of 24 h-ABPM compared to a standard Head-up Tilting (HUT) in diagnosing OH in patients with parkinsonian disorders.

Methods: 44 patients (17 MSA, 27 PD) underwent cardiovascular autonomic screening tests and 24 h-ABPM. Patients were classified into 2 groups: patients with OH (OH + group; $N = 28$) and without OH (OH-; $N = 16$). The number of patients with abnormal circadian BP rhythms were compared between groups. Standing tests were included during 24 h-ABPM. The sensitivity and specificity in detecting OH from the 24 h-ABPM standing test was compared with HUT.

Results: During HUT, BP was significantly lower in OH+ group compared to OH− and the degree of BP fall during HUT was significantly greater in OH+ group (both $p < 0.01$). With 24 h-ABPM, OH+ patients had a higher proportion of patients with abnormal BP and reversed circadian rhythms than OH- groups (both $p < 0.01$). Using 24 h-ABPM with the diary, a fall of 20 mmHg or more in SBP showed a sensitivity and specificity of 82 % and 100 % (AUC 0.91, 95 % CI 0.84–0.98) in differentiating OH+ from OH−, respectively.

Conclusions: This study demonstrates that 24 h-ABPM with the diary has reasonably high sensitivity and specificity in detecting OH compared to a standard HUT tests in patients with parkinsonian disorders.

Disclosure: Nothing to disclose.

Epilepsy 2

OS3207

Long-term follow-up of genetic generalized epilepsy with typical absence seizures and generalized paroxysmal fast activity in adulthood

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Introduction: Generalized paroxysmal fast activity (GPFA), a rhythmic EEG pattern of unknown significance was reported in a few patients with genetic generalized epilepsy (GGE) presenting with typical absence seizures (TAS). Our aim was to report the long-term follow-up and genetic findings in GGE patients with TAS having GPFA in their EEG.

Methods: We had investigated all EEGs of the adult GGE patients with TAS between the years of 1997 and 2002 for another study and eventually recorded GPFA in 12 of them. Afterwards these patients were followed up for their clinical and electroencephalographic course and their genetic features were also investigated. The control group was composed of 24 adult GGE patients who also had TAS without GPFA with similar follow-up duration in the same epilepsy center.

Results: Durations of epilepsy and TAS were significantly longer in the GPFA group. There is no significant difference between the groups in comparison of the electroclinical characteristics except EEG photosensitivity, which was significantly common in GPFA Group. The age at detection of GPFA was 33 ± 16.6 (16–71) and 80 % still have GPFA in their last EEG .60 % of the GPFA group had consanguineous parents whereas only 4.17 % had consanguinity in the Control Group. Five relatives with epilepsy from GPFA Group were also evaluated but GPFA could not be seen in their 30 evaluated EEGs. We could not show the responsible mutations.

Conclusions: GPFA is an ignored EEG pattern of adult GGE patients with TAS, indicating life-long course for epilepsy and TAS.

Disclosure: Nothing to disclose.

OS3208

Screening for anxiety in epilepsy clinics. A comparison of conventional and visual-analog methods

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Introduction: Up to 60 % of people with epilepsy (PwE) have psychiatric comorbidity including anxiety. Anxiety remain underrecognized in PwE. This study investigates if the screening tools for depression could be used to pick up anxiety as well.

Methods: 261 participants with a confirmed diagnosis of epilepsy were included. Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) and Emotional Thermometers (ET), both validated to screen for depression were used. Hospital Anxiety and Depression Scale-Anxiety (HADS-A) with a cut off for moderate and severe anxiety was used as the reference standard. Sensitivity, specificity, positive and negative predictive value and ROC analysis as well as multivariate regression analysis were performed.

Results: Patients with depression (n = 46) were excluded as multivariate regression analysis showed that depression was the only significant determinant of having anxiety in the group. Against HADS-A, NDDI-E T (0.874) and ET-7 (0.882) showed highest level of accuracy in recognising anxiety as per ROC curve. ET4 showed highest negative predictive value (NPV = 0.968).

Conclusion: Our study showed that reliable screening for moderate to severe anxiety in PwE without depression is feasable with conventional and visual analogue tools. Both scales can be recommended. The cut off values for anxiety are different from those for depression in both tests. As no test performed well in a case-finding role, we recommend that these tests should be used as a screening tools as an initial first step to rule out patients who are unlikely to have anxiety.

Disclosure: Nothing to disclose.

OS3209

Is serotonin transporter implicated in mesial temporal lobe epilepsy development?

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Background: Human and animal studies demonstrated that deregulation of serotonergic neurotransmission can be involved in the pathophysiology of epilepsy. Serotonin transporter (5-HTT) plays a key role in the regulation of serotonin levels. It has been described that expression of the 5-HTT gene could be modulated by a 17 bp variable number of tandem repeats (VNTR) in the second intron (5-HTTVNTR). This VNTR can have 9, 10 or 12 repeats. The 12-repeat allele has been associated with higher transcriptional activity. Investigation of the association between 5-HTTVNTR and the development of Temporal Lobe Epilepsy (TLE) has been inconclusive. Our aim was to analyse evaluate the association between 5-HTTVNTR and Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS) in a Portuguese population.

Methods: A cohort of 119 MTLE patients (65F, 54 M, mean age = 44 ± 11 years, age of onset = 13 ± 9 years, 62 with Febrile Seizures antecedents) was compared with a cohort of 236 healthy individuals (HI). HTTVNTR genotyping was performed by PCR fragment sizing.

Results: The genotype 12/9 was overrepresented in MTLE-HS patients compared to controls (2.5 % in MTLE vs 0.0 % in HI, p = 0.037 OR = 1.026 (0.997–1.056). MTLE-HS sub-groups (with and without febrile seizures antecedents) showed no differences in 5-HTTVNTR allelic or genotypic frequencies.

Conclusion: These results suggest that serotonin transporter gene may play a role in MTLE-HS susceptibility. Variations in the 5-HTT gene expression may lead to changes in serotonergic neurotransmission and consequently in brain homeostasis, lowering the threshold for seizure development. Supported by a BICE Tecnifar Grant 2012.

Disclosure: Nothing to disclose.

OS3210

Family impact and parental perception of childhood epilepsy

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Introduction: Epilepsy is a real public health problem; patients living with epilepsy suffer from psychological and socio-cultural problems which are barriers to their development and social integration. Our objective was to assess the impact of epilepsy on quality of life of parents and their perception of the disease.

Methods: For 1 year, 146 children (2–16 years) with epilepsy were recruited, and their parents were interviewed, the parent interviewed lived with the patient for at least 1 year. The presence of major life changes during the previous 3 months on the social or economic conditions of the family unrelated to epilepsy, significant comorbidities and mental retardation was an exclusion criteria.

Results: Epilepsy has an impact on the health of mothers, 73 % of mothers had sleep disorders, and 33 % had headaches. More than half of mothers had seen a considerable impact on their work, 85 % of mothers felt that family economy was affected by the disease. If 18 % of parents believe that their child's epilepsy brought them together, 68 % believe it has not led to conflicts in their married life, and 14 % thought the opposite.

According to 9.5 % of the mothers, their child's epilepsy removed any desire to conceive again.

Conclusions: Epilepsy is a major neurological problem in developing countries and is associated with significant psychosocial maladjustment among both children involved and family members.

Disclosure: Nothing to disclose.

OS3211

Reflex seizures induced by reading, rub, music and startle: a video-EEG analysis

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Introduction: Reflex epilepsies are a group of disorders in which seizures are habitually provoked by a specific sensory stimulus or cognitive process. The nosological status of reflex epilepsies remains unclear. Analysis of reflex seizures can help identify the cortical networks underlying each specific type of seizure.

Methods: We undertook a clinical and video electro-encephalographic (EEG) analysis of 2 cases each of primary reading epilepsy and rub epilepsy, and 1 case each of epilepsy relating to music and startle.

Results: Two cases of reading epilepsy exhibited myoclonic jerks of the jaw and tongue during silent reading. EEG was normal in one, and in the other showed 3–4 Hz rhythmic spike wave in the central region suggesting involvement of the left precentral cortex. Both patients with rub epilepsy showed asymmetric tonic posturing of the limbs with stimulation of the susceptible area. EEG showed spikes and rhythmic slow activity frontocentrally, suggesting involvement of the supplementary motor area. The patient with musicogenic epilepsy, on being played a specific song during EEG recording exhibited jerking of the right arm and jaw, followed by loss of awareness, and

secondary generalisation. EEG showed rhythmic spike wave discharges in the left fronto-temporal region. The patient with startle epilepsy exhibited asymmetric tonic spasm of the limbs with a gelastic component in response to unexpected auditory stimulation. EEG showed right frontocentral rhythmic activity.

Conclusions: Our results help confirm the location of epileptogenic networks in patients with reflex seizures provoked by various stimuli. Video and EEG data will be presented.

Disclosure: Nothing to disclose.

OS3212

Psychiatric disease, social aspects and life events in young men with epilepsy

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Introduction: We investigated psychiatric disease, adverse social aspects and life events in men with epilepsy.

Methods: This study was based on the Norwegian Mother and Child Cohort Study (MoBa). Data included information on diagnoses, symptoms from validated diagnostic instruments and adverse social aspects from 71,700 men, registered as fathers of children in MoBa around week 18 of pregnancy.

Results: 658 men (mean age 31.8 years) reported epilepsy, 36.9 % using antiepileptic drugs (AEDs). Men with epilepsy more often screened positive for present depression (3.9 % vs. 2.5 %, $p = 0.023$) compared to the references without epilepsy. Symptoms of anxiety was linked to untreated epilepsy (7.0 % vs. 4.6 %, $p = 0.004$), as was self-reported ADHD (3.4 % vs. 0.4 %, $p < 0.001$), bipolar disorder (2.2 % vs. 0.3 %, $p = 0.003$), unspecified psychiatric disorders (5.6 % vs. 2.3 %, $p = 0.008$), low self-esteem (2.5 % vs. 1.3 %, $p = 0.011$) and episodes of physical violence (3.3 % vs. 1.5 %, $p = 0.021$). Low satisfaction with life (1.7 % vs. 0.7 %. $p = 0.010$) and serious somatic illness (10.7 % vs. 4.3 %, $p < 0.001$) was more often reported among AED treated men compared to the references. Unemployment due to disability was linked to both AED treated (9.1 % vs. 1.4 %, $p < 0.001$) and untreated epilepsy (2.9 % vs. 1.4 %, $p = 0.009$), as were low income (10.3 % vs. 5.4, $p = 0.031$ and 9.7 % vs. 5.4 %, $p = 0.011$).

Conclusions: Epilepsy in young men was associated with a higher frequency of psychiatric disorders, adverse socioeconomic aspects, and lower satisfaction with life. Men with untreated epilepsy appear to be the most vulnerable group concerning psychiatric comorbidity, and this may be relevant for their children's development.

Disclosure: Nothing to disclose.

Infection and AIDS

OS3213

Which viral encephalitis do we treat? A review of four-year data

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Introduction: To determine the prevalence of herpes encephalitis, known as the most common, potentially mortal and treatable cause of sporadic encephalitis, in a sample Turkish population.

Methods: Demographic, clinical, laboratory, imaging, electrophysiology and PCR-DNA results of patients examined with a pre-diagnosis of encephalitis, i.e. ICD-10 of A81–86, G04, G05, B00, in our clinic between June 2010–December 2013 were examined retrospectively.

Results: A total of 68 patients were included. The most common presenting symptom was altered behavior (67.6 %), followed by headache and seizures. Neurological examination was mainly normal in 14.7 %, whereas isolated findings of altered consciousness was determined in 66.2 %. Temporal T2 hyperintensity was determined in the MRI of 27.9 %, and EEG abnormalities were determined in 35.3 % of patients. Lymphocytic pleocytosis was determined in the CSF of 35 patients, whereas increased leukocyte count was determined in 20 patients; and CSF protein count was increased overall in 27 patients. In the end, 57 patients had been diagnosed with viral encephalitis, 3 bacterial meningitis, 3 tuberculous meningitis, 2 sporadic Creutzfeld-Jacobs disease, 2 acute disseminating encephalomyelitis, and 1 brucella encephalitis. Seven (10.2 %) cases of viral encephalitis were HSV DNA PCR positive.

Conclusions: Viral encephalitis is the most common cause of infectious encephalitis; however, other atypical causes and tuberculous and brucella encephalitis should be noted, particularly in the Turkish population. Negative HSV DNA PCR results do not always exclude the need for antiviral therapy in patients with a strong pre-diagnosis of herpes encephalitis since several microbiological factors might result in false negativity.

Disclosure: Nothing to disclose.

OS3214

Stroke in HIV infected patients: a case series reviewing etiologic mechanisms

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Introduction: A high incidence of stroke is observed in younger patients with uncontrolled human immunodeficiency virus (HIV) infection and severe immunosuppression. In previous studies, opportunistic infections and HIV coagulopathy/vasculopathy explained more than 60 % of the strokes.

Methods: We made a retrospective transversal study of patients with stroke between 2006 and 2013 and who had a previous or concomitant diagnosis of HIV infection. The Stroke mechanism was classified according to the Trial of Org 10172 in Acute Stroke Treatment (TOAST) criteria. The aim of this study was to characterize this population and categorize the possible etiologic mechanisms of stroke.

Results: Nineteen (17 men) HIV (18 HIV-1, 1 HIV-2) patients were included. The mean age at the stroke diagnosis was 49.5 (SD 11.6) and stroke occurred at a median of 9.5 years (0–22) after HIV infection diagnosis. The median of CD4 cells was 225.5/μL (0–853) and the median viral load was 0.0 copies/mL (0–1220000). There were 16 ischemic strokes and 3 transient ischemic attacks. The mean admission NIHSS was 7.3 (SD 6.5). The stroke aetiology according to the TOAST criteria was: 3 large-artery atherosclerosis (15.8 %), 4 cardioembolism (21.0 %), 7 small-vessel occlusion (36.8 %), 1 other determined aetiology (5.2 %) (cocaine) and 4 undetermined aetiology (21.0 %) (incomplete evaluation). Central nervous system opportunistic infections or HIV vasculopathy/coagulopathy were not diagnosed.

Conclusions: Many mechanisms may concur to the aetiology of stroke in HIV infected patients. In this HIV patients' cohort, and contradicting previous studies, vascular factors and cardiac mechanisms were highly recognized mechanisms of stroke.

Disclosure: Nothing to disclose.

OS3215

Tuberculomas of brain: an unpredictable entity

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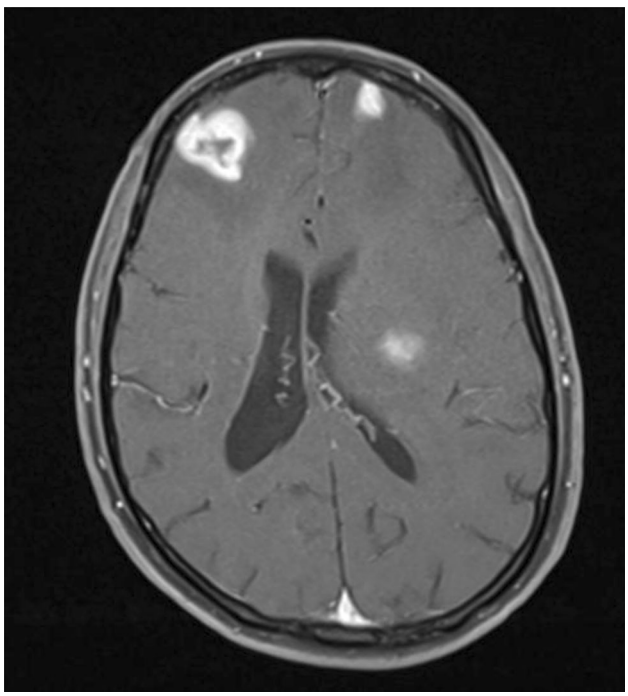
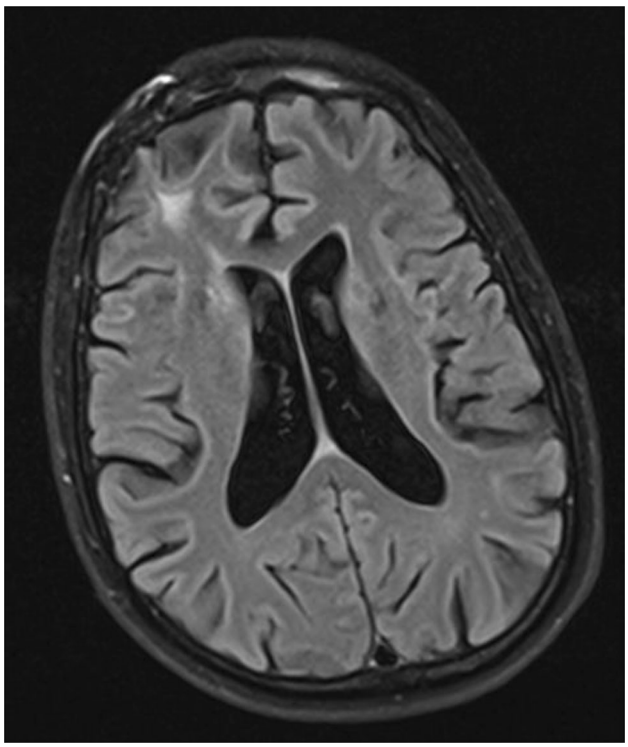
Introduction: Mycobacterium tuberculosis is one of the commonest causes of central nervous system (CNS) infections. They cause tuberculous meningitis, vasculitis, encephalopathy, abscesses tuberculomas and caries spine. The nature of the lesion depends on the host immunity and virulence of the bacteria. Of the CNS lesions, the tuberculomas are the most unpredictable. Keeping this in mind, we decided to retrospectively study the cases of tuberculomas of brain and their response to anti-tubercular drugs in order to formulate a standard treatment plan.

Methods: This was a retrospective study conducted in our hospital. The patients who had an MRI diagnosis of CNS tuberculoma with minimum 6-month follow-up were included.The diagnosis of tuberculomas was either confirmed by brain biopsy or was supported by evidence of tuberculosis in the cerebrospinal fluid or in other organs like lungs.

Results: 6 patients met the selection criteria. Their age ranged from 11 to 70 years. Duration of receiving anti-tubercular treatment varied from 6 months to 2 years. 1 patient, aged 70 years died to septicaemia. Of the remaining five, 1 patient had complete resolultion of the lesion. 2 patients had incomplete resolultion, inspite of more than 1 year ATD (anti-tubercular drug) treatment. Remaining 2 patients had significant decrease in size of the lesions after 1 year of treatment.





Conclusions: The results show that the response to treatment is mixed. However presence of multiple tuberculomas and larger lesions heralded worse prognosis. A more elaborate study with larger patient number is needed to formulate a standardized treatment plan.

Disclosure: Nothing to disclose.

OS3216

Serum glucose adjusted cut-off values for normal cerebrospinal fluid/serum glucose ratio

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Introduction: Calculation of the cerebrospinal fluid/serum glucose (CSF/S-Glu) ratio is part of the routine CSF work-up, however, different cut-off values ranging from 0.3 to 0.5 have been suggested so far to distinguish physiological from pathological conditions.

Objective: To determine normal cut-off values of the CSF/S-Glu ratio.

Methods: As an Austrian reference laboratory we screened our database for paired CSF and serum samples, which have been collected by lumbar puncture, were processed within one hour after

withdrawal, showed cell count < 5/μl, erythrocyte count < 500/μl and age-related normal CSF total protein resulting in 1036 sample pairs. Glucose concentrations in CSF and serum were measured by enzymatic spectrophotometry.

Results: Glucose concentrations in CSF were approximately 60 % of those in serum. CSF/S-Glu ratios negatively correlated with serum glucose levels ($R = -0.586$, $p < 0.001$) and cut-off values for normal CSF/S-Glu ratio defined as the 5th percentile were 0.5 for patients with a serum glucose concentrations <100 mg/dl, 0.4 for those with a glucose level of 100–149 mg/dl and 0.3 for serum glucose concentrations ≥150 mg/dl.

Conclusions: CSF/S-Glu ratio inversely correlates with serum glucose concentrations in a non-linear manner. These findings suggest that cut-off values for normal CSF/S-Glu ratio must be adjusted to serum glucose levels, probably explaining the considerably varying cut-offs that have been reported so far.

Disclosure: Nothing to disclose.

OS3217

Migration of toxocara canis into the spinal cord in poorly treated patients

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Introduction: Although *Toxocara* myelitis is a rare entity, 17 cases were recently diagnosed in Lebanon and published. Radiological features of the Visceral Larva Migrans (VLM) infection of the spinal cord seem to be specific. Lesions on the magnetic resonance imaging (MRI) showed fusiform enlargement with focal nodular enhancement after Gadolinium injection. Two of these patients were initially poorly treated and had multiple MRIs.

Methods: Serial MRI pictures of two patients with prolonged *Toxocara* myelitis were reviewed and compared.

Results: One patient was followed up for a period of 4 months with an unknown myelitis. The lesion was noticed in this patient to migrate upward from C8 to C2–C3 level with time. The patient was eventually diagnosed to have *Toxocara* infection and treated with anti-helminthic agents with complete resolution. The second patient had a C2–C3 myelopathy that was diagnosed to be a *Toxocara* infection and treated for a 2 week period. He relapsed 2 months later with a new lesion at C4 level. Treatment for 2 more months cleared the lesion permanently.

Conclusion: In untreated or poorly treated *Toxocara canis* myelitis, the lesion in the spinal cord seems to migrate from one area to another as seen on MRI. This worm which can migrate in blood and solid organs seems also to migrate within the spinal cord if poorly treated. In this particular condition, treatment with anti-helminthic agents should be continued until complete resolution of the clinical symptoms and normalization of the MRI.

Disclosure: Nothing to disclose.

OS3218

Assessment of HIV-infected patients with neurological complications in a multi-disciplinary platform

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Introduction: Despite combination antiretroviral therapy (cART), neurological complications, in particular the cognitive ones, remain a challenge in HIV-infected patients. Frequently, co-morbidities are intermingled with HIV infection, rendering the management of these patients difficult.

Methods: We set up a multi-disciplinary Neuro-HIV Platform composed of infectiologists, neurologists, neuropsychologists, psychiatrists, and neuroradiologists. During a day-hospitalization, the patient benefits from a clinical evaluation by all these specialists, together with blood work-up, brain MRI and lumbar puncture.

Results: From March 2011 to November 2013, we evaluated 80 consecutive patients (52 men, 49.6 ± 9.1 y, nadir CD4+ T cells 172.2 ± 142.7 cells/mm^3, current CD4$^+$ 568.8 ± 257 cells/mm^3, 76 % with undetectable plasma HIV RNA, 89 % with undetectable CSF viral load, 99 % on cART). Main referral cause was cognitive complaints (90 %), which were confirmed in 78 % of those. Main causes of cognitive disorders were psychiatric conditions (41 %) and HIV-associated neurocognitive disorders (HAND) (30 %). Neurological deficits were evidenced in 46 % of the cohort. Brain MRI was abnormal in 54 %, mostly due to slight to moderate cortical/subcortical atrophy. The presence of HAND was correlated with a lower nadir CD4+ T cells ($p = 0.02$). No other correlation was found between HIV disease status and neurological deficits.

Conclusions: Neurological/neuropsychological complications are frequent in well-treated HIV+ patients. The latter are more often ascribed to a psychiatric condition than to HIV infection itself. A multi-disciplinary approach is a real asset to take care of these complex patients.

Disclosure: We are indebted to AbbVie, Gilead, and Bristo-Myers Squibb who made this Neuro-HIV platform possible.

Neurogenetics

OS3219

Autosomal-dominant proximal spinal muscular atrophy caused by mutations in a novel gene-motor adaptor BICD2

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Introduction: Spinal muscular atrophy (SMA) refers to a group of genetic disorders characterized by degeneration of anterior horn cells of the spinal cord. Although the most common SMA cases are inherited in autosomal-recessive trait and caused by homozygous deletion or mutation of the survival of motor neuron 1 (SMN1), rare families with dominant inheritance have been reported.

Materials and methods: A four-generation Bulgarian family with 11 affected members and one sporadic patient afflicted with autosomal dominant proximal SMA were involved in the study. The evaluation included detailed neurological examination and testing of muscle strength. Evaluation of serum creatine phosphokinase (CPK) levels and electromyography (EMG) were performed of 6 patients. The molecular-genetic analysis encompassed genome-wide linkage analysis and whole-exome sequencing.

Results: The clinical onset age varied between 1 and 6 years (mean 3.17 ± 1.70 years), and individuals presented with delayed motor milestones, such as walking, difficulties in getting upright from a squatting position and in climbing stairs, a waddling gait, and slow running. The weakness was limited to the lower limbs and did not progress significantly over time, given that affected individuals still remained ambulatory into the fifth decade. The genome-wide linkage analysis and whole-exome sequencing found a heterozygous de novo c.320C>T (p.Ser107Leu) mutation in bicaudal D homolog 2 (Drosophila) (BICD2) in the 11 affected from the four-generation family and c.2321A>G (p.Glu774Gly) in the sporadic case.

Conclusion: Our study identifies BICD2 gene mutations as a novel cause of non-5q linked SMA and highlights its importance in the motor neuron function in humans.

Disclosure: Nothing to disclose.

OS3220

Molecular diagnosis and disease gene identification in neurological disorders using exome sequencing

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Introduction: Genetic and clinical heterogeneity make the molecular diagnosis of various neurological disorders challenging. One example are disorders arising from faulty oxidative phosphorylation. Despite good progress in the field, most disease causing mutations still have to be identified.

Methods: We applied exome sequencing to 300 unrelated individuals with suspected mitochondrial disease. Variant filtering was performed to prioritize likely pathogenic mutations. Cellular studies were conducted to establish the disease-causing role of mutations in new disease genes and to gain insights into the physiological role of encoded proteins.

Results: In one quarter of patients, we identified mutations in known disease genes (e.g. *POLG1, TWINKLE*). In another quarter, we detected defects in genes previously not associated with mitochondrial disease. Clear candidate mutations were rare, predicted a loss-of-function, and affected evolutionary conserved genes such as *MGME1,* the first exonuclease to be involved in mitochondrial replication. The pathogenicity of other defects is supported by statistical evidence with one example being mutant *ACAD9* detected in 15 cases. More difficult is the interpretation of mutations in genes coding orphan proteins such as FBXL4 associated with reduced mitochondrial content. Evolving issues are factors involved in mitochondrial protein translation (tRNA synthetases, *ELAC2*, *MTO1*, and a new tRNA modifying enzyme) as well as perturbations of cofactor metabolism. The latter offer therapeutic perpectives such as riboflavin supplementation in hRFT2/3 defects.

Conclusion: Genome wide sequencing comprehensively detects causal mutations and enables identification of novel disease genes. Technological advances hold promise for improvement of the diagnostic yield and implementation in routine clinical testing.

Disclosure: Nothing to disclose.

OS3221

ATM mutations are not exclusively associated with ataxia-telangiectasia but may also cause focal or generalized dystonia

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Introduction: Ataxia-telangiectasia (A-T) is an autosomal recessive inherited disease characterized by progressive childhood-onset cerebellar ataxia, oculomotor apraxia, telangiectasias of the conjunctivae, and immunodeficiency caused by homozygous mutations in the *ATM* gene. Besides this classic manifestation several other non-classic forms exist including milder or incomplete A-T phenotypes. Recently, *ATM* mutations were found in 13 Canadian Mennonites with primary-appearing dystonia, a French family with generalized dystonia and in a Muslim Indian family with dopa-responsive cervical dystonia.

Methods: A 45-year-old German female patient reported delayed motor development, speech and swallowing difficulties, impaired trunk and head control, and abnormal posturing since childhood. Physical examination revealed generalized dystonia including torticollis and dystonic head tremor. Ataxia of stance and gait and telangiectasias were absent. There was no family history of neurological disease. The further diagnostic workup including brain MRI, neuronal electrophysiology, cerebrospinal fluid, and neuropsychological testing was unremarkable.

Results: Alpha fetoprotein was highly increased to 208 kIU/l (normal < 5.8). Genetic testing revealed compound heterozygous mutations in the *ATM* gene. The c.8147T>C, p.V2716A variant is a known causative A-T mutation, and the novel variant c.8578_8580delTCT is predicted to be pathogenic. Previous treatment with botulinum toxin, L-Dopa (300 mg/day), benzodiazepines and deep brain stimulation had no benefit.

Conclusions: This patient adds to the recent literature that *ATM* mutations are not exclusively associated with A-T but may also cause focal or generalized dystonia.

Disclosure: Nothing to disclose.

OS3222

Influence of *MTHFR*, *eNOS*, *ACE* and *ApoE* haplotypes in modulating serum vitamin profiles among ischaemic stroke patients

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Introduction: Hyperhomocysteinemia, endothelial dysfunction, deregulation of blood pressure and impaired cholesterol metabolism may increase the risk of individuals towards ischaemic stroke. The aims of this study are to (i) investigate the association of methylenetetrahydrofolate reductase (*MTHFR*), endothelial nitric oxide synthase (*eNOS*), angiotensin converting enzyme (*ACE*) and apolipoprotein E (*ApoE*) gene polymorphisms and/or haplotypes with

ischaemic stroke susceptibility and (ii) to compare serum vitamin profiles with *MTHFR*, *eNOS*, *ACE* and *APOE* gene polymorphisms and/or haplotypes.

Methods: Cases (n = 297) and controls (n = 297) originating from three generations of Kelantan's Malays were recruited. The rs1801133 and rs1801131 in *MTHFR*; rs2070744, variable number tandem repeat (VNTR) and rs1799983 in *eNOS*; rs4646994 in *ACE* and rs429358-rs7412 in *ApoE* were genotyped and the haplotypes were inferred. Serum vitamin profiles (homocysteine, folate, vitamin B_{12}) were determined.

Results: Both rs1801133 [adjusted OR = 5.67; 95 % ± CI:2.27–14.19; p = 0.001] and *eNOS* VNTR [adjusted OR = 16.77; 95 % ± CI:8.71–32.29; $p < 0.001$] were significantly associated with ischaemic stroke susceptibility due to their effects on serum homocysteine and vitamin B_{12} levels. Amongst the haplotypes, *MTHFR* $T_{rs1801133}A_{rs1801131}$ [adjusted OR = 1.98; 95 % ± CI:1.41–2.78; $p < 0.001$] and eNOS $T_{rs2070744}a_{VNTR}T_{rs1799983}$ [adjusted OR = 3.51; 95 % ± CI:2.51–4.89; $p < 0.001$] showed higher risk towards ischaemic stroke by increasing serum homocysteine [adjusted $\beta = 0.04$, p = 0.002 and adjusted $\beta = 0.04$, $p < 0.001$ respectively] and vitamin B_{12} levels [adjusted $\beta = 0.04$, p = 0.031 and adjusted $\beta = 0.05$, $p < 0.001$ respectively] when compared to controls.

Conclusions: $T_{rs1801133}$ and a_{VNTR} are potential biomarkers for ischaemic stroke susceptibilities by influencing serum homocysteine and vitamin B12 levels leading to endothelial dysfunction and predisposition to ischaemic stroke.

Disclosure: The authors declare that there are no conflicts of interests.

OS3223

Genotype and phenotype heterogeneity of transthyretin-associated amyloidosis: a report from the German Amyloidosis referral center

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Introduction: Transthyretin (TTR)-associated amyloidosis is a rare, fatal protein-deposition disease characterized by a wide spectrum of genotypes and heterogeneous phenotypes. The aim of the present study is to describe genotypes and phenotypes of patients with TTR-amyloidosis evaluated at the Heidelberg Amyloidosis Center between 2001 and 2013.

Methods: Records of 220 patients with mutations within the TTR gene and/or histologically confirmed TTR amyloidosis were reviewed regarding cardiac and neurologic parameters to define different phenotypes, i.e. polyneuropathy (TTR-FAP), cardiomyopathy (TTR-FAC), mixed phenotype, wild-type amyloidosis (senile systemic amyloidosis, SSA), and asymptomatic gene carriers. TTR-FAC was diagnosed in patients with heart failure, diastolic dysfunction, LV-hypertrophy, pseudoinfarction pattern and/or bundle branch block. TTR-FAP was defined as neurologic symptoms consistent with sensorimotor polyneuropathy. The mixed phenotype was diagnosed if criteria for both, TTR-FAP and TTR-FAC, were present.

Results: Cardiac phenotype was present in 13 %, neurologic phenotype in 4 %, and mixed phenotype in 30 % of patients. SSA was diagnosed in 54 pts. Sixty patients were asymptomatic gene carriers. There were 29 different TTR-mutations, the most common being Val30Met and Val20Ile. Patients with SSA were almost exclusively male (93 %) and had cardiac involvement, whereas 72 % of mixed phenotype and 59 % of cardiac phenotype were male.

Conclusions: Mixed-type hereditary and wild-type amyloidosis were the two largest groups in our national referral center. A pure neurologic phenotype is rare. In patients with polyneuropathy of unknown etiology, cardiac involvement may provide an important clue towards the diagnosis of TTR-amyloidosis.

Disclosure: JP received travel support from Pfizer.

OS3224

Adult-onset leukoencephalopathies with predominant involvement of brainstem and cerebellum can be related to histiocytosis

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Introduction: Histiocytoses are disorders resulting from abnormal histiocyte proliferation, and—in children—they can determine neurological dysfunctions associated with a characteristic pattern of white matter abnormalities, predominantly involving cerebellum and brainstem (henceforth "infratentorial leukoencephalopathy" [ITL]). We aim to report the clinical and paraclinical features of nine adults admitted to our Institute with a diagnosis of ITL.

Methods: We reviewed the clinical and laboratory information of 7 males, and 2 females (all isolated cases) with prominent T2- and FLAIR-weighted signal abnormalities in the posterior fossa structures, unremarkable CSF examination, and no evidence of autoimmune or hereditary diseases.

Results: Mean age at presentation was 49 years (range 38–59); clinical features were a variable combination of ataxia, spasticity, cranial nerve dysfunction, cognitive decline, neurogenic bladder, and diabetes insipidus. Supratentorial white matter abnormalities and spinal cord lesions were present in three and four individuals, respectively. Tc99 m bone scintigraphy was consistent with histiocytosis in five individuals, and one had histiocytic (hairy-cell) leukemia. Retroperitoneal or bone biopsies confirmed the diagnosis in the four investigated cases.

Conclusions: Adult-onset ITL can be related to histiocytoses, and therefore the search for bone lesions is mandatory. There are substantial clinical and MRI similarities among the individuals with histologically proven histiocytosis and those with no evidence of systemic manifestations compatible with histiocytosis. Consequently, our cases support the hypothesis that the brain involvement—supposed to be paraneoplastic—may appear years before the onset of systemic manifestations, thus making a definite diagnosis impossible without a long-term follow-up.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 2

OS4101

Continue or stop pre-stroke antihypertensive therapy in acute stroke: main results from the efficacy of nitric oxide in stroke (ENOS) trial

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Background: A majority of patients are taking antihypertensive medication before their stroke. However, management of such treatment(s) remains unclear and is the subject of the ENOS trial.

Methods: ENOS is an international multicentre prospective randomised open-label blinded-endpoint trial. Patients with acute ischaemic stroke (IS) or intracerebral haemorrhage (ICH), systolic BP 140–220 mmHg, and taking antihypertensive therapy immediately before their stroke were randomised to continue or stop this for 7 days; all patients were also randomised to transdermal glyceryl trinitrate (GTN) or no GTN (single-blind, results reported separately). The primary outcome is shift in modified Rankin Scale at 3 months. Patients or relatives gave written informed consent and all sites had research ethics approval. Analysis is by intention-to-treat.

Results: 2,097 patients were enrolled from 152 sites in 23 countries across 5 continents between July 2001 and October 2013 (with 82 % patients recruited from start of 2007). At baseline: age 73 (SD 11); male 51 %; recruitment from Asia 10 %, Europe 19 %, UK 65 %; number of BP drugs before stroke, 1: 44 %, 2: 35 %, 3: 16 %, 4: 4 %, >4: 1 % (median 2); angiotensin modifier 64 %, beta-blocker 39 %, calcium channel blocker 35 %, diuretic 35 %, alpha-blocker 7 %; prior stroke 20 %; diabetes 23 %; atrial fibrillation 22 %; mean BP 167 (19)/88 (13) mmHg; severity (Scandinavian Stroke Scale) 33 (13)/58; total anterior circulation syndrome 33 %; IS 85 %, ICH 12 %; median time to recruitment 26 (IQR 20) hours.

Summary: The main results will be available for presentation in quarter 2 2014. ENOS is large enough to influence clinical practice.

Disclosure: Nothing to disclose.

OS4102

Exosomes reduce brain injury in a rodent stroke model via immunomodulatory actions and stimulation of post-ischemic neuroregeneration

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Introduction: Mesenchymal stem cells (MSCs) induce neuroprotection against cerebral ischemia without being integrated into residing neural networks. Rather, MSCs seem to modulate post-ischemic immune responses in a paracrine way. Recent findings suggest that immunomodulatory properties of MSCs are mediated by exosomes. Accordingly, these small extracellular vesicles (70–140 nm) might provide a powerful, alternative therapeutic tool in experimental stroke research.

Methods: Male C57BL6 mice were exposed to cerebral ischemia for 30 min. MSC-derived exosomes or PBS were intravenously administered on days 1, 3 and 5 post-stroke. To compare exosome efficacy, MSCs were injected on day 1 followed by PBS injections on days 3 and 5. Brain injury, functional outcome, neurogenesis and peripheral/cerebral immune states were analyzed for up to 28 days post-stroke.

Results: In comparison to PBS controls, application of MSC-derived exosomes reduced the extent of brain injury and enhanced functional recovery during the 4 week lasting observation period in a similar manner as did injected MSCs. Ongoing experiments revealed that MSC-derived exosomes promote neuroregeneration by fostering endogenous neurogenesis and—as revealed via flow cytometric analysis—by affecting the immune state in the peripheral blood and within the affected brain hemispheres.

Conclusions: Intravenous delivery of MSC-derived exosomes is neuroprotective. It enhances neuroregeneration and modulates post-ischemic immune responses. Thus, MSC-derived exosomes provide a non-cellular tool for stroke treatment, which might prove qualified for clinical treatment of stroke patients in the future.

Disclosure: Nothing to disclose.

OS4103

B-type natriuretic peptide predicts stroke of presumable cardioembolic origin in addition to coronary artery calcification

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Introduction: B-type natriuretic peptide (BNP) is a marker of cardiac dysfunction that is released from myocytes in response to ventricular wall stress. Previous studies suggested that BNP predicts stroke events in addition to classical risk factors. It was suggested that the BNP-associated risk results from coronary atherosclerosis, atrial fibrillation or heart failure.

Methods: 3675 subjects from the population-based Heinz Nixdorf Recall study (45–75 years; 47.6 % men) without previous stroke, coronary heart disease, myocardial infarcts, open cardiac valve surgery, pacemakers and defibrillators were followed up over 9.2 ± 1.9 years. Cox proportional hazards regressions were used to examine BNP as stroke predictor in addition to vascular risk factors (age, gender, systolic blood pressure, LDL, HDL, diabetes, smoking), renal insufficiency, atrial fibrillation/heart failure and coronary artery calcification.

Results: Eighty-nine incident strokes occurred (80 ischemic, 9 hemorrhagic). Subjects suffering stroke had significantly higher BNP values at baseline than the remaining subjects (26.3[Q1;Q3 = 12.9;51.0] vs. 17.4[9.4;31.4]; $p < 0.001$). In a multivariable regression, $\log_{10}$BNP was an independent stroke predictor (hazard ratio = 1.96[95 %-confidence interval = 1.13–3.41]; $p = 0.017$) in addition to age (1.24 per 5 years[1.04–1.49]; $p = 0.016$), systolic blood pressure (1.25 per 10 mmHg[1.14–1.38]; $p < 0.001$), smoking (2.05[1.24–3.39]; $p = 0.005$), atrial fibrillation/heart failure (2.25[1.05–4.83]; $p = 0.037$) and computed tomography-based $\log_{10}$ (coronary artery calcification + 1) (1.47[1.15–1.88]; $p = 0.002$). Log_{10}BNP predicted stroke in men, but not women, both in subjects ≤65 and >65 years. In subsequent analyses, BNP discriminated the incidence of cardioembolic stroke (p for trends = 0.001), but not stroke of macroangiopathic ($p = 0.555$), microangiopathic ($p = 0.809$) or unknown ($p = 0.367$) origin.

Conclusion: BNP predicts presumable cardioembolic stroke independent of coronary calcification.

Disclosure: Nothing to disclose.

OS4104

HMG-CoA reductase inhibition promotes stroke recovery perilesional tissue remodeling and contralesional pyramidal tract plasticity

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Introduction: 3-Hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors are widely used for secondary stroke prevention. Besides their lipid-lowering effects, pleiotropic effects on neuronal survival, angiogenesis and neurogenesis have been described. In view of these promising actions, we were interested whether post-acute HMG-CoA reductase inhibition promotes functional neurological recovery, perilesional and contralesional neuronal plasticity.

Methods: We examined effects of rosuvastatin (0.2–2 mg/kg/day i.c.v.), administered starting 3 days after 30 min of middle cerebral artery occlusion, on motor-coordination, perilesional tissue remodeling and contralesional axonal plasticity.

Results: Rosuvastatin, administered at a dose of 2 but not 0.2 mg/day, significantly increased the motor grip strength and coordination of ischemic mice, promoted exploration behavior and reduced anxiety. Neurological recovery was associated with structural remodeling of peri-lesional brain tissue, reflected by increased neuronal survival, enhanced angiogenesis, and reduced corpus callosum and striatal atrophy. Increased sprouting of contralesional pyramidal tract fibers crossing the midline in order to innervate the ipsilesional red nucleus was noticed in rosuvastatin compared with vehicle treated ischemic mice, as shown by anterograde tract tracing experiments using dextran amines injected in the motor cortex.

Conclusion: Our data support the idea that HMG-CoA reductase inhibition promotes brain plasticity far beyond the acute stroke phase.

Disclosure: Nothing to disclose.

OS4105

Motor recovery after ischemic stroke in mice is age-dependent and correlates with brain BDNF levels

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Objective: Ischemic stroke frequently affects motor function. This is of particular relevance in elderly patients who have a lower ability to recover from ischemic brain injury. Brain derived neurotrophic factor (BDNF) modulates activity-dependent synaptic plasticity in the motor cortex and improves motor symptoms after cerebral ischemia in young and otherwise healthy rodents. To uncover a potential age-dependent effect of BDNF on motor recovery after stroke, we investigated whether BDNF-expression after stroke correlates with age and whether different BDNF levels in young and aged mice may influence motor function.

Methods: 8-week- and 1-year-old wild-type (WT) as well as 8-week-old $bdnf^{+/-}$ mice were subjected to 30 or 60 min transient middle cerebral artery occlusion (tMCAO). 24 h after 60 min tMCAO BDNF protein levels and subcellular localization were determined. Motor recovery was assessed in mice undergoing 30 min tMCAO from day 1 to day 24 using a foot fault score (FFS).

Results: At day 1 after 60 min tMCAO, BDNF protein levels were significantly increased in young (8-week) versus aged (1-year) WT mice. Motor function analysis up to day 24 post stroke revealed an age-dependent correlation between BDNF content and motor recovery as young WT mice showed a significant improvement in the FFS compared to $bdnf^{+/-}$-mice and 1-year-old WT mice, respectively.

Conclusion: Motor recovery after stroke is age-dependent and depends on the expression of BDNF. Modulation of BDNF levels might become a promising strategy to improve stroke outcome especially in older patients.

Disclosure: Nothing to disclose.

OS4106

Cooperative hand movements in stroke patients: impaired neural coupling

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Introduction: Recent research indicates that task-specific, interhemispheric neural coupling is involved in the control of the cooperative hand movements required for activities of daily living. This neural coupling is reflected in bilateral electromyographic (EMG) reflex responses in the arm muscles to unilateral nerve stimulation and an exclusive activation of secondary somatosensory (S2) cortical areas during functional magnetic resonance imaging. The aim of this study was to investigate these reflex responses in the forearm muscles in chronic post-stroke patients.

Methods: EMG responses in forearm muscles were reorded in 15 stroke patients and 12 healthy volunteers following unilateral electrical stimulations of the ulnar nerve during a dynamic-cooperative (dyn-coop) task and two control tasks.

Results: When the nerve of the unaffected arm was stimulated during dyn-coop, bilateral EMG responses were generated, similar to those seen in healthy subjects. Stimulation of the affected arm only evoked ipsilateral responses. The presence of contralateral EMG responses correlated with the clinical motor impairment as measured using the Fugl-Meyer test. Only ipsilateral EMG responses were recorded during the control tasks.

Conclusions: These observations suggest impaired processing of afferent input leading to defective neural coupling during cooperative hand movements after stroke. In severely affected patients, movement execution seems to rely on the involvement of the ipsilateral tract arising in the non-damaged hemisphere. The rehabilitation of stroke patients, currently focused on reach and grasp movements of the affected arm/hand, should be supplemented with the training of the cooperative hand movements required during activities of daily living.

Disclosure: Nothing to disclose.

Multiple sclerosis and related disorders 3

OS4201

Active-controlled study to investigate the ability of the HAP score to predict responders to Octagam 5 % in patients with early relapsing multiple sclerosis (PREDICT study)

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Introduction: Since three decades treatment of multiple sclerosis (MS) patients with intravenous immunoglobulin (IVIG) has been employed. However, after somewhat contradicting study results, it seems possible that only a subgroup of patients benefits from IVIG therapy. We hypothesise, based on results from open-label, exploratory predecessor study GAM-25 in 33 patients with relapsing-remitting multiple sclerosis (RR-MS) that responsiveness to IVIG therapy might be individually predictable by combination of immunologic and genomic parameters.

Methods and results: Patients on glatiramer acetate or IFN-beta will be randomised to IVIG treatment (0.6 g/kg Octagam® 5 % at 4-week intervals) or alternate first-line therapy. Before enrolment, 9 predictive genotypes will be combined with quartile based scores of 66 immune parameters—including leukocyte phenotypes, plasma cytokine levels as well as basic and induced gene expression. In a stepwise approach for each genotype 0–4 biomarkers will be added using linear discriminant analysis. Non-responders are defined as being positive for 5 or more out of 9 individually calculated scores.

Clinical response is defined after 2 years treatment if a) no relapses, b) Expanded Disability Status Scale (EDSS) not increasing by $\geq$1.0 step, and c) no MRI activity. Confirmatory, active-controlled, rater-blinded PREDICT study (GAM-27) started enrolling 216 adult patients with early relapsing MS and EDSS $\leq$3.5 in December 2013.

Conclusions: Combining genomic and functional immune parameters into a biomarker panel could be the first step to support personalised medicine by prospectively allowing the discrimination of individual immunotypes into responders and non-responders to IVIG therapy in patients with relapsing MS.

Disclosure: The study is sponsored by Octapharma AG, Seidenstrasse 2, 8853 Lachen, Switzerland.

OS4202

Patients who switch to natalizumab have better outcomes than those who continue on the same platform therapy after a relapse

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Introduction: Randomized clinical trials comparing treatment options for patients who relapse on a platform therapy (interferon-beta [IFN-beta] or glatiramer acetate [GA]) are not available. Propensity-matching patients from observational cohorts can approximate randomization by comparing patients with similar baseline characteristics. Clinical outcomes and treatment discontinuation were compared between propensity-matched patients who either switched to natalizumab or who continued on the same platform therapy after an on-treatment relapse.

Methods: 759 patients from the MSCOMET study who remained on IFN-beta or GA after relapse were propensity-matched based on age, sex, disease duration, EDSS score, number of prior treatments and relapse history to 759 patients from the TOP study who switched to natalizumab within 12 months of relapse on IFN-beta or GA (Table 1). Times to next relapse on treatment and to treatment discontinuation were compared using Cox time-to-event analysis with propensity-matched patients jointly censored.

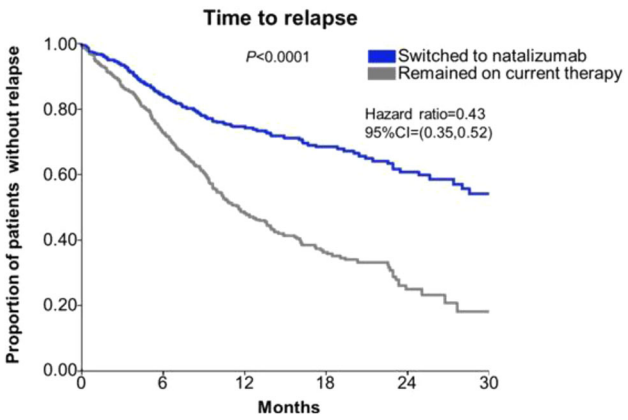
Results: Switching to natalizumab decreased the risk of future relapse by 57 % (HR = 0.43; 95 %CI = 0.35–0.52; $P < 0.0001$) (Fig. 1) and decreased the risk of treatment discontinuation by 52 % (HR = 0.48; 95 %CI = 0.40–0.58; $P < 0.0001$) (Fig. 2) compared to remaining on the same platform therapy after relapse (follow-up, years, mean[SD]: TOP, 1.80[1.24]; MSCOMET, 0.91[0.82]).

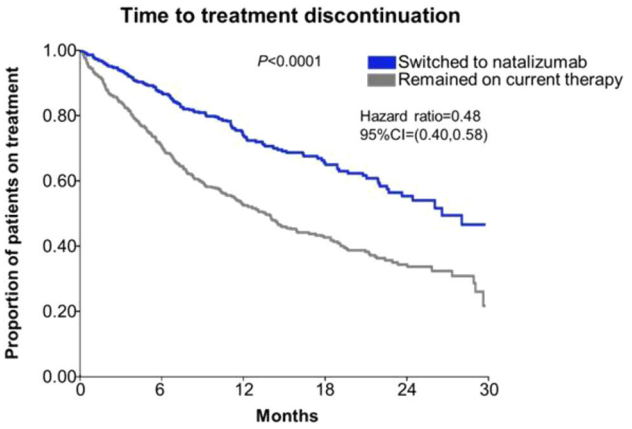
Conclusions: Switching to natalizumab after a relapse on IFN-beta or GA may improve clinical outcomes and reduce the risk of treatment discontinuation in MS patients. In the absence of relevant randomized clinical trials, comparisons of propensity-matched patients from large, observational cohorts are useful to estimate the relative risks associated with various treatment decisions in a clinical practice setting.

Table 1. Baseline characteristics of propensity matched patients

Baseline Characteristic	TOP (switched to natalizumab; n=759)	MSCOMET (remained on platform therapy; n=759)	*P*-value
Age, years, mean (SD)	39.28 (9.30)	39.15 (10.27)	0.5866
Sex, % female	72	73	1.0000
Disease duration, years, mean (SD)	9.80 (6.87)	9.88 (7.20)	0.9942
Percentage of disease on treatment, mean (SD)	58 (38)	57 (26)	0.8587
No. of prior treatment starts, mean (SD)	1.53 (0.80)	1.55 (0.84)	0.4970
EDSS, median (IQR)	3 (2,4)	2.5 (2,4)	0.9679
No. of relapses in prior year, mean (SD)	1.21 (0.58)	1.26 (0.63)	0.2239
Steroid-treated relapses in prior year, mean (SD)	0.72 (0.66)	0.75 (0.68)	0.0923
No. of relapses in prior 2 years, mean (SD)	1.73 (0.94)	1.78 (1.04)	0.4770
Steroid-treated relapses in prior 2 years, mean (SD)	0.99 (0.88)	1.05 (0.96)	0.0826

Abbreviations: EDSS = Expanded Disability Status Scale; IQR = interquartile range; nat = natalizumab; SD = standard deviation





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OS4203

After a relapse, patients who switch to natalizumab have better outcomes than those who switch between platform therapies

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Introduction: Randomized clinical trials comparing treatment options after patients relapse on platform therapies (interferon-beta [IFN-beta] or glatiramer acetate [GA]) are not available. Propensity-matching techniques approximate randomization by comparing patients with similar baseline characteristics. Using propensity-matched groups, clinical outcomes and treatment discontinuation were compared between patients who switched to natalizumab and those who switched between IFN-beta and GA after an on-treatment relapse.

Methods: From MSBase and TOP observational studies, 578 patients switching from IFN-beta to GA and 165 patients switching from GA to IFN-beta were propensity-matched (based on age, sex, disease duration, EDSS score, prior number of treatments and relapse history) to equivalent numbers who switched to natalizumab (Table 1); treatment switches occurred $\leq$12 months after relapse. Times to next relapse on treatment and to treatment discontinuation were compared using Cox time-to-event analysis with propensity-matched patients jointly censored (mean follow-up = 1.69–2.24 years).

Results: Switching to natalizumab reduced relapse risk by 63 % (Fig. 1) and discontinuation risk by 62 % (Fig. 2) compared to switching from IFN-beta to GA. Switching to natalizumab reduced relapse risk by 53 % (HR = 0.47; 95 %CI = 0.30–0.74; $P < 0.001$) and discontinuation risk by 48 % (HR = 0.52; 95 %CI = 0.36–0.75; $P < 0.001$) compared to switching from GA to IFN-beta.

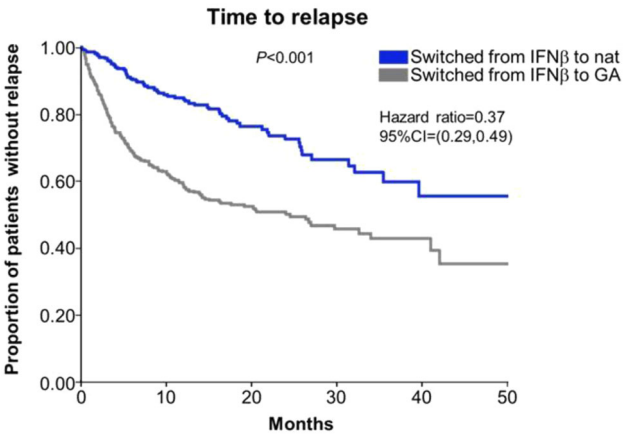
Conclusions: When considering treatment sequence for MS patients who relapse on platform therapies, switching to natalizumab rather than switching between IFN-beta and GA may improve clinical outcomes and reduce the risk of treatment discontinuation. In the absence of randomized clinical trials, propensity-matching techniques can compare the risks associated with various treatment decisions in a clinical practice setting.

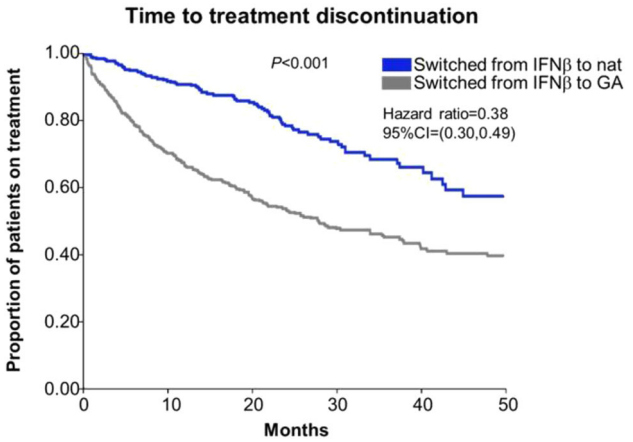
Table 1. Baseline characteristics of propensity matched patients' groups*

Baseline Characteristic	TOP IFNβ to nat (n=578)	MSBase IFNβ to GA (n=578)	TOP GA to nat (n=165)	MSBase GA to IFNβ (n=165)
Age, years, median (IQR)	38 (31,44)	37 (30,43)	38 (30,45)	38 (32,46)
Sex, % female	76.5	76.1	80.0	78.8
Disease duration, years, median (IQR)	6.3 (3.2,11.9)	5.8 (2.8,11.2)	6.4 (3.1,10.3)	5.5 (2.6,10.3)
Percentage of disease time on treatment, median (IQR)	40 (20,70)	40 (20,70)	30 (10,50)	30 (10,60)
No. of prior treatment starts, median (IQR)	1 (1,2)	1 (1,2)	1 (1,1)	1 (1,1)
EDSS, median (IQR)	3 (2,4)	3 (2,4)	3 (2,4)	2.5 (2,4)
No. of relapses in prior year, mean (SD)	1.6 (0.8)	1.6 (0.9)	1.76 (0.85)	1.84 (0.95)
Steroid-treated relapses in prior year, mean (SD)	1.0 (0.8)	1.0 (0.9)	1.15 (0.87)	1.19 (0.97)
No. of relapses in prior 2 years, mean (SD)	2.4 (1.2)	2.4 (1.3)	2.6 (1.3)	2.6 (1.4)
Steroid-treated relapses in prior 2 years, mean (SD)	1.4 (1.1)	1.4 (1.3)	1.6 (1.3)	1.6 (1.3)

Abbreviations: EDSS = Expanded Disability Status Scale; IQR = interquartile range; nat = natalizumab; SD = standard deviation

* P>0.05 for all post-matching comparisons of baseline characteristics





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OS4204

Clinical efficacy and safety of peginterferon beta-1a in patients with relapsing-remitting multiple sclerosis: 2-year data from the pivotal phase 3 ADVANCE study

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Objectives: At Year 1 of the ADVANCE study, in patients with relapsing-remitting multiple sclerosis (RRMS), subcutaneous peginterferon beta-1a (PEG-IFN; 125 μg administered every 2 [Q2W] or 4 [Q4W] weeks) provided benefits versus placebo. Here, we evaluate the interim 2-year efficacy and safety of PEG-IFN in ADVANCE.

Methods: During Year 2 all patients received dose-regimen blinded PEG-IFN (at the end of Year 1 patients on placebo were re-randomised to PEG-IFN 125 μg Q2W or Q4W). Interim analyses were conducted for patients with 2 years of data at cut-off. Post-hoc analyses compared the efficacy of Q2W versus Q4W.

Results: For patients continuing PEG-IFN in Year 2, annualised relapse rate (ARR) was maintained (for Q4W) or further numerically reduced (for Q2W) versus Year 1, and new or newly-enlarging T2 lesions were numerically lower for both regimens. Versus those originally assigned to placebo, reductions in ARR, risk of relapse and disability progression were seen for patients on PEG-IFN over 2 years. Q2W provided numerically larger treatment effects over 2 years versus Q4W for the majority of efficacy measures. Over 2 years, adverse events (AEs) were reported in 96% of patients on both Q2W and Q4W; the majority were mild or moderate in severity. Incidences of serious AEs were 16% on Q2W and 21% on Q4W.

Conclusions: Interim 2-year results support the maintained benefits of PEG-IFN beyond 1 year in RRMS, with numerically greater efficacy for Q2W versus Q4W, and a safety profile consistent with Year 1 of ADVANCE and other beta interferons.

Disclosure: Study sponsored by Biogen Idec Inc. (Cambridge, MA, USA). BCK: honoraria from Bayer Schering, Biogen Idec Inc., Merck Serono, Novartis, Roche, Sanofi Aventis, and Teva Neurosciences, and financial support for research from Bayer Schering, Biogen Idec Inc., Merck Serono, and Teva; LB: consulting fees from Biogen Idec Inc., Vaccinex, Questcor, and Novartis; AB: consulting fees from Bayer Schering, Merck Serono, Teva, Novartis, Biogen Idec Inc., Nycomed-Takeda, and Genzyme-Sanofi; JP: consulting fees, grant and research support from Allergan, Biogen Idec Inc., Bayer Schering, Merck Serono, Genzyme, Novartis, Sanofi, and Teva; SL, YZ, AS, SH, AD: employees of Biogen Idec Inc.

OS4205

Oral versus intravenous high doses of methylprednisolone in multiple sclerosis relapses, a double blinded randomised controlled trial (COPOUSEP): results at 1 month (primary end-point)

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Introduction: Intravenous (IV) high doses of Methylprednisolone (MP) for 3–5 days are commonly recommended to accelerate Multiple Sclerosis (MS) relapses recovery. MP administered orally would simplify and consistently minimize the procedure's cost. To date, insufficient data have been published to validate the use of MP orally in MS relapses. This study aims to compare oral versus IV efficacy and safety of MP, 1 g/day for 3 days, for the treatment of MS relapses.

Methods: COPOUSEP is a French multicenter, double blinded randomized, non-inferiority, controlled trial. 200 relapsing MS patients were randomized to receive MP 1 g/day for 3 days orally or IV. Main inclusion criteria were: residual EDSS 0–5 before relapse; relapse onset 15 days or less before MP 1st administration; at least 1 increased point of Kurtzke EDSS scale functional system and raising a score of 2 points or more (3 or more for the "sensory" function). EDSS scores were measured at 3, 8, 28 and 180 days, new relapses were recorded prospectively; tolerance was

evaluated by auto-questioners at 2, 3, 4, 8 and 28 days and safety data were collected up to 180 days. Primary end-point was the percentage of patients improved at day 28 (decrease by at least 1 point of the most affected functional system), without retreatment with MP.

Results: Efficacy at Day 28 (primary end-point) and safety results will be available in June 2014.

Conclusion: COPOUSEP is the first non-inferiority trial comparing oral versus IV administration of MP for the treatment of MS relapses with sufficient power.

Disclosure: Nothing to disclose.

OS4206

Effect of teriflunomide on MRI activity in patients with early MS: outcomes from the phase 3 TOPIC study

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Introduction: Teriflunomide is a once-daily oral immunomodulator for relapsing-remitting multiple sclerosis (RRMS). The phase 3 TOPIC study (NCT00622700) assessed use of teriflunomide in patients with a first clinical episode consistent with MS plus $\geq$2 lesions. This analysis evaluated treatment effect on magnetic resonance imagining (MRI) activity.

Methods: Randomised patients received once-daily teriflunomide 14 mg, teriflunomide 7 mg, or placebo. When reaching the primary endpoint (risk of relapse determining clinically definite MS), patients could enter an open-label extension. MRI was performed at screening, 12, 24, 48, 72, and 108 weeks (pre-defined main timepoint for analysis), and processed at a centralised analysis centre.

Results: Baseline characteristics were generally balanced ($n = 618$). At baseline, 31.4 % had $\geq$1 gadolinium (Gd)-enhancing lesion and mean total lesion volume (TLV) was 8.66 mL. Teriflunomide 14 mg significantly reduced TLV increase from baseline at 108 weeks ($p = 0.04$ vs placebo), at all other timepoints and as early as 12 weeks ($p \leq 0.04$ vs placebo). Teriflunomide 14 mg reduced number of Gd-enhancing T1 lesions per scan vs placebo (0.40 vs 0.95); relative risk reduction 58.5 % ($p < 0.001$); total enhanced volume per scan 0.03 vs 0.08 ($p < 0.0001$ vs placebo). Teriflunomide 14 mg significantly reduced the volume of T2-lesion component at every visit ($p < 0.05$ vs placebo), except 12 and 108 weeks ($p = 0.0503$). Apart from week 24 ($p = 0.0524$), teriflunomide 14 mg significantly decreased T1-hypointense lesion volume from baseline ($p < 0.05$ vs placebo) at all visits.

Conclusions: In patients with early MS, teriflunomide 14 mg had a significant, positive impact on MRI activity supporting the observed beneficial clinical effects.

Disclosure: Study supported by Genzyme, a Sanofi company. Authors supported by Abbvie (JW), Alkermes (JW), Acorda Therapeutics (AM), Actelion (GC, LK), Allozyne (LK), Almirall (GC), Bayer (GC, LK), Bayer Schering Pharma (LK), Bayhill (LK), Biogen (GC), Biogen Idec (AM, LK), Chemicon International (JW), CLC Behring (LK), EMD Serono (AM, JW), Genentech (AM), GeNeuro SA (LK), Genmab (LK), Genmark (LK), Genzyme (GC, AM, JW, LK), GlaxoSmithKline (AM, LK), Hoffman LaRoche (JW), Jansen RND (JW), Lilly (LK), Medscape CME (JW), Merck Serono (GC, LK), Mitsubishi Pharma (LK), Novartis (GC, AM, JW, LK), Novonordisk (LK), Nuron Biotech (AM), ONO (AM), Osmotica (AM), Peptimmune (LK), PRIME (JW), Questcor (AM), Roche (AM, LK), Sanofi (GC, AM, JW, LK), Santhera (LK), Teva (GC, AM, JW), Teva Neurosciences (JW), UCB (LK), Xenoport (LK), Wyeth (LK). DB is an employee of Sanofi. PT is an employee of Genzyme, a Sanofi company.

ePoster sessions

Ageing and dementia 1

EP1101

Neuronal correlates of anosognosia for memory impairment in Alzheimer disease: the role of posterior cingulate cortex

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Introduction: Anosognosia for memory deficits has major impact on caring for Alzheimer's disease (AD). However, the neural mechanisms of anosognosia in AD remain unclear. The aim of this study was to acquire multimodal brain imaging in a sample of patients, to search for brain regions that differ between patients and elderly controls and to evaluate the contribution of brain regions to anosognosia in AD.

Methods: We compared 31 patients with probable AD and 19 cognitively intact healthy volunteers using Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET). Participant's awareness of current memory functioning was assessed with the memory awareness rating scale (MARS). We used statistical parametric mapping (SPM8) to compare both groups in each modality and to correlate brain imaging measurements and anosognosia scores in AD patients, controlling for dementia severity, age, gender and education.

Results: In the group comparison, we found a significant hypometabolism of the posterior cingulate cortex (PCC) and parietofrontal associative cortices in Alzheimer patients with PET. Additional analysis with voxel based morphometry (VBM) also showed cortical atrophy of the PCC and the medial temporal regions. Finally, in Alzheimer patients, correlation between anosognosia scores and hypometabolism extending from ventral to dorsal PCC was evidenced.

Conclusions: The PCC is a hub region of the default mode network, notably involved in self-referential processing. In addition to confirming the vulnerability of the PCC in AD, these results suggest that the disturbance of the PCC is implicated in loss of self-knowledge in AD.

Disclosure: Nothing to disclose.

EP1102

A fMRI graph theory study of the effect of gender and aging on topology of functional brain networks

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Introduction: To analyze age- and gender-related effects on large-scale functional brain networks using a graph theory approach.

Methods: Graph theoretical analysis was applied to resting state (RS) fMRI data from 132 healthy controls (62 men and 70 women, mean age = 40.6 years, range = 8–84 years). The global topology of functional networks was examined by computing the average degree, clustering coefficient, characteristic path length, global and local efficiency, hierarchy and assortativity. Regional network properties, including the integrated degree and local efficiency of each network node, were also assessed. The effects of age, gender and "age *x* gender" interactions on global functional network measures were assessed by using linear regression models.

Results: Significant age-related abnormalities (i.e., lower degree, clustering coefficient, local and global efficiency and hierarchy; and higher path length and assortativity) were detected in both genders. Males showed higher average network values than females. Both genders experienced a significant age-related decline of nodal degree and local efficiency of several regions of the frontal lobe (including the bilateral anterior cingulate cortex, middle and superior frontal gyrus, orbitofrontal cortex, precentral gyrus and supplementary motor area), temporal regions, posterior cingulate cortex/precuneus and deep gray matter nuclei. No significant "age *x* gender" interaction was found for global and regional network metrics.

Conclusions: Age-related decline of functional network measures were detected in both genders. The effect of aging was more severe in regions of the frontal lobes and the basal ganglia than in the other brain areas. Gender does not influence such an altered network connectivity with aging.

Disclosure: MAR speakers honoraria from Biogen Idec and Serono Symposia International Foundation. FA funding for travel from Teva and speaker honoraria from Bayer, Biogen, Sanofi Aventis, SSIF.MF received compensation for consulting and/or speaking from Bayer, Biogen Idec, Merck Serono, and Teva.

EP1103

[^{18}F]FDG-PET evidence of selective medial temporal lobe dysfunction in prodromal Alzheimer's disease

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Introduction: [^{18}F]FDG-PET imaging is a fundamental prognostic marker in mild cognitive impairment (MCI), supporting the presence of Alzheimer's Disease (AD) pathology by the evidence of the typical temporo-parietal pattern. A limbic-predominant AD subtype has been defined on the basis of the prevalent distribution of neurofibrillary tangles in the hippocampus compared with the cortex. In this study, we evaluated [^{18}F]FDG-PET brain metabolic changes and hippocampal volume in a sample of amnestic MCI subjects with long-term disease course (range 3–7 years).

Methods: Within a large series of MCI subjects, we selected 13 cases with persistent, selective long-term memory impairment. Optimized voxel-based statistical parametric mapping (SPM) procedure was used to assess brain metabolic changes in single subjects. Medial temporal lobe atrophy was measured with voxel-based morphometry (VBM). Clinical-neuropsychological features and CSF profile were also obtained.

Results: The majority of cases showed an unusually selective medial temporal hypometabolism. None showed the typical AD pattern. VBM analysis showed significant atrophy in the hippocampal structures, less extended than the hypometabolic pattern. Low CSF A-beta42 values supported the diagnosis of prodromal AD.

Conclusion: In this MCI group with predominant episodic memory deficits and very slow rate of progression of memory impairments, [^{18}F]FDG-PET and VBM findings suggest a specific and more limited anatomo-functional pattern, in comparison to the typical prodromal AD, compatible with the pathological limbic-predominant subtype. Single-subject [^{18}F]FDG-PET imaging can be useful in revealing MCI subtypes with more favourable prognosis and in subject selection for clinical trials.

Disclosure: Nothing to disclose.

EP1104

Clock drawing test: validation studies with multiple forms of dementia

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Introduction: The Clock Drawing Test (CDT) is a classic instrument preferably used for the assessment of constructive/visuospatial functions. Its clinical and investigational use has shown potential for the detection of cognitive impairment in populations with dementia, especially Alzheimer's disease (AD).

Methods: We selected patients with a clinical diagnosis of mild stage AD, frontal variant Frontotemporal dementia (fv-FTD), vascular dementia (VaD), Dementia with Lewy Bodies (DLB) and Parkinson's disease (PD). All subjects were assessed with the Mini-Mental State Examination, the Montreal Cognitive Assessment, the Clinical Dementia Rating scale and the CDT. The CDT was scored according to three scoring systems: Rouleau et al., 1992; Cahn et al., 1996; and Babins et al., 2008.

Results: We included 557 subjects (225 AD, 102 fv-FTD, 126 VaD, 51 DLB and 53 PD), 50.6 % female. The results showed the existence of significant differences between the several diagnoses, for the three scoring systems, with the following pattern of results: AD, DLB < fv-FTD, VaD. Once we controlled the effects of cognitive screening test scores and age, only the Cahn scoring system was able to significantly discriminate AD and DLB patients from fv-FTD and VaD patients. This particular discriminatory capacity was due to the qualitative analysis of the clock drawing errors, namely stimulus-bound response and conceptual deficit, both considered typical of AD patients.

Conclusions: Our results support the CDT potential as a cognitive screening measure particularly sensitive to AD pathology and similar cognitive deficits, a fact more evident for the Cahn scoring system.

Work supported by the Lundbeck Foundation.

Disclosure: Nothing to disclose.

EP1105

Cross-sectional clinical, neuropsychological, neuroimaging, and neurophysiological characterization of mild cognitive impairment patients in WP5 PharmaCog/E-ADNI study

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Parnetti[7], P. Payoux[12], A. Picco[11], D. Quaranta[10], J.-P. Ranjeva[6], L. Roccatagliata[11], P.M. Rossini[10], N. Salvadori[7], P. Schonknecht[13], A. Soricelli[14], M. Tsolaki[15], F. Vecchio[2], P.J. Visser[16], J. Wiltfang[17], G.B. Frisoni[1,18], on behalf of the PharmaCog Consortium

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Introduction: Workpackage5 of PharmaCog (E-ADNI) is a serial multicenter European study aimed to identify new cognitive, neuroimaging, neurophysiological, and biochemical biomarkers of disease progression in patients with amnestic mild cognitive impairment (aMCI).

Methods: We report cross-sectional data of the 147 patients enrolled in 13 memory clinics in Italy (Brescia, Genoa, Naples, Perugia, Rome), France (Marseille, Toulouse, Lille), Spain (Barcelona), Germany (Essen, Leipzig), Greece (Thessaloniki), and The Netherlands (Amsterdam). Patients underwent clinical and neuropsychological evaluation, high resolution 3T MRI with MPRAGE, T2*, FLAIR, resting state, and DTI acquisitions, EEG with resting state and auditory P300 recording, lumbar punctures assessing Abeta42, tau and p-tau, and blood samples. Patients were divided into Abeta positive (CSF-POS) and negative (CSF-NEG) based on CSF Abeta42 levels.

Results: CSF-POS have worse performance relative to CSF-NEG patients on visual memory (delayed matching to sample test 72.0 ± 15.1 vs 62.7 ± 16.9 respectively, $p = .002$ and spatial recognition memory 67.5 ± 12.5 vs 58.8 ± 12.9 respectively, $p < .0005$), and working memory (spatial working memory score 48.3 ± 21.3 vs 39.4 ± 20.8 respectively, $p = .02$). Moreover, CSF-POS have reduced volumetric (hippocampus, caudate, putamen, pallidum and lateral ventricles), thicknesses (enthorinal, fusiform and parahippocampal gyrus), and diffusion (splenium of the corpus callosum) measures, and a specific EEG pattern of cortical sources relative to CSF-NEG patients.

Conclusions: We found significant clinical, neuroimaging, and neurophysiological differences between aMCI patients with high and low CSF Abeta42 levels, suggesting that these two populations show different underlying pathology. Longitudinal data acquisition is ongoing and will clarify the impact of these biomarkers in predicting progression of the disease.

Disclosure: Nothing to disclose.

EP1106

Retinal plaques in Alzheimer's disease

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Objectives: To evaluate the existence of pathologic retinal deposits in patients with possible Alzheimer's Disease (AD).

Methods: We examined 20 patients with mild cognitive impairment, 10 of whom had family history of AD. Also, 10 patients with no complaints were examined. The age range was between 45 and 86. We performed fundus autofluorescence (FAF) test and optical scanning tomography (OCT) test on all of them. The retinal regions with hypofluorescent and hyperfluorescent images were taken into consideration and OCT was also performed through these lesions to detect the layer of the abnormality.

Patients with diabetic retinopathy and vascular occlusions were excluded.

Results: In 16 patients with mild cognitive defects we were able to find abnormal accumulations in the ganglion layer and nerve fiber layer. Some of the accumulations were hypofluorescent and others were hyperfluorescent on FAF.

In the other group of patients who had no complaints, only drusen on the pigment epithelium layer could be seen.

Conclusions: We believe that abnormal retinal deposits (possibly containing beta amyloid protein) can be observed in the ganglion and retinal fiber layers in patients who have high risk for AD. Retinal examination can be very helpful in the evaluation of these patients.

Disclosure: Nothing to disclose.

EP1107

Cognitive impairment in healthy Filipino adults with MRI white matter hyperintensities

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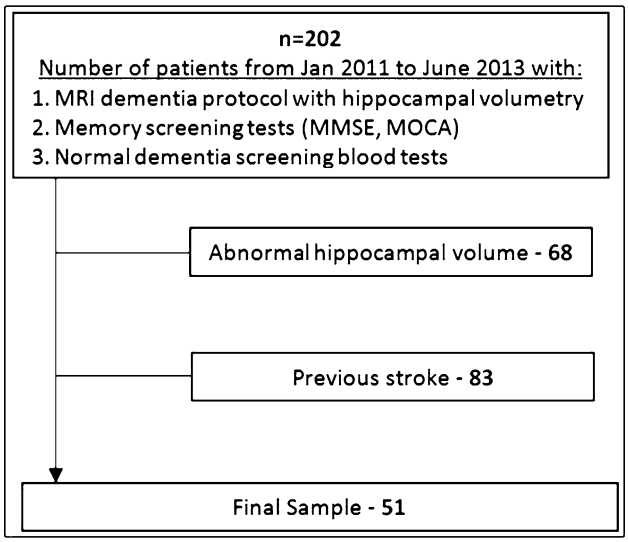
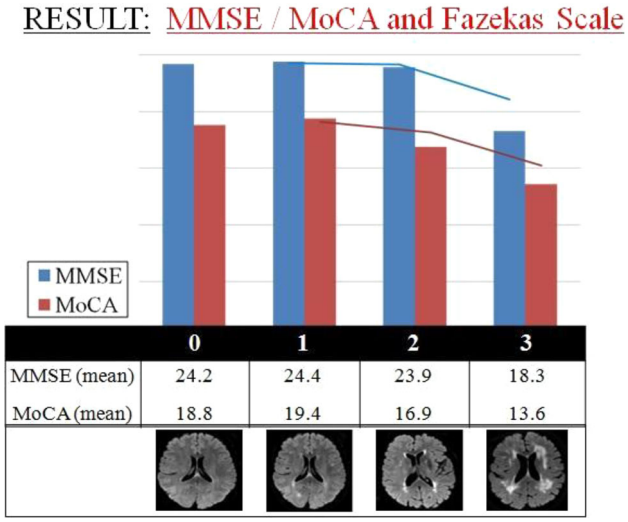
Introduction: White matter hyperintensities (WMH) are frequently seen in MRI of patients presenting with stroke or dementia, but are also observed to be present in healthy adults with no neurologic or cognitive impairment. Are they radiological findings of uncertain clinical significance? Or are they pre-clinical signs of dementia and cognitive decline. This paper studies the relationship of WMH and cognitive function of healthy Filipino adults with normal hippocampal volume and with no previous history of strokes.

Methods: 202 Filipinos with MRI hippocampal volumetry, neurocognitive screening tests and normal metabolic parameters were studied. Hippocampal volume was determined using NeuroQuant®, a software utilized by US-NIH studies for dementia. Those with low hippocampal volume and evidence of stroke were excluded. MRI were reviewed and WMH were graded using Fazekas scale. 51 patients were included in the final sample. Correlational statistics was used to determine relationship of WMH to neurocognitive scores.



Results: The higher the age, the greater is the Fazekas Score and WMH ($p = 0.004$). There is a clinically significant decrease in Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) Scores with the greater WMH. Most significant drop in scores between Fazekas 2 and 3.



Conclusions: This paper to the best of our knowledge is the first to use hippocampal volumetry to exclude subjects with Alzheimers and vascular dementia. Our results show that there is a clinically significant drop in neurocognitive scores with increasing WMH in healthy adults with no apparent clinical signs of dementia but only has WMH on MRI.

Disclosure: Nothing to disclose.

EP1108

Factors that predict cognitive decline in patients with subjective cognitive impairment

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Introduction: Current evidence supports the concept of a preclinical phase of Alzheimer's disease (AD) where pathological and imaging changes are present in asymptomatic individuals. Subjective cognitive impairment (SCI) may represent the earliest point on the continuum of AD. A better understanding of the baseline characteristics of this group of patients will enhance our knowledge of the very early disease process and facilitate preventive strategies, early diagnosis, timely follow-up and treatment. The aim of this study was to investigate which factors in SCI predict cognitive decline defined as a progression to a diagnosis of amnestic mild cognitive impairment (aMCI) or dementia at follow-up.

Methods: A retrospective observational study comparing baseline characteristics of patients with SCI who declined cognitively and those who did not.

Results: Patients who declined took significantly more medications for physical illnesses at baseline, were older by 9.78 years ($p = .001$) and reported that the onset of their memory problems was 10.3 years later than those that did not decline ($p = .001$). There were significant differences in test scores on the Trail Making B test and CAMCOG-R (attention subscale). Survival analysis demonstrated significant cut off points on key variables that predicted later decline (age of onset, age at first assessment, trail making test B and NART score). These cut-offs suggest differences in executive function, attention and cognitive reserve even at the stage of SCI.

Conclusions: Knowing which factors and test results in SCI predict conversion to aMCI or dementia can facilitate early detection, decision about frequency of follow-up and timely treatment.

Disclosure: Nothing to disclose.

EP1109

Study of Alzheimer's disease patients in a cohort of aged adults on the island of Crete, Greece suggests genetic predisposition for the disease

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Introduction: The aim of this project was to investigate the clinical, epidemiological and genetic characteristics of a cohort of aged adults on the island of Crete, Greece diagnosed with Alzheimer's disease (AD), mild cognitive impairment (MCI) and depressive disorder (DD).

Methods: A total of 3200 adults over 65 years of age visiting selected primary care physicians in the town of Heraklion, Crete and nearby villages were tested using a detailed questionnaire. Individuals scoring less than 23 or 24 (if <6 or ≥6 years of education, respectively) on the MMSE test were referred to the second phase physicians of the study (neurologists, psychiatrists, and geriatricians) and underwent neuropsychological evaluation. An interim analysis was performed in the first 138 consecutive patients diagnosed with AD (NINCDS/ADRDA criteria; $n = 45$), MCI (IWG criteria; $n = 71$) or DD ($n = 22$).

Results: Mean age (years) was 77.4, 77.2 and 76.2 for patients with AD, MCI and DD, respectively. The majority in all groups were females (60.0, 73.2 and 86.4 % for AD, MCI and DD, respectively). The mean MMSE was lower for AD (19.8) than for MCI (21.6) and DD (20.7) patients. The 3 groups were comparable concerning history of hypertension, diabetes mellitus, arthritis, osteoporosis and dyslipidemia. In this cohort, 46.5 % of AD patients had history of

dementia in a first degree relative, compared with 16.9 % of the MCI and DD patients examined together ($p = 0.001$).

Conclusion: The high frequency of dementia in first degree relatives of AD patients suggests a genetic component for the disease in our cohort.

Disclosure: Nothing to disclose.

EP1110

The Retzius–Cajal neuron in Alzheimer's disease

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Introduction: Retzius–Cajal neuron is the prominent neuron of the layer I of the brain's cortex. This is a large multipolar solitary neuron, mostly surrounded by astrocytes.

Methods: The structural morphology of the layer I of the temporal and occipital areas of the cortex of twenty cases of Alzheimer's disease was studied in rapid Golgi staining, Golgi–Nissl method and electron microscopy.

Results: In case of Alzheimer's disease Cajal–Retzius neuron, was dramatically reduced in comparison with normal controls brains of the same age. The electron microscopy revealed alterations of dendritic branches, decrease in spite density and morphological alterations of the mitochondria in the soma, the dendrites and the dendritic spines of Retzius–Cajal neurons. Tau pathology in the form of paired helical filaments were very rare in Retzius–Cajal neurons.

The synapses between the Retzius–Cajal neurons and the corticipetal fibers were dramatically reduced.

Conclusions: Retzius–Cajal neurons serve mainly in the development of horizontal connections in the cortex. Their loss in Alzheimer's disease may result in substantial alteration of the local functional fields of the cortex.

Disclosure: Nothing to disclose.

EP1111

Five-line fluency test is brief and effective screening for mild Alzheimer disease: norms and cut-offs

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Introduction: Figure fluency test may be a visual analogy of word fluency tasks and may briefly detect new distinct deficits in Alzheimer disease different from those measured by common tests. We aimed to establish norms for senior population and to find out cut-offs for mild AD patients.

Methods: We asked 645 normal elderly people (NEP) (the Mini-Mental State Examination (MMSE) 28 ± 2 points) and 46 patients with mild dementia due to Alzheimer disease (AD) (MMSE 23 ± 3 points) fulfilling NIA-AA recommendations to draw as many different figures using exactly five lines as possible within three minutes (five-LIne Fluency Test, LIFT).

Results: Mild AD patients produced significantly less figures than NEP in several aspects: total numbers (average: 9 vs 13), repeating figures (2 vs 3), repetition rate (16 vs 26 %), wrong figures (0 vs 3) and original correct numbers (4 vs 11) (all $p < 0.01$). The optimal cut-off of 6 correct figures yielded sensitivity 83 % and specificity 85 % with area under curve of receiver operating characteristic 0.9. LIFT scores in NEP are not influenced by gender, but they are significantly, yet poorly associated with age ($r = -0.15$) and education ($r = 0.2$).

Conclusions: LIFT is a short, simple, yet complex cognitive test that can be useful in everyday screening for AD with pencil and paper only. We provide normative data for the elderly which may be easily used in other countries due to non-verbal nature of the test.

Supported by grant IGA NT 13183, PRVOUK 34/LF3 and DRO (PCP, 00023752).

Disclosure: Nothing to disclose.

EP1112

The use of biomarkers for the etiologic diagnosis of mild cognitive impairment in Europe: a survey of the European Alzheimer's disease consortium

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Introduction: Revised diagnostic criteria for Alzheimer's Disease (AD) acknowledge a key role to imaging and biochemical markers for the early diagnosis of AD. We aimed to investigate the use of AD biomarkers in the European Alzheimer's Disease Consortium (EADC) centres and assess perceived usefulness for the etiologic diagnosis of mild cognitive impairment (MCI).

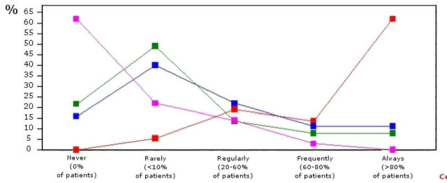
Methods: We surveyed the availability, the frequency of use, and the confidence in diagnostic usefulness of markers of brain amyloidosis (cortical amyloid burden on PET and CSF Abeta levels) and neurodegeneration (medial temporal atrophy [MTA] on MRI, temporoparietal and posterior cingulate hypometabolism on FDG-PET, and CSF tau levels). Questionnaires were filled by physicians of EADC centres in charge of patient care.

Results: The most frequently used biomarker is visually rated MTA (75 % of the 37 responders using it "always" or "frequently"), followed by CSF markers (22 %), FDG-PET (16 %) and amyloid PET (3 %) (Fig. 1). Although MTA is reported in clinical reports by 89 % of centres, only 45 % of them perceive it as contributing to diagnostic confidence, and contribution is rated as "moderate". 79 % of responders feel "very" or "extremely" comfortable delivering a diagnosis of MCI due to AD when both amyloid and neuronal injury biomarkers are abnormal ($p < .02$ versus any individual biomarker) (Fig. 2).

Conclusions: EADC Memory Clinics make fairly extensive use of biomarkers for the etiological diagnosis of MCI. Responders largely agree that a combination of amyloidosis and neuronal injury biomarkers is a persuasive AD signature.

Figure 1. Frequency of biomarker use in the assessment of patients with MCI in EADC centres.

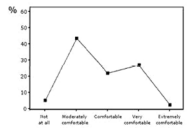
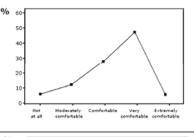
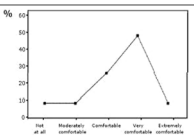
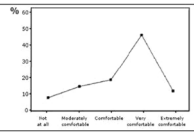
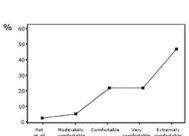
Values are presented as % and number of the 37 participating EADC centres. % reported in the graph corresponds to the one reported in the cells. Column headings of the table correspond to x-axis points on the graph.



						Centres using the biomarkers
Medial Temporal Atrophy	0 (0%)	2 (6%)	7 (19%)	5 (13%)	23 (62%)	37 (100%)
FDG PET	8 (22%)	18 (49%)	5 (13%)	3 (8%)	3 (8%)	29 (78%)
CSF abeta/tau	6 (16%)	15 (40%)	8 (22%)	4 (11%)	4 (11%)	31 (84%)
Amyloid PET	23 (62%)	8 (22%)	5 (13%)	1 (3%)	0 (0%)	14 (38%)

Figure 2.
Clinical vignette: physicians' diagnostic confidence.

Values are presented as % of responders.
P-value denotes significance at Mann-Whitney U-test.

		Difference in perceived strength of diagnostic confidence versus:			
		TP and PC hypo-metabolism ALONE	abnormal CSF Aβ and tau ALONE	abnormal amyloid PET ALONE	at least ONE abnormal amyloid + ONE abnormal
Medial temporal atrophy ALONE n=37		*p=0.019*	*p=0.010*	*p=0.026*	*p<0.00001*
TP and PC hypo-metabolism ALONE n=32		---	p=0.737	p=0.771	*p=0.004*
Abnormal CSF Aβ and tau ALONE n=35		---	---	p=0.988	*p=0.008*
Abnormal amyloid PET ALONE n=26		---	---	---	*p=0.016*
At least ONE abnormal amyloid + ONE abnormal neuronal injury marker n=36		---	---	---	---

Disclosure: Nothing to disclose.

EP1113

Crossed aphasia in a dextral patient with nonfluent/agrammatic variant of primary progressive aphasia

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Introduction: To describe a case of "crossed" nonfluent/agrammatic variant of primary progressive aphasia (nfv-PPA) evolving to an extrapyramidal syndrome.

Methods: We collected clinical/cognitive and neuroimaging data over 2 years from a 55-year old right-handed lady presenting with language disturbances, including ^{18}F-FDG PET; ^{123}I-DaTscan, and structural MRI. fMRI during verbal fluency generation was also performed to establish language hemispheric dominance, and diffusion tensor MRI was applied to evaluate the language network relative to controls.

Results: The patient presented with motor speech impairment characterized by slowness, difficulty on initiation with frequent stuttering, prosodic changes, hypophonia and frequent pauses. Mild agrammatism and difficulties in complex sentence comprehension were also present. ^{18}F-FDG PET and structural MRI revealed a selective involvement of the right middle and inferior frontal gyri (Broca's area). The clinical picture was highly suggestive of nfv-PPA. Over 2 years, language deficits worsened evolving to a full apraxia of speech with an overlapped mixed dysarthria. The patient developed a left-sided mild extrapyramidal bradykinetic-rigid syndrome. ^{18}F-FDG PET and structural MRI at year 2 showed a progression of brain damage to the right dorsolateral frontal cortex, frontal operculum, caudate nucleus and putamen. Homologous regions on the left hemisphere were mildly involved. DaTscan showed a decreased right putamen ^{123}I uptake. FMRI demonstrated a left hemispheric language dominance. Tractography showed a right superior longitudinal fasciculus severe damage.

Conclusions: Functional and structural imaging indicate a non-dominant hemisphere-related degeneration in patient with nfv-PPA. The occurrence of a left-sided extrapyramidal motor syndrome might suggest an underlying corticobasal degeneration.

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Disclosure: FA funding for travel from Teva and speaker honoraria from Bayer, Biogen, Sanofi Aventis, SSIF. CG received compensation for consulting and/or speaking from Novartis, Teva, Sanofi, Genzyme, Merck Serono, Biogen, Bayer, Actelion, SSIF. MF received compensation for consulting and/or speaking from Bayer, Biogen Idec, Merck Serono, and Teva.

Cerebrovascular diseases 1

EP1114

Association of asymptomatic peripheral arterial disease and ischemic stroke in Nigerians

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Introduction: The burden of stroke is likely to increase substantially over the next few decades in developing countries. The identification of asymptomatic PAD, a condition associated with increased vascular events and mortality in ischemic stroke, will help to reduce the economic and social burden associated with stroke.The primary aim of this study was to determine the association between asymptomatic PAD and ischemic stroke in Nigerians.

Methods: An analytical study carried out in the National Hospital, Abuja. One hundred patients (all confirmed by neuroimaging) and 100 controls were consecutively recruited and studied. Ankle-brachial index (ABI) was obtained in all participants using a hand-held 8-MHz

continuous-wave Doppler (Huntleigh 500 D) and a mercury sphygmomanometer (Accosson).

Results: The mean age of patients was 58.17 ± 12.29 years; while control group was 58.68 ± 10.8 years (P = 0.756). Among cases, male to female ratio was 2.2: 1. The mean ABI was lower among cases (1.03 ± 0.14 vs. 1.07 ± 0.14, P value = 0.043). The frequency of PAD in ischemic stroke patients was 18 %. PAD was associated with over 2-fold increased risk of ischemic stroke on univariate analysis (odds ratio (OR) 2.52, 95 % CI 1.042–6.113; P = 0.036).Multivariate analysis washowever not significant. PAD was associated with older age, diabetes mellitus, previous stroke, left ventricular hypertrophy and hyperlipidemia, after adjustment for potential confounders.

Conclusions: This study concludes that asymptomatic PAD increased the risk of ischemic stroke in Nigerians (univariate analysis). However, an independent association was not established. Further studies are needed to make firm conclusions.

Disclosure: Nothing to disclose.

EP1115

Magnetic resonance imaging patterns associated with cerebral venous thrombosis and cerebral arterial infarctions: a comparison using voxel-based lesion-symptom mapping

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[1]Department of Neurology, Amiens University Hospital, Amiens; [2]Department of Neurology, Rouen University Hospital, Rouen, France

Introduction: Information available about MRI parenchyma pattern of cerebral venous thrombosis (CVT) is scarce. The study's primary objective was to establish whether the brain parenchyma lesions observed in CVT and cerebral artery infarction (CAI) can be distinguished by analysis of the corresponding MRI patterns.

Methods: We performed an observational, two-centre study of consecutive patients hospitalized for CVT and CAIs. We included 91 patients (CVT with parenchymal lesions: n = 44; CAI: n = 47, 80 % with an anterior cerebral artery infarct) admitted to either of two university hospital stroke units between January 2000 and December 2011. Clinical data were collected prospectively. Brain lesions were imaged using a fast fluid-attenuated inversion recovery imaging sequence. The MRI patterns for CVT and CAIs were then analyzed using two validated methods: region-of-interest analysis and voxel-based lesion symptom mapping (VLSM).

Results: The mean ± SD age of the study population was 50.5 ± 17 years. Patients with CAI were less likely than patients with CVT to have lesions located in the posterior cortex (34 % vs. 70 %; p = 0.001) but were more likely to have lesions in deep structures (47 % vs. 5 %; p < 0.001). In a VLSM analysis, the presence of a CAI (relative to CVT) was primarily associated with lesions in two small regions: the putamen (X, Y, Z coordinates: 31, -7.13; T-score = 2.89) and the centrum ovale (X, Y, Z coordinates: 25, −14, 23; T-score = 2.89).

Conclusion: There are substantial differences between CVT and CAI in terms of the location of brain infarcts seen on MRI.

Disclosure: Nothing to disclose.

EP1116

Migraineurs are more susceptible to infarct growth in acute stroke

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[1]Radiology, A.A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Boston, MA, USA; [2]Neurology, Hacettepe University, Faculty of Medicine, Ankara, Turkey; [3]Radiology, Neurovascular Research Laboratory, Massachusetts General Hospital; [4]Neurology, Stroke Service, Massachusetts General Hospital, Boston, MA, USA

Introduction: Epidemiological data indicate that migraine is an independent stroke risk factor. Recent data suggest that migraine mutations increase brain vulnerability to ischemia via excitatory mechanisms. Migraine mutant mice develop higher number of ischemic depolarizations with accelerated infarct growth during hyperacute stroke leading to worse tissue and neurological outcomes. In this study, we assessed whether a similar untoward effect of migraine was evident on stroke evolution in humans.

Methods: We retrospectively determined lesion volumes on diffusion-weighted imaging (DWI), and mean transit time (MTT) maps on perfusion-weighted imaging (PWI) in consecutive patients with a reliably documented migraine history. DWI-PWI mismatch was calculated on spatially co-registered DWI and MTT maps, as a marker for viable tissue at risk for infarction.

Results: Stroke patients with a history of any migraine or migraine with aura were younger and more often female, compared to patients without migraine. Migraineurs less frequently had coronary artery disease or diabetes. The frequency of posterior circulation lesions was significantly higher in migraineurs. In migraineurs with aura, a larger proportion of the perfusion defect had restricted diffusion, resulting in smaller DWI/PWI mismatches. A significantly larger proportion of migraineurs with aura showed no mismatch (i.e., DWI/PWI > 0.9), indicating that the entire perfusion defect was already infarcted.

	Migraine		No migraine
	Any	With Aura	
Number of patients with DWI/PWI scans	25	9	25
DWI/PWI [median (range)]	0.8 (0.8)	1.0 (1.7)	0.5 (0.6)
Patients with DWI/PWI>0.9	9* (36%)	5† (56%)	1 (4%)

*p=0.011 migraine vs no migraine, †p=0.002 migraine with aura vs no migraine

Conclusions: Our data show that a history of migraine, particularly with aura, is associated with accelerated acute infarct growth, consistent with data obtained in migraine mutant mice.

Disclosure: The study was funded by NIH grants R01NS061505 and R01NS059710.

EP1117

Glyceryl trinitrate for acute stroke: main results from the efficacy of nitric oxide in stroke (ENOS) trial

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Background: High blood pressure (BP) is common during the acute phase of stroke and is associated with a poor outcome. Although small and medium-sized trials have assessed the effect of altering BP on outcome, the management of high BP remains unclear. We tested whether transdermal glyceryl trinitrate (GTN), a nitric oxide that lowers BP, is safe and effective in improving outcome after acute stroke.

Methods: ENOS is an international multicentre prospective randomised single-blind blinded-endpoint trial. Patients with acute ischaemic stroke (IS) or intracerebral haemorrhage (ICH) and systolic BP 140–220 mmHg were randomised to GTN or no GTN (and, where relevant, to continue or stop pre-stroke antihypertensive therapy—results reported separately). The primary outcome is shift in modified Rankin Scale at 3 months. Patients or relatives gave written informed (proxy) consent and all sites had research ethics approval. Analysis is by intention-to-treat.

Results: 4,011 patients were enrolled from 173 sites in 23 countries across 5 continents between July 2001 and October 2013 (with 79 % patients recruited from start of 2008).

At baseline: mean age 70 (SD 12); male 57 %; recruitment from Asia 14 %, Europe 16 %, UK 64 %; prior hypertension 65 %; prior stroke 15 %; diabetes 17 %; atrial fibrillation 17 %; mean BP 167 (19)/90 (13) mmHg; severity (Scandinavian Stroke Scale) 34 (13)/58; total anterior circulation syndrome 30 %; IS 81 %, ICH 16 %; stroke-recruitment time <12 h 18 %.

Summary: The main results will be available for presentation in quarter 2 2014. ENOS is large enough to influence clinical practice.

Disclosure: Nothing to disclose.

EP1118

The impact of neurosonology in the emergency department

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Introduction: The neurosonological study is a non-invasive technique, broadly used in assessing the stroke patient. It is useful in detecting cerebrovascular pathology of both extra and intracerebral arteries, as well as hemodynamic changes not detected by other ancillary tests. However, its usefulness in the emergency department (ED) when evaluating a patient with suspected stroke, is not yet documented. The purpose of this work is to determine whether the information provided by the neurosonological study in the ED changes the clinical conduct when facing a patient with suspected acute cerebrovascular disease.

Methods: We made a retrospective analysis of the neurosonological studies preformed in the ED in the period between January 2011 and August 2013. The neurosonological study was considered positive if at least one of the following was present: symptomatic extracranial stenosis $\geq$50 %; any intracranial stenosis; arterial dissection; cardiac shunt; temporal arteritis. We preformed a univariate analysis with Chi square test, and multivariate analysis with logistic regression. Statistical significance was defined when $p < 0.05$.

Results: We included 319 patients, 198 males (62 %), aged between 19 and 92 years old (mean 55.5). In 64 patients (20 %) the study was considered positive. We hospitalized 48 patients (75 %) with a positive study, and 83 (32.5 %) without neurosonological changes. With multivariate analysis adjusted to vascular risk factors, the statistically significant association was maintained.

Conclusions: The presence of changes in the neurosonological study led more frequently to hospitalization. These results suggest that neurosonology preformed in the ED has impact on decision-making in the stroke patient.

Disclosure: Nothing to disclose.

EP1119

Platelet activation and nitric oxide synthesis in patients with leukoaraiosis

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Introduction: The importance of endothelial dysfunction in cerebrovascular disease has been established. The endothelial dysfunction is associated high frequency of white matter lesion (hyperintensity lesions in MRI which is the hallmark of leukoaraiosis). The endothelial dysfunction may enhance the platelet activity. While these phenomenons of endothelial dysfunction and platelet activity were studied in stroke patients, there are limited data regarding these pathophysiological mechanisms in leukoaraiosis patients. The objective of this study is to investigate the endothelial dysfunction and platelet activity in patients with leukorariosis.

Methods: We compared 50 healthy volunteers with 105 patients with leukoaraiosis. Cerebral infarction was excluded by MRI examination. Staging of leokoaraiosis was made in 4 grades according to lesions severity and their advancement. Haemodinamic assessment was made by carotid Doppler ultrasonography. Endothelial dysfunction was evaluated by plasma determination of NO metabolites (NOx) and platelet activity by platelet aggregation test.

Results: NOx plasma concentration was reduced comparative with healthy subjects. Platelet aggregation was greater in leukoaraiosis patients comparative with healthy subjects. These results were correlated with leukoaraiosis grade.

Conclusions: These results may provide details of leukoaraiosis pathogenesis revealing that the endothelial dysfunction and prothrombotic changes may play an important role. Because leukoaraiosis is an important risk factor for cerebral infarction therapies which may stabilize the endothelial function and antiplatelet therapy may considerable help the prevention of cerebral infarction.

Disclosure: Nothing to disclose.

EP1120

Inhibition but not activation of neuronal P2X7 receptors plays roles in brain injury after optic nerve transaction and focal cerebral ischemia

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Introduction: P2X7 receptors (P2X7R) are members of the family of cationic-selective ion channels gated by extracellular ATP. They are involved in the regulation of receptor trafficking, inflammation and ATP-mediated cell death.

Methods: Here, we have analyzed cellular expression patterns of P2X7 on neuron, glia and retinal ganglion cells (RGCs) and evaluated roles of P2X7 receptor modulation and activation in the cell survival after optic nerve (ON) transection and focal cerebral ischemia in mice.

Results: We observed neuronal but not glial expression of P2X7 receptors in brain and retina. Activation of P2X7 receptor with different concentration of BzATP has no effect on neuronal. However, modulation of P2X7 receptors by Brilliant Blue G (BBG) improved neuronal and RGC survival injury after ON transection and cerebral ischemia. The number of Fluoro-Gold positive RGCs were significantly higher in BBG treated animals. Furthermore, inhibition of P2X7 receptors decreased infarct volume, brain swelling and neurological scores 90 min after cerebral ischemia and 24 h reperfusion. In addition, inhibition of P2X7 receptors decreased DNA fragmentation and increased neuronal survival after 30 min of cerebral ischemia which was assocciated with increased phosphorylation of survival kinases AKT and ERK-1/2.

Conclusions: Here, we provide evidence that the cellular expression of P2X7 receptors is mainly observed on the neuronal cell and the significance of P2X7 receptor modulation on neuronal cell death. We predict that the clinical implementation of P2X7 receptor antagonists can be beneficial not only in patients with acute ischemic stroke, but also with more delayed degenerative neurological diseases.

Disclosure: Nothing to disclose.

EP1121

A prospective study of diagnostic accuracy and outcomes in cerebellar infarction

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Introduction: Early and accurate diagnosis of cerebellar infarction (CI) is challenging because of non-specific symptoms and absence of localizing signs. Delayed or misdiagnosis may result in increased morbidity and mortality.

Methods: Fifty-six consecutive patients admitted to Liverpool Hospital with CI were prospectively analysed over 2 years (2012–2013) to determine factors associated with delayed diagnosis.

Results: Mean age was 61 years, M:F = 39:17. Ten patients had prior general practitioner presentations while five had prior Emergency Department (ED) presentations. 28 (50 %) presented within 4.5-h, 9 between 4.5–24 h and 19 (34 %) > 24 h after symptom onset. TIA/stroke was not the principal ED diagnosis in 20 (36 %). The most common presenting symptoms in patients presenting <4.5 h were dizziness, gait ataxia and nausea/vomiting compared to dizziness, gait ataxia, and headache in those presenting >24 h. The most common signs were limb ataxia and nystagmus. ED detection of clinical signs was significantly less than that found by the neurology team.

Isolated CI was present in 32 patients (57 %), the most frequent site being posterior inferior cerebellar artery (72 %). 24 patients had additional territory involvement (posterior circulation 62 %; anterior 17 %). Complications included brain oedema and recurrent stroke in 11 patients, of whom 8 had multiple territory strokes. Eleven (20 %) died within 3-months. Patients with isolated CI had less complications and were more likely to be discharged home ($p < 0.05$).

Conclusions: Late presentation in CI and infarction in other vascular territories were common. Although involvement of additional arterial territories did not predict earlier presentation, these patients experienced more complications.

Disclosure: Nothing to disclose.

EP1122

Clinical results of carotid artery stenting versus carotid endarterctomy; a single center experience

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Introduction: We aim to review our results of carotid artery stenting (CAS) and carotid endarterectomy (CEA).

Methods and results: The records of all our patients who undergone carotid artery revascularization between 2001 and 2013 were evaluated. CAS or CEA procedures were performed in patients with asymptomatic carotid stenosis >70 % or symptomatic stenosis >50 %. Demographic data, procedural details, and clinical outcomes were also recorded.

194 CEA and 115 CAS procedures were performed for symptomatic and/or asymptomatic carotid artery stenosis. Primary outcome measures were in-30 day stroke/transient ischemic attacks (TIA)/amaurosis fugax or death. Secondary outcome measures were bleeding complications, length of stay in hospital and ICA patency as well as stroke or all-cause death during long-term follow-up. No significant differences were found with respect to 30-day mortality and neurologic morbidity between CAS and CEA procedures (13 % and 7,7 % respectively). Length of stay in hospital (CAS 4,5 ± 4,4 and CEA 5,9 ± 5,8; $p < 0,001$) were significantly longer in CEA group. In the post-procedural follow up, only in symptomatic patients, restenosis rate was significantly higher in the CEA group (CEA 16.4 % vs CAS 4.4 %; $p = 0.045$); the other endpoints did not differ significantly.

Conclusions: Endovascular stent treatment of carotid artery atherosclerotic disease is an alternative for vascular surgery, especially for patients that are high risk for standard CEA. The increasing experience, development of cerebral protection systems and new treatment protocols increases CAS feasibility.

Disclosure: Nothing to disclose.

EP1123

Antithrombotic treatment and initial stroke severity in patients with acute ischemic stroke and atrial fibrillation: 10 year observation of single academic hospital in Korea

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Introduction: Clinical practice guideline recommended appropriate use of oral anticoagulants for the patients with AF. However, warfarin has not been widely used in Korea. Here, we elucidated the relationship between international normalized ratio (INR) values on admission and clinical outcomes in patients with acute ischemic stroke and atrial fibrillation.

Methods: We identified 5,407 consecutive patients who visited our hospital within 7 days after onset. We adopted INR values extracted in emergency room, and the initial stroke severity and functional outcome were assessed by baseline NIHSS and 3 month mRS.

Results: A total of 640 patients had persistent or paroxysmal AF. 277 patients (43 %) were aware of their AF before admission. The awareness was not increased over the 10 years. Among them, 334 (52.2 %) were not on antithrombotic treatment, 208 (32.5 %) were receiving antiplatelet treatment, 98 (15.3 %) were receiving warfarin. In addition, the patients who were taking warfarin with a therapeutic INR ($\geq$ 2.0) were only 21 (3.3 %). Admission NIHSS score was significantly lower in the group of patients taking warfarin (median 5, interquartile range [3,12]) compared with the groups of no antithrombotic treatment (8[4,16]) and antiplatelet treatment (8[3,15]). Admission NIHSS score had negative linear trend relationship in the patients with higher admission INR. (INR $\geq$ 2.0, 3[1,8], INR = 1.5–2.0, 4[2,12], and INR $<$ 1.5, 8[3,15], p = 0.017).

Conclusions: Awareness of AF has been poor in Korean ischemic stroke patients with AF. In addition, underuse and inappropriate use of warfarin was widespread. Therefore, the education about appropriate anticoagulation is needed to general public and health professionals.

Disclosure: Nothing to disclose.

EP1124

Posterior reversible encephalopathy Syndrome (PRES): a series of 22 patients

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Introduction: Posterior reversible encephalopathy syndrome, is a syndrome characterized by headache, lethargy, visual complaints or seizures.On imaging, PRES presents with abnormalities of the white matter and the grey matter, predominantly affecting the posterior regions. The diagnosis currently relies on clinical manifestations and typical neuroimaging findings. In this study, we aimed to discuss causes, clinical aspects, imaging findings and prognosis of PRES.

Methods: The patients who met the diagnosis of PRES were involved in our study. Datas of the patients (demographics, presenting symptoms, medical history, risk factors, cranial imaging findings, biochemical markers, treatment, neurologic status after treatment) were collected retrospectively from hospital records.

Results: Total number of patients were 22 (18 female/4 male). The mean age of the patients was 40 (min 19, max 64). Main clinical symptoms were encephalopathy, seizure and visual loss. In our group, hypertension and eclampsia were the major etiologic factors. Relation between etiologic factors, cranial magnetic resonance imaging findings, biochemical markers (serum ürea, creatin, LDH levels) and neurologic sequel was evaluated.

Conclusions: PRES is a clinicoradiological entity. Early recognition and resolution of the underlying cause is the keystone of management. So, its different kind of etiologic factors, clinical presentation and radiologic findings should be known.

Disclosure: Nothing to disclose.

EP1125

Prospective comparison of continuous cardiac monitoring and holter on a stroke unit

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Introduction: Continuous cardiac monitoring (CCM) is commonly used in the stroke unit to detect arrhythmias in stroke patients. Before marketing, cardiac monitoring algorithms are typically validated by comparison with a historic data set, however prospective validation against the gold standard Holter in a real-life setting is not typically performed. The goal was to determine the diagnostic accuracy of continuous cardiac monitoring with an atrial fibrillation (AF) detection algorithm with Holter in a stroke unit.

Methods: We prospectively included patients with a TIA or acute ischemic stroke. During holter monitoring (HM) (ELA Spiderview, ELA Medical SYNESCOPE MultiChannel-MultiDay Version3.10 SN software), CCM (Philips Intellivue 2 MP30, ST/AR Arrhythmia Algorithm software)was obtained. We included patients with duration of HM $>$ 17.5 h and less than 4 h absence of overlap of recording times. The rate of bradyarrhythmias (rate $<$ 50/min), tachyarrhythmias (rate $>$ 120/min) and AF were compared between CCM and Holter. The holter events were classified by a cardiologist, the monitor events primarily by a neurologist (seconded by a blinded cardiologist).

Results: We included 95 patients (49 % females) with a mean age of 71 years. During the CCM, we detected AF in 4 patients, with 2 additional patients on Holter (sensitivity 67 %). On CCM tachy- and bradyarrhythmias were respectively seen in 14 versus 24 patients (sensitivity 58 %) and 22 versus 29 (sensitivity 76 %) patients on Holter. Specificity of CCM was more than 90 % for all arrhythmias.

Conclusions: CCM had lower sensitivities than HM for detection of bradycardia, tachyarrhythmia and AF. Arrhythmia detection algorithms should be validated in real-life circumstances.

Disclosure: Nothing to disclose.

EP1126

Treating experimental stroke with adult neural progenitor cells: an analysis of optimal intravenous cell delivery time points and their underlying mechanisms

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Introduction: Neural progenitor cells (NPCs) induce histological/functional recovery after stroke, albeit grafted cells are not integrated into the residing neural network. Although the most ideal NPC delivery route remains elusive, intravenous cell delivery is not inferior to intracerebral cell transplantation. However, systematic analyses of optimal time points for intravenous NPC delivery and their long-term consequences do not exist.

Methods: Male C57BL6 mice were exposed to cerebral ischemia for 30 min and NPCs were grafted via cannulation of the femoral vein during reperfusion, on day 1 or on day 28 post-stroke. Animals were allowed to survive for up 84 days post-stroke, followed by behavioral tests and immunohistochemical analyses.

Results: Numbers of grafted NPCs within the ischemic hemisphere were increased on days 56 and 84 after transplantation on day 28 post-stroke. Likewise, transplantation on day 28 yielded enhanced neuronal differentiation rates of grafted cells. However, reduced post-ischemic brain injury was only found after acute NPC delivery for as long as 56 days post-stroke. On the contrary, late NPC transplantation on day 28 resulted in reduced functional deficits on day 84, albeit tissue injury was not affected. Reduced brain injury after acute NPC transplantation was associated with enhanced blood-brain-barrier (BBB) stabilization and reduced microglial activation. On the other

hand, late NPC transplantation stimulates neural regeneration via enhanced angioneurogenesis within the lesion site.

Conclusions: Acute NPC delivery yields long-term but not stable reduction of brain injury via stabilization of the BBB, whereas late NPC delivery enhances post-ischemic neuroregeneration via mechanisms involving increased angioneurogenesis.

Disclosure: Nothing to disclose.

EP1127

Neuroprotective role of statins in acute phase of ischemic stroke

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Introduction: The pleiotropic effects of statins are receiving increasing attention in stroke patients. We performed a prospective, open-label, observational study to investigate the pleiotropic effects of early statin treatment on stroke-induced changes in the levels of circulating endothelial progenitor cells (EPCs), vascular endothelial growth factor (VEGF) and matrix metalloproteinase (MMP)-9.

Methods: 44 Patients admitted within 48 h after ischemic stroke onset were enrolled. 22 patients were assigned to receive 20 mg atorvastatin and the other were not. Circulating EPCs, VEGF and MMP-9 were determined at 1st day and 7th day for each individual. Stroke severity was assessed by a certified neurologist using National Institute of Health Stroke Scale (NIHSS) at admission and functional outcome was evaluated at the 30th day using modified Rankin Scale at 30th day.

Results: MMP-9 remained in an elevated level within the first 48 h after onset, and then distinctly decreased in the acute phase. Moreover, patients received statin-treatment show a significantly larger MMP-9 decrement than those not. On the other hand, statin therapy is associated with an increase in the number of circulating EPCs in patients with ischemic stroke. However, no significantly influence of statins use on VEGF was observed.

Conclusions: In summary, treatment with statins initiated in the acute phase of ischemic stroke enhance the post-ischemic vascular repair consequent on augmentation of circulating EPCs as well as attenuate the inflammatory injury on account of decrement of MMP-9 expression.

Disclosure: Nothing to disclose.

EP1128

Genetic aspects of inflammatory response mediated by IL-6 following spontaneous intracerebral hemorrhage (SICH): a case control study

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Introduction: The activity of IL-6, a well-recognized mediator of immunological post-stroke response, is regulated on multiple levels of which IL-6 genetic polymorphism is crucial. The objective of this prospective, clinical, controlled study was to assess the relations between IL-6 genetic variations, extent of inflammatory response and outcome in SICH patients.

Methods: 44 consecutive SICH patients and 36 age and sex matched healthy controls were enrolled. DNA was isolated and a 500 bp upstream DNA sequence of the IL-6 gene was sequenced in order to identify 5 common promoter haplotypes (B, C, D, E and F). Serum concentrtion of IL-1, IL-6, CRP and leukocytes count were analyzed once in the controls and four times (days1,2,3,7) in the SICH patients. Clinical outcome was assessed in SICH patients by means of NIHSS (National Institute Stroke Scale) on admission and mRS (modified Rankin Score) at day 30 and 90 after stroke onset.

Results: IL-6 promoter haplotype F, equally frequent in both cases and controls, was associated with:

1) lower IL-6 levels in patients reaching twofold means difference on day2 ($p = 0.038$, CI: −1,1,51 to −47.38),

2) ten times lower IL-1 concentration on day 7 ($p = 0.006$, CI: −1.53 to −0.29),

3) non-significantly lower leukocytes count and CRP level in patients,

4) no differences were found in the control group.

IL-6 serum level correlated positively with the CRP level and leukocytes count in all measurement time points. Patients with lower IL-6 level had lower NIHSS and mRS on days 1 to7 ($p < 0.05$).

Conclusion: IL-6 promoter haplotype F seems to be associated with lower inflammatory response after SICH, which, in turn, determines better short and long term clinical outcome in SICH patients.

Disclosure: Nothing to disclose.

Movement disorders 1

EP1129

Positive effects of granulocyte-colony stimulating factor on a rat model of Parkinson's disease

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Introduction: Granulocyte-colony stimulating factor (G-CSF) is a glycoprotein structured molecule, and releases from monocytes, macrophages, endothelial cells. Previous studies have revealed that it is present in many areas including substantia nigra in central nervous system. This study aims to investigate the effects of G-CSF on rat model of Parkinson's disease.

Methods: Eighteen Sprague–Dawley adult male rats were included in the study and were devided into 3 groups. Rotenone + Dimethyl sulfoxide (DMSO) was sterotactically injected to left substantia nigra compacta and ventral tegmental area of the group 1 and group 2. Only DMSO was applied to the same location of the third group as a sham group. Rotation test was applied to rats after 10 days by administering intraperitoneally apomorphine. Rats having continuous rotation in the same direction 7 times per minute in apomorphine-induced rotation test (AIRT) were considered as PD. Group 1 was administered with 100 μg/kg G-CSF, and group 2 with isotonic saline for 28 days. Then, apomorphine-induced rotation numbers were recorded for 10 min, and malondialdehyde levels in plasma and thyrosine hydroxylase (dopamine degradation product) (THA) measures in brain of the rats were examined.

Results: AIRT scores and malondialdehyde levels of the group 1 were lower than the group 2, while THA levels were higher ($p < 0.005$). There was no significant differences in terms of malondialdehyde and THA levels between the group 1 and 3.

Conclusions: G-CSF was detected to have positive effects on rat model of PD. This positive effect may be associated with of G-CSF's neuroprotective effect.

Disclosure: Nothing to disclose.

EP1130

Progressive encephalomyelitis with rigidity and myoclonus: a new variant with DPPX antibodies

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Introduction: Progressive encephalomyelitis with rigidity and myoclonus (PERM) is a variant of the Stiff Person Syndrome. Associated antibodies are mainly directed against glutamic acid decarboxylase (GAD), glycine receptors (GlyR), or amphiphysin. Here, we report a distinct variant of PERM comprising marked hyperekplexia, cerebellar ataxia, and trunk stiffness who tested negative for the antibodies hitherto described, but positive for a new antibody directed against the dipeptidyl peptidase-like protein 6 (DPPX or DPP6).

Methods: Case series describing the clinical, paraclinical, and serological features of three patients with PERM. A recombinant, cell-based indirect immunofluorescence assay with DPPX-expressing HEK293 cells was used to detect DPPX antibodies in conjunction with mammalian tissues.

Results: All patients presented with a distinct syndrome involving hyperekplexia, prominent cerebellar ataxia with marked eye movement disorder, and trunk stiffness of variable intensity. Additional symptoms comprised allodynia, neurogenic pruritus, and gastrointestinal symptoms. Symptoms began insidiously and progressed slowly. An inflammatory CSF profile with mild pleocytosis and intrathecal IgG-synthesis was found in all patients. High DPPX antibody titers were detected in the patient's serum and CSF, with specific antibody indices suggestive of intrathecal synthesis of DPPX antibodies. Response to immunotherapy was good, but constant and aggressive treatment may be required.

Conclusions: These cases highlight the expanding spectrum of both PERM and anti-neuronal antibodies. Testing for DPPX antibodies should be considered in the diagnostic work-up of patients with acquired hyperekplexia, cerebellar ataxia, and stiffness, as such patients might benefit from immunotherapy.

Disclosure: C. Probst, I. M. Blöcker, R. Bahtz and L. Komorowski are employees of Euroimmun. W. Stöcker is a board member of Euroimmun.

EP1131

Epidemiological genetic study of familial dystonia in Tunisia

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Introduction: Familial dystonia have been described and reflect the genetic origin. No studies have been conducted on this topic in Tunisia.

We report on clinical, genealogical and genetic characteristics of primary dystonia in 22 Tunisian families.

Methods: From 2009 to 2013, we conducted an epidemiological genetic study including 84 patients with primary dystonia. A field survey was conducted and 22 families were visited. family tree, neurological examination, video and blood sample from the index case and all family members were made. A molecular study was performed in 8 families and the results were analyzed.

Results: Epidemiological genetic study revealed 9 secondary cases belonging to 3 families. A high rate of consanguinity was noted (40 %). Generalized dystonia were observed in 12 cases with phenotypic variability (blepharospasm, generalized dystonia and hemiparkinsonism) in a DYT1 family. 10 had focal dystonia, including 2 torticollis. A mutation in TOR1A gene was noted in eight cases. Three had dopa-responsive dystonia with GCH1 gene mutation. Whole exome sequencing was performed in two patients with cervical dystonia.

Conclusion: Our study is the first to report 22 families with primary dystonia in Tunisia. The high rate of consanguinity in our study suggests autosomal recessive inheritance. The frequency of familial forms motivates a battery of genetic tests to reach a clear diagnosis and adequate management.

Disclosure: Nothing to disclose.

EP1132

Corpus callosum damage and motor function in Parkinson's disease

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Introduction: To investigate corpus callosum (CC) microstructural damage and its relationship with motor impairment in Parkinson's disease (PD) patients at different disease stages.

Methods: We enrolled 173 PD patients (98: Hoehn and Yahr score [HY] = 1–1.5; 37: HY = 2–2.5; 29: HY = 3–3.5; 9: HY = 4–5) and 39 controls (HC). Diffusion tensor (DT) MRI tractography was performed to obtain the CC and its main three partitions: CC-genu, CC-body, and CC-splenium. Mean tract fractional anisotropy (FA) and mean diffusivity (MD) values were measured. Pearson's correlations were used to explore the relationship between CC DT MRI metrics and UPDRSIII.

Results: All PD patients relative to HC showed decreased FA and increased MD of the whole CC and its partitions. CC microstructural damage was more marked with increasing severity, being only mild in PD with HY = 1–1.5 (who showed the greatest damage in the CC-body) and severe (same degree of damage in all partitions) in patients at the later disease stages. UPDRSIII correlated ($p < 0.001$) with FA of the whole CC ($r = -0.399$), CC-genu ($r = -0.199$), CC-body ($r = -0.481$), and CC-splenium ($r = 0.270$) and MD of the whole CC ($r = 0.367$), CC-body ($r = 0.438$), and CC-splenium ($r = 0.257$).

Conclusions: PD is associated with CC microstructural damage that becomes more significant with disease worsening. In PD, the best predictor of motor functions is the involvement of the CC-body, which includes the transcallosal motor tracts. Assessing CC alterations may improve the understanding of the pathogenetic mechanisms associated with motor impairment in PD.

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EP1133

Intensive rater training to standardize cognitive assessment: a study to assess the effect of rasagiline on mild cognitive impairment in Parkinson's disease patients

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Introduction: Parkinson's disease (PD) trials using cognition endpoints are relatively new. Formal rater training is critical to increase success.

Methods: The MODERATO study examines effects of rasagiline on cognition in PD patients. Endpoints include the Montreal Cognitive Assessment (MoCA) and the Scales for Outcomes of Parkinson's Disease—Cognition (SCOPA-COG). To maximize rater reliability, a training program preceded study start. Raters completed on-line didactic and video training requiring 100 % correct and video recorded administrations to mock patients which were reviewed by calibrated expert raters. Errors affecting item scores were labeled "major" and required submission of another video.

Results: 80 raters started training and 71 completed it. 30 % were classified as inexperienced ($\leq$ 10 pre-trial administrations) on MoCA, 73 % were inexperienced on SCOPA-COG. Using a paired samples t-test there was no significant difference between the MoCA and SCOPA-COG online assessment accuracy (MoCA 90 % $\pm$ 10.9; SCOPA-COG 93 % $\pm$ 14.2; $p = 0.07$). There was no difference between experienced and inexperienced raters on MoCA errors (3.71 ± 2.93 and 3.96 ± 2.87, respectively; $p = 0.74$) but experienced SCOPA-COG raters made significantly more errors than inexperienced raters (7.94 ± 3.39 vs. 5.21 ± 2.87; $p = .001$). Of 71 raters submitting videos, 38 (54 %) required re-submission. Of 28 raters providing a second submission, 10 (36 %) required further training.

Conclusions: Results support enhanced training designed to maximize reliability, regardless of pre-trial clinical or direct scale experience. Multi-step, multi-modal training can standardize raters to fidelity with scale instructions, minimizing error variance and increasing study power.

Disclosure: ElizaBeth Grubb and Azhar Choudhry are employees of Teva Pharamaceuticals.

EP1134

Levodopa/carbidopa intestinal infusion complications: the experience of 3 Neurology Departments in North-West Italy and a case report

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Introduction: Levodopa/carbidopa intestinal infusion represents one of the therapeutic options for advanced Parkinson's disease (PD) patients with motor fluctuations and diskynesias unresponsive to other treatments. It relieves symptoms of advanced PD and it improves quality of life. The most common complications of levodopa/carbidopa intestinal infusion are related to the infusion device, especially intestinal tube dislocation, occlusion, kinking or looping. Other complications are peristomal infections, localized peritonitis, pneumo-peritoneum or hemo-peritoneum. Adverse events may be also related to levodopa/carbidopa infusion, such as acute psychosis, weight loss, polyneuropathy.

Case report: From 2007 67 patients underwent levodopa/carbidopa intestinal infusion in our Departments. Among complications, in our experience 5 patients had tube occlusion due to bezoars. We report on a 61 years old patient with advanced PD who started levodopa/carbidopa intestinal infusion in October 2010. Some days later transient obsessive ideation occurred. 3 months later agitation, delusions of persecution, hallucinations, false recognition and aggression occurred, alternating with drowsiness and severe brady-akinesia. There were also proteinuria with renal failure and anemia (with a negative gastroscopy). He needed clozapine therapy, transfusion of packed red blood cells and hydratation. Subcutaneous continuous infusion of apomorphine was started in association with levodopa/carbidopa intestinal infusion. Patient was discharged after 4 weeks; he presented motor and cognitive improvement.

Conclusion: Also in our experience levodopa/carbidopa intestinal infusion adverse events are similar to those reported in literature.

Disclosure: Nothing to disclose.

EP1135

Gastrointestinal dysfunction in PD patients with morning akinesia

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Introduction: It is well established that gastroparesis is common in PD causing delayed gastric emptying of L-dopa with a delayed onset of symptomatic effect. However, little is known about which measures can be used to identify patients that have this problem.

Methods: The AM-IMPAKT study is a Phase IV study designed to assess the effect of apomorphine HCl subcutaneous injection in L-dopa-treated PD patients with morning akinesia. At screening, patient gastrointestinal function was assessed using the SCOPA-Autonomic (SCOPA-AUT) scale and the Gastroparesis Cardinal Symptom Index (GCSI). We present an interim baseline analysis of gastrointestinal function in 50 patients who have completed the study. Patients were categorized according to duration of PD (0–5, 6–10, 11–15 and 15+ years).

Results: In this interim population, mean $\pm$ SD age was 63.9 ± 11.1 years and duration of levodopa treatment was 49.6 ± 81.6 months. In these patients with delayed time-to-ON, GSCI was variable, although bloating and postprandial fullness subscores were increased. In contrast, baseline SCOPA-AUT total scores ranged from 15.2–16.8, and were driven mainly by GI dysfunction (scores 4.0–5.0) and urinary dysfunction (scores 5.0–6.5). Abnormal SCOPA-AUT total and subscores were already present in patients with PD duration of 0–5 years, and scores were similar to patients with a longer disease duration.

Conclusions: In PD patients with morning akinesia, the SCOPA-AUT appears to be helpful in identifying underlying gastroparesis. Once recognized, the presence of gastroparesis suggests that non-oral drug delivery may be useful to ensure a rapid and reliable ON in patients with morning akinesia.

Disclosure: S. Isaacson reports consulting fees for US WorldMeds LLC.

EP1136

ANDANTE safety review: a placebo controlled, randomized, study of rasagiline as an add-on therapy to stable dose of dopamine agonists in early Parkinson's disease

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Introduction: Dopamine agonists (DA)s are used as initial symptomatic therapy for early PD, escalating dose or addition of levodopa needed over time to maintain symptom control. Increasing DA dose is associated with a higher risk of AEs and addition of levodopa with the emergence of motor complications. Rasagiline is a selective, irreversible MAO-B inhibitor complementing the direct stimulation of dopamine receptors provided by DA monotherapy.

Methods: ANDANTE is a Phase-IV, 18-wk study of PD patients sub-optimally controlled on stable DA dosages ($\geq$6 mg/day ropinirole or $\geq$1.0 mg/day pramipexole). Patients were randomized to rasagiline (RAS) 1 mg or placebo (PL); DA dosage remained stable throughout; 11 patients required rescue levodopa during the study.

Results: Among 326 patients included in the safety cohort, 204 reported AEs (104RAS vs. 100PL). The most common AEs experienced by patients in any group were dizziness (7.4 % RAS vs 6.1 % PL), peripheral edema (7.4 % RAS vs 4.3 % PL), nausea (6.2 % RAS vs 4.3 % PL), and falls (5.6 % RAS vs 1.2 % PL). Somnolence, confusion, and hallucinations were not increased. AE severity was similar between rasagiline and placebo treated groups. A total of 13 patients experienced SAEs (4.9 %RAS vs. 3.0 %PL). No impulse control disorders (ICD) were reported during the study.

Conclusions: In the ANDANTE study, addition of rasagiline to DA monotherapy was safe and well-tolerated. No significant difference in percentage of patients with AEs (64.2 % RAS vs. 61.0 % PL) or serious AEs (4.9 % RAS vs. 3.0 % PL) was observed. In early PD patients sub-optimally controlled on DA monotherapy, improvement in motor control by the addition of rasagiline was not accompanied by limiting adverse effects.

Disclosure: Stuart Isaacson, MD, Honoraria or payments for consulting, advisory services, speaking services and research support over the past 12 months from Teva Neuroscience and Lundbeck; Azhar Choudhry is an employee of Teva.

EP1137

Pisa syndrome in Parkinson's disease: demographic and clinical correlations in an Italian Multicenter study

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Idiopathic Pisa syndrome (PS) in Parkinson's disease (PD) is a rare entity with only sporadic single case descriptions. Therefore, its pathophysiology has been poorly investigated.

We performed this multicenter cross-sectional study with the aims to estimate the proportion of patients developing PS in a large cohort of patients with PD and to assess relationships between PS and demographic/clinical variables.

Patients with PD were selected from consecutive outpatients. Age, sex, age at PD onset, UPDRS III and IV, PDQ8, antiparkinsonian therapy and any information on lateral trunk flexion present at the time of the study were recorded.

A total of 1631 patients (F:M = 679:936) with PD met the eligibility criteria and entered into the study. Mean age and mean duration of parkinsonian motor symptoms were 69 (SD 9.6) and 7.1 (SD 4.9) years, respectively. Mean UPDRS III score was 22.1 (SD 11.2) and Hoehn and Yahr was 2.1 (0.7). The mean daily dose of Levodopa was 424.9 mg (sd 307,3). PS was detected in 150 out of 1631 patients (9.2 %). The mean degree of lateral flexion of the trunk was 16.5 (SD 7.7). Concomitant camptocormia was detected in 63 (43.2 %) patients with PS.

Patients with PS were significantly older, had longer duration of disease and of treatment with antiparkinsonian drugs than patients without PS; the UPDRS III and IV, H-Y were significantly higher in patients with PS.

These results suggest that PS is a frequent and disabling complication in PD in the advanced phase.

Disclosure: Nothing to disclose.

EP1138

Self completed non motor symptoms questionnaire (NMSQuest) score used to set up Parkinson's disease burden in the outpatient clinic

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Introduction: The Non Motor Symptoms Questionnaire (NMSQuest) is a widely used self completed tool to assess NMS in patients with Parkinson's disease (PD). We had previously recommended a simple grading system using the total NMSQuest score to address the burden of NMS in PD [1]: NMS levels as very mild 0–5, mild 6–12, moderate 13–20 and severe >20.

Methods: We analysed preliminary data from 100 PD patients consecutive completed NMSQuest (mean age 67 years; range 29–92 years), 38 females, disease duration 6 years (range 0.5–49 years). We classified using the NMSQuest total score in four severity levels as NMS burden and correlated with Hoehn and Yahr stages (HY) as motor symptom burden.

Results: In the whole sample, severity of NMS as assessed by NMSQuest levels were very mild (22 %), mild (41 %), moderate (24 %) and severe (13 %). 14 % of our PD patients in moderate and 7 % in severe NMSQuest level were in HY 1 while 16 % with moderate and 6 % with severe NMSQuest level were in HY 2 showing discordance between NMSQuest levels and HY stage. Furthermore, four patients with drug naive PD at HY 1 and HY 2 had moderate (n = 2) and severe (n = 1) NMSQuest level whereas only 1 patient had mild NMSQuest level.

Conclusions: This observation further outlines the importance of assessing NMS in PD patients. A substantial proportion of patients, in spite of being in early "motor" stage, had considerable NMS burden prompting the need of specific treatment which would have been otherwise missed.

Disclosure: Nothing to disclose.

EP1139

The effect of subthalamic nucleus deep brain stimulation on restless legs syndrome in patients with Parkinson's disease

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Introduction: Sleep disorders and restless legs syndrome (RLS) are common in Parkinson's disease (PD) patients. Some of these sleep abnormalities may improve after subthalamic nucleus (STN) deep brain stimulation (DBS). We investigated the effect of STN DBS on RLS in PD patients.

Methods: This study included 59 PD patients (32 male, 54.2 %). Patients were detected for RLS before and on the sixth month of the STN DBS according the International Restless Legs Syndrome Study Group criteria and patients fulfilled the four essential criteria accepted as RLS. The severity of clinical symptoms were measured using Unified Parkinson's Disease Rating Scale (UPDRS) II and III; and dopaminergic treatment dosage calculated as levodopa equivalent dose (LED).

Results: The mean age was 53.93 ± 10.06 and the mean disease duration was 14.09 ± 6.88 years. 32 (54.2 %) and 18 (30.5 %) patients were noted for having RLS before and after STN DBS. Fourteen patients reported significant improvement of their RLS symptoms ($p < 0.001$), and recently developed RLS was not detected. After STN DBS mean 55.15 %; 57.55 %; and 50.02 % reduction found on UPDRS part II; III scores, and LED respectively.

Conclusions: Our findings indicated that notable improvement of RLS reported by nearly half of PD patients after STN DBS.

Disclosure: Nothing to disclose.

EP1140

The study of oxidative status and mitochondria functionality in human neuronal models of pantothenate kinase associated neurodegeneration

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Introduction: Pantothenate Kinase-Associated Neurodegeneration (PKAN) is an early onset autosomal recessive movement disorder, caused by mutations in the Pantothenate Kinase-2 (*PANK2*) gene that encodes a mitochondrial enzyme involved in Coenzyme A synthesis. The pathology is hallmarked by severe iron accumulation in the brain. Our previous results on patient's fibroblasts suggested that Pank2 deficiency promotes an increased oxidative status further enhanced by the addition of iron. To clarify the molecular mechanism leading to iron homeostasis dysfunction in more suitable models of disease, we developed and characterized new human neuronal models obtained by patients fibroblast's direct reprogramming.

Methods: Primary skin fibroblasts from three PKAN patients and three unaffected subjects were infected with lentivirus carrying the three-transcription factors Mash1, Nurr1 and Lmx1a to obtain induced neurons (iNs). They were evaluated for radical oxygen species (ROS), mitochondrial functionality and glutathione measurements by specific fluorescence probes at single cell level.

Results: The efficiency of fibroblasts reprogramming was around 5 %, as identified by the expression of TuJ1, Tyrosine hydroxylase and N-CAM neuronal markers. In basal condition, PKAN iNs showed an increase in ROS level, about 50 % higher respect to the iNs from healthy subjects. The reduced form of glutathione resulted decreased by about 15 % in PKAN iNs compared to controls. Evaluation of TMRM signal indicated that the mitochondrial membrane potential is not affected in PKAN iNs.

Conclusions: The data indicated that neurons can be reprogrammed from PKAN fibroblasts. They partially confirmed the results obtained in fibroblasts, indicating an altered oxidative status probably due to iron mishandling.

Disclosure: Nothing to disclose.

EP1141

Pallidal deep brain stimulation in the treatment of Huntington's chorea

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Background: Stereotactic lesions have been occasionally performed in Huntington's chorea since the dawn of functional stereotactic surgery, however, with modest results. Despite the success of deep brain stimulation (DBS) in surgical treatment of Parkinson's disease and dystonia, the interest of testing DBS in Huntington's Disease (HD) has been limited. So far, promising results of pallidal DBS in 7 patients with HD have been reported in the literature.

Objectives: To present the results of pallidal DBS in a patient with HD.

Methods: A 59 year old woman with HD since 12 years and severe motor symptoms was implanted bilaterally in the Globus pallidus internus. The patient was evaluated at 12 months after surgery.

Results: The effect of DBS was deemed satisfactory concerning the patient's choreo/dystonic symptoms. The improvement according to the unified Huntington's disease rating scale was modest, with a score reduction from 92 before surgery to 81 at one year.

Conclusions: The results of pallidal DBS were deemed satisfactory in the patient presented here, confirming previous reports of the role of DBS in HD. However, further randomized studies are needed to ascertain the role of DBS in HD, especially considering the progressive nature of the disease.

Disclosure: Nothing to disclose.

Multiple sclerosis and related disorders 1

EP1142

Spinal cord glutamate-glutamine is elevated at onset of cervical cord relapse in multiple sclerosis

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Introduction: Previous ^{1}H-magnetic resonance spectroscopy (MRS) studies in Multiple Sclerosis (MS) have found elevated levels of Glutamate in active brain lesions compared with healthy controls. Glutamate excitotoxicity is considered to be an important mechanism of neurodegeneration in MS. We aimed to: (a) quantify the glutamate-glutamine (Glx) levels in the cervical cord at the onset of a SC relapse using an advanced MRS protocol, and (b) explore their relationship with clinical disability.

Methods: SC metabolites were quantified in 20 RRMS patients (14F; mean age 41 years.) within 4 weeks of upper SC (C1-C3) relapse and 22 controls (17F; mean age 44 years) using a cardiac-gated PRESS sequence; TE = 30 ms; MOIST water suppression on a 3T Philips scanner. Clinical scales, including MS Functional Composite tests and the Expanded Disability Status Scale (EDSS) were obtained for patients.

Results: Following SC relapse, N-acetyl-aspartate (NAA) was reduced [3.32 (SD 1.19) mMol/L vs 4.69 (SD 1.62) mMol/L, $p = 0.023$] and Glx was elevated [7.6 (SD 3.71) mMol/L vs 5.1 (SD 2.18) mMol/L, $p = 0.036$] compared to controls. In patients, no statistically significant association was found between Glx levels and clinical scales, when correcting for age, gender and cord cross sectional area.

Conclusions: Glx was significantly elevated at the site of a new lesion which causes a SC relapse, suggesting an altered glutamate metabolism, but it was did not associated with acute disability. We are going to explore whether elevated Glx at onset of a SC relapse predicts clinical outcome.

Disclosure: OC receives research grant support from the Multiple Sclerosis Society of Great Britain and Northern Ireland, the Department of Health Comprehensive Biomedical Centre, the International Spinal Cord Research Trust (ISRT) and the Engineering and Physical Sciences Research Council (EPSRC); she has received honoraria from Bayer Schering and GE. AT has received honoraria for consultancy from Eisai Ltd, BTG International, Novartis; honoraria and support for travel for lecturing from Serono Symposia International Foundation and Novartis. Support for travel for consultancy from MSIF; honorarium from Sage for editorship of Multiple Sclerosis Journal. BS receives funding from Philips medical. CAMW is on the advisory board for BG12 (Biogen) and receives grants (PI and co-applicant) from ISRT, EPSRC, Wings of Life, MS Society, Biogen Idec and Novartis.

EP1143

Alemtuzumab demonstrates improvement in MRI outcomes across baseline subgroups versus subcutaneous interferon beta-1a in relapsing-remitting multiple sclerosis patients who relapsed on prior therapy

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Introduction: Alemtuzumab demonstrated superior efficacy to subcutaneous (SC) IFNB-1a including reduction in magnetic resonance imaging (MRI) activity and slowing brain atrophy in active relapsing-remitting multiple sclerosis (RRMS) patients who relapsed on prior therapy. This study examined MRI outcomes in subgroups stratified by baseline demographic and disease characteristics.

Methods: In the 24-month, phase 3 CARE-MS II (NCT00548405) study, patients were randomised to alemtuzumab 12 mg/day intravenously on 5 days at baseline and on 3 days 12 months later, or SC IFNB-1a (44μgTIW). Treatment effects on risk of gadolinium (Gd)-enhancing, new/enlarging T2 and new T1-hypointense lesions, and brain atrophy (brain parenchymal fraction change) over 2 years were analysed for subgroups stratified by gender, age, race, geographic region, baseline MRI, Expanded Disability Status Scale score and other clinical parameters. Odds ratios (OR) were calculated by logistic regression (covariate adjustment for baseline lesion count).

Results: Alemtuzumab ($n = 426$) significantly reduced the risk of new/enlarging T2 lesions (OR range: 0.11–0.37, $p < 0.01$) and new T1 hypointense lesions (0.07–0.33, $p < 0.05$) versus SC IFNB-1a ($n = 202$) at Month 24 in all subgroups. Risk of Gd-enhancing lesions was lower with alemtuzumab in all subgroups, with significant risk reductions (0.19–0.38, $p < 0.05$) in most. All subgroups tended to develop less brain atrophy with alemtuzumab, which was statistically significant for younger subgroups with less extensive MRI lesions.

Conclusions: MRI benefits of alemtuzumab versus SC IFNB-1a were observed in all examined subgroups of RRMS patients who relapsed on prior therapy. These findings support the superior efficacy of alemtuzumab over SC IFNB-1a in RRMS.

Disclosure: Study supported by: Genzyme, a Sanofi company, and Bayer Healthcare Pharmaceuticals Frederik Barkhof reports receiving consulting fees from Bayer-Schering Pharma, Sanofi-Aventis,

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EP1144

Vitamin D status and vitamin D receptor gene Fok1 and Taq1 polymorphisms in Portuguese patients with multiple sclerosis

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Introduction: Multiple Sclerosis (MS) is recognized as a T-cell-mediated autoimmune disease. Vitamin D has a strong immune modulating potential and is known to suppress T-cell activation by binding to vitamin D receptor (VDR). Several studies have addressed the role of VDR gene polymorphisms in MS with conflicting results.

Objective: To investigate the association of Fok1 and Taq 1 with MS in a group of Portuguese patients and to study vitamin D status in the same group of patients.

Methods: A total of 426 patients (275 females, mean age at onset 30.0 ± 9.1 years, mean disease duration 11.1 ± 8.6 years, mean EDSS 3.1 ± 2.3) and 261 ethnicity-matched controls were genotyped for the Fok1 and Taq1 polymorphisms using TaqMan® assays. Serum 25(OH)D levels were available for only 154 MS patients and were determined using an electrochemiluminescence immunoassay.

Results: The Fok 1 ff genotype frequency was significantly higher in the patient's group relative to controls (16.4 % vs. 10.0 %, $p = 0.018$, OR = 1.77 (1.10–2.87)). No significant associations were found for the Taq1 polymorphism. Serum 25(OH)D levels revealed vitamin D deficiency or insufficiency in 66.9 % of the patients. A negative correlation between vitamin D levels and disability (EDSS and MSSS) was also found.

Conclusions: These results support a role for VDR in MS development in this group of patients, and suggest that vitamin D may function as a disease modifier. Geographical latitude could be a factor influencing the differences reported in the literature.

Disclosure: Nothing to disclose.

EP1145

The effect of teriflunomide on lymphocyte and neutrophil count in patients with a first clinical episode consistent with multiple sclerosis: results from the TOPIC study

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Introduction: Teriflunomide is a once-daily oral immunomodulator approved for the treatment of relapsing-remitting multiple sclerosis (RRMS). Teriflunomide significantly reduced the risk of relapse determining clinically definite MS in patients with a first clinical episode consistent with MS in the phase 3 TOPIC trial (NCT00622700). To further characterise teriflunomide usage in early MS, we assessed its effect on lymphocytes and neutrophils in TOPIC.

Methods: Patients (n = 618) with a first clinical episode consistent with MS received once-daily teriflunomide 14 mg, 7 mg or placebo for up to 108 weeks. Blood samples were collected at randomisation, then every 24 weeks and at treatment end.

Results: Mean baseline lymphocyte and neutrophil counts were similar across groups. At week 108, mean percent change from baseline in lymphocyte and neutrophil count was <14 % in all groups; mean counts remained within normal range. The decreases observed with teriflunomide occurred within the first 12 weeks, and counts remained stable thereafter. Per protocol, patients with neutrophils $<1 \times 10^9$/L discontinued treatment permanently. One (14 mg) and two (7 mg) patients discontinued due to neutrophil count decrease and neutropenia. No evidence of a link between neutrophil or lymphocyte count decreases and serious infection was observed.

Conclusions: Mean reductions in lymphocyte and neutrophil counts associated with teriflunomide were small, as in the phase 3 TEMSO and TOWER studies, and were not associated with an increased risk of infections. This is consistent with the immunomodulatory mechanism of action and the manageable clinical safety profile of teriflunomide.

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EP1146

Artificial intelligence techniques in the diagnosis of multiple sclerosis

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Introduction The early identification of patients at risk of developing multiple sclerosis (MS) represents the main purpose of diagnostic criteria and of clinicians in everyday clinical practice.The integration of all risk factors into an estimate of absolute risk is the starting point

for an accurate and personalized risk management at the onset of the disease. The aim of this study is to develop an artificial neural networks-based (ANNs) diagnostic model integrating both clinical and paraclinical baseline data.

Methods: Patients admitted to our Department within 3 months from CIS onset have been included. We evaluated baseline clinical data as well as MRI, multimodal evoked potentials (EPs) and CSF data. A Multi-Layer Pereceptron with a Back Propagation algorithm was used to recognize a pattern for the early prediction of MS.

Results: 227 CIS patients have been included: 71 (31 %) developed CDMS at 24 months and 120 (52.9 %) during the entire follow-up (6.82 years SD 2.78). 80 % of the patients provided training data, 20 % were the validation group for performance evaluation of the model. By changing the types of ANN and the number of input factors applied, we created models that demonstrated up to 87 % accuracy. The best accuracy was obtained with a ANN topology of Multi-Layer Perceptron with two hidden layers for models including both clinical, MRI, CSF and EPs data.

Conclusion: This study demonstrated the feasibility of using ANNs in medical decision support systems for predicting early conversion to MS by integrating baseline clinical and paraclinical data.

Disclosure: G. Dalla Costa, G. Di Maggio and L. Moiola have nothing to declare. V. Martinelli has received personal compensation for activities with Biogen Dompe, Merck Serono, Bayer Schering, Teva and Sanofi Aventis as a speaker. L. Leocani and R. Furlan have nothing to declare. M. Filippi has received honoraria for lectures and travel expenses and consulting fees as an investigator in previous and current treatment trials from Teva, Merck Serono, Bayer Schering Pharma AG, Biogen-Dompe and Genmab, and has received research support from Teva, Merck Serono, Bayer Schering Pharma, Biogen-Dompe and Genmab. G. Comi has received compensation for consulting services and/or speaking activities from Bayer Schering Pharma AG, Serono Symposia International Foundation, Merck Serono International, Teva, Sanofi-Aventis and Biogen Dompe.

EP1147

Interferon-beta specifically affects mitochondrial activity in CD4$^+$-lymphocytes: potential mechanism of action

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Introduction: Cellular immunity crucially depends on energy supply, determined by mitochondrial function. Interferon-b (IFN-b) is a mainstay in the treatment of multiple sclerosis; however mechanisms of action are incompletely understood. Here we assess the influence of IFN-b on mitochondrial function of CD4$^+$-T-cells in vitro and ex vivo.

Methods: We analysed intracellular ATP (iATP) and mitochondrial transmembrane potential ($\Delta\Psi$m, flow cytometry) in mitogen-stimulated CD4$^+$-cells of IFN-b ($n = 65$), glatiramer acetate ($n = 22$), azathioprine ($n = 8$) and mitoxantrone ($n = 22$) treated MS-patients and controls (untreated MS ($n = 70$); healthy controls ($n = 59$)). Expression of genes involved in cellular energetics in ex vivo IFN-b treated CD4$^+$-cells of healthy donors were quantified and genetic variants in key metabolism regulators correlated with MS IFN-b responders/non-responders (responders: < 1 clinical relapse and < 1 gadolinium enhancing lesion in MRI per year).

Results: IFN-b led to decreased iATP in a dose dependent manner (365.0 ± 17.8 mean $\pm$ SEM) in contrast to other immunotherapies (glatiramer acetate; 476.6 ± 29.0). This was reflected by a dose dependent depolarisation of $\Delta\Psi$m upon IFN-b treatment in vitro. iATP-levels in responders were reduced compared to non-responders ($p < 0.05$). We could demonstrate a reduced iATP level for the genotype 101 compared to genotype 102 ($p < 0.01$) of *PGC-1α*, a key regulator of mitochondrial functions.

Conclusion: Reduced iATP-synthesis in addition to depolarization of $\Delta\Psi$m and differential gene expression of OXPHOS point to specific IFN-b effects on mitochondrial function of CD4 + -cells. Our data reveal the so far unknown effect of IFN-b on immune cellular energy metabolism and imply a possible mechanism for therapeutic response/non-response in MS-patients.

Disclosure: Nothing to disclose.

EP1148

Predictors of freedom from detectable disease activity in patients with clinically isolated syndrome treated with interferon beta-1b in the BENEFIT trial

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Introduction: Identification of factors that might predict freedom from detectable disease activity is of clinical interest for patients in the early stages of multiple sclerosis.

Objective: To analyze baseline characteristics that predicted no evidence of detectable disease activity (NEDA) in the BENEFIT trial of early vs delayed treatment with interferon beta-1b for patients presenting with clinically isolated syndrome.

Methods: Patients were categorized into 2 groups: NEDA (i.e., no relapses, no EDSS progression, no new T2 or gadolinium enhancing lesions) vs. those experiencing ≥ 1 these outcomes. Clinical and MRI assessments were made every 6 and 12 months, respectively. Univariate, bivariate (treatment plus 1 other factor), and stepwise multivariate regression models were used to analyze baseline factors that potentially predicted NEDA up to 5 years.

Results: In the delayed treatment group, active treatment was delayed by a mean of 1.50 years (median 1.94 years). 447/468 patients were analyzed, 49 of whom (11.0 %) remained with NEDA (early treatment, 39 [14.0 %]; delayed treatment, 10 [6.0 %]). No evidence of clinical (vs. MRI) disease was observed in 197 patients (44.1 %). Early treatment was a strong predictor of NEDA in univariate analyses (OR 0.39, 95 % CI 0.19–0.80, $p = 0.01$) and multivariate models that included all covariates. Significant predictors of occurrence of disease activity included presence of McDonald 2010 MS, dissemination in time (McDonald 2010), dissemination in space (McDonald 2010 or 2001) and several MRI measures.

Conclusions: Despite the short time difference in the start of therapy, early treatment proved to be an advantage for remaining NEDA.

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EP1149

Fingolimod in paediatric multiple sclerosis: design of a double-blind study versus interferon beta-1a IM

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Introduction: Paediatric multiple sclerosis (MS) is a rare disorder. To date, no controlled studies have been conducted to evaluate disease modifying treatments (DMTs) in children with MS. Fingolimod is an S1P modulator which is approved for the treatment of adults with RRMS. Here we present the design of the PARADIGMS study [fingolimod versus intramuscular interferon beta-1a (IFN-beta-1a IM) in paediatric MS patients].

Study design: PARADIGMS is a 24-month, randomised, double-blind, active controlled, multicentre study in paediatric MS patients aged 10–17 years. The primary objective is to evaluate the efficacy of oral fingolimod versus IFN-beta-1a IM in reducing the frequency of relapses in paediatric MS patients treated for up to 2 years. Secondary objectives include assessment of magnetic resonance imaging (MRI) lesions, brain volume loss, additional clinical disease activity parameters, effect on cognition, pharmacokinetics and safety of fingolimod. Key inclusion criteria include Expanded Disability Status Scale score of 0–5.5 and 1 MS relapse during the previous year. Key exclusion criteria include patients with progressive MS or with an active, chronic disease of the immune system other than MS. Approximately 190 patients will be randomised to receive fingolimod or IFN-beta-1a IM 30 μg (1:1). Fingolimod will be administered at 0.5 mg/day in patients with body weight >40 kg and at 0.25 mg/day in patients with body weight ≤40 kg.

Conclusions: This study of fingolimod in paediatric MS will be the first prospective, randomised-controlled study to evaluate the therapeutic potential of any DMT for such patients.

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EP1150

4-year follow-up of delayed-release dimethyl fumarate treatment in relapsing-remitting multiple sclerosis (RRMS): integrated MRI outcomes from DEFINE, CONFIRM, and the ENDORSE extension study

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Introduction: Here we present a 2-year interim analysis of MRI outcomes from ENDORSE, an ongoing, 5-year, dose-blind extension of the Phase 3 DEFINE and CONFIRM studies evaluating delayed-release dimethyl fumarate (DMF) in RRMS.

Methods: Patients randomized to delayed-release DMF 240 mg twice (BID) or three times daily (TID) in DEFINE/CONFIRM continued the same dosing regimen in ENDORSE. Placebo (PBO; DEFINE/CONFIRM) and glatiramer acetate (GA; CONFIRM) patients were randomized 1:1 to delayed-release DMF BID or TID. Brain MRI scans were obtained yearly in ENDORSE. Efficacy was analyzed (June 12, 2013 cutoff) by parent/extension study arm: BID/BID, TID/TID, PBO/BID, PBO/TID, GA/BID, GA/TID.

Results: 718 patients (MRI cohort) were dosed in ENDORSE (n = 206 [BID/BID], 215 [TID/TID], 96 [PBO/BID], 93 [PBO/TID], 48 [GA/BID], 60 [GA/TID]). During the second year of ENDORSE, among patients continuing delayed-release DMF treatment: 68 % (BID/BID) and 61 % (TID/TID) were free of new/enlarging T2 lesions; 76 % (BID/BID) and 70 % (TID/TID) were free of new T1-hypointense lesions; and at 2-year assessment, 88 % (BID/BID) and 84 % (TID/TID) were free of gadolinium-enhancing lesions. Among patients switching from PBO to delayed-release DMF, no new/enlarging T2 lesions were observed in 33 % (PBO/BID) and 31 % (PBO/TID) during the second year on placebo in DEFINE/CONFIRM and 73 % (PBO/BID) and 77 % (PBO/TID) during the second year on delayed-release DMF in ENDORSE.

Conclusions: Reduced frequency of new MRI lesions was maintained over 4 years in patients continuing delayed-release DMF. In patients switching from placebo to delayed-release DMF, MRI outcomes were similar to those observed with delayed-release DMF in DEFINE/CONFIRM.

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EP1151

Assessment of disability status with long-term natalizumab treatment in the STRATA study

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Introduction: The Safety of TYSABRI® Re-dosing and Treatment (STRATA) study is an open-label multinational study of natalizumab treatment in patients with relapsing-remitting multiple sclerosis who completed previous randomized controlled trials and their open-label extension studies. Rates of disability progression over time in STRATA were assessed by Expanded Disability Status Scale (EDSS) scores.

Methods: The proportion of patients with 6-month confirmed progression to an EDSS score of ≥4.0 or ≥6.0 was evaluated in those patients with ≥2 post-baseline EDSS assessments. Analyses were conducted at the 6-year time point and excluded patients who had already reached the milestone at STRATA baseline. Proportions were estimated using the Kaplan–Meier (KM) method.

Results: A total of 1094 patients were enrolled in STRATA; at STRATA baseline, 300 had an EDSS score ≥4.0 and 109 had an EDSS score ≥6.0. Excluding the 300 patients with an EDSS score ≥4.0 at STRATA baseline, 56 of 617 patients with ≥2 post-baseline assessments reached a confirmed EDSS score ≥4.0 by the 6-year time point in STRATA (estimated KM proportion, 12 %). Similarly, of 770 assessed, 37 reached a confirmed EDSS score ≥6.0 (estimated KM proportion, 6 %). Sensitivity and subgroup analyses based on original feeder study treatment assignment will also be presented. The adverse event profile of natalizumab remained unchanged from previous observations.

Conclusions: With long-term natalizumab treatment in STRATA, few patients progressed to significant disability milestones and the safety profile was consistent with postmarketing experience.

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EP1152

Efficacy of daclizumab HYP across subgroups of varying relapsing-remitting multiple sclerosis disease severity: results from the SELECT study

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Introduction: Daclizumab high-yield-process (DAC-HYP) treatment has shown significant benefits on annualised relapse rate, gadolinium-enhancing (Gd +) and new/newly enlarging T2 MRI lesions, and 3-month sustained disability-progression in RRMS. The objective of this study was to evaluate the effects following 1-year of DAC-HYP in patients with relapsing-remitting multiple sclerosis (RRMS) across baseline disease subgroups.

Methods: Post-hoc analyses from SELECT patients randomized to placebo (n = 196) vs. pooled DAC-HYP 150 mg (n = 201) and 300 mg (n = 203) groups. Subgroups were defined according to demographic and baseline disease characteristics. Cox proportional hazards was used to compare time to relapse adjusted for prior relapse.

Results: DAC-HYP vs. placebo reduced the relapse-risk (Hazard Ratio [95 %-CI]) for the demographics: age ≤35 years, 57 % (0.35 [0.23–0.55]) vs. >35 years, 29 % (0.67 [0.41–1.09]); male, 65 % (0.28 [0.16–0.49]) vs. female, 31 % (0.65 [0.43–0.98]); and for baseline disease characteristics: disease duration, <3 years, 53 % (0.43 [0.24–0.80]), ≥3–<10 years, 42 % (0.52 [0.32–0.86]), ≥10 years, 44 % (0.48 [0.26–0.89]); <2 relapses, 31 % (0.65 [0.43–0.98]) vs. ≥2 relapses in previous 12 months, 64 % (0.28 [0.16–0.49]); EDSS < 3.5, 51 % (0.44 [0.29–0.67]) vs. ≥3.5, 36 % (0.57 [0.34–0.96]); absence, 52 % (0.44 [0.27–0.70]) vs. presence of Gd+ lesions, 38 % (0.54 [0.34–0.85]); and T2-lesion volume ≤ median, 47 % (0.48 [0.30–0.77]) vs. >median, 45 % (0.49 [0.31–0.77]). DAC HYP was similarly effective on MRI outcomes.

Conclusions: DAC-HYP treatment may be effective for important patient subgroups, including those with more aggressive RRMS. Data support the therapeutic option of DAC-HYP across the spectrum of RRMS.

Disclosure: Drs. Giovannoni and Gold served on the Steering Committee for the SELECT study and received consultancy fees from Abbvie & Biogen Idec; Drs. Elkins and Riester are full time employees of Biogen Idec. Drs Tsao and Greenberg are full time employess of AbbVie. Study sponsored by AbbVie and Biogen Idec.

EP1153

Efficacy and safety of anti LINGO-1 for the treatment of relapsing forms of multiple sclerosis: design of the phase 2 SYNERGY trial

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Introduction: BIIB033 is a monoclonal antibody directed against LINGO-1, a CNS-specific glycoprotein that suppresses oligodendrocyte differentiation and myelination. In Phase 1 studies of healthy volunteers and participants with MS, BIIB033 was well tolerated and showed typical IgG pharmacokinetics, lending support for further development of BIIB033 in Phase 2.

Methods: SYNERGY is a Phase 2, dose-ranging study of BIIB033 in ~400 participants with active RRMS/SPMS who are being randomized to intravenous infusions of 3, 10, 30 or 100 mg/kg BIIB033 or placebo every 4 weeks for 72 weeks. Participants are also receiving once-weekly interferon beta-1a. The primary efficacy endpoint is confirmed improvement (≥3 months) in neurophysical/cognitive function; confirmed worsening (≥3 months) is the key secondary endpoint. Both are composite measures defined based on pre-specified changes on at least one of the following: Expanded Disability Status Scale, Timed 25-Foot Walk, 9-Hole Peg Test and 3-s Paced Auditory Serial Addition Test. Exploratory endpoints include MRI and electronic patient-reported outcomes (PROs). Safety, tolerability, immunogenicity and pharmacokinetics will be assessed.

Results: SYNERGY was designed to study the efficacy of BIIB033 on repair of new and pre-existing lesions in participants with active relapsing MS. Primary and secondary endpoints were selected to allow "Go/No Go" decisions for Phase 3 and dose selection based on clinical effects. Novel MRI and PROs will be described.

Conclusions: Results of the SYNERGY study will establish whether BIIB033 can facilitate CNS repair in patients with active RRMS/SPMS while receiving concomitant immunomodulatory treatment and will help inform decisions on further clinical development.

Disclosure: RMM Hupperts has received honoraria, consultancy fees and research grants from Biogen Idec, Novartis, Merck, sanofi-aventis and Teva. G Phillips, T Dong-Si, JQ Tran, L Xu and D Cadavid are employees of Biogen Idec.

EP1154

Efficacy benefits of fingolimod 0.5 mg once daily in patients previously treated with glatiramer acetate: pooled analysis of phase 3 FREEDOMS and FREEDOMS II studies

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Introduction: In order to assess the consistency of fingolimod efficacy vs. placebo in subgroups of relapsing-remitting multiple sclerosis (RRMS) patients previously treated with disease modifying therapies, we conducted post hoc subgroup analyses of the 24-month (M) FREEDOMS and FREEDOMS II studies. Here we present the results from subgroup of patients who were treated with glatiramer acetate (GA) within the year prior to study entry and had disease activity (DA) within past 2 years.

Methods: DA is defined as.

(i) $\geq$1 relapse in past year (Y-1) and either $\geq$1 gadolinium-enhancing (Gd +) lesion or T2 lesion count $\geq$9 at baseline;

(ii) equal or more relapses in Y-1 than Y-2.

For prior GA-treated patients fulfilling one or both definitions, annualised relapse rates (ARR; negative binomial regression [NBR]), proportion relapse-free (logistic regression), 3- and 6 M- confirmed disability progression (CDP; Cox proportional hazard models), number of lesions (Gd + , new/newly enlarging [N/NE] T2; NBR) and median percent change in brain volume from baseline (PCBV; Wilcoxon) are presented.

Results: The pooled subgroup included 69/783 fingolimod 0.5 mg and 87/773 placebo patients. Fingolimod patients had reduced ARR (ARR ratio = 0.473, p = 0.004), higher odds being relapse-free (odds ratio = 2.2, p = 0.042) and reduced risk of 3 M- (Hazard Ratio, HR = 0.42, p = 0.042) and 6 M-CDP (HR = 0.59, p = 0.28) vs. placebo. Fingolimod patients also had fewer Gd + lesions (93 % reduction, $p < 0.001$) and N/NE T2 lesions (84 % reduction, $p < 0.001$) vs. placebo. The median PCBV decreased by 56 % vs. placebo (p = 0.004).

Conclusions: Fingolimod was effective in reducing clinical and MRI activities in patients with previous GA treatment.

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EP1155

Anti-JC virus antibody prevalence in a Finnish cohort of patients with multiple sclerosis and clinically isolated syndrome

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Introduction: To determine the seroprevalence of anti-JC virus (JCV) antibodies and evaluate the rate of seroconversion/seroreversion in a cohort of patients with multiple sclerosis (MS) and clinically isolated syndrome. To assess whether age, gender, MS subtype, duration of disease from the first symptoms, Expanded Disability Status Scale, number of relapses within 2 years preceding study and prior immunological treatment influence on anti-JCV antibody seropositivity.

Methods: The JCV seroprevalence was analysed in 503 patients from 4 Finnish MS centres. To assess the rate of JCV seroconversion, a subset of 97 patients underwent annual evaluation over a period of 4.5 years. A confirmatory second-generation ELISA was used for testing sera for anti-JCV antibodies.

Results: In cross-sectional study, anti-JCV antibody seroprevalence was 57.4 % (95 %CI 52.6–62.2). The rate of seropositivity was higher in males (67.3 % versus 54.1 %, p = 0.02), tended to increase across age groups (from 46.9 % in patients aged <30 years to 78.9 % in patients $\geq$60 years, p = 0.085), and was not affected by prior immunosuppressive or natalizumab therapy. In longitudinal analysis, 4 out of 19 (21 %) patients converted to seropositivity over 4.7 years, whereas 4 out of 48 (8.3 %) patients reverted from antibody-positive to seronegative status over 4.5 years. In 3 out of 67 patients serostatus fluctuated over 4.5 years.

Conclusions: Our results demonstrate anti-JCV antibody seroprevalence in half of the patients and its association with gender and age, but not with prior disease modifying therapies. Due to the fluctuations in serostatus, further studies are warranted to evaluate predictive value of anti-JCV antibody measurements.

Disclosure: This project was partially funded by Biogen Idec Inc.

EP1156

Investigation of ceralifimod's (ONO-4641) effect on lymphocytes in comparison with fingolimod

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Introduction: Ceralifimod (ONO-4641) is an oral, selective, non-prodrug, sphingosine-1-phosphate receptor-1 and -5 agonist. We assessed the effects of four ceralifimod (ONO-4641) doses on lymphocytes and lymphocyte subsets compared with placebo and fingolimod.

Methods: Healthy volunteers were randomized to ceralifimod (ONO-4641; 0.01, 0.025, 0.05 or 0.1 mg) or placebo or fingolimod (0.5 mg) once daily for 14 days. Absolute lymphocyte count (ALC) and lymphocyte subsets (CD3+ [T], CD4+ [T helper], CD8+ [cytotoxic T], CD19 [B], CD4+/CD25high and NK cells) were determined at baseline and several timepoints during treatment and recovery periods.

Results: In total 144 volunteers were randomized; the mean (standard deviation) age was 34.9 (9.0) years and 62 (43 %) subjects were female. Ceralifimod (ONO-4641) treatment was associated with a dose-dependent decrease in lymphocytes. After 14 days' treatment (Day 15), mean ALC percentage change from baseline was −3 % (placebo), −62 % (fingolimod), −8 % (ceralifimod 0.01 mg), −25 % (ceralifimod 0.025 mg), −45 % (ceralifimod 0.05 mg) and −56 % (ceralifimod 0.1 mg). After treatment discontinuation, mean ALC in the ceralifimod groups recovered faster than with fingolimod such that the proportion of subjects reaching ≥80 % of baseline ALC 14 days post-treatment was >85 % in placebo and all ceralifimod groups, versus 33 % in the fingolimod group. A dose-dependent decrease in lymphocyte subsets (CD3+, CD4+, CD8+, CD19, CD4+/CD25high) was observed for ceralifimod; NK cells remained unaffected. A similar pattern for subsets was observed with fingolimod.

Conclusions: Ceralifimod (ONO-4641) was associated with a dose-dependent decrease in lymphocytes, and lymphocyte recovery was faster in the ceralifimod than the fingolimod group.

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Peripheral nerve disorders

EP1157

Adult polyglucosan body disease: clinical and histological heterogeneity of an Italian family

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Introduction: Adult Polyglucosan Body Disease (APBD) is a rare autosomal recessive leukodystrophy due to mutations of glycogen branching enzyme gene (GBE1), leading to accumulation of polyglucosan bodies (PB) in central and peripheral nervous system. The disease mainly affects the Askenazi Jewish descent.

Methods: Three siblings from a non-Jewish Italian family, affected with APBD.

Results: The proband, a 57-years-old man, presented with progressive distal paresthesia at the age of 55 years. A sensory-motor demyelinating neuropathy was diagnosed at nerve conduction study (NCS). Subsequently, gait ataxia and urinary urgency were reported. His sister, now aged 56 years, has been showing a slowly worsening paraparesis since the age of 52 years, complicated by neurogenic bladder in the last months. The youngest affected sister, aged 53 years, had a recent, transitory, episode of orthostatic vomit and mild ataxia. The MRI of all subjects showed diffuse hyperintense infra- and supratentorial white matter abnormalities, with bulbar and spinal cord atrophy. In both sisters NCS was normal, whereas their muscle biopsies only showed non-specific alterations. In the proband, both muscle and nerve biopsies showed PB, which prompted molecular investigation for GBE1. All siblings were compound heterozygous for a previously described mutation (c.1604A>G), and a novel one (c.1064G>A).

Conclusions: We demonstrated that in a large APBD family, common clinical signs occurred together with "atypical" ones (demyelinating neuropathy/transient symptoms) featuring a peculiar intrafamilial variability. Indeed, PB detection at muscle/nerve biopsy correlates with NCS alteration, which makes the integration between peripheral and central nervous system findings necessary for a correct diagnosis.

Disclosure: Nothing to disclose.

EP1158

Long-term prognosis and health-related quality of life (HRQol) in multifocal motor neuropathy (MMN)

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Introduction: MMN evolves with asymmetric weakness, conduction blocks (CB), antibodies to glycolipid GM1. Purpose of our study was to assess if demographic, clinical, neurophysiological variables could be useful to identify disease progression in MMN.

Methods: Forty one Caucasian patients (34 males and 7 females, median age 47 years) were followed for median duration of 92 months (range 12–264). Eight patients (19.5 %) had GM1 IgM antibodies at diagnosis, 36.5 % became positive during study frame. UE tremor was observed in 60 % of patients. Strength was assessed separately in UE, LE with Medical Research Council Scale (MRC), disability with Overall Disability Sum Score (ODSS) and Ranking scale. Effects of IVIg treatment on progression was included in analyses conducted at 1, 3, 5, 10, 15 years by separate Mann–Whitney U test and Wilcoxon matched pair test. Human leukocyte antigen (HLA) antigen distribution was compared between patients and 3,528 controls. Health-related quality of life (HRQol) was assessed using Short-Form Health Survey (SF-36).

Results: At 1 and 3 years, total MRC score and the subscore related to lower extremities significantly decreased ($T = 113$; $p = 0.009$ and $T = 70{,}5$; $p = 0.002$, respectively) without benefit from IVIg. At 10 years, overall MRC subscores significantly decreased ($p = 0.003$ and 0,001). There was no significant differences between demographic features, number of definite CBs, disability outcome measures. Analysis of distribution of 9 selected HLA allelles with frequency ≥15 % either in patients or controls showed that DQB1*06 prevailed in anti GM1 positive MMN ($p = 0.02$).

Conclusions: Our results provide evidence that MRC grading is reliable prognostic marker. The finding of HLA DQB1*06 prevalence in patients with detectable anti GM1 confirms that HLA locus contributes to immune response.

Disclosure: Nothing to disclose.

EP1159

Prognostic factors and health-related quality of life (HRol) in polyneuropathy with IgM antibodies to myelin associated glycoprotein (MAG)

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Introduction: Polyneuropathies with IgM antibodies to MAG are immunologically mediated disorders. Purpose of this cohort study was to assess effects on disease progression of demographic (age of onset/diagnosis, gender), clinical, neurophysiological variables.

Methods: Forty Caucasian patients (25 males,15 females, median age 70.5 years) were followed for a median duration of 91 months (range 12–225). Median anti-MAG titer determined by ELISA was 17,452 U. Electrophysiological type of neuropathy (demyelinating, axonal or mixed), muscle strength, assessed with Medical Research Council Scale (MRC), disability, assessed with Overall Disability Sum Score (ODSS), Ranking scale, type of treatment, serum IgM level were included in the analyses. Worsening was considered significant if MRC difference between first and last esamination was at least 12 points. Survival analysis with Cox regression model was performed. Human leukocyte antigen (HLA) antigen distribution was compared between patients and 3,528 controls. Health-related quality of life (HRQol) was assessed using Short-Form Health Survey (SF-36).

Results: Survival analysis showed that patients with higher IgM level ($p = 011$), electrophysiological evidence of demyelinating damage ($p = 0.05$), absence of either immnunomodulating, immunosuppressive treatments during disease course (p.0021) had significantly higher risk of worsening. Analysis of distribution of 9 selected HLA allelles with frequency $\geq$15 % either in patients or controls showed that B44 and DRB1*07 prevailed significantly in patients ($p = 0.004$ and $= 0.03$ respectively) Variations of clinical measures did not affect HRQol.

Conclusion: IgM level, electrophysiological type of neuropathy at onset could be considered prognostic markers in polyneuropathies with IgM antibodies to MAG. The finding of HLA B44 and DRB1*07 prevalence in patients could point possible association of anti-MAG antibody production with this molecule.

Disclosure: Nothing to disclose.

EP1160

Morphological study of the human corneal sub-basal plexus using in vivo confocal microscopy in patients with symptomatic diabetic polyneuropathy compared to controls

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Introduction: Diabetic neuropathy (DN) is a common clinical condition. The currently recommended diagnostic tests have low sensitivity. With the advent of in vivo corneal confocal microscopy (CCM) it was observed changes in the innervation of the cornea in patients with DN.

Methods: We evaluated the characteristics of the innervation of the cornea through the in vivo MCC in 35 diabetic patients with symptomatic distal symmetric polyneuropathy (DSP), compared to 55 controls. We sought to determine a pattern of morphological changes between stages of DSP severity, comparing clinical, laboratory, and nerve conduction variables.

Results: Differences between control and diabetic groups were observed for the following variables: age (44.9 ± 13.24 vs 57.02 ± 10.4, p value < 0.001), fiber density (29.7 ± 10.2 vs. 16.6 ± 10.2, p value < 0.001), number of fibers (4.76 ± 1.30 vs 3.14 ± 1.63, p value < 0.001), number of Langerhans cells (4.64 ± 8.05 vs 7.49 ± 10.3, p value $= 0.035$), tortuosity (p value < 0.05) and thickness (p value < 0.05). Furthermore, inverse relationship was found between fiber density and age (p value < 0.01) and fiber density and clinical severity (p value < 0.05). Another highlight was a positive relationship between conduction velocity of peroneal nerve and fiber density (p value < 0.05).

Conclusions: MCC is a fast, non-invasive and reproducible method for the diagnosis and monitoring of diabetic DSP.

Disclosure: Nothing to disclose.

EP1161

Modelling pathogenesis and treatment of Mitofusin 2 disease using patient-specific iPSCs

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Introduction: Patients-derived human induced pluripotent stem cells (iPSCs) are promising strategy for studying diseases mechanisms and therapeutic approaches, due to their potentiality to recapitulate disease features. Mitofusin 2 gene mutations are associated to a broad spectrum of human diseases in which Charcot Marie-Tooth disease-2A2 (CMT2A2), an hereditary axonal neuropathy with progressive distal muscle weakness, atrophy and sensitivity loss, is the most frequent phenotype. Mitofusin 2 encodes a protein responsible for mitochondrial outer membrane fusion. The mechanism of neuron loss and the role of mitochondrial dysfunction are poorly understood owing to the lack of an appropriate human model system and no effective treatment is still available.

Methods: We generated iPSC lines derived from human skin fibroblasts of CMT2A2 patients with *viral* vectors, capable of expressing the four Yamanaka factors and with a *non-viral* episomal iPSC reprogramming plasmids. iPSCs were differentiated using a protocol to promote neuronal phenotype. The phenotype of these cells was analyzed by morphological, functional, gene expression, and protein analysis.

Results: Patient-derived cells show no morphological and replication features modifications compared to WT cells. We observed perturbation in mitochondrial organization, suggesting that this is a key mechanism of CMT pathogenesis. Indeed, biochemical analysis demonstrated a reduction in the respiratory chain. Furthermore, CMT2A-iPSCs were used to test candidate therapeutic strategies. In particular, we evaluated a possible shRNA strategy, to reduce MFN2 protein.

Conclusions: The present study demonstrates that iPSCs can be an essential tool in the understanding of human Mitofusin 2 pathogenesis and to test possible new treatments.

Disclosure: Nothing to disclose.

EP1162

Churg Strauss syndrome neuropathy: characterization from a retrospective series of 700 biopsies

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Objectives: Although Churg Strauss syndrome CSS is frequently complicated with peripheral neuropathy, few cases of CSS with examination of the peripheral nerve biopsy have been published.

Methods: Biopsy specimens were selected from over 700 sural nerve biopsies performed at the Section of Neurology, Neurological Clinic of Athens University Hospital, from1991–2011. A total of 71 biopsies fulfilled the pathological criteria for vasculitis. 22 cases

were diagnosed as non-systemic vasculitis. 49 cases were considered as systemic vasculitis and 9 cases of these were diagnosed as CSS, according to the criteria of the American College of Rheumatology. Clinical, electrophysiological, histopathological and morphometrical features of were obtained retrospectively from medical files.

Results: Nine out of 700 biopsies (1.3 % of all biopsies) performed in our laboratory were diagnosed as CSS. The pathological features were vasculitis with predominant axonal degeneration and a varying pattern of myelinated fiber loss. The vasculitic changes were found mainly in small epineural blood vessels. Mononeuritis multiplex and distal symmetrical and asymmetrical sensorimotor neuropathy, were equally frequent. Asthma was the most frequently observed manifestation. Hypereosinophilia (>10 %) was the main biological feature of CSS. The number of male and female was equally distributed in our study.

Conclusions: This retrospective study confirms that diagnosis of polyneuropathy is based on clinical and electrophysiologic studies, but precise immunolohistochemistry and morphometric study of the peripheral nerve biopsy may be decisive in establishing the diagnosis. Although CSS is rare, it is important to recognize it, because remission depends on immunosuppressive therapy introduced in the early stage.

Disclosure: Nothing to disclose.

EP1163

Genotypic and phenotypic presentation of TTR-FAP in Turkey

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Introduction: Transthyretin-related familial amyloid polyneuropathy (TTR-FAP) is an autosomal dominant disorder caused by mutations of the transthyretin (*TTR*) gene. More than 100 different mutations of the transthyretin gene were identified worldwide, but still the first described Val30Met is the most common one. The mutant amyloidogenic transthyretin protein causes systemic accumulation of amyloid fibrils that results in organ dysfunction and death.TTR-associated FAP is a progressive and fatal disease if left untreated and should be considered in the differential diagnosis of any patient with a progressive polyneuropathy, especially with an accompanying autonomic involvement.

Methods: We studied clinical, electrophysiological, histopathological, and genetic characteristics in 14Turkish patients (4 female, 10 male) from 9 families withpolyneuropathyand mutations in *TTR*.

Results: Mean age of onset was 43.6 ± 13.3 years (between 21–66 years). Nine of them were late-onset TTR-FAP. At onset, all the patients exhibited sensory loss of the lower and upper limbs, three patients also experienced severe autonomic symptoms. Five patients had autonomic nervous system manifestations, and nine demonstrated evidence of amyloid cardiomyopathy, two of them had renal involvement. Five patients (4 male) had carpal tunnel syndrome. One patient with Gly53Glu mutation showed episodes of dysarthria and hemiparesis which were already described to be associated with this genotype. Four patients died during follow-up due to the systemic involvement. Sequence analysis of TTR gene revealed the presence of six different mutations (Val30Met [in 3 unrelated families], Glu89Gln, Gly53Glu, Glu74Gly, Gly47Glu, Glu109Gly).

Conclusions: Our study suggests that the TTR-FAP patients from Turkey exhibit a wide clinic and genetic heterogeneity.

Disclosure: Nothing to disclose.

EP1164

Neuropathy in Tangier disease mimicking leprosy

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Introduction: Tangier disease (TD) is a rare autosomal recessive disorder of lipid metabolism resulting from mutations in the ABC1 gene, leading to decreased levels of plasma HDL. Peripheral neuropathy is present in about 50 % of cases. We report a patient diagnosed with TD in which a leprosy neuropathy was first considered.

Methods: A 51-year-old man complained of weakness and numbness in the limbs. Neurological examination showed facial diplegia, weakness and wasting in the four limbs, hyporreflexia and asymmetrical decrease in vibratory, touch and pain sensations in limbs. Pain and temperature anesthesia was found over a back hypopigmented skin lesion. He suffered from myocardial infarction at the age of 48, thrombocytopenia and spontaneous splenic rupture.

Results: Electromyography revealed bilateral facial palsy and a demyelinating sensorimotor polyneuropathy. Sural nerve biopsy showed onion bulb formation, macrophagic cells with foamy cytoplasm and dense bodies accumulation compatible with bacillary degeneration. Histiocytic cells with foamy cytoplasm surrounding capillaris in the dermis were seen in the skin biopsy. A diagnosis of leprosy neuropathy was considered and he was treated without neurological improvement. 6 years later, during a diagnostic study of thrombocytopenia and splenomegaly in a brother, a lipid profile revealed very low HDL-C and LDL-C levels with low ApoA-1, that were later seen in other brothers, as well as in our patient, confirming TD diagnosis.

Conclusions: Peripheral neuropathy may be the presenting symptom in TD and may simulate leprosy neuropathy. We suggest that a lipid profile should be included in the screening of chronic demyelinating neuropathy.

Disclosure: Nothing to disclose.

EP1165

Bochum ultrasound score versus clinical and electrophysiologal parameters in distinguishing acute-onset chronic from acute inflammatory demyelinating polyneuropathy

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Introduction: We aimed to evaluate prospectively a recently introduced nerve ultrasound score (Bochum ultrasound score, BUS) [1] (Overview in Table 1) clinical and electrophysiological parameters in distinguishing sub- acute chronic (CIDP) from acute inflammatory demyelinating polyneuropathy (AIDP).

Overview of the Bochum Ultrasound Score

Anatomic Sites	Points
CSA of the ulnar nerve in Guyon's canal	1
CSA of the ulnar nerve in the upper-arm	1
CSA of the radial nerve in spiral groove	1
CSA of the sural nerve between the gastrocnemius muscle	1
Sum Score	**4**

Legend
CSA = cross sectional area

The Bochum Ultrasound score has two simple rules:

1) The patient receives 1 point, for each of the above anatomic sites, where he showes a pathological cross sectional area enlargement, compared the reference values of our lab (Kerasnoudis et al., Clin Neurophysiol 2013)

2) If the patient showes on both sides of the body a pathological cross sectional area nerve enlargement of the concrete nerve, he also receives only 1 point

Considering the above, each patient can receive a minimum sum score of 0 points and a maximum sum score of 4 points. Following the previous report in the literature (Kerasnoudis et al, 2013a) we used as a cut-off value for differentiating a sub- acute CIDP from AIDP a sum score of ≥ 2 points

Methods: BUS, clinical [sensory symptoms or signs, bulbar palsy, autonomic nerve system (ANS) dysfunction, preceeding infections and respiratory muscle involvement] and electrophysiological parameters (A-waves, sural nerve sparing pattern, sensory ratio > 1) underwent prospective evaluation in a group of 10 patients (mean age 53.4, SD $\pm$ 10.3, 6 women), who referred to our department between January 2012 and May 2013 with clinical presentation of sub- acute polyradiculoneuropathy.

Results: Sensitivity and specificity in distinguishing sub-acute CIDP from AIDP were as follows: BUS: 83.3 %, 100 %; sensory symptoms: 100 %, 75 %; lack of ANS dysfunction: 83.3 %, 75 %; lack of bulbar palsy 83.3 and 50 %; lack of preceding infections 66.6 % and 50 %; lack of respiratory muscle weakness or need for mechanical ventilation 100 % and 50 %; negative sural sparing pattern: 100 %, 50 %; lack of sensory ratio >1 100 % and 25 %; presence of A-waves 33.3 % and 25 % (Tables 2, 3).

	Polyradiculoneuropathies (n=10)					
	CIDP (n=6)	AIDP (n=4)	Sensitivity	Specificity	PPV	NPV
Sensory symptoms	6	1	100%	75%	85.7%	100%
No bulbar palsy	5	2	83.30%	50%	71.40%	67%
No ANS dysfunction	5	1	83.30%	75%	83%	75%
No preceeding infections	4	2	66.60%	50%	66.60%	50%
No respiratory muscle weakness or need for mechanical ventilation	6	2	100%	50%	75%	100%

	Polyradiculoneuropathies (n=10)					
Electrophysiology	CIDP (n=6)	AIDP (n=4)	Sensitivity	Specificity	PPV	NPV
A-waves	2	3	33.3%	25%	40%	20%
No Sural sparing (definition 1)	6	2	100%	50%	75%	100%
No Sural sparing (definition 2)	6	3	100%	25%	66.6%	100%
No Sural sparing (definition 3)	6	2	100%	50%	75%	100%
No Sural sparing (definition 4)	6	2	100%	50%	75%	100%
No Sensory ratio > 1	6	3	100%	25%	66.6%	100%
Nerve ultrasound						
Bochum ultrasound score ≥ 2 pt	5	0	83.30%	100%	100%	75%

Legend
Sural sparing definition 1 = normal sural SNAP amplitude with abnormal median SNAP amplitude (low or absent) (Murray and Wade, 1980)
Sural sparing definition 2 = normal sural SNAP amplitude with absent median SNAP amplitude (Bromberg and Albers, 1993)
Sural sparing definition 3 = normal sural SNAP amplitude with abnormal median or ulnar SNAP amplitude (low or absent) (Albers et al, 1985)
Sural sparing definition 4 = normal sural SNAP amplitude with at least two abnormal (low or absent) sNAPs amplitudes in the upper extremities (radial, ulnar, median nerves) (Al-Shekhlee A et al, 2005)
Sensory ratio = (sural + radial) / (ulnar + median) SNAP amplitudes (Al-Shekhlee A et al, 2007)

Conclusions: BUS seems to have a comparable high sensitivity and specificity with certain clinical parameters (presence of sensory symptoms, lack of ANS dysfunction), but a higher sensitivity and specificity compared to electrophysiological parameters, in distinguishing sub-acute CIDP from AIDP.

References

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Disclosure: Nothing to disclose.

EP1166

Early and paradoxical worsening after rituximab infusion for anti-MAG neuropathy

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Introduction: A recent study demonstrated clinical benefit of rituximab in anti-MAG neuropathy on secondary endpoints (Léger 2013). Conversely, some authors report cases of worsening after rituximab infusion (Stork 2013, Broglio 2005, Gironi 2006). Here we report two cases of neurological worsening after the third (out of four) weekly infusion of rituximab (375 mg/m2).

Case report: Both patients had a typical chronic, distal, predominantly sensory impairment with ataxia. Anti-MAG antibody titre was above 10.000 BTU and electrophysiological study (EDX) disclosed predominantly distal demyelinating abnormalities in both patients.. Treatment by IVIG and/or plasma exchange was inefficient; neurological condition worsened with the occurrence of distal weakness in feet. Rituximab therapy was thus undertaken. In the days following the third infusion, both patients experienced worsening of neurological status.

Patient 1 experienced an increase of his sensory signs with extension from the calves to the knees, appearance of errors of position sense of big toes, and loss of 3 points on Norris score.

Patient 2 experienced worsening of ataxia requiring a second aid for walking (+1 point in ONLS score), lower limbs distal weakness (-4 points MRC score) and an extension of sensory loss to fingers. EDX in Patient 2 confirmed worsening of demyelinating features.

We discontinued immediately rituximab infusion and resumed treatment by IVIG which allowed improvement in patient 1 and stabilization in patient 2.

Conclusion: Rituximab treatment in anti-MAG neuropathy requires close monitoring to detect this paradoxical worsening. Further prospective analysis is necessary to identify pathogenic mechanisms and predisposing factors.

Disclosure: Nothing to disclose.

EP1167

Teachings from the French database of TTR familial amyloid polyneuropathy (TTR-FAP): sporadic, genetic and phenotypic heterogeneity in late onset cases

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Introduction: TTR-FAP is progressive, disabling and life-threatening neuropathy due to a point mutation of TTR gene with autosomal dominant transmission. Median survival ranges from 7 to 12 years after onset. France is considered as a prototype of non endemic country. To study the impact of labeling French reference center for FAP (NNERF) and building of a national network.

Methods: In 1986–2013 period, 460 FAP patients were registered in NNERF's database. All carried amyloidogenic TTR gene mutations and Congo positive amyloid deposit (CPAD).We report genotypic characteristics in all database and the phenotypic varieties of FAP in France in 2008–2013 period.

Results: TTR-FAP are actually identified in 80/100 geographical departments. Ethnical origin: French-56 %, Portuguese-34 %, other-10 %. 41 TTR mutations identified: Met30–60 %, Tyr77–12 %, Phe77–6 %, Val107–5 %, Ile122–2 %; 22 variants TTR in single cases.In 2008–2013 period: 158 new cases, mean age 59y (22–89), Portuguese origin 21 %, positive family history of FAP 52 %, walking with aid 38 %, a late onset (≥50 y) in 69 % including 22 % older than 70y. Diagnosis of FAP was delayed by 3y (0.2–13.5) after first symptoms. Two phenotypes were common in all origins: Small Fiber Length-Dependent PNP (20 %) and Autonomic NP (16 %). Four new phenotypes: All-Fiber SM-PNP (16 %), Upper Limbs NP (17 %), Ataxic NP (12 %), Motor NP (0.7 %). CPAD after nerve biopsy in 18/24pts (75 %), LSGB in 78/111 pts (70 %); 76 % required multiple biopsies.

Conclusions: A better knowledge of the phenotypes of FAP and the larger use of TTR gene analysis in idiopathic aggressive polyneuropathy cases will help to accelerate diagnosis of TTR-FAP.

Disclosure: Nothing to disclose.

EP1168

Anti-sulfatide IgM antibodies in peripheral neuropathy: to test or not to test?

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Introduction: Anti-sulfatide IgM antibodies have been associated with different neuropathies and were variably associated with serum IgM monoclonal gammopathy and antibodies to the meylin-associated glycoprotein (MAG). This heterogeneous association has induced some skepticism on the pathogenetic relevance of this reactivity.

Methods: We reviewed the clinical association of anti-sulfatide IgM antibodies in 570 patients with neuropathy and related disorders examined in our Institution since 2004. Anti-sulfatide antibodies were measure by ELISA at the initial serum dilution of 1:32,000 and titrated by serial two-fold dilution. Patients were also tested for anti-MAG IgM antibodies by western blot.

Results: High titers of anti-sulfatide IgM (1.32,000 or more) were found in 39 patients, including 19 with titers up to 1:64,000, and 20 with titers of 1:128,000 or more. In 33/39 positive patients (85 %) anti-MAG IgM were also found. In these patients the neuropathy had the features of neuropathy associated with anti-MAG antibodies. Six patients did not have anti-MAG antibodies. Five of them had moderately increased anti-sulfatide titers (up to 1:64,000) that were associated with various neuropathies including a chronic sensory axonal neuropathy associated with IgG monoclonal gammopathy, POEMS syndrome, transtiretin neuropathy, asymptomatic neuropathy and paraneoplastic sensory neuropathy. One patient with a demyelinating neuropathy associated with IgM monoclonal gammopathy had markedly increased antibodies (1:256,000).

Conclusions: Anti-sulfatide IgM antibodies are not infrequent in patients with neuropathy but are often associated with anti-MAG reactivity. A selective reactivity to sulfatide is rarely found and is associated with different forms of neuropathy raising some doubts on their diagnostic relevance.

Disclosure: Eduardo Nobile-Orazio reports personal compensation for serving in the Steering or Advisory Board of Baxter, Italy, CSL Behring, Italy, Kedrion, Italy, and Novartis, Switzerland. He received honoraria for lecturing from Baxter, CSL Behring, Grifols, Spain, and Kedrion and travel supports for Scientific Meetings from Baxter and Kedrion. All compensations and supports are outside the submitted work.

EP1169

Distal polyneuropathy as initial manifestation of sporadic Creutzfeldt-Jakob disease: early sural biopsy findings

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Introduction: The co-existence of central nervous system (CNS) and peripheral nervous system (PNS) involvement in Creutzfeldt-Jakob disease (CJD) has been reported in only few previous cases.

Case report: A 67-year-old man with stocking-like hypoesthesia, loss of vibration sense, ataxic gait was suspected of polyneuropathy. Standard cerebrospinal fluid (CSF) analyses were negative. Electromyography suggested an axonal-demyelinating distal neuropathy. Motor and sensory evoked potentials were pathological, whereas spinal cord MRI was normal. The patient received a cycle of iv Methylprednisolone without any benefit.

Sural nerve biopsy [fig. 1] showed the coexistence of both demyelinating and axonal pathology with marked fiber loss, occasional onion bulbs, predominantly axonal damage [fig. 2] at teasing examination. The ultrastructural analysis of the sural nerve showed predominant axonal pathology [fig. 3]. The patient́s gait ataxia markedly worsened and spasticity, bradykinesia, resting tremor, limb rigidity, hypophonia and memory impairment became evident with bilaterally positive Babinski signs. The diagnosis of CJD was suggested by brain MRI scan, although electroencephalography was atypical. CSF examination showed marked 14-3-3 positivity, and tau was increased.

The patient died 11 months after disease onset. On autopsy, histological analysis of the brain confirmed the diagnosis. Immunohistochemistry for PrPsc revealed kuru-like amyloid plaques in the cerebellum. A complete analysis of the PRNP gene was negative for known mutations. The CJD subtype of this patient was MV2.

Conclusions: Our case underscores that the PNS can be involved early in sCJD. Clinical and pathological similarities among the reported cases of sCJD with ataxia and sensory polyneuropathy are discussed.

Disclosure: Nothing to disclose.

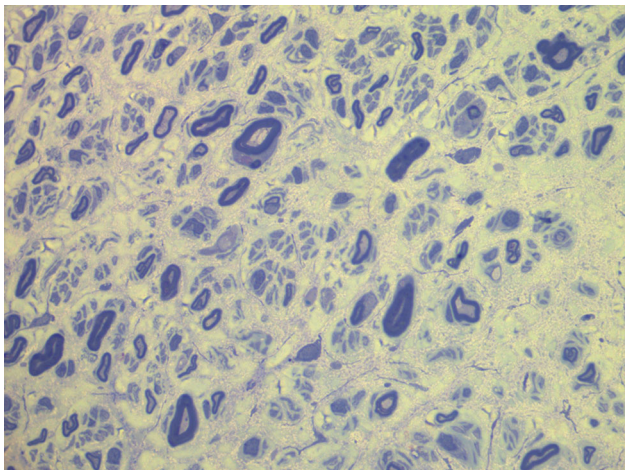

Figure 1

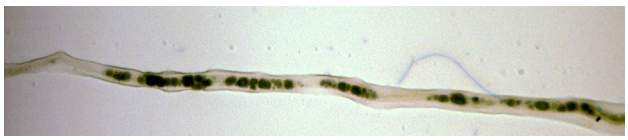

Figure 2

Figure 3

EP1170

Combined skin biopsy and neurophysiological study in TTR-amyloidosis allows early detection of small fiber neuropathy

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Introduction: Small-fiber neuropathy (SFN) is most frequent and early manifestation of transthyretin familial amyloid polyneuropathy (TTR-FAP). Evaluation of the value of intraepidermal nerve fibers density (IENFD) by skin biopsy and neurophysiological investigation of small nerve fibers to detect SFN in TTR-FAP.

Methods: We evaluated 11 patients with clinical polyneuropathy (7M/4W; 40–75 ys) and 9 asymptomatic carriers (4M/5W; 30–56 ys) with 5 types of pathogenic ATTR-variants: V30M (n = 16), V28M (n = 1), S77T (n = 1), S77P (n = 1) and T49I (n = 1). Skin biopsies performed at thigh (proximal) and leg (distal); IENFD measured after immunofluorescence staining of PGP9.5 in nerve terminals. Lower limit of normal values were 12.8 f/mm at thigh and 7.6 at leg (Devigili et al., 2008). Congo red staining was performed to detect amyloid deposits. Neurophysiological investigation including laser evoked potentials (LEP), quantitative sensory testing (QST), sympathetic skin response (SSR) and heart-rate variability (HRV).

Results: In 11 patients with overt neuropathy, skin biopsy evidenced SFN, with proximal IENFD (mean ± SD) at 4.3 ± 3.9 f/mm, distal IENFD at 2.3 ± 1.6 f/mm. Neurophysiological investigation showed abnormal LEP (n = 9), QST (n = 6), SSR (n = 6), and HRV (n = 8). In 9 asymptomatic carriers, proximal IEFND was decreased in 9/9 at 7.1 ± 4.3 f/mm, and distal IENFD in 6/9 at 3.8 ± 1.9 f/mm. Neurophysiological investigation showed abnormal LEP (n = 4), QST (n = 0), SSR (n = 2), and HRV (n = 3). Finally, congo stain disclosed amyloid deposits in 6/11 patients, 1/9 carriers in skin biopsy.

Conclusions: This pilot study showed that a combined approach may detect TTR-FAP at a presymptomatic stage and therefore identify potential candidates for innovative therapeutic strategies.

Disclosure: Nothing to disclose.

EP1171

Bortezomib: new option for chronic inflammatory demyelinating polyradiculoneuritis (CIDP)

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Introduction: CIDP is an acquired, immune-mediated disorder that is progressive or relapsing over a period of at least 8 weeks. CIDP is thought to be mediated by both cellular and humoral immune reactions directed against the peripheral nerve myelin or axon. Only three treatment regimens for CIDP have demonstrated benefit in randomized, controlled studies: corticosteroids, plasma exchange, and intravenous immunoglobulins (IVIg). Approximately 25 % of patients respond inadequately to corticosteroids, plasma exchange or IVIg. We aimed to evaluate bortezomib as a new treatment option in CIDP patients aiming at immune cells with high metabolism.

Methods: Six patients with CIDP were consecutively treated with bortezomib. The patients failed to standard and escalating treatments and had an excessively high need of IVIg. Subjects were neurologically and neurophysiologically examined every 3 months after a series of 4 bortezomib injections (1.3 mg/m^2), accompanied by antibiotic and virustatic protection for 4 weeks.

Results: Subject had an INCAT-Score (Inflammatory Neuropathy Cause and Treatment Scale) between 2–10 prior to bortezomib. Meanwhile three patients were examined. In these three patients the INCAT-Score and the nerve conduction velocity studies remain stable. Electromyography in two patients showed reinnervation in musculus brachioradialis and musculus interosseous dorsalis. No severe side effects occured.

Conclusion: Our case series is the first report of a positive effect of bortezomib in CIDP patients who failed standard treatment algorithms. Although preliminary our case series show promising results in CIDP patients with highly active disease course. Further research is needed to evaluated bortezomib's effect in CIDP patients.

Disclosure: Nothing to disclose.

Autonomic nervous system disorders

EP1201

Orthostatic intolerance is frequent in patients with clinically isolated syndrome

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Objectives: The aim of this study was to determine the prevalence of pathologic response to orthostatic challenge in patients with clinically isolated syndrome (CIS) suggestive of multiple sclerosis (MS) and to correlate autonomic dysfunction with clinical and MRI findings and serum catecholamine levels.

Methods: We included 40 CIS patients, 18 males and 22 females, aged 16–53 years. The pain-provoked head up tilt table test (PP-HUTT) was used to provoke an orthostatic reaction.

Results: Altogether 32 patients (80 %) had a pathological response: orthostatic hypotension (OH) (N = 13, 32.5 %), vasovagal syncope (N = 10, 25 %) and postural orthostatic tachycardia (POTS) (N = 9, 22.5 %). There was no significant difference ($p = 0.177$) between type of CIS and type of response to orthostatic provocation (OH, POTS or syncope). There was no significant correlation between presence of autonomic dysfunction and presence of lesions in the brain hemispheres (Spearman coefficient -0.136, $p = 0.403$), brainstem (Spearman coefficient 0.025, $p = 0.878$), cerebellum (Spearman coefficient 0.153, $p = 0.346$) or the spinal cord (Spearman coefficient 0.048, $p = 0.784$). Pathological response to orthostatic provocation correlated with difference in norepinephrine levels (standing-supine) (Pearson coefficient -0.419, $p = 0.012$), indicating that MS patients with pathological response to orthostatic provocation have higher increase in norepinephrine upon standing. This increase is mainly due to high percentage of patients with postural orthostatic tachycardia who had statistically higher difference in norepinephrine levels (standing–supine) compared to patients with normal response to orthostatic provocation ($p = 0.03$).

Conclusions: This study has shown that orthostatic intolerance is frequent in the initial phases of MS.

Disclosure: Nothing to disclose.

EP1202

Evaluation of autonomic nervous system in acute stroke through the assessments of heart rate variability and catecholamine levels

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Introduction: This study aimed to evaluate changes in autonomic nervous system caused by cerebral lesions in acute stroke according to the hemispheric localization of the lesion by assessing heart rate variability and catecholamine levels.

Methods: Sixty stroke patients and 31 healthy controls were included. Plasma epinephrine and norepinephrine levels were measured on the 1st, 3rd and 7th days. Heart rate variability (time-domain and frequency-domain analyses) was analyzed on 24-hour Holter recordings. Stroke patients were grouped according to the site of lesion: those with right hemisphere lesion (n = 24), those with left hemisphere lesion (n = 28), those with brain stem-cerebellum lesion (n = 8).

Results: Norepinephrine levels on the 1st and 3rd days were significantly higher in all patient groups than in the controls. Epinephrine levels on the 1st, 3rd and 7th days were significantly higher in the group with right hemisphere lesion than in the controls. On frequency-domain analysis, the group with right hemisphere lesion had higher low frequency and low frequency/high frequency values than the controls. Time-domain analysis revealed significant decreases in standard deviation of the mean of 5-min 288 R–R intervals values of the groups with right hemisphere and brain stem-cerebellum lesions compared to the controls.

Conclusions: In conclusion, among acute stroke patients, significant autonomic dysfunction was determined in those with right hemisphere lesion. These findings indicated autonomic dysfunction in favor of sympathetic activity. Closer monitoring and treatment of stroke patients, particularly in acute phase, may favorably affect their prognosis.

Disclosure: Nothing to disclose.

EP1203

Comparison of sudoscan and Q-sweat for assessment of sudomotor function

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Introduction: Autonomic neuropathy is poorly investigated. As sweat glands are innervated by sympathic C-fibers, measurement of sweat function has been suggested for assesment of early autonomic dysfunction. Quantitative Sweat Measurement System (Q-sweat) is the commercially available version of Quantitative Sudomotor Axon Reflex Test (QSART), the reference method for sweat function assessment. It is a time-consuming and highly qualified method.

This sudy aimed to compare SUDOSCAN a quick, simple, non invasive and quantitative method for assessment of sudomotor function to Q-Sweat.

Methods: 100 patients were measured for Q-Sweat on forearm (FA), distal leg (DL) and foot (F). References valueswere issued from literature. Sweat function using SUDOSCAN was measured on hands and feet. Results were expressed in microSiemens (μS) and electrochemical sweat conductance (ESC) >60 μS were considered as normal. Comparison between the two methods were performed for each corresponding site using Chi2 test and focusing on distal sites due to the length dependence of sweat function.

Results: 72 % of patients had concordant results between feet ESC and DL Vol. In our group a good correlation was observed between feet ESC and DL Vol or Foot Vol ($p = 0.00002$ and $p = 0.002$ respectively), and no correlation was found between hand ESC and FA Vol.

Conclusions: These preliminary results that must be confirmed on a larger population, show that SUDOSCAN allowing quick and quantitative assessment could be an interesting tool for early screening of sudomotor function impairment.

Disclosure: Nothing to disclose.

EP1204

Abstract withdrawn

EP1205

Comparison of SUDOSCAN and cardiovascular testing for assessment of cardiovascular autonomic neuropathy

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Introduction: Despite its frequency autonomic neuropathy is often poorly investigated. Cardiovascular Autonomic Neuropathy (CAN) has been shown to be one risk factor of morbi-mortality. Measurement of sweat function has been suggested for early assessment of autonomic dysfunction. SUDOSCAN, a quick, non-invasive method to assess sudomotor function, was compared to Ewing tests currently used for CAN investigation.

130 patients addressed for autonomic assessment in various neurologic diseases (suspected small fiber neuropathy, parkinsonian syndromes,…) were investigated using Ewing tests. CAN severity was defined according to the "Ewing Score" (ES) based on HR variations during controlled breathing, stand test (30/15 ratio) and Valsalva maneuver, BP variations during orthostatic and hand grip tests. To measure sweat function patients were asked to place the palms of the hands and the soles of the feet on large electrodes. Results are provided as Electrochemical Sweat Conductance (ESC) of hands and feet in microSiemens (μS) and risk score for CAN calculated from these conductances.

Results: For a cut-off value of 40μS and 60 μS for foot ESC, the OR for having Ewing score >1 (vs others) were 14.0 [3.1–63.5] and 6.4 [2.4–17.0] respectively. The highest correlations were observed between Sudoscan risk score and deep breathing and standing 30/15 ratio (-0.50, $p < 0.0001$).

These results suggest that SUDOSCAN allowing quick, reproducible and quantitative assessment of sudomotor function could be an interesting tool for autonomic neuropathy detection and follow-up. This has to be confirmed by assessment of sensitivity/specificity in a large number of patients with different diseases.

Disclosure: Nothing to disclose.

EP1206

Autonomic nervous system functional status analysis in type 1 Gaucher disease patients

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Introduction: Type 1 Gaucher disease (GD) is a rare hereditary progressive lysosomal storage disorder with pathological features caused by accumulation of glycosphingolipids in various tissues. GD has been classified into three types based on the presence and severity of neurological involvement. For type 1 it was thought not to involve nervous system, but recent studies suggest peripheral neurological manifestations. Till now, activity of the autonomic nervous system in type 1 GD was not tested.

Methods: Present study included 20 type 1 GD patients and 20 age and gender-matched healthy controls. Evaluation of the autonomic nervous system function was performed with Ewing defined battery of tests. Task Force® Monitor software (use of adaptive autoregressive parameters algorithm and Fourier transform velocity) enabled the RR interval spectral analysis of low frequency (sympathetic tone), high frequency (parasympathetic tone), sympathetic-vagal balance and power spectral density as well as baroreceptor sensitivity sequential analysis at rest and upright posture.

Results: Patients with type 1 GD had higher scores of handgrip and deep breathing tests ($p < 0.01$), together with orthostasis and Valsalva maneuver tests ($p < 0.05$) in comparison to healthy subjects. A significant difference was found in overall autonomic score between the two groups ($p < 0.01$). Low frequency RR interval spectral analysis revealed statistically significant lower values in type 1 GD patients ($p < 0.05$) in comparison to healthy individuals.

Conclusions: Our results suggest decreased sympathetic outflow in type 1 GD patients.

Disclosure: Nothing to disclose.

EP1207

Metabolic concentrations alternations of bilateral prefrontal lobes and hippocampus after taking codeine phosphate: quantified by ^{1}H-MRS and LCModel

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Introduction: To offer experimental data reference for the further study of codeine habituation.

Methods: Twenty right-handed healthy youth were included (10 males,10 females, mean age22 ± 2 years). MRS data were collected by GE 1.5T MR scanner, using point resolved spectroscopy (PRESS) sequence (TE/TR 30 ms/3000 ms). The regions of interest (ROI) were located over the bilateral prefrontal lobes and hippocampus, size of ROI was 2 cm × 2 cm × 2 cm. The data of spectra were post-processed by LCModel software and the concentrations of metabolites were ultimately measurement. The metabolite concentraction of each people was analyzed by paired-samples t test of spss19.0.

Results: Before taking codeine phosphate, the concentration of NAA in left prefrontal lobe was higher than that in the same-sided hippocampus. After taking codeine phosphate, GPC increased in the left prefrontal lobe while Ins declined.

Conclusions: Codeine Phosphate can change the metabolites' concentrations alternations of the left prefrontal lobes. It is considered that the concentrations of GPC and Ins are related with the drug-dependent.

Disclosure: Nothing to disclose.

EP1208

Another cause of dizziness in posterior inferior artery territory cerebellar infarction: orthostatic hypotension

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Introduction: Orthostatic hypotension (OH) is the cause of dizziness that is occurred during supine to sitting or sitting to standing. OH can occur in lesions such as the rostral ventrolateral medulla or spinal cord. Cerebellum also modulates cardiovascular control of

vestibular system. But there was no report about OH in cerebellar infarction.

Methods: We identified 23 patients with unilateral cerebellar infarction in posterior inferior cerebellar artery (PICA) territory diagnosed by MRI. Standadized autonomic function test including head up tilt test (HUT) using Finapres for recording of beat to beat blood pressure for checking OH were performed. The patients with OH who had no risk factor or showed no OH in follow-up study were sorted by as the OH group.

Results: We identified 8 patients with OH during the tilting. There is no difference in age, sex or risk factor between OH group and comparison group. The mean SBP increase during the tilting was 35 mmHg. Patients with OHT showed mild autonomic dysfunction, among which adrenergic dysfunction was most common abnormality. Lesion subtraction analyses revealed that damage to medial part of superior semilunar lobule was more frequent in patients with OH compare to patients without OH.

Conclusion: We speculate that cerebellar hemispheric areas may participate in regulating BP response in human. Clinician should be aware of the possibility of OH as cause of dizziness in patient with PICA cerebellar infarction, if patient complained of postural lightheadedness typically triggered by standing from sitting or supine.

Disclosure: Nothing to disclose.

EP1209

Gender-related differences in the cardiac autonomic function in patients with Parkinson's disease

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Objective: The study aimed to evaluate the influence of gender on the cardiovascular autonomic function in patients with Parkinson's disease.

Materials and methods: Fifty-five PD patients (32 male and 23 female) at mean age 64.5 ± 8.9 years and 40 age-matched healthy controls were included in the study. The Bulgarian version of the SCOPA-AUT scale (SCOPA-AUT-BG) was used for assessment of the autonomic symptoms. The autonomic modulation of HRV was investigated by short-term heart rate (HR) monitoring at rest and after head-up tilt (HUT) with subsequent calculation of the time and frequency parameters of HRV.

Results: The self-reported cardiovascular and thermoregulatory symptoms from SCOPA-AUT-BG were significantly higher in females in the PD group ($p < 0.05$). No significant gender differences of the HRV parameters at rest could be found. In the healthy controls and only in the PD men the HUT provoked sympathetic excitation with significant decrease in the duration of the R–R interval ($p < 0.05$). In contrast, the test did not induce changes in the duration of the R–R interval in PD women.

Conclusion: The existence of gender differences in the cardiac autonomic function in patients with Parkinson's disease suggests possible sex-related effect in their expression.

Disclosure: Nothing to disclose.

EP1210

Orthostatic intolerance in bariatric surgery patients

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Introduction: The obesity epidemic is increasing worldwide and with it, the healthcare costs of treating the related conditions. Bariatric medicine is attempting to halt this with weight loss and exercise programmes and, with increasing frequency, surgery. This surgery has heralded tremendous success but not without complications.

Methods: The London Clinical Autonomic Neurosciences (LoCAN) group have seen a cohort of 13 patients in the last 10 years who have experienced varying degrees of orthostatic intolerance post bariatric surgery, e.g. the Postural Tachycardia Syndrome (PoTS), syncope. PoTS is characterised by a rise in HR of 30b/m or more, or a HR of >120b/m with orthostasis either during a 10 min tilt or on standing. All 13 patients underwent a variety of clinical autonomic testing in our units.

Results: Autonomic testing revealed 4 patients exhibiting PoTS, 6 patients with pre-syncope/syncope and 9 patients with low resting blood pressure.

Conclusions: The findings of PoTS and syncope post-surgery are substantiated by the small number of previous studies in this area. As this surgery is becoming an intrinsic part of the health service nationally and internationally, it is imperative that the associated complications be identified and remedied.

Disclosure: Nothing to disclose.

EP1211

The peripheral sympathetic neuron is intact in Alzheimer's disease and frontotemporal dementia behavioural variant

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Introduction: 2012, Zakrzewska-Pniewska reported on a considerable high frequency (27 %) of Alzheimer's disease (AD) patients with pathologic sympathetic skin response test. The question arises whether peripheral sympathetic sudomotor neurons might be involved in tauopathies in analogy to involvement in alpha-synucleinopathies. A specific method to evaluate the postganglionic sympathetic sudomotor function is the Quantitative Sudomotor Axon Reflex Test (QSART). To our knowledge, this is the first prospective study to evaluate QSART in frontotemporal dementia behavioural variant (bvFTD) and AD.

Methods: Patients were recruited from the Department for Neurology, General Hospital, City of Linz. QSART was recorded from 4 standard recording sites (1 arm and 3 leg).

Results: 15 AD (7 female) and 14 bvFTD (9 female) patients were included. Mean age (± SD) of AD patients was 74 ± 9, of bvFTD 71 ± 10 years. Pathologic QSART was present in 3 AD patients and 0 of bvFTD patients ($p = 0.037$). In the AD patients with pathologic

QSART one had severe dysfunction and suffered concomitant diabetes mellitus; two minor dysfunction of unknown origin. In no patient the arm was involved, the only site where sweating tested with QSART persists with increasing age. Sweat results of the 4 recording sites did not differ between both groups.

Conclusions: There are no signs of sudomotor involvement in bvFTD in this exploratory study. Although a similar frequency of sudomotor involvement was observed in AD compared to Zakrzewska-Pniewska, our data suggests, that this finding is not part of the AD disease process but might rather be attributed to the high age.

Disclosure: This project was supported by a grant of the National Bank of Austria (OeNB 13240).

EP1212

Catecholaminergic polymorphic ventricular tachycardia presenting with pseudoseizures:Head-up tilt test as a provocation method of adrenergically mediated ventricular tachycardia

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Introduction: Patients with potentially lethal cardiac channelopathies often present to medical care with history of syncope or seizures due to episodic ventricular arrhythmias and associated cerebral hypoperfusion. We suspected an adrenergically mediated syncope in a patient previously diagnosed with epilepsy and psychogenic non-epileptic seizures (PNES) due to anxiety-induced episodes with loss of consciousness, sometimes associated with head injury. We attempted to use head up tilt test (HUT) as a provocation method for an adrenergic response.

Methods: The 27-year-old institutionalised female patient with recurrent emotionally-induced loss of consciousness was diagnosed with syncopes when her seizures were recorded on EEG. To study mechanisms of her syncopes, she underwent 60° passive HUT with continuous heart rate, blood pressure and EEG monitoring.

Results: Two minutes after tilting-up, the patient reported feeling anxious, became pale and lost consciousness with generalised myoclonic jerks, respiratory arrest and cyanosis. ECG revealed polymorphic ventricular tachycardia and ventricular fibrillation which spontaneously reverted to sinus rhythm. Genetics testing revealed catecholaminergic polymorphic ventricular tachycardia. The patient was started on a betablocker and has had a cardioverter defibrillator implanted. Her attacks stopped and she regained full independence.

Conclusion: HUT can be used to induced an adrenergic response and appears to be a more potent stressor than standing in some situations. Our clinical case emphasizes the importance of including CPVT in differential diagnosis of PNES and seizures.

Disclosure: Nothing to disclose.

EP1213

Cardiac autonomic activity among orphans

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During the past decade there has been rapid progress in understanding of the effects of exposure to traumatic life experiences on psychophysiology in children. Research indicates that response to stressors is not a purely cognitive construct, but is also associated with physiological and neuroendocrine-mediated mechanisms. Though there seems to be little published work on changes in autonomic activity in orphan children.

Heart rate variability (HRV) as noninvasive measure of autonomic input to heart rate has been used to estimate modulation of autonomic tone. HRV was measured in 30 orphans (12.57 ± 0.29 year old; 20 boys) and aged-matched non-orphans ($n = 31$) using five-minute recordings through a standardized protocol and time and frequency domain HRV indices were derived.

Although no significant difference was observed in resting HR and time domain HRV indices between two groups, spectral parameters such as HF and HFn were significantly decreased, while LFn and LF/HF ratio were significantly higher in orphans ($p < 0.001$), suggesting increased sympathetic nervous system functioning as stress response. Distribution of spectral components in orphans was VLF > LF > HF, while in non-orphans we revealed higher HF band power (HF > LF > VLF), that also suggests reduction in HRV and signs of sympathetic activation in orphans, which is often presented before the clinical manifestation of autonomic disbalance.

This study suggests that cardiac autonomic activity among orphans is associated with increased autonomic arousal and reveals the degree of autonomic dysfunction experienced by this population. As cardiovascular risk is highly related to variations of HRV our findings suggest that orphans more vulnerable to cardiovascular problems.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 2

EP1214

Clinical factors related to severity of post stroke dementia

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Introduction: The results of clinical studies about the severity of post stoke dementia patients are limited in Korea. We nvestigate clinical factors related to severity of dementia and to inspect the clinical factors related to the progression of dementia severity.

Methods: The patients who visited the hospital by first time between March 2010 and September 2012, among the patients with post stoke dementia admitted to 50 geriatric hospitals spread all over Korea, formed the analysis cohorts. Retrospective review of medical records was performed.

Results: A total of 2965 patients were included. The average duration of illness is 24.61 ± 28.18 months. By the severity of illness, mild cases were 1032 patients (34.81 %), moderate 1278 (43.10 %), severe 655 (22.09 %), and mean score of MMSE was 14.82 ± 6.24. The severity of dementia is higher in patients with overweight by 3.10 times ($p = 0.017$) existence of inmate by 5.92 times ($p = 0.0002$), past history of aphasia symptom by 0.18 times ($p = 0.0004$). Among the clinical factors related to the progression of dementia severity, female patients showed longer duration of illness by 2.89 times compared with average, by the results of univariate analysis of 120 severe dementia patients.

Conclusions: Among the clinical factors related to severity of post stroke dementia in an inpatients of 50 geriatric hospital in Korea, severity of dementia is higher in patients with overweight, existence of inmate, past history of aphasia symptom. The progression speed of dementia is suggested to be slow in female, regarding longer duration of illness in severe dementia patients.

Disclosure: Nothing to disclose.

EP1215

Changes in brain thyroid hormone receptors after permanent cerebral ischemia in male rats

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Introduction: Thyroid hormones (TH) may play an important role in the pathophysiology of acute cerebral ischemia. We investigated whether serum T3/T4 and brain thyroid receptors (TRα1, TRβ1) change during the subacute phase of experimental stroke.

Methods: Male adult Wistar rats were subjected to permanent filament middle cerebral artery occlusion (group P) and compared to sham-operated controls (group S). Clinical evaluation and blood sampling was performed on days 2, 7 and 14. On day 14, tissues were collected from the infarction (E1), peri-infarction hemisphere (E2) and non-infarcted hemisphere (E3) for Western-blot (WB) and confocal microscopy (CM) analysis of TRa and TRb.

Results: Serum T4 was reduced in P vs S group ($p < 0.05$) on day 2, while half of the animals in group P displayed "low-T3" serum values ($p < 0.05$) on day 14. Compared to S group, TRβ1 (WB analysis) was reduced within the infarct core area (E1) ($p < 0.01$) while TRβ1 nuclear fraction was increased in the peri-infarcted area (E2); TRβ1 protein expression did not differ in the contralateral, non-ischemic, hemisphere (E3). TRα1 nuclear fraction (WB data) only demonstrated a mild, nonsignificant ($p = 0.1$) reduction in the infarct core. CM analysis revealed that TRα1 was strongly expressed by the activated macrophages/microglia within the infarct core and weakly in the reactive astrocytes; TRβ was strongly expressed in the nucleus of reactive astrocytes in the infarct.

Conclusions: Our data support that brain ischemia induces a low-T3 and T4 response, associated with significant medium-term total and local changes in brain TRs expression.

Disclosure: Nothing to disclose.

EP1216

Setting up a neuroscience stroke and rehabilitation centre 12,000 km away with the help of telemedicine: to teach to treat–to treat to teach

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Introduction: Due to the world-wide aging population there is a need for specialist neurological knowledge. Our project in Brunei Darussalam (BD) offers to overcome distances and also a long-time benefit for patients.It comprises the set up of a specialized local stroke unit, neurological intensive care unit, normal wards and neurorehabilitation. This has been achieved by continuous medical education and telemedical consultation.

Methods: Set up of the Bruneian Neuroscience Stroke and Rehabilitation Centre (BNSRC) started 7/2010. In order to overcome the distance, a telemedical network between the Department of Neurology of Krankenhaus Nordwest, Frankfurt am Main, Germany (KHNW) and the BNSRC was established. This international cooperation includes the development of a "specialist in neurology" training program, accredited in BD and an international advisory board. Daily tele-teaching as well as 24/7 tele-neurology services are offered. All neurological laboratories have been set up on site, tele-cytology, tele-electrophysiology including EEG and ultrasound.Awareness campaigns, telescience have been successfully started.

Results: So far patients with stroke, intracerebral hemorrhage, aneurysms, myasthenia gravis, multiple sclerosis, Parkinson's disease, encephalitis and other neurological diseases as in- and outpatients. We evaluated 85 % ischemic strokes and 15 % hemorrhagic. Thrombolysis, hemicraniectomy, hypothermia, invasive intracranial pressure measurement have been also performed. 1st intravenous thrombolysis had a door to needle time of 24 min. We have achieved world class neurological intensive care standards in a brief period. Training programs and the back up with telemedicine are ideal for teaching and treating in Neurology.

Conclusion: Stroke is a major disease at the present time and prevention is more important than ever. Treatment in a stroke unit has been proven to be effective. Setting up BNSRC is not only a useful tool, for more it proved to be feasible and successful to cooperate irrespective of distance, religion and culture.

Disclosure: Nothing to disclose.

EP1217

Hypomorphic NOTCH3 allele in an Italian family with CADASIL features

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Introduction: The cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL) is a hereditary disease whose diagnosis may require a multidisciplinary approach to its clinical, radiological, pathological and genetic features. Significant efforts have been doing to clarify whether hypomorphic NOTCH3 mutations are neutral polymorphisms, or, causative for a distinct cerebrovascular entity. In this view, we explored, for the first time, clinical, radiological, pathological, genetic and molecular findings in a family carrying a novel NOTCH3 nonsense mutation in exon 3 (c.307C>T, p.Arg103$_*$).

Methods: A non-consanguineous family from Naples (Italy) was examined because of recurrent cerebrovascular disorders. All the recruited subjects underwent clinical evaluation, MRI scans, skin biopsy with ultrastructural analysis, genetic studies and protein activity evaluation.

Results: Seven members of the family were included in the present study, five of them carried the novel NOTCH3 mutation in exon 3 (c.307C>T, p.Arg103$_*$). The clinical picture of the family was suggestive of CADASIL, with an autosomal dominant inheritance and a typical symptom timeline through generations. At MRI scans, mutation carriers presented significant cerebrovascular signs. Ultrastructural investigations did not show any granular osmiophilic material (GOM) but only non-specific signs of vascular damage. Furthermore, studies were performed to evaluate protein activity.

Conclusion: Clinical, radiological, pathological, genetic and molecular findings are widely discussed to clarify the importance of this NOTCH3 nonsense mutation.

The present study broadens the spectrum of CADASIL mutations and, therefore, opens new insights about the mechanism of Notch3 signaling.

Disclosure: Nothing to disclose.

EP1218

Ischemic stroke in patients under anticoagulation therapy: new options, old problems!

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Introduction: Anticoagulation with vitamin K antagonists or novel oral anticoagulants (NOACs) reduces acute ischemic stroke (AIS) in atrial fibrillation and other high-risk thrombogenic conditions. However, AIS remains a problem in patients under anticoagulation therapy (AT).

Methods: Hospital based retrospective descriptive study of cardioembolic AIS in patients under AT during 1 year (2013).

Results: Of 632 hospitalized patients, 33 (5.2 %) had AIS under AT. The majority were males (18/58 %). Median age was 72 [53–82]. Patients were receiving warfarin/acenocumarol (25/80.6 %), dabigatran (5/16.1 %), and rivaroxaban (1/3.3 %). Most (25/80.6 %) had atrial fibrillation, with mean and median CHA2DS2-VASc score of 4.75 and 5 respectively. The majority 17 (68 %) of patients on warfarin/acenocumarol were under-anticoagulated. Regarding the NOACs, all were receiving the lowest recommended dose, with adherence problems in all except one. At hospital presentation 25 (80.6 %) patients were not eligible for thrombolysis: INR $>=$ 1.7 (13/41.9 %), delayed presentation (11/35.4 %), miscellaneous factors (7/22.5 %). There was no absolute contra-indication for thrombolysis in 6 (19.4 %) patients under treatment with warfarin (3), dabigatran (2), and rivaroxaban (1). Two patients on warfarin were treated with alteplase without complications. No fatalities occurred. Medication adherence reinforcement in all, dose escalation of anticoagulants (13), addition of an antiplatelet drug (2), and switch to a NOAC (3) were treatment strategies adopted.

Conclusions: Undercoagulation remains a major problem in patients receiving vitamin K antagonists. AIS in patients receiving NOAC is a new problem to be discussed. As with the older anticoagulants, perhaps even more important, adherence appears as a major issue in patients receiving NOACs.

Disclosure: Nothing to disclose.

EP1219

Blood genomic signatures in extracranial- and intracranial atherosclerosis in ischemic stroke patients

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Introduction: Extracranial- and intracranial atherosclerosis (ECAS and ICAS) have different pathogeneses. Blood genomic profiling may identify their unique molecular signatures.

Methods: Whole gene microarray of peripheral blood was performed in 24 patients with acute ischemic stroke (ECAS, n = 12; ICAS, n = 12) and 12 healthy controls. Differential gene expression and gene set enrichment analysis (GSEA) were conducted. Plasma resistin levels were compared across independent samples of stroke patients with ECAS (n = 39), ICAS (n = 20), and small vessel disease (SVD, n = 57).

Results: Compared to controls, microarray revealed that 144 and 24 transcripts were altered in ECAS and ICAS, respectively. All of transcripts that were differentially expressed in ICAS were also differentially expressed in ECAS, and 120 transcripts were differentially expressed only in ECAS. Gene sets related to immune response and protein metabolism were altered in both ECAS and ICAS, but the magnitude of gene alteration was higher in ECAS than in ICAS. Several genes of interest that encode resistin (RETN, fold difference [FD]:2.11), interferon regulatory factor 5 (IRF5, FD: 1.59), CD163 (CD163 transcript variant 1, FD: 1.59, CD163 transcript variant 2, FD: 1.59), and CHST13 (carbohydrate sulfotranferase 13, FD: 1.55) showed higher gene expression in ECAS than ICAS. Circulating resistin levels were elevated in independent samples of ECAS, but not in those of ICAS, compared to those of SVD.

Conclusions: ECAS and ICAS had different blood genomic alterations in acute ischemic stroke. Several genes, including resistin, were more associated with pathogenesis of ECAS than ICAS.

Disclosure: Nothing to disclose.

EP1220

Comparison of duplex ultrasonography with digital substraction angiography in the assessment of symptomatic carotid artery stenosis

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Introduction: Conventional duplex ultrasonography (dUS) is a noninvasive imaging modality widely used as a first tool for the evaluation of carotid stenosis. Our aim was to assess the accuracy of dUS in the assessment of symptomatic carotid stenosis, compared to digital subtraction angiography (DSA) now considered to be a "gold standard".

Methods: The study included 135 patients with anterior circulation stroke or transient ischemic attacks, which were admitted during a 6-year period and submitted to both dUS and DSA. Estimates of carotid stenosis obtained by dUS were compared to data from DSA. Stenosis was classified as mild (0–49 %), moderate (50–69 %), significant (70–79 %), severe (80–99 %) and total occlusion (100 %).

Results: A very significant correlation between dUS and DSA was found when carotid stenosis was classified according to the aforementioned criteria (Spearman's coefficient: 0.9, $p < 0.001$). DUS showed the greatest sensitivity (96.8 %) in the mild stenosis group (n = 190 vessels) as well as in the total occlusion group (92.6 %, n = 27 vessels). In the intermediate groups, dUS underestimated the stenosis; its sensitivity was 36.4 % in the moderate (n = 22 vessels), 33.3 % in the significant (n = 9 vessels) and 22.7 % in the severe stenosis group (n = 22 vessels).

Conclusions: DUS is very reliable for the noninvasive assessment of carotid stenosis. However its accuracy is lower in severe, significant and most importantly in moderate stenosis, potentially affecting

the appropriate surgical management. Further studies are needed for the potential use of combined noninvasive imaging techniques as a substitute of DSA in the assessment of carotid stenosis.

Disclosure: Nothing to disclose.

EP1221

Decision analysis for thrombolysis in acute ischemic stroke of various degrees of severity

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Introduction: Thrombolysis for acute ischemic stroke (AIS) has proven results on decrease of disability/mortality. Mild and rapidly remitting AIS were excluded from clinical trials, and are often excluded during the therapeutic decision.

We quantified 5-year's gain with thrombolysis according to initial stroke severity.

Methods: We developed a decision analysis model on TreeAge Pro2011©, analysing gains as increased years of life expectancy (YLE) and lesser years lost to disability (YLD) at 5 years. It was applied to Code Stroke patients with AIS admitted during 2 years.

Stroke severity was based on National Institutes of Health Stroke Scale (NIHSS): mild as NIHSS $\leq$ 4, moderate as 5–10, and severe >10. Patients with rapidly remitting symptoms were included as mild if best score $\leq$4.

Results: From 406 Stroke Code admissions, 261 (64.3 %) were AIS (55.2 % male, median age 71 years).

In 254 patients with NIHSS information, mild stroke was found in 91 (35.8 %), moderate in 77 (30.3 %), and severe in 86 (33.9 %). Ninety-four patients (36.0 %) underwent thrombolysis.

Estimated gains with thrombolysis in 5 years for mild stroke were more 0.39 YLE and less 0.05 YLD. For moderate stroke 0.70 YLE were gained with 0.02 less YLD. Severe stroke benefited with more 1.07 YLE and less 0.03 YLD, although the later was less 0.22 YLD when mortality was discounted.

Conclusions: Thrombolysis benefits in YLE increased with stroke severity. Our model favours thrombolysis even in mild stroke, with additional YLD reduction. Decision analysis modelling may have a role supporting intravenous thrombolysis in all stroke severity groups.

Disclosure: Nothing to disclose.

EP1222

Adherence with post-stroke follow-up clinic visits and factors influencing compliance in a large urban hospital in the USA of America

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Introduction: Referral to a Stroke Prevention Clinic (SPC) is associated with a one-quarter reduction in mortality after ischemic stroke or transient ischemic attack (TIA). We investigated adherence with post-stroke follow-up visits to SPC and tried to identify factors influencing compliance with such visits in a large urban hospital.

Methods: A retrospective chart review was performed in patients discharged in 2011 and 2012 who were admitted with an acute stroke (ischemic or intra-parenchymal hemorrhage) or TIA. Only patients who were provided with a documented follow-up appointment before discharge were analyzed. The patients were divided into "missed" and "visited" groups. Descriptive statistical tools and binary logistic regression forward conditional method was used for analysis of this data.

Results: 198 (41.9 %) of 472 eligible patients returned to clinic, with an average duration of 51 days post-discharge. Regression analysis showed that gender, modified Rankin score at discharge, and insurance status did not affect SPC attendance, but several other factors did (Table 1). The likelihood of SPC attendance decreased by a factor of 0.976 for every 1 year increase in patient age. Patients discharged to home were more likely to visit SPC. Patients with a TIA were less likely to return for follow up than patients with a stroke (ischemic or hemorrhagic). Non African-American (AA) patients (25.6 % of the patients) were more likely to attend SPC than AA patients (Table 1).

Characteristics		"Missed" group (n = 274)	"Visited" group (n = 198)	Odds Ratio (95% Confidence interval)	p-value
Disposition	Home	121 (44.2%)	115 (58%)	Home vs. Rehab 1.716 (1.126-2.615)	0.012
	In-patient rehab	153 (55.8%)	83 (42%)		
Type of vascular event	Ischemic	211 (77%)	158 (79.8%)	Ischemic stroke vs TIA: 3.84 (1.729- 8.53)	0.001
	Hemorrhagic	32 (11.7%)	30 (15.1%)	Hemorrhage vs TIA: 4.845 (1.907-12.306)	0.001
	TIA	31 (11.3%)	10 (5.1%)		
Race	Non-AA	60 (21.9%)	61 (30.8%)	Non AA vs AA 1.63 (1.055-2.518)	0.028
	AA	214 (78.1%)	137 (69.2%)		

Table 1. Factors found to affect clinic visit after logistic regression analysis.

Conclusions: We found poor compliance with SPC visits, which seems to be influenced by age, discharge disposition, race and type of vascular event.

Disclosure: Nothing to disclose.

EP1223

Inhibition of plasma kallikrein protects mice from ischemic stroke by combined antithrombotic, antiinflammatory and antiedematous mechanisms

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Introduction: Plasma kallikrein (PK) is an important component of the kallikrein-kinin system (KKS). The KKS contributes to stroke pathophysiology by mediating inflammation, edema and thrombus formation. Activation of PK triggers the cleavage of kininogen to release kinins—highly inflammatory mediators that participate in the attraction of immune cells and increase vascular permeability. In the present study we investigated the pathophysiological role of PK in mouse models of ischemic stroke.

Methods: Focal cerebral ischemia was induced by middle cerebral artery occlusion (MCAO) in PK-deficient (Pk-/-) and control (Pk +/+) mice as well as in mice receiving PK-specific blocking antibodies. Infarct volumes and neurological scores were assessed between day 1 and day 7, and findings were confirmed by magnet resonance imaging. Evans Blue tracer was applied to quantify the extent of blood-brain barrier (BBB) damage. Local inflammatory responses and thrombus formation were assessed post stroke by qRT-PCR, Western blot and histological approaches.

Results: Inhibition of PK by both targeted deletion (Pk−/−) and pharmacological blockade led to significantly smaller brain infarctions, improved neurological outcome and improved long-term survival. Reduced BBB damage, attenuation of the local inflammatory response and reduced intracerebral thrombus formation could be identified as underlying mechanisms.

Conclusions: The present together with our previous findings further corroborate the major pathophysiological relevance of the KKS during ischemic neurodegeneration. Selective inhibition of distinct members of the KKS might become a promising strategy to combat ischemic brain damage in the future.

Disclosure: Nothing to disclose.

EP1224

Prognostic evaluation of cerebral vein and dural sinus thrombosis

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Introduction: Although the overall outcome of cerebral vein and dural sinus thrombosis (CVT) is good, about 25 % of patients develop complications, and mortality rate is 3–15 %. Identification of prognostic factors is crucial for selecting the proper treatment for each case (more aggressive versus conservative). A risk score comprising six clinical variables with different hazard ratios was proposed to predict CVT outcome (Ferro et al., Cerebrovasc Dis 2009).

Aim: To evaluate the ability of this prognostic score in predicting the prognosis of our population of CVT patients.

Methods: We conducted a retrospective analysis of consecutive adult patients diagnosed with CVT from 2006 to 2012. The prognostic score and the six variables were analysed and compared with the outcome at 6 months, using a simplified regression model ($R > 0.5$ suggesting a stronger relationship).

Results: 60 patients were studied, 83.3 % females; mean age: 39.8 years-old. The value of R between the result of the weighted risk scale and outcome was 0.345. When the 6 variables were combined but not weighted, and compared with outcome, the value of R was 0.529. For the combination of the variables "malignancy" and "intracranial haemorrhage on admission", R was 0.460. There was no significant correlation between other variables independently or combined.

Conclusion: In our population, the proposed risk score did not show a strong correlation with prognosis. However, the combination of intracranial haemorrhage and malignancy had a stronger correlation with outcome, being probably the most important predictive factors in clinical practice.

Disclosure: Nothing to disclose.

EP1225

The aetiology of spontaneous intracerebral haemorrhage: insights from a neuropathological series

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Introduction: The therapeutic and prognosis of spontaneous intracerebral haemorrhage (ICH) depend on the underlying aetiology; however, it remains undetermined in many patients. We aim to assess the impact of the histopathology study in the etiologic diagnosis of encephalic ICH and describe the findings from a 10-year neuropathological series.

Methods: The setting is a tertiary hospital in Northern Portugal; all the patients with ICH admitted in the last 10 years were identified and histologic samples of surgically drained ICH retrieved. Blinded from histologic results, a presumable clinical aetiology was attributed to these patients, using clinical and imaging records. The histopathology samples were reviewed and immunohistochemistry to beta-amyloid was performed in undetermined cases.

Results: From 2003 to 2013, 52 patients with ICH underwent surgical drainage and had histopathology samples. The average age was 49.2 years (SD = 19.5), 56 % were men. Clinical and imaging data defined a presumable aetiology in 27.1 %, including 7.9 % under anticoagulation and 19.2 % with suspected structural pathology. The histological data allowed definitive diagnosis in 65.4 %. The arteriovenous malformations (28.6 %) and cavernous hemangiomas (19.3 %) represented the most common structural abnormalities. In 7 patients (13.5 %) with average age of 67.1 years (SD = 8.5) the vessels showed changes related to amyloid angiopathy.

Conclusions: The histopathology study established a definite aetiology in an additional 38.3 % of patients than using the clinical and imaging data. Although the patients from this series are younger and with major bleedings, we identified a significant number of amyloid angiopathy, in agreement with what has been described in the few published series.

Disclosure: Nothing to disclose.

EP1226

Diabetes and stroke: liraglutide is associated with a decreased risk of stroke in type 2 diabetes mellitus. A nested case-control study

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Introduction: Diabetes mellitus (DM) is associated with an increased risk of stroke. We investigated antidiabetic drugs and their effect on stroke incidence in DM patients.

Methods: We conducted a nested case-control study. Cases were DM patients who subsequently suffered from stroke; controls were DM patients with no subsequent stroke. Using the Danish National Hospital Discharge Register, we included DM patients with information on date of DM diagnosis, date of stroke, and comorbidities. From the Central Region of Jutland, Denmark, medication use and biochemical parameters were collected.

Results: 15,773 DM patients were included. Biguanides (OR: 0.592, 95 %CI: 0.422–0.832), DPP-4 inhibitors (OR: 0.553, 95 %CI: 0.339–0.903) and liraglutide (OR: 0.351, 95 %CI: 0.208–0.592) decreased the risk of stroke, whereas insulin (OR: 0.923, 95 %CI: 0.735–1.158), β-cell stimulating drugs (OR: 1.260, 95 %CI:0.879–1.808), pioglitazone (OR: 0.682, 95 %CI: 0.166–2.805) and exenatide (OR: 0.848, 95 %CI:0.390–1.843) had no significant effect. A dose- and duration-response trend was shown for liraglutide. When limited to type 2 DM patients (n = 11,202), the associations remained.

When results were adjusted for biochemical parameters (LDL, HDL, total cholesterol, HbA_{1c} and creatinine), none of the antidiabetic drugs reduced the risk of stroke.

Conclusions: An association between liraglutide and a reduced risk of stroke in type 2 DM patients was present. Of the antidiabetic drugs, liraglutide had the most pronounced effect, which may indicate that liraglutide could be recommendable as part of first-line treatment in stroke prophylaxis in diabetic subjects.

Disclosure: None.

EP1227

Persistent barriers to help-seeking for stroke and TIA after a national media campaign (Face, Arm, Speech, Time to Call 999 (FAST))

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Introduction: National media campaigns (e.g. Face Arm Speech Time (FAST)) have encouraged the public to dial emergency services ("999") immediately for stroke symptoms. However many patients still reach hospital too late for thrombolysis and optimal care. Reasons for delays in calling 999 after stroke/TIA are poorly understood.

Methods: We interviewed consecutive patients admitted to the stroke service in Sheffield, UK with stroke/TIA in August 2013 where informed consent was available. Carers were interviewed if they had called for help on the patients' behalf. We recorded timings of symptoms and medical consultations, perceptions of symptoms and barriers to calling 999.

Results: 61 patients were included; 9 had major stroke (NIHSS > 5), 38 minor stroke, and 14 TIA. 13 carers were also interviewed. 50 (82 %) patients/carers were aware of the FAST campaign pre-admission, and 54 (89 %) patients had ≥ 1 "FAST" symptom. The median (IQR) time between symptoms onset to first call for medical help was 57.5 min (10–1021) but 30 (49 %) called the family doctor first. Only 21 (34 %) patients reached hospital within 4 h of symptoms onset. There were several important barriers to calling 999 e.g. 35 (57 %) callers had not thought the symptoms were serious, 21 (34 %) did not want to trouble hospital services and 16 (26 %) were embarrassed or afraid to call 999.

Conclusions: Despite widespread awareness of the FAST campaign, most patients/carers delay or avoid calling 999 after stroke/TIA. Future campaigns need to emphasize the seriousness of stroke/TIA and the need to call emergency services promptly.

Disclosure: Nothing to disclose.

EP1228

Expansive arterial remodeling: risk factors for ischemic complication after carotid artery stenting?

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Introduction: Expansive artery remodeling and vulnerable plaque are considered risk factors of cerebral ischemic events. However it is not well known wether these can be risk factors of medical complication for carotid artery stenting (CAS). The purpose of this study is to investigate association between carotid artery remodeling retio (RR) and ischemic complication in patients treated with CAS for their high grade carotid artery stenosis.

Methods: Forty three patients with >50 % stenosis (15 symptomatic and 28 asymptomatic) treated with CAS were included to the study.

Results: New ischemic signals on DWI-MRI were detected in 34.9 % (15/43). Vulnerable plaques were detected 15/43 patients on T1-weighted MRI and associated significantly high new ischemic signals of 8/15 compared with patients with non vulnerable plaque (7/28). ($P = 0.063$)Remodeling ratio (RR) was calculated by dividing the outer vessel circumference at the site of greatest stenosis by a normal reference-segment vessel circumference by using multidetector row CT. There is no statistical significant between RR and new ischemic signals ($P = 0.541$) and also present of vulnerable plaque ($P = 0.558$).

Conclusions: Remodeling Ratio has the potential for more accurate selection for CAS treatment.

Disclosure: Nothing to disclose.

Headache and pain 1

EP1229

The effects of transcutaneous electrical nerve stimulation (TENS) for patients with low back pain: first two randomized contolled trials in Russia with dynamic TENS devices

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Introduction: TENS is well known for management of different pains. But randomized controlled trials (RCTs) that could be analysed and included into Cochrane reviews are still not too many, and the effects of TENS are still in the focus of interest for clinicians and researchers. New compact devices for dynamic TENS need even more attention as those that can be used in out-patient clinics and at home for patients with low back pain (LBP).

Methods: We designed and completed two RCTs to evaluate if compact dynamic TENS (cDENS) devices are helpful for LBP management. Trial I (blind) compared cDENS effects with placebo (sham device produced for this study by the manufacturer); Trail II compared cDENS and clasical TENS device used for in-patients at neurology ward of our University hospital.

Results: There were 100 patients in 4 groups:

Group 1 (sham device) and

Group 2 (cDENS device) included 15 patients each in the first pilot RCT;

Group 3 (36 patients used cDENS) and

Group 4 (34 patients used classical TENS at neurology ward) were included into Trial II.

All patients showed improvement after therapy ($p < 0.01$), but the results in Group 2 were better than in Group 1 since Day 9 ($p = 0.016$), and the pain reduction was faster and better in Group 3 vs Group 4 after Day 6. We also calculated which characteristics could predict response for cDENS therapy.

Conclusions: Both TENS methods helped for LBP management, but cDENS device showed even more effect than classical one.

Disclosure: Grants from the Russian Ministry of Science and Education (Moscow, Russia) and from DENAS Corporation (Ekaterinburg, Russia) for these trials.

EP1230

Effects of stimulating melanopsin-containing retinal ganglion cells in migraine patients using multifocal objective pupillometry

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Objectives: To establish the effects of stimulating intrinsically-photosensitive retinal ganglion cells (ipRGCs) using multifocal pupillographic objective perimetry (mfPOP) on migraine severity parameters and pupillary response characteristics.

Methods: A randomized case-control crossover study tested migraineurs and normal controls using mfPOP utilising a blue protocol (BP) to stimulate ipRGCs and a yellow protocol (YP) to stimulate cone photoreceptors. Migraine diaries were obtained a week prior to, and a week after, each testing. Responses were analysed according to response time-to-peak and standardised amplitude (AmpStd). The percentage area under the receiver operator characteristic (%AUC) was used to predict migraine status.

Results: 38 migraineurs (41.97 ± 16.02 years, 23 females) and 24 normal controls (39.17 ± 14.84 years, 14 females) were enrolled. There was no significant difference in the mean number of migraine attacks/subject in the weeks prior to, or following, testing with either protocol. The AmpStds (in dB) were lower for migraineurs than controls: 9.04 ± 11.2 (mean ± SE) vs. 9.48 ± 10.4 for BP, and 10.74 ± 4.96 vs. 11.4 ± 5.23 for YP, though these differences did not reach statistical significance. A migraine attack occurring in the 2 weeks prior to testing had a significant independent effect in lowering AmpStd while a history of triptan use increased AmpStd. The %AUC was highest for AmpStd (77.2 % for YP and 84.6 % for BP).

Conclusions: Stimulating ipRGCs did not affect migraine severity. Pupillary response characteristics were influenced by recent attacks of a migraine and a history of triptan use.

Disclosure: Nothing to disclose.

EP1231

Neuromuscular transmission studied with SFEMG in migraine with aura: phenotypic correlations in 93 patients

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Introduction: Single-fiber electromyography (SFEMG) showed mild subclinical abnormalities of neuromuscular transmission in subgroups of migraine patients with complex neurological auras. The objective of this study was to test the hypothesis that distinct neuromuscular abnormalities are correlated with different aura phenotypes.

Methods: Stimulation SFEMG in m. extensor digitorum communis was performed in 21 healthy controls and 127 migraineurs, 34 without aura, 93 with aura; in the latter group, 77 had typical aura with Headache (MTA), 6 brainstem aura (BM), 7 sporadic hemiplegic migraine (SHM), 3 familial hemiplegic migraine (FHM). Among MTA 35 patients had only visual auras, 25 complex auras (visual plus somatosensory and/or language disturbances) and 17 prolonged auras. Results were expressed as the average mean MCD (mean consecutive difference) and single endplate abnormalities (i.e. percentage of fibers with increased jitter and presence of intermittent impulse blocking).

Results: Average mean MCD did not differ between controls and migraineurs, or in migraine subgroups, but it was significantly higher in SHM. Mild single endplate abnormalities were observed in BM and S/FHM. Increased average mean MCD was associated with aphasic or motor aura, increased jitter with sensory aura, and with a diagnosis of complex aura and S/FHM.

Conclusions: We confirm that mild subclinical neuromuscular transmission abnormalities can be identified in subgroups of migraineurs with aura. As they vary with the aura phenotype, they could be due to different pathophysiological mechanisms involving ion channels or muscle metabolism, and hence to different genotypes.

Disclosure: Nothing to disclose.

EP1232

Visual and auditory evoked potentials in migraine: sensitivity and specificity as diagnostic tools

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Introduction: There are at present no reliable instrumental tests for the diagnosis of migraine. Many migraineurs are characterized interictally by a habituation deficit of visual evoked potentials (VEP) and/or increased intensity dependence of auditory evoked potentials (IDAP). In this retrospective study we tested the usefulness of VEP and IDAP as diagnostic tools in episodic migraineurs (EM).

Methods: We analyzed recordings from 360 healthy volunteers (HV) and 624 EM. VEP50 (5 blocks of 50 responses) were obtained in 77 HV and 231 EM, VEP100 (6 blocks of 100 responses) in 240 HV and 280 EM, IDAP in 86 HV and 328 EM. Some subjects underwent both VEP and IDAP tests. Thresholds were calculated by Receiver Operating Curve analysis, and used to calculate sensitivity, specificity and efficacy of each test.

Results: Sensitivity was 61.0 % for VEP50, 61.4 % for VEP100 and 45.7 % for IDAP. Specificity was 77.9 % for VEP50 and VEP100 and 87.2 % for IDAP. Efficacy was 65.3 % for VEP50, 69.0 % for VEP100 and 54.3 % for IDAP. In subjects who underwent both VEP and IDAP recordings, abnormality of at least one of them had a 83.4 % sensitivity, 66.7 % specificity and 81.1 % efficacy.

Conclusions: Taken alone, none of VEP or IDAP has sufficient diagnostic efficacy. However, when both tests are combined in the same patient, abnormality of at least one of them is highly predictive of migraine, suggesting that VEP and IDAP can contribute to the migraine diagnosis.

Disclosure: Nothing to disclose.

EP1233

Medication overuse headache: a-12 year follow-up study of 77 patients

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Objective: To assess the long-term outcome of patients with medication overuse headache (MOH).

Background: MOH is a common disease and management is complicated by treatment failure and relapses.

Methods: The study population consisted of 77 consecutive patients treated and followed between 2001 and 2013 in our tertiary headache centre. MOH patients included in this study according to the classification of headache disorders of the International Headache Society 2004.

Results: A total of 77 patients (67 female/10 male, mean age 40.71) completed this study. Based on headache characteristics on

evaluation, 58 (75.3 %) were diagnosed with migraine. Sixteen patients (20.7 %) gave a history of tension-type headache. Three patients (4 %) reported a combination of migraine and tension type headache. The most commonly used drugs were nonsteroid antiinflammatory drugs (NSAID) (54 %), combination of ergot and NSAID (28.5 %), and ergots (17 %). The duration of medication use was between 1 and 29 years (mean: 5.4 years). They underwent a structured detoxification programme and were subsequently closely followed. At 12-year follow-up, fifty eight patients (77 %) remained cured of MOH, reduction in headache frequency of more than 50 % occured in 16 patients (20 %), and 3 patients (3 %) reverted to episodic headache.

Conclusion: This long-term follow-up study revealed a marked decline in the frequency of MOH. Patients with MOH previously regarded treatment-resistant benefit considerably from multidisciplinary treatment and close follow-up.

Disclosure: Nothing to disclose.

EP1234

Abnormal thalamic function in patients with vestibular migraine

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Introduction: Vestibular migraine (VM) has been increasingly recognized as a possible cause of episodic vertigo, but its pathophysiology is still unclear. Here, we used advanced non-invasive neuroimaging to examine the functional response of neural pathways associated with vestibular stimulation in patients with VM.

Methods: Twelve patients with VM underwent whole-brain blood oxygen level-dependent (BOLD) fMRI during ear irrigation with cold water. The functional response of neural pathways to this stimulation in patients with VM was compared to age- and gender-matched patients with migraine without aura (MwoA) and healthy controls (HC). Secondary analyses explored associations between BOLD signal change and clinical features of migraine in patients.

Results: We observed a robust cortical and subcortical pattern of BOLD signal change in response to ear irrigation across all participants. Patients with VM showed significantly increased thalamic activation in comparison with both patients with MwoA and HC. The magnitude of thalamic activation was positively correlated with the frequency of migraine attacks in patients with VM.

Conclusions: We provide novel evidence for abnormal thalamic functional response to vestibular stimulation in patients with VM. These functional abnormalities in central vestibular processing may contribute to VM pathophysiology.

Disclosure: Nothing to disclose.

EP1235

Q-No: a questionnaire to predict nocebo in outpatients seeking neurological consultation

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Introduction: Nocebo affects significantly adherence and treatment outcome and varies considerably among neurological conditions. We aimed to evaluate a questionnaire to predict nocebo in outpatients seeking neurological consultation.

Methods: A four-item (rating range 4–20) self-fulfilled questionnaire (Q-No) was given in outpatients seeking neurological consultation at the Athens Naval Hospital. A blind to Q-No scoring neurologist rated outpatients as nocebo or no-nocebo after follow-up of >6 months.

Results: 338 (71.6 % females) patients with mean age 46.9 (± 13.8) years fulfilled the Q-No and the mean total score was 13.2 (± 3.7). The Crombach's alpha coefficient was 0.627. Neurologist suggested 80 patients (23.7 %) as nocebo and 258 as no-nocebo (mean Q-No score = 12.4 95 % CI: [12.0–12.9] and 15.8, 95 %CI: [15.1–16.6], respectively). By using a cut-off at score 16 the Q-No predicts nocebo with 82.6 % specificity and 61.3 % sensitivity.

Conclusions: Q-No may serve as a useful tool to predict nocebo in outpatients seeking neurological consultation.

Disclosure: Nothing to disclose.

EP1236

Sexual dysfunction in migraine patients receiving preventatives: evaluation with two screening test

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Introduction: We aimed to evaluate sexual functioning in migraine patients and sexual dysfunction attributable to preventive treatment.

Methods: Patients attended in two outpatient headache offices. Included during follow-up visit after initiation of preventive therapy. Answered Massachusetts General Hospital-Sexual Functioning Questionnaire (MGH-SFQ) (5 multiple choice items considering different phases in sexual response) and Psychotropic-related sexual dysfunction questionnaire (SALSEX) (2 dicotomic items assesing any change in sexual activity and if it was spontaneously reported, and 5 multiple choice items considering specific dysfunctions).

Results: 55 patients (13 males, 42 females), age 36 ± 9 years (range: 19–57). 22 (40 %) with chronic migraine and in 7 (12.7 %) medication overuse. Time from migraine onset 16.6 ± 12.4 years (1–37). 9.6 ± 9 (1–30) headache days during previous month. As preventive treatment 20 (36.3 %) received beta-blockers, 26 (47.3 %) anticonvulsants, 5 (9.1 %) calcium-channel blockers, and 4 (7.3 %) antidepressants. In MGH-SFQ in 13 (23.6 %) at least moderate decrease in overall sexual satisfaction. In 2 of 13 males (15.3 %) at least moderate erectile dysfunction. SALSEX detected change in sexual activity since the beginning of treatment in 19 (34.5 %) patients, but in none spontaneously reported. Mean age was higher among patients with at least moderate decrease in sexual satisfaction in MGH-SFQ (40.5 ± 9.9 vs 34.6 ± 8.3, p: 0.04). No other relationship between demographic and clinical variables and MGH-SFQ or SALSEX scores.

Conclusion: Sexual dysfunction assessed by screnning test is common among migraineurs. Though dysfunction related to preventatives is frequent, it is not spontaneously reported.

Disclosure: Nothing to disclose.

EP1237

Headache in cerebral venous-sinus thrombosis, pattern and location: a series of 60 consecutive patients

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Introduction: Headache is the most frequent presenting symptom of cerebral venous thrombosis (CVT), most commonly associated with other manifestations.

Methods: From a prospective study of 60 consecutive patients diagnosed with CVT over 12 months, we selected those who presented with headache only. Diagnosis of CVT was made by magnetic resonance imaging (MRI) combined with MR venography (MRV): both increased signal on MRI T1 and T2 weighted images and the absence of flow was required to confirm diagnosis.

Results: During the inclusion period, a total of 30 patients were diagnosed with CVT. Twelve patients (40 %) had headache as the only presenting symptom.

The majority of these were young (mean age 39.9 years old), female (91.7 %) patients, with only one third having a past medical history of headache (in all compatible with the diagnosis of migraine without aura).

Conclusions: This stresses the idea to systematically look for CVT in patients with recent persistent headache, thunderclap headache or pain worsening with straining, sleep or Valsalva maneuvers, even in the absence of papilledema or focal signs.

Disclosure: Nothing to disclose.

EP1238

Association between cranial autonomic symptoms (CAS) and main migraine's features in a juvenile population with migraine

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Introduction: Recently we have noted that Cranial autonomic symptoms (CAS) are frequently reported during migraine attacks also in paediatric age and were significantly associated to the frequency of attacks, supporting the role of the trigemino-autonomic reflex in the pathophysiology of migraine.

However the main observed CAS subserve different parasympathetic functions (secretomotor fibers: lacrimation, nasal obstruction, sweating and vasomotor fibers: red ear and facial flushing) with possible different predictive significance in migraine attacks. The aim of this study was to evaluate the association between most frequent CAS and the main characteristics of migraine in a juvenile population with migraine, examining every single CAS individually.

Methods and results: A total of 198 children suffering from migraine with/without aura (94 M, 104F, 4–17 years) were enrolled in 2 years time. A questionnaire investigating the presence of CAS and the main characteristics of migraine was administered to them. CAS were present in % of migrainous subjects and at the univariate analysis we found that conjunctival injection, lacrimation and sweating were positive related with frequency of attacks, lacrimation with duration of disease and allodynia, obstruction nasal with pulsantig pain.

Conclusions: These findings confirm that CAS are rather common in the course of paediatric migraine attacks. Generally CAS are related to frequency of attacks but the analysis of association between single CAS and main migraineus features shows that secretomotor parasympathetic functions are more related to pain while vascular control has less important function.

Disclosure: Nothing to disclose.

EP1239

Impulsivity among migraine patients: study in a series of 129 cases

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Introduction: Unlike mood disorders, impulsivity has not been extensively studied in headache patients. We aimed to assess influence of impulsivity on Chronic Migraine (CM) or Medication Overuse (MO).

Methods: Patients attended in an outpatient headache office in a tertiary hospital (January 2013-January 2014). Episodic migraine (EM), CM, MO diagnosed accordingly ICHD-III. We gathered demographic and nosological characteristics. Patients answered Hospital Anxiety and Depression Scale (HADS), considering Anxiety or Depression when scored >10 in any of subscales. Impulsivity assessed with Plutchik scale (15 multiple choice items, positive if score >20).

Results: 129 patients (15 males, 114 females), mean age 38.4 ± 11.7 years (range: 18–70). 85 cases (65.9 %) CM and, among them, 64 (75.2 %) with MO. Mean scores of 7.8 ± 4.4 (0–17) in HADS-Anxiety, 3.7 ± 4 (0–18) in HADS-Depression and 13.8 ± 6.5 (1–32) in Plutchik scales; 27.9 % of patients met criteria for anxiety, 7 % for depression and 14.7 % for impulsivity.

We first compared CM and EM groups; HADS-Anxiety (8.6 ± 4.6 vs 6.3 ± 3.7, p: 0.003), and HADS-Depression scores (4.6 ± 4.4 vs 1.9 ± 2.3, $p < 0.001$) were higher among CM cases. When considering CM with or without MO, HADS-Anxiety score (9.2 ± 4.5 vs 5.1 ± 4.7, p: 0.02) was increased in patients with MO. No differences in Plutchik score or presence of impulsivity in both comparisons.

Conclusion: In our population, impulsivity assessed by Plutchik scale is common, but, unlike mood disorders, does not correlate with CM or MO.

Disclosure: Nothing to disclose.

EP1240

Prevalence of headache disorders diagnosed according to ICHD-3beta in three different social settings

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Introduction: The aim of our study was to estimate the prevalence of headache disorders in three different social settings using the newly published International Classification of headache Disorders (ICHD-3beta).

Methods: The study population consisted of:1042 students (719 females, mean age 20.6, range 17–40), 1075 workers (146 females, mean age 40.4, range 21–67), 1007 blood donors (484 females, mean age 34.1, range 18–64). All patients were interviewed using a semi-

structured validated interview conducted by a neurologist or by trained senior medical students and diagnosed according to ICHD-3beta.

Results: In the whole material, 1-year prevalence of headache was 67 %, migraine 17 % and tension type headache (TTH) 58 %. In females the prevalence of migraine in students (39 %) was significantly higher than in workers 16 % and blood donors 19 %, $p < 0.0001$. In males the prevalence of migraine in students (21 %) was also significantly higher than in workers 4 % and donors 5 %, $p < 0.0001$. The prevalence of TTH in females was respectively 69, 65 and 66 %. The prevalence of TTH in males was significantly higher in students (90 %) than in workers 32 % and blood donors 59 %, $p < 0.0001$, the prevalence of TTH was also significantly higher in donors than in workers, $p < 0.0001$. Only few (18 %) had consulted because of headache. The prevalence of migraine and TTH was significantly different in three social settings. Reasons for this will be analyzed and presented.

Conclusions: We show for the first time convincingly that headache disorders have different prevalence according to social setting. They represent a huge health problem in Russia.

Disclosure: Nothing to disclose.

EP1241

Grey matter in migraine with aura patients

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Introduction: A few studies assessed cortical thickness in patients with migraine, with heterogeneous results. Previous investigations reported a thickening of the somatosensory cortex (SSC) and visual motion processing areas (V3A/MT+) both in migraine without (MO) and with aura (MA) whereas other studies showed thinning in several cortical regions and a recent study showed no abnormalities.

Objective: To investigate regional cortical thickness/atrophy in MA (ICHD III-beta) patients.

Patients and methods: We compared 15 MA patients (age 30.2 ± 5.7, 8 females) vs 21 controls (age 34.9 ± 4.7, 13 females). Cortical thickness was measured in 146 regions using FreeSurfer and volumetric T1 weighted images.

Results: MA patients presented a mild focal thinning of the grey matter of the right ventral posterior cingulate cortex ($p = 0.001$). Thickening of left inferior frontal sulcus ($p = 0.043$) and of the left postcentral gyrus ($p = 0.0001$) that is part of SSC, of the left occipito-temporal gyrus ($p = 0.017$), particularly of the medial occipito-temporal gyrus ($p = 0.027$) belonging to the visual cortical areas MT+, was observed.

Conclusion: The thinning of several cortical regions reported in MA was not confirmed; our preliminary result of a cortical thinning of the right ventral posterior cingulate cortex needs to be confirmed. Our finding of a thickening in the SSC and of the MT+ areas is in keeping with previous observations. The thickening in MT+ warrants the study of a larger sample of MA patients, to be analyzed according to the type of aura. These results support the hypothesis that repetitive MA attacks could lead to neuroplastic changes in grey matter.

Disclosure: Nothing to disclose.

EP1242

Visual evoked potential habituation in migraineurs: a longitudinal study with a blinded design

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Introduction: Lack of habituation has been called the neurophysiological hallmark of migraine, but the results of earlier studies have been discrepant. We investigated if VEP habituation changes in relation to an attack, and if lack habituation in interictal migraineurs could be reproduced with a blinded design.

Methods: 50 migraineurs and 31 headache-free controls were included. VEPs were recorded once in controls and four times on different days in migraineurs. Investigators were blinded. VEPs were averaged in 6 blocks of 100 responses. VEP peaks were determined without knowledge of diagnosis or block number. Linear change over blocks of N70–P100 amplitude was applied as main habituation measure. Habituation in controls and in the first interictal recording in migraineurs was compared with an independent samples Student's t-test.

Results: Habituation was more pronounced in ictal (-0.47 ± 0.43 μV/block) than interictal (-0.31 ± 0.25 μV/block) recordings ($p = 0.029$). No habituation differences were found between interictal and preictal or postictal recordings. No VEP habituation differences were found between headache-free controls and interictal recordings.

Conclusion: VEP habituation increased significantly in relation to the migraine attack while no changes were detected preictally. Earlier studies reporting changes in VEP habituation over the migraine cycle have mostly applied a cross-sectional design, which may not have been ideal. In this blinded replication study we could not confirm that migraineurs lack habituation compared to controls. This confirms our recently published data and, as far as we know, no studies that applied blinding during VEP recordings have found lack of habituation in migraineurs.

Disclosure: Nothing to disclose.

EP1243

Reversible cerebral vasoconstriction syndrome as a cause of thunderclap headache: a retrospective case series study

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Introduction: Thunderclap headache (TCH) is a common Emergency Department presentation. Although subarachnoid hemorrhage (SAH) should be the first diagnosis to exclude, reversible cerebral vasoconstriction syndrome (RCVS) is another important cause. RCVS is characterized by multifocal narrowing of cerebral arteries, typically manifested by acute- severe headache with or without neurological deficits.

Objective: To compare and discuss the clinical and radiological characteristics of patients with RCVS.

Case reports: We report four cases of RCVS, all presented with TCH, while half of them had additional neurological symptoms such as right homonymous hemianopia, right sided weakness and slurred speech. Brain CT was normal in two of our patients, however subsequent cerebrospinal fluid analysis revealed xanthochromia consistent with SAH. The remaining two patients demonstrated intracerebral hemorrhage on CT. All of our patients underwent Digital Subtraction Angiography (DSA) that showed segmental narrowing and dilatation of one or more cerebral arteries without any signs of

aneurysm. Repetitive DSA after 3 months was entirely normal prompting the diagnosis of RCVS.

Conclusions: TCH requires urgent work up to identify the underlying cause. Although SAH is the most important diagnosis to exclude in the first instance, physicians should be aware of other causes and how they present, such as RCVS. Early recognition of this condition can prevent complications such as hemorrhagic and ischemic stroke.

Disclosure: Nothing to disclose.

EP1244

A cross-sectional study of migraine improvement after diet/exercise-induced weight loss or bariatric surgery

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Introduction: Obesity seems to be associated with severity and frequency of migraine headache. Great weight loss by bariatric surgery seems to result in an improvement of migraine headache. Whether smaller amount of weight loss or the other methods of weight loss had similar effect on migraine is remained to be answered. We designed this study to assess the effect of 7–10 % reduction of body weight either shortly after bariatric surgery or through combined diet and exercise.

Methods: In this prospective cross-sectional study, frequency and intensity of migraine were assessed before and after weight loss in 49 obese women (18–60 years) with migraine headache (24 persons underwent bariatric surgery and 25 received diet and exercise plan).

Results: The mean intensity (visual analog scale) and frequency of migraine headaches per month were reduced from 6.8 ± 2.0 and 17.6 ± 11.5 at baseline to 1.5 ± 2.6, 0.4 ± 0.6 after surgery (both $p < 0.001$). Non-surgical weight loss reduced the intensity and frequency of migraine headaches from 6.9 ± 1.8 and 7.2 ± 6.5 to 4.6 ± 3.3 ($p < 0.001$) and 3.9 ± 6.6 ($p = 0.001$) respectively. Losing similar amount of weight by surgery resulted in more reduction of the intensity ($p < 0.001$) and frequency ($p = 0.002$) of migraine comparing with non-surgical modifications.

Conclusions: Although weight reduction with diet/exercise had a significant effect on migraine, the effect was less than losing a similar amount of weight by surgery. Our observations highlighted the needs for a deeper insight into hormones and appetite mediators which affected by bariatric surgery and have shared roles in migraine and obesity.

Disclosure: Nothing to disclose.

EP1245

Chronic migraine: characteristics in a prospective headache registry

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Introduction: We aimed to analyze clinical and demographic characteristics of patients with chronic migraine (CM) in a prospective registry.

Methods: Patients attended in an outpatient headache office in a tertiary hospital (January 2013–January 2014). Referred from primary care or general neurology offices. CM diagnosed accordingly to ICHD-2R criteria. We gathered demographic and clinical data, previous therapies, comorbidities and risk factors. We assessed headache impact administering six-item Headache Impact Test (HIT-6).

Results: 150 patients (24 males, 126 females), mean age of 40.4 ± 14.1 years (15–71), age at onset of migraine 18.1 ± 8.2 years (6–45). Latency from onset of CM to diagnosis 44.3 ± 85 months (3–480). Considering risk factors, in 105 (70 %) medication overuse (MO), in 63 (42 %) stressful life events, in 18 (12 %) mood disorders, and in 9 (6 %) obesity. Among comorbidities, in 73 cases (48.7 %) vascular risk factor, especially smoking, in 19 (12.7 %) other chronic pain, and in 7 (4.7 %) respiratory disease. 34 of 126 female patients (26.9 %) described menstrually-related migraine. Mean HIT-6 score of 61.6 ± 6.5 (42–78), and HIT-6 score ≥ 55 (at least substantial headache-related impact) in 82.3 %. Only 25.3 % of patients had previously received triptans as symptomatic treatment and in 47.3 % at least one preventive drug had been used.

Conclusion: Latency between onset and diagnosis of MC is prolonged in our series. In our MC population MO and stressful events are frequent risk factors. We consider that previous use of preventatives and triptans is insufficient.

Disclosure: Nothing to disclose.

Infection and AIDS; Neurotoxicology; Education in neurology; History of neurology

EP1246

Which disorders may mimic Whipple's disease?

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Introduction: Whipple's disease (WD) is a differential diagnosis of rapidly progressive dementias (RPD), important not to miss since it's a treatable disorder. It is often suspected in clinical practice, although infrequently confirmed.

Methods: Characterization of a group of patients in which WD was suspected but not confirmed. Identification of patients submitted to polymerase chain reaction detection of *Tropheryma whipplei* on CSF between 2007 and 2013. Clinical files review.

Results: Thirty-one patients were identified, two excluded because WD was confirmed. From the remaining 29, 17 were females, mean age at presentation of 64.4 years (SD $\pm$ 12.6). 20 patients presented with dementia (RPD in 10), 5 extrapyramidal syndrome, two cerebellar syndrome, one gait disorder with myoclonus, one vertigo. Five patients had systemic symptoms: diarrhea (2), weight loss (1), fever (1), arthralgia (1). During follow up nine patients developed myoclonus, five ataxia and three ophthalmoplegia. All performed MRI, showing diffuse white matter lesions (18), global atrophy (4), lobar atrophy (2), midbrain-hypothalamic lesions (2), cortical hyperintensities (1). 23 performed EEG, disclosing slow background activity (9), slow focal activity (3), epileptiform activity (4), periodic activity (1). After a median follow-up of 2.4 years (0.1–14.5) 17 remained stable, 5 deteriorated, 5 died, 2 improved. Most frequent final diagnosis were: Lewy body disease (3), fronto-temporal dementia (3), RPD with parkinsonism (3), Parkinson's disease (3), Creuztfledt Jacob disease (2), Alzheimer's disease (2); four patients remain without final diagnosis.

Conclusions: In our group of patients the main reason for considering WD a possible etiology was RPD, independently of the presence of systemic symptoms. This group revealed to be heterogeneous, notwithstanding the majority having atypical presentations of common neurodegenerative disorders.

Disclosure: Nothing to disclose.

EP1247

Sporadic Creutzfeldt-Jakob disease: the 'forme fruste'

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Objective: To elucidate the clinical features of sporadic Creutzfeldt-Jakob disease (sCJD) which does not fulfill the WHO criteria.

Background: An incomplete form, aka forme fruste (FF), of sCJD grows popular owing to the diffusion-weighted imaging (DWI). However its clinical features remain unclear.

Methods: Twenty patients with prion disease were surveyed (with V180I mutation 5 cases, probable sCJD (pCJD) 8 and FF 7). Mean age and male to female ratio were as follows respectively. V180I 81.0, 2:3; pCJD 70.4, 3:5; FF 69.1, 5:2. FF showed progressive dementia and high signal intensity cortical lesions in DWI, but represented only less or equal one out of four clinical features advocated by WHO. We compared symptoms and signs, MRI and EEG among three groups.

Results: Myoclonus and PSD was found in 60 %, 0 % of V180I, both 88 % of pCJD and both 43 % of FF. The average time to its appearance from the onset was 9 months in V180I, both 2 months in pCJD and 18, 14 months in FF. Some cases showed the prolonged focal sign before the rapid decline of dementia. DWI abnormality was observed in all cases. It appeared from the early stage of the illness even in FF. The whole duration of illness was 19 months in V180I, 18 months in pCJD and 41 months in FF on average.

Conclusions: The 'forme fruste' is a distinct subtype of sCJD characterized by slow progression, delayed and rare appearance of myoclonus and PSD. Early MRI examination including DWI is needed for diagnosis.

Disclosure: Nothing to disclose.

EP1248

Neurophobia: localising the deficit

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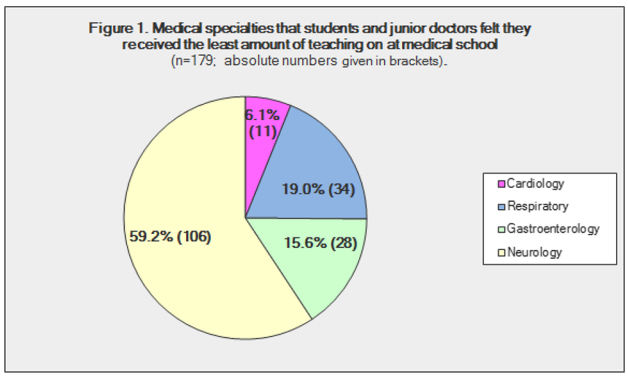
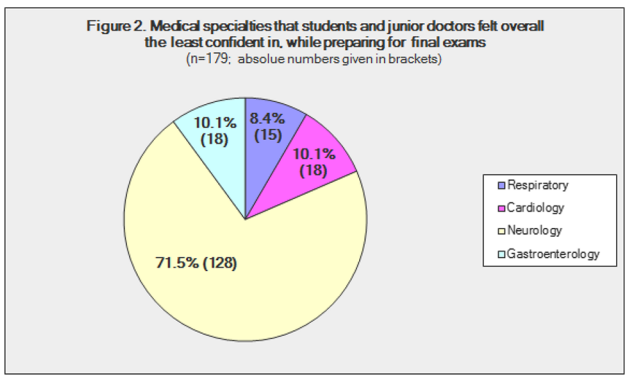
Introduction: Neurophobia is prevalent among medical students and junior doctors (Flangan et al., 2007). We investigated the extent and underlying reasons for neurophobia, prompting the creation of a junior doctor-led ("near-peer") neurology revision course for final year medical students.

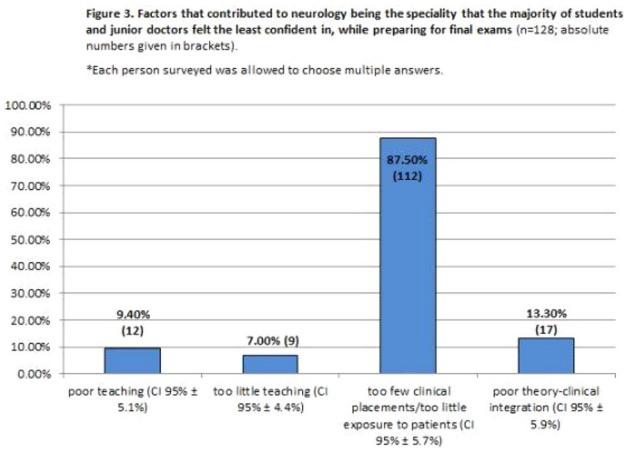
Methods: An online questionnaire was designed to evaluate which specialties were perceived to be most challenging to learn at medical school and why. Final year students and junior trainees in London participated voluntarily. Following analysis of the results, a one day neurology revision course was organised and offered to London final year students by junior doctors. Pre course standardisation briefing of teachers was undertaken. The course included interactive lectures, an EMQ session, and clinical examination circuit of patients. Course feedback was collected from both students and tutors.

Results: The online questionnaire received 179 responses: 136 (76 %) were medical students and 43 (24 %) junior trainees. The majority of respondents identified neurology as the specialty they found most challenging at medical school (59.2 %; CI 95 % ± 7.2 %) and were least confident in when taking their final exams (71.5 %; CI 95 % ± 6.6 %) (Figs. 1–3). All students and tutors (n = 44) felt their skills, knowledge and confidence in neurology had improved following participation in the revision course. The most useful aspect of the course was the examination circuit (75 %).

Conclusions: Students and trainees feel most challenged when assessing neurological patients. This diffidence may be related to perception of limited dedicated undergraduate teaching in neurology. Near-peer teaching improves confidence in neurological assessment and may desensitize neurophobia.







Disclosure: Nothing to disclose.

EP1249

Abstract withdrawn

EP1250

Empedoclis and Galen on the functional expression of the soul

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Introduction: Empedoclis was a pre-Socratic philosopher and Galen a doctor of Hellenistic era.

Methods: We attempted to fine common places between Empedoclis philosophy on the soul and brain, based on the fragments of his poems and Galen's theories based on his numerous dissertations.

Results: The functions of the soul are continuously renewed, since they are generated and grow by the production of the cerebral spirit. The reasoning faculty of the soul is mortal. Galen clamed that the anterior part of the brain is able to receive sensations to form imaginations and to apprehend any kind of thoughts. The sensus communis is perceptive to new impressions and able to support the creation of new thoughts Abnormal sense perception may result to illusions and hallucinations. When the thinking faculty is paralyzed the patient suffers from dementia. The degree of awareness depends mainly on the state and the condition of the brain itself. Memory is the retention and conservation of those impressions, which soul discerned at an earlier time. Virtue seems to require an act of good will. Reason must be trained in order to control the erroneous thoughts and the inappropriate behaviour. Anger and desire are regarded as afflictions of the soul. They may be restrained and controlled by the judgment of the reason. Empedoclis clamed that soul is eternal. The brain tries to create ideal condition for the function of the soul by establishing love and tranquility in the place of fear and enemity.

Disclosure: Nothing to disclose.

EP1251

Tuberculous meningoencephalitis: clinico-radiological correlations and therapeutic response

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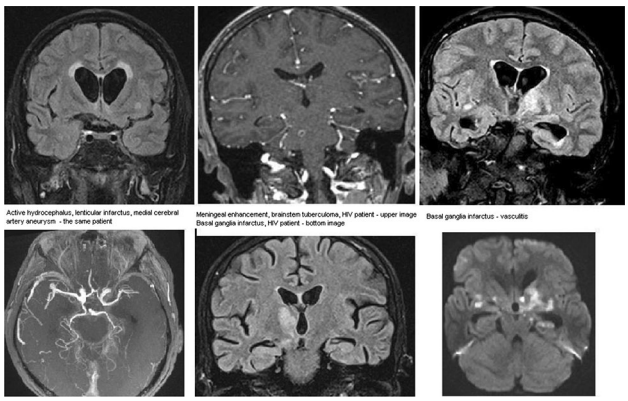
Introduction: Cerebral tuberculosis is the most severe complication of secondary dissemination of Koch bacillus. Though it frequently presents as tuberculous meningitis, we encounter brain involvement as vasculitis, tuberculomas, hydrocephalus, aneurysms. With the advent of efficacious antibiotherapy, its early introduction in the management plan may ameliorate the clinical picture.

Methods: We present six cases of tuberculous meningoencephalitis in adults showing clinical and radiological profiles that illustrate the whole range of cerebral involvement with the corresponding diagnostic and management pitfalls.

Results: There was commonly an insidious neurological onset for 3–10 days, culminating into a coma in 3 patients while the brain MRI showed various lesions ranging from tuberculomas and hydrocephalus to vasculitis and medial cerebral artery aneurysm. (Please find a sample of the radiological findings in the attachement.) The results of the lumbar puncture oriented the diagnostic but failed to sustain it by a positive PCR or cultures in one patient, whose definite diagnostic was established late on CSF cultures drawn from the ventricular shunt. As for the management, the main challenge was optimizing the blood brain barrier penetration of antituberculous drugs though fortunately only one of the cultures demonstrated multidrug-resistant Mycobacterium.



Conclusions: With a still low sensibility of the TB PCR and the delayed results of Mycobacterium cultures, a high degree of suspicion and early initiation of antituberculous treatment are requisite for a favourable outcome. However, the issues to discuss would be the optimal dose of intravenous steroids as well as the correct management of brain tuberculomas.

Disclosure: Nothing to disclose.

EP1252

The contribution to neuological research by professor Michailo Lapinsky

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Introduction: Professor M.M. Lapinsky was the founder of neurology as a clinical discipline at medical faculties of Kyiv St. Volodymyr University (Ukraine) and Zagreb University (Croatia). At the beginning of the XX century he gained wide European recognition for his clinical, pathomorphological and experimental works on neurology. Nevertheless the most data of his professional activity are slightly known by modern medical community.

Methods: This paper presents a brief review of the literature regarding the main approaches of professor M.M. Lapinsky's scientific research.

Results: Throughout his career, the first Head of the Nervous Disease Department of Kyiv University, Professor Michailo Lapinsky published more than 150 articles and monographic works. He has noted the stages of arterial lesions caused by peripheral nerve transaction, changes of brain capillaries under different pathological conditions, role of a. carotis sympathetic innervation and phenomena of visceral pain (Lapinsky's pelvic syndrome, Lapinsky's femoral reflexive point). He experimentally generated epileptic seizures by irritation of frog brain cortex with salts of bile acids. His works on efferent system developed the conception of motor functional

presentation in the spinal cord. Thus the clinical variety of spinal cord injuries and phenomena of diaschisis have been recognized.

Conclusions: The repercussions of Lapinsky's findings are essential to the current fields of medical science. His has given a significant impulse to raising the profile for neurology in Ukraine and worldwide as his many ideas have become the cornerstone of different neurological concepts and principles.

Disclosure: Nothing to disclose.

EP1253

Paralytic rabies: two case reports

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Background: There are two forms of human Rabies: the well-known encephalitic (furious) and the paralytic (dumb) form. Both are progressive and generally lead to death. Paralytic rabies (PR) accounts for 20 % of all rabies.

Objective: We report two atypical cases of PR followed by furious encephalitis.

Case reports: A 30-year-old woman and a 44-year-old man were admitted for progressive weakness initially of lower limbs followed after 1 week by the upper limbs. Examination found quadriplegia with areflexia, without meningeal signs. Brain MRI was normal. Laboratory tests showed normal amount of white blood cells and C reactive protein. Cerebrospinal fluid examination showed albumin-cytological dissociation. The two patients were diagnosed initially as acute polyradiculoneuritis. Viral tests for hepatitis markers and HIV were negative. Over a hospital stay of 2 days, they developed confusion, agitation, furiousness, vomiting, and breathlessness, followed by consciousness deterioration. The first patient expired on day 5 and the second on day 7. Autopsy confirmed the diagnosis of rabies. No history of animal bite was found.

Discussion: PR is recognized to be more difficult to diagnose, as more than 50 % of patients lack the classical symptoms such as hydrophobia or aerophobia. Our patients also did not have these symptoms, and their initial presentation was mimicking Guillain-Barré syndrome. The pathological basis of paralysis in PR is not well understood, peripheral nerve demyelination seems to be the main mechanism.

Conclusion: PR should always be suspected regardless of history of animal exposure where clinical findings are not typical for Guillain-Barré syndrome.

Disclosure: Nothing to disclose.

EP1254

Caffeine prevents human prion protein-mediated neurotoxicity through induction of autophagy

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Introduction: The human prion protein fragment PrP (106–126) possesses a majority of the pathogenic properties associated with the infectious scrapie isoform of PrP, known as PrP^{Sc}. Accumulation of PrP^{Sc} in the brain of humans and animals affects the central nervous system.

Methods: Recent epidemiologic studies suggest that caffeine, one of the major components of coffee, has a protective effect against the development of neurodegeneration; however, a protective function of caffeine in prion disease has not been reported.

Results: We therefore investigated the effect of caffeine on prion-mediated neurotoxicity. Expression of the autophagy marker LC3-II protein was dose-dependently increased by caffeine, and the autophagy induced by caffeine protected neuronal cells against PrP (106–126)-induced cell death. On the other hand, down-regulation of LC3-II with the autophagy blockers 3-methyladenine and wortmannin prevented the caffeine-mediated neuroprotective effects.

Conclusions: This report provides the first evidence that caffeine treatment protects human neuronal cells against prion-mediated neurotoxicity and this neuroprotection effect is mediated by caffeine-induced autophagy signals. We suggest that caffeine treatment may be a therapeutic strategy for prion peptide-induced apoptosis.

Disclosure: Nothing to disclose.

EP1255

Abstract withdrawn

Movement disorders 2

EP1256

The oligomer modulator anle138b is effective in the prodromal phase of a transgenic mouse model of Parkinson's disease

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Introduction: Currently for neurodegenerative diseases like Parkinson's disease (PD) only symptomatic treatment is available. PD is characterized by deposition of aggregated alpha-Synuclein (αSyn) in neurons. Recent studies showed that the oligomer modulator anle138b might provide a disease-modifying therapy. As published previously, treatment of mice transgenic for human A30P-αSyn with anle138b resulted in significantly prolonged disease-free survival and reduction in deposition of αSyn.

To determine if the effect of anle138b is already detectable in early disease phase, a detailed analysis of the motor performance and deposition of αSyn was conducted during the prodromal phase of the disease.

Methods: Transgenic mice were treated with anle138b or placebo. Disease progression was evaluated by Rotarod measurements and determination of body weight. To detect deposition of αSyn sucrose gradient centrifugation, histopathological and immunohistochemical studies were conducted.

Results: Anle138b significantly reduced fluctuations in motor performance in the prodromal phase approaching the level of non-transgenic control mice and led to normal increase in body weight and decreased deposition of aggregated αSyn.

Conclusions: Treatment with the oligomer modulator anle138b leads not only an increased disease-free survival, but also to a better motor performance and a decreased deposition of aggregated αSyn in the prodromal phase of the disease. These results point to a key role of protein aggregation in the pathogenesis of PD and therefore, anle138b is holding promise for a disease-modifiying therapy in synucleinopathies.

Disclosure: Nothing to disclose.

EP1257

Cerebellar signs in spinocerebellar ataxia type 37 at the start of follow up

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Introduction: Spinocerebellar ataxia 37 (SCA37) is a new type of pure spinocerebellar ataxia (SCA) with important alteration of vertical eye movements. The clinical cerebellar phenotype is still to be carefully explored. The objective of the study was to analyse the SCA37 phenotype using SARA scale.

Methods: Twelve affected patients were recruited from two different families in Spain. Cerebellar affection was assessed by SARA scale at the beginning of the follow-up (2010). Sex, referred age at onset and time of evolution were also collected. Relationships between SARA items and these variables were studied by the use of network analysis. Patterns of affection were examined by hierarchical clustering after multiple correspondence analysis.

Results: Sitting remained normal in all patients. Although the rest of the items were positively correlated, a tightly correlation exist between gait, speech and stance items. Time of evolution is a central parameter in the network, and its correlation is particularly strong with gait, speech and stance items. Women have a longer time of evolution. Three patterns of patients were defined according to the affection.

Conclusions: As previously described in other SCAs, our study shows that time of evolution is critical in the intensity of cerebellar sings, particularly in gait, stance and speech. Women seem to have longer time of evolution and the intensity of affection establishes 3 types of patients at the start of the follow-up highlighting the variability of the phenotype.

Disclosure: Nothing to disclose.

EP1258

Opicapone effect on levodopa pharmacokinetics in comparison with placebo and entacapone when administered with immediate release 100/25 mg levodopa/carbidopa in healthy subjects

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Introduction: Opicapone (OPC) was developed to fulfil the need for more potent, safer and longer acting COMT-inhibitors.

Objectives: To investigate the effect of a once-daily (QD) OPC (25, 50 and 75 mg) on levodopa pharmacokinetics (PK), in comparison to placebo and 200 mg entacapone (ENT).

Methods: This was a single-centre, double-blind, randomized and placebo-controlled study in 4-groups of 20 (10 male and 10 female) subjects each. The study consisted of QD administration of OPC or placebo for 11 days followed by thrice-daily (every 5 h) 100/25 mg levodopa/carbidopa (LC), 200 mg ENT or placebo on Day 12.

Results: Levodopa extent of exposure (AUC) was significantly increased up to 78.9 % and 73.7 % with 75 mg-OPC in comparison to placebo and ENT, respectively. Levodopa-AUC_{0-24} was higher when LC was administered with any OPC dose than when administered concomitantly with ENT. Peak exposure (C_{max}) to levodopa increased (> 30 %) with 75 mg-OPC following LC administrations. A significantly long-lasting and sustained S-COMT inhibition occurred with OPC. Maximum S-COMT inhibition ranged from 67.1 % (200 mg-ENT) to 94.2 % (75 mg-OPC) and was higher than ENT for all OPC doses. The 50 and 75 mg-OPC were somehow similar (75 mg was slightly superior); thus, the 75 mg-OPC may not bring a significant advantage to 50 mg-OPC with regard to S-COMT inhibition. The tolerability profile of OPC was favourable.

Conclusion: OPC may offer a therapeutic advantage in relation to ENT in patients with Parkinson's disease receiving levodopa therapy. The dosages of 25 and 50 mg-OPC likely provide the most adequate enhancement in levodopa availability as adjunct to levodopa/carbidopa therapy.

Disclosure: Nothing to disclose.

EP1259

Opicapone long-term efficacy and safety in Parkinson's disease BIPARK-II study: a one-year open-label follow-up

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[1]R&D Department, Bial, Portela & C[a], S.A., S. Mamede Coronado; [2]Pharmacology and Therapeutics Department, Faculty of Medicine, University Porto, Porto, Portugal

Introduction: Opicapone (OPC) was developed to fulfil the need for more potent, safer and longer acting COMT inhibitors.

Objectives: To follow the efficacy and safety of 1-year, open-label (OL), once-daily (QD) OPC-treatment in patients with Parkinson's disease (PD) on levodopa-therapy and with motor fluctuations.

Methods: After completion of the placebo-controlled double-blind (DB) part, 367 (97.6 %) patients continued to a 1-year OL-part, in which all subjects were treated with OPC (25 or 50-mg OPC). All subjects began with 25-mg OPC QD for 1-week. Then, the investigator freely adjusted the levodopa therapy and/or OPC based on the dopaminergic response and/or associated adverse events. The efficacy variable was the change from baseline in OFF-time, based on patient diaries. Secondary endpoints include proportion of responders, course of OFF/ON-time, UPDRS-III, PDQ-39, NMSS, PDSS and safety assessments.

Results: After 1-year treatment with OPC, reduction in absolute OFF-time in relation to the DB baseline was consistent with that observed at DB-part ($\sim$2.0-h). For subjects that were under placebo in the DB-part, a decrease of $\sim$0.5 h in relation to OL baseline and a relevant decrease of $\sim$1.5-h in relation to the DB baseline, were observed. OFF-time responders' (67.5 %), OFF-time reductions (12.5 %) and increase in absolute ON-time without or with non-troublesome dyskinesias ($\sim$1.7-h), were also consistent with the DB results. OPC was safe and well tolerated.

Conclusion: Long-term use of OPC was safe, well tolerated, and presented a sustained efficacy in reducing the OFF-time in patients with PD on levodopa-therapy and with motor fluctuations.

Disclosure: Nothing to disclose.

EP1260

Transcranial parenchymal sonography findings and the structure of depression in patients with Parkinson's disease

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Introduction: The reduced raphe echogenicity on transcranial parenchymal sonography (TCS) is associated with depression in PD patients, suggesting the involvement of serotonergic depletion in the pathogenesis of mood disturbances in PD. The aim was to investigate.

(1) raphe echogenicity in depressed vs. non-depressed PD patients using TCS and

(2) the structure of depression in PD patients with normal vs. hypoechogenic raphe structures.

Methods: Depression, anxiety and apathy were assessed using Hamilton Depression Rating Scale-21 (HDRS), Montgomery-Asperg Depression Rating Scale, Hamilton anxiety rating scale and Apathy scale. All patients underwent TCS in order to estimate raphe structures.

Results: Thirty nine percent of 120 consecutive PD patients were depressed. Raphe hypoechogenicity was found in 51 out of 118 patients (43.2 %). Twenty seven (58.7 %) depressed and 24 (33.3 %) non-depressed patients had hypoechogenic raphe on TCS ($p = 0.07$). Logistic regression analysis revealed that the probability for PD patients with hipoechogenic raphe to be depressed is 3.5 times higher than in patients with normal raphe system (OR = 3.48). Patents with raphe hypoechogenicity were more frequently apparently sad ($p = 0.03$), reporting sadness ($p = 0.01$) and pessimistic thoughts ($p = 0.05$) more commonly compared to patients with normal raphe, who had more frequent suicidal thoughts ($p = 0.03$).

Conclusions: Serotonergic mesencephalic midline structures are more frequently altered in depressed than in non-depressed PD patients. Distinct depression characteristics suggest its heterogeneity in PD, presumably depending on the differences in underlying neurotransmitters interactions.

Disclosure: Nothing to disclose.

EP1261

Peripheral alpha-synuclein markers in subjects harboring the G209A mutation in the SNCA gene

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Introduction: The potential use of α-synuclein concentration as a biomarker for synucleinopathies remains controversial, with great variability in results across studies. This variation could reflect technical/methodological differences, but also biological factors, such as the biological and pathophysiological heterogeneity of PD, especially as it pertains to the relative contribution of α-synuclein. We have undertaken a study to assess α-synuclein concentration in a biologically homogeneous group of Greek PD patients harboring the G209A mutation in the SNCA gene encoding for α-synuclein, leading to an A53T substitution; in this group we have also included non-manifesting carriers of the same mutation (total N = 29, with 8 non-manifesting carriers). α-Synuclein levels in this group were compared with an age-matched healthy control group (N = 29).

Methods: The levels of total α-synuclein in plasma and serum were measured using an in-house ELISA assay with high sensitivity and reproducibility.

Results: We have found a significant decrease in serum α-synuclein concentration in the ASYN MUT as compared to the control group (16.3 ± 2.2 vs. 27.2 ± 2.8 ng/ml, mean ± SEM respectively, $p = 0.001$ by parametric t-test). This result was verified by measurements of α-synuclein in the plasma of ASYN MUT and control subjects (7.11 ± 1.8 vs. 16.0 ± 4.2 ng/ml, mean ± SEM respectively, $p = 0.012$ by non-parametric Mann–Whitney U test).

Conclusions: Our data indicate that the G209A SNCA mutation leads to lower circulating α-synuclein levels. Whether this reflects lower production of α-synuclein from blood cells, decreased α-synuclein release or altered distribution between periphery and CNS remains to be determined.

Disclosure: Nothing to disclose.

EP1262

A reclassification rate of clinical diagnoses and diagnostic impact of imaging tests in parkinsonian disorders: a 2 year follow-up study

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Introduction: Since the diagnosis of parkinsonian disorders is made on clinical grounds and only computed tomography (CT) is formally incorporated into step two (exclusion) criteria for diagnosing idiopathic Parkinson's disease (IPD), the aim of the study was to review a reclassification rate of clinical diagnoses and to evaluate possible diagnostic impact of paraclinical imaging tests in parkinsonian disorders after a 2-year follow-up period.

Methods: Overall 480 consecutive patients with movement disorders were referred for transcranial ultrasound (TCS) examination in 2011, and were recruited into the study. All clinical and imaging data of these patients were reassessed in 2013. After a 2-year follow-up period, 47 (9.8 %) cases were reclassified according to clinical diagnosis. They were included into further analysis.

Results: The mean age (±SD) of the patients (n = 47) was 66.9 ± 10.3 years (min.45–max.85), 27 (57.4 %) were female, with the symptom duration of 8.7 ± 11.3y, and 15 (31.9 %) denoted positive family history. The majority (n = 37, 78.7 %) were referred from Out-patient Neurological Department at Kaunas Clinics. The number of prospective paraclinical imaging tests was as follows: TCS (n = 42, 89.4 % as five patients had bilateral acoustic window insufficiency), brain CT (n = 20, 42.6 %), DaTscan (n = 14, 29.8 %), conventional MRI (n = 8, 17 %). The initial and final clinical diagnoses, also the main imaging results are presented in Tables 1 and 2.

Diagnosis (n=47)	Initial clinical diagnosis (n, %)	Final clinical diagnosis after 2-year follow-up (n, %)	Relative reclassification rate (%)
Parkinson's disease (**PD**)	15 (31.9)	13 (27.7)	-4.2
Essential tremor (**ET**)	17 (36.2)	5 (10.6)	-25.6
ET, but with observation for PD (**ET-PD**)	9 (19.1)	16 (34)	+14.6
Parkinsonian syndromes unspecified (**PSu**)	1 (2.1)	5 (10.6)	+8.5
Healthy subject (**HS**)	0	1 (2.1)	+2.1
Secondary parkinsonism (**SecP**)	4 (8.5)	4 (8.5)	0
Mild cognitive impairment (**MCI**)	0	1 (2.1)	+2.1
Dementia (**Dem**)	0	1 (2.1)	+2.1
Dystonia (**Dyt**)	1 (2.1)	0	-2.1
Hereditary degenerative parkinsonism (**HDP**)	0	1 (2.1)	+2.1

Diagnosis (n=47)	DaTscan (n=14)		TCS-SN (substantia nigra echogenicity, n=42)		
	Normal n	Abnormal 123^I-Ioflupane binding n	Normal (<=0.19 cm^2) n	Abnormal moderate (0.20-0.25cm^2) n	Abnormal high (>=0.26cm^2) n
PD	2	5	0	0	11
ET	0	1	3	2	0
ET-PD	4	1	3	5	7
PSu	1	0	1	2	2
HS	N/A	N/A	1	0	0
SecP	N/A	N/A	0	1	2
MCI	N/A	N/A	0	0	0
Dem	N/A	N/A	1	0	0
Dyt	N/A	N/A	0	0	0
HDP	N/A	N/A	0	1	0

Conclusions: The majority of patients were reclassified to negative clinical diagnosis for IPD after paraclinical tests and follow-up. DaTscan and TCS-SN with a threshold value of 0.26 cm^2 had the highest diagnostic impact for IPD diagnosis, however with limited specificity.

Disclosure: Nothing to disclose.

EP1263

Effects of high altitude exposure on physiological tremor

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Introduction: Various neurological symptoms can occur after arising from ascent to altitudes greater than 2,500. So far, no data exist on the effects of high altitude on physiological tremor under natural conditions.

Methods: One female and five male healthy non-professional mountaineers undertook an expedition to Cho oyu (8,201 m) in Nepal. We used a smartphone triaxial accelerometer to record postural tremor at 3,400, 5,700, and 7,100 m height after a minimum acclimatization time of 12 h. Tremor peak frequency and total power were calculated using offline fast Fourier transforms.

In addition, blood oxygen saturation (measured non-invasively), heart rate and the Lake Louise Score (LLS) for Acute Mountain Sickness (AMS) were performed at all three heights.

Results: At 3,400 m mean peak frequency of postural tremor was 5.0 Hz and mean tremor amplitude was 0.001 milliG. At 5,700 m (camp 1) peak tremor frequency decreased to 3.3 Hz and amplitude increased to 0.002 milliG. Three participants reached camp 2 (7,100 m). Tremor frequency was 4.2 Hz and tremor amplitude increased to 0.003 milliG. This increase in tremor amplitude was accompanied by a decrease in average blood oxygen saturation, an increase in mean heart rate, and worsening of the average LLS.

Conclusion: Under natural conditions in high altitude—and exposure to hypoxia—an increase of the amplitude of physiological tremor was found. This effect of hypoxia mainly results from activation of the hypothalamic–pituitary–adrenal axis causing elevated catecholamine levels, leading to threefold increase in tremor amplitude paralleled by raised heart rate.

Disclosure: Nothing to disclose.

EP1264

Power of olfaction impairment on the etiopathogenesis of Parkinsonism in animal model: experimental study

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Introduction: It is known that olfaction impairment is a characteristic and the first feature of Parkinsonism (1). Olfactory dysfunction is involved in various neurodegenerative diseases and fMRI may be good candidates to detect neurodegeneration related decreased volume of nigrostriatal pathways (2). We examined conversely that olfaction disorders may cause Parkinsonism by causing neurodegenerative changes in substantia nigra in an animal model.

Method: Twenty hybrid rabbits were used. Five of them used as control for the evaluation of olfactory bulbs and related connections. The remaining animals were done frontal burr hole at the level of midorbital line. Ten of them were applied to bilateral olfactory bulb ablation and five of them used as SHAM group. The remaining animal were applied bilateral olfactory bulb ablation and used as study group. After 3 months follow up period, all animals were decapitated under general anesthesia and their olfactory bulbs and degenerated-apoptotic neuron densities of substantia nigra were examined stereological methods. Results were analysed statistically.

Result: All animals belong to study group were observed having apathia, mental disorders, psychomotor retardation, sexual aversion, decreased self care and reduced motor functions and muscular kinesia disorders similar to Parkinson symptoms. Gross anatomical examinations revealed that olfactory bulbs of these animals were atrophied. Prominent neuronal loss due to apoptosis were detected in substantia nigra in study group by histopathological examinations.

Conclusion: In contrary to common believe, we argued that olfaction disorders cause Parkinsonian disorders via neuronal degeneration in substantia nigra.

Disclosure: Nothing to disclose.

EP1265

Myoclonus after treatment of cobalamin deficiency: an unusual complication in adult

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Introduction: Myoclonus is not a classic feature of vitamin B12 (VB12) deficiency in adults, though they are frequent in infant cases.

Methods: We report an adult patient with cobalamin deficiency that developed temporary myoclonus exaggerated after the initiation of VB12 treatment.

Results: A 56 year old woman presented an acute mental confusion with gait disturbance and urinary dysfunction. Neurological examination showed a disoriented and hallucinated patient, a pyramidal and coronal syndromes, associated to peripheral sensory signs. Mild myoclonus of the upper limbs was noted initially. The VB12 blood level was very low. The MRI showed an extensive posterior cervical and dorsal myelitis. 48 h after VB12 therapy, she developed head myoclonus persisting even during sleep, and contrasting with an improvement of the mental confusion. The electroencephalogram was comitial. The myoclonus improved within a few days after the administration of low doses of clonazepam.

Conclusions: In infantile cobalamin deficiency, variable movement disorders were reported (tremors, chorea, dystonia, myoclonus) usually occurring early in the disease and worsening after treatment. In the literature, there were only two reported adult patients with cortical and spinal myoclonus, one of them appearing after treatment. This phenomenon may be explained by the sudden stimulation of folate and cobalamin pathways and producing a temporary imbalance of the complicated metabolic pathways of cobalamin. To our knowledge, this is the third report of myoclonus in an adult patient with VB12 deficiency. Myoclonus should be considered as one of the extraordinary neurological manifestations of VB12 deficiency in adults.

Disclosure: Nothing to disclose.

EP1266

Evaluation of olfactory function in Friedrich's ataxia: a case–control study

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Introduction: Olfactory dysfunction is present in a number of neurodegenerative diseases and some types of spinocerebellar ataxias. However, olfactory dysfunction in Friedreich's ataxia has not yet been reported.

Methods: Seventeen patients with Friedreich's ataxia (FA) confirmed with DNA testing were evaluated. All patients were evaluated, including age of onset, duration of disease, gender, co-morbidities, ataxia severity (as measured by the Scale for the Assessment and Rating of Ataxia). Olfaction was tested using the 12 Sniffing Sticks Diagnosis Test. A matched-control group of 34 individuals was also evaluated. Intra- and inter-groups comparisons were performed with a $p < 0.05$ statistical significance level (Spearman's test, Student's *t* test).

Results: The FA group consisted of seven females and ten male patients Mean age of onset of disease was 15.8 ± 10.0 years, mean age of patients 30.5 ± 14.7 years (control group 35.5 ± 9.7) (ns). Nine out of 17 patients (52.9 %) had a normal olfaction test. Eight (five men, three women) showed hyposmia (Fisher's test $p < 0.0001$) when compared to the control group. Spearman's correlation coefficient between olfactory function vs. age at onset of symptoms was 0.29 ($p = 0.25$), vs. disease duration -0.01 ($p = 0.96$), vs. SARA 0.2 ($p = 0.42$), vs. allele I (number of GAA repeats) -0.38 ($p = 0.12$), and vs. allele II 0.2 ($p = 0.39$).

Conclusions: A significant proportion of FA patients had hyposmia ($p < 0.00$, Fisher's test). However, there was not a significant correlation between the findings of the smell test with age of onset, duration of disease, SARA and genetic profile (number of GAA repeats).

Disclosure: Nothing to disclose.

EP1267

The spectrum of movement disorders in chronic liver disease: a cross-sectional study

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Introduction: Chronic liver failure has been associated with neurological symptoms such as parkinsonism, ataxia and cognitive decline, globally termed ''acquired hepatolenticular degeneration'', a distinct condition from hepatic encephalopathy. Parkinsonism has been explained with manganese accumulation in basal ganglia, but the spectrum of movement disorders in chronic liver disease is not completely known, and few data are available on patients without cirrhosis.

Methods: 71 patients with chronic liver disease were evaluated. Demographic characteristics, aetiology and duration of liver disease were obtained from medical records. Motor symptoms were scored using the UPDRS-III scale. A subset of patient with movement disorders underwent brain MRI.

Results: Patients' mean age at assessment was 67 years, and mean liver disease duration 13.5 years. Mean age at onset of hepatic disease and neurological symptoms were 53 and 67 years. Prevalence of movement disorders was 56.3 %, including bradykinesia (80 %), tremor (57.5 %) and rigidity (40 %). Severe parkinsonism was present in 14 subjects (mean UPDRS-III 27/108). Mean duration of neurological symptoms was 3.8 years. Among patients with movement disorders, 70 % were subjectively impaired, while 30 % were only affected subclinically. The most common aetiology was HCV-related cirrhosis (47.5 %), followed by alcoholic cirrhosis (20 %) and chronic C hepatitis (15 %). 12 patients underwent brain MRI, with bilateral T1 pallidal hyperintensity in 50 % of cases.

Conclusions: Parkinsonism and isolated tremor are common in chronic liver disease; we observed movement disorders also in patients with chronic hepatitis without liver failure, which may indicate that neurodegeneration takes place early in the course of liver disease.

Disclosure: Nothing to disclose.

EP1268

Mapping regional grey and white matter damage in patients with progressive supranuclear palsy syndrome

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Introduction: This study investigated the pattern of grey matter (GM) atrophy and white matter (WM) microstructural damage in patients with probable progressive supranuclear palsy syndrome (PSPs) using advanced magnetic resonance imaging (MRI) techniques.

Methods: We enrolled 21 patients with probable PSPs and 21 healthy controls. Patients underwent clinical and neuropsychological evaluation, and brain structural and diffusion tensor (DT) MRI. The regional patterns of brain GM atrophy and WM microstructural damage were assessed using voxel-based morphometry and tract-based spatial statistics, respectively ($p < 0.05$ FWE).

Results: PSPs patients were in a moderate stage of disease (mean Hoehn and Yahr score: 3.3) and showed mild to moderate cognitive impairment involving especially attentive-executive functions. PSPs patients did not show significant GM atrophy relative to controls. On the contrary, they showed a significant reduction of fractional anisotropy and a significant increase of mean, axial and radial diffusivities in the main WM tracts bilaterally, including body and splenium of corpus callosum, cingulum, inferior fronto-occipital, superior longitudinal and uncinate fasciculi, anterior and superior corona radiata, corticospinal tract, and thalamic radiations. Superior cerebellar peduncles and internal capsules showed a significant increase of diffusivity values, but no FA changes.

Conclusions: In PSPs patients, WM microstructural damage is prominent compared to GM atrophy even in the moderate stage of the disease, suggesting that diffuse WM damage in tauopathies is not merely a function of disease severity. Regional differences in DT MRI metrics might reflect a different vulnerability of WM tracts.

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Disclosure: FA funding for travel from Teva and speaker honoraria from Bayer, Biogen, Sanofi Aventis, SSIF. CG received compensation for consulting and/or speaking from Novartis, Teva, Sanofi, Genzyme, Merck Serono, Biogen, Bayer, Actelion, SSIF. MF received compensation for consulting and/or speaking from Bayer, Biogen Idec, Merck Serono, and Teva.

EP1269

Anxiety and depression in hemifacial spasm

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Introduction: Hemifacial spasm is characterized by intermittent tonic or clonic twitching of the muscles innervated by ipsilateral facial nerve. It must be differentiated from other causes of involuntary facial movements, all of which can potentially lead to social embarrassment. Onset is generally between the second and eighth decades of life and averages 45–51 years of age. Facial twitchings are frequently leads to stress and anxiety. Symptoms of hemifacial spasm are frequently aggravated by stress, fatigue, anxiety, and voluntary facial movements.

Methods: We examined the prevalence of anxiety and depressive symptoms (using Becks Depression and Anxiety Inventory and clinical assessment) in hemifacial spasm (HFS). In a case study, we evaluated anxiety and depression symptoms in 90 patients with HFS; and found the anxiety and depression score to be significantly greater in HFS compared to normal population. We compared their sex, age, marital status, peripheral facial paralysis history also.

Results: There were 90 HFS patients with a mean age of $56 \pm 15{,}19$ (35–79) years, comprising of 65.6 %($n = 59$) women and 34.4 % ($n = 31$) men. Among the HFS patients, the mean anxiety and depression score was significantly higher in HFS than in normal population. 24.4 % of HFS patients have peripheral facial paralysis. We found that female gender was a risk factor for anxiety and depression in HFS.

Conclusions: It is important that diagnosis and appropriate management of anxiety and depression symptoms can improve quality of life in HFS patients.

Disclosure: Nothing to disclose.

EP1270

Was pallidotomy abandoned too early in Parkinson's disease treatment?

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Introduction: In recent years deep brain stimulation (DBS) has established therapeutic benefits for otherwise treatment-resistant movement disorders, such as Parkinson's disease (PD).

Infection and rejection of the implanted device poses a significant risk in DBS and a subgroup of patients tend to develop repeated infections that, in some cases, prompt the removal of the entire system.

Published data shows that pallidotomy may improve rigidity, tremor and dyskinesias, with minimal neuropsychological decline and a very acceptable risk profile but, after the success of DBS, lesional surgery has been almost abandoned.

Methods: We present three patients who underwent DBS with successful control of PD's motor symptoms, but who had their implants removed due to rejection or infection. Unilateral pallidotomy, by radiofrequency ablation, was then performed.

Neuroanatomical localization of the GPi was set using stereotactic CT and MRI fusion and postoperative MRIs were performed to assess lesion's characteristics.

Clinical outcome measurements included the UPDRS scale and medication reduction up to 2 years.

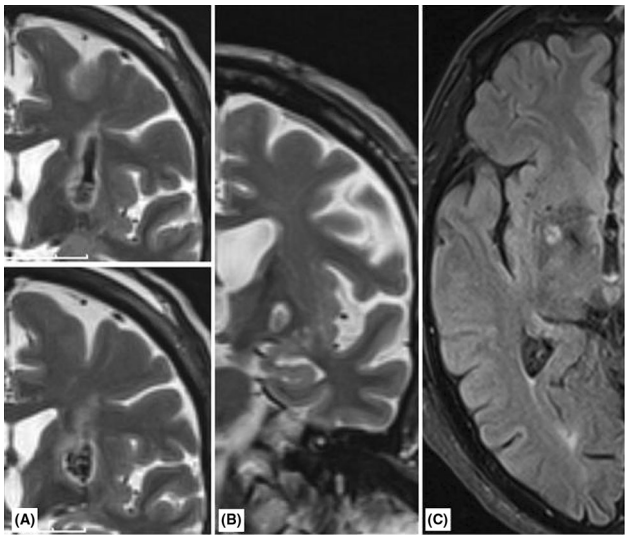
	Patient 1 (female, 69 y-old)	Patient 2 (male, 72 y-old)	Patient 3 (male, 73 y-old)
Parkinson's disease diagnosis	1992	1995	1998
Deep brain stimulation (bilateral STN)	June 2008	December 2010	October 2008
Complete removal of implanted devices	June 2009 *(Rejection of device due to metal allergy)*	April 2011 *(St. aureus infection)*	February 2010 *(St. aureus infection)*
Pallidotomy	July 2010 *(Target left GPi)*	October 2012 *(Target left GPi)*	October 2012 *(Target right GPi)*

Results: After implant removal, the consequent worsening of motor symptoms resulted in great reduction on patient's autonomy

and quality of life. In all cases, this situation was reversed after unilateral pallidotomy.

Despite follow-up showed different imaging outcomes, all patients experienced reasonable motor benefits, sustained improvement in UPDRS scale, medication reduction and resolution of drug-related dyskinesias.

		Patient 1 (female, 69 y-old)	Patient 2 (male, 72 y-old)	Patient 3 (male, 73 y-old)
UPDRS III	with deep brain stimulation ON	8	10	11
	after removal of implanted devices	30	24	22
	after pallidotomy	11	8	10



Conclusions: Unilateral pallidotomy should always be considered for patients in whom DBS hardware needs to be removed, and for patients with advanced disease that, for some reason, are not good candidates for DBS.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 3

EP2101

NT-proBNP level as a predictor of progressive clinical course of non-cardioembolic ischemic stroke

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Introduction: The purpose of a prospective cohort study—determination of the relationship between the level of amino-terminal brain natriuretic propeptide (NT-proBNP) with clinical course of non-cardioembolic ischemic stroke (IS).

Methods: The study included 45 patients with IS; mean age—66.8 ± 11.4 years; the median time from stroke onset up to blood sampling was 22.5 {16.0; 27.0} h. NT-proBNP level in plasma were determined by ELISA. Patients with atrial fibrillation were excluded.

Results: NT-proBNP level at the first day was 309 {34; 851} ng/L, and on the tenth day fell up to 28 {0.1; 233} ng/L; $p = 0.023$. Progressive course of IS with increasing of neurological deficit ≥2 NIHSS points or death at first 7 days was characterized by significantly higher level of NT-proBNP than at favorable clinical variant of IS. Thus, when the concentration of NTproBNP < 460 ng/L, progressive clinical course of IS occurred in 3 (11.1 %) cases, and when the level of NTproBNP ≥ 460 ng/L in 8 (44.4 %); $p = 0.014$. The severity of the initial neurological deficit in patients with NT-proBNP level < 460 ng/L was 3 {1; 4} NIHSS score, in patients with NT-proBNP ≥ 460 ng/L 5 {3; 8}; $p = 0.047$. Hyperexpression of NT-proBNP at stroke onset was associated with unfavorable functional outcome (mRS score 4–6); $p = 0.032$, as well as with severe functional disturbances at the hospitalization time (NIHSS score ≥ 15); $p = 0.022$.

Conclusions: Elevated NT-proBNP levels in debut of non-cardioembolic IS were associated with progressive clinical course of stroke, what had been accompanied neurological deterioration.

Disclosure: Nothing to disclose.

EP2102

Influence of sphingosine-1-phosphate receptors on blood brain barrier and processes of angiogenesis in vivo

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Introduction: Based on the knowledge that high density lipoprotein (HDL) and its component sphingosine-1-phosphate (S1P) have promoting effects on vasculogenesis after ischemic events, it raises the question how the S1P receptors are involved in post-ischemic events and if these receptors could be a therapeutic target for better outcome after stroke.

Methods: In a model of transient ischemia male C57BL/6 mice were subjected to 30-min intraluminal middle cerebral artery occlusion, followed by 24 h of reperfusion. After filament withdrawal animals received intraperitoneal injections of antagonists of the S1P receptors S1P1, S1P2 and S1P3 (W146, JTE-013, and Suramin, respectively).The edema and infarct sizes, the endothelial proliferation, and the expression of ATP-binding-cassette (ABC)-transporters and occludin were analyzed with immunohistochemical and western blot technique.

Results: Edema and infarct sizes are significantly increased after S1P1 receptor inhibition compared to control conditions whereas infarct size is significantly decreased after inhibition of S1P3 receptor. In addition, endothelial proliferation is markedly increased in the ischemic and non-ischemic area after S1P3 receptor inhibition. Expression of ABCB1, ABCC1 and occludin is upregulated after inhibition of S1P2 and S1P3-receptors, particularly in the non-ischemic hemisphere.

Conclusion: First results indicate that S1P receptors seem to play an important role after stroke and that inhibition of S1P1 worsens ischemic damage whereas inhibition of S1P3 has a beneficial effect after ischemia. How these mechanisms could help for better therapy results in patients has to be investigated.

Disclosure: Nothing to disclose.

EP2103

Trends in yield of code stroke program for enhancing thrombolysis

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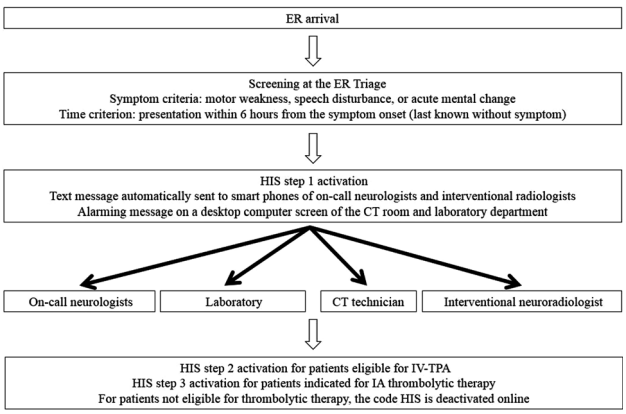
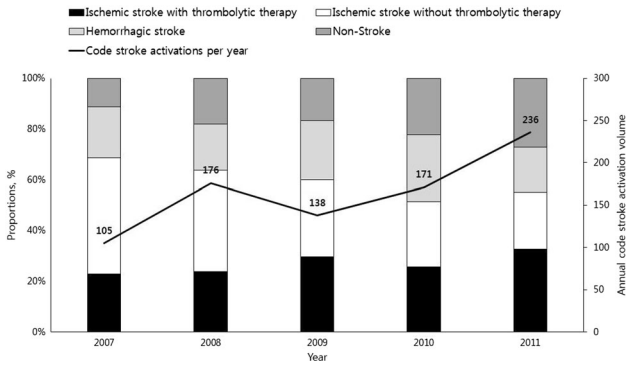
Introduction: Since the benefit of thrombolytic therapy in acute ischemic stroke is time-dependent, a code stroke program needs to be implemented, maintained, and improved with continuous efforts to expedite the thrombolytic therapy. We analyzed the long-term yield and efficiency of our code stroke program.

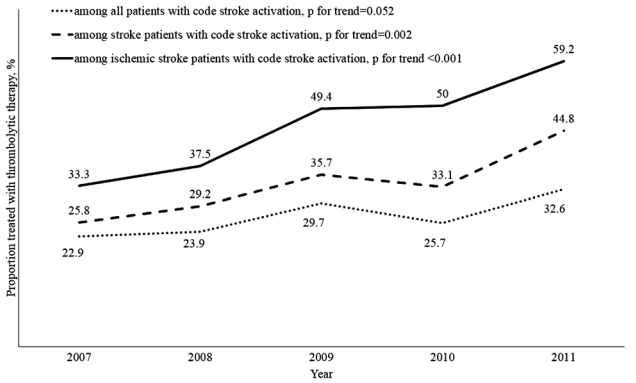
Methods: Using a prospective single-center registry, we assessed the rates of stroke diagnosis and thrombolysis, door-to-CT and door-to-needle times, and their annual trends in patients with the code stroke activation between May 2007 and December 2011.

Results: Of the 791 patients with the code stroke activation during the 4.7-year study period, 626 (79.1 %) had a stroke: 461 (58.3 %) ischemic strokes and 165 (20.9 %) hemorrhagic strokes. Along with an increase of the code stroke activation (from 105/year to 236/year) and thrombolytic therapy volumes (from 24/year to 77/year), the rate of thrombolytic therapy among ischemic stroke patients increased from 33.3 % to 59.2 % (p for trend = 0.0001). However, code activations for a non-stroke case also significantly increased (p for trend = 0.0001). Door-to-CT time (p for trend = 0.0011) and proportion of CT initiation ≤25 min after arrival improved (p for trend = 0.0022), resulting in 18.4 min and 76.7 % in 2011. Although the door-to-needle time and proportion of door-to-needle time ≤60 min did not significantly improve, they were 43.3 min and 83.1 % in 2011.

Conclusions: Our code stroke program yielded a high rate of detecting thrombolytic candidates and a continuous increase of thrombolytic therapy. These findings support that the stroke team members' collaborative effort to treat more and faster.







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EP2104

QuALiCoMe questionnaire: the possible role of cognitive and linguistic reserve in the recovery from post-stroke aphasia

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Introduction: By extending the concept of Cognitive Reserve (CR) to the domains of linguistic, communicative and metalinguistic competence, we suppose that the wide variability of recovery among post-stroke aphasic patients with similar initial clinical and demographic characteristics, as well as comparable therapeutic intervention, may be at least partly due to a sort of linguistic subset of CR, namely a "Linguistic Reserve", which may influence a patient's brain plasticity and neural language networks implied in recovery processes. To investigate this hypothesis we developed an informant-based instrument, named QuALiCoMe (Questionario su Attitudine Linguistica, Comunicativa e Metalinguistica), aimed at

providing an estimate of premorbid linguistic abilities in patients with post-stroke aphasia.

Methods and results: The QuALiCoMe was drafted in the framework of a wider research aimed at studying language recovery of post-stroke aphasic patients, assessed since acute phase of stroke. The initial pool of items was submitted to classical test theory and factorial analysis. The resulting questionnaire addresses educational attainment, major lifetime occupation, reading abilities and habits, writing abilities and use of widely available technology. It has been tested on a sample of healthy subjects in terms of applicability, internal consistency, reliability, external validity and informativeness. It has also been used in a pilot study on post-stroke aphasic patients to evaluate its applicability and possible prognostic implications.

Conclusions: We report the final version of the questionnaire after a preliminary validity evaluation and application on post-stroke patients. It shows good properties and appears a promising tool to estimate premorbid linguistic reserve in post-stroke aphasic subjects.

Disclosure: The present research is performed under a grant from the Ente Cassa di Risparmio di Firenze, a no-profit banking foundation pursuing social goals.

EP2105

Can we predict asymptomatic atrial fibrillation as strong stroke risk factor in patients with pacemakers

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Introduction: Intention of this study was to define asymptomatic atrial fibrillation occurrence in homogenous patients group. Those were patients with complete atrioventricular block. All patients with known risk factors for atrial fibrillation such as heart failure, heart cavity dilatation, structural heart disease, hyperthyroidisms were excluded.

Methods: In the enrollment period 194 patients with complete heart block and indication for pacemaker implantation were hospitalized. According to defined criteria in third month after pacemaker 65 patients meat asymptomatic atrial fibrillation criteria (cumulative AF time of more than 1 %). Same criteria in 24th month after implantation meat 60 % of enrolled patients.

Results: History of hypertension was steady risk factor for asymptomatic atrial fibrillation in third month after implantation ($P = 0.036$) and 24 months after implantation as well ($P = 0.02$). Group of patients with asymptomatic atrial fibrillation had higher occurrence of atrial signal width of more than 50 ms, but statistically insignificantly. On the other side patients with later developed asymptomatic atrial fibrillation had higher occurrence of P wave width of more than >100 ms ($P < 0.001$). In this way standard electrocardiogram superiority over intracardial recordings was shown. Patients with later developed asymptomatic atrial fibrillation had significantly higher level of BNP at implantation ($P = 0.031$). After the follow-up period difference in mortality neither major cardiovascular events was not shown.

Conclusions: Our study indicated some new risk factors for asymptomatic atrial fibrillation. These risk factor measurement is very simple. However new studies should reevaluate clinical implication of this parameters in stroke risk stratification.

Disclosure: Nothing to disclose.

EP2106

Diagnosis and management strategy of peadiatric moyamoya disease and moyamoya syndrome: the Zurich Moyamoya Center experience

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Introduction and objectives: Moyamoya (MM) is a progressive stenoocclusive angiopathy of the circle of Willis. It includes both disease (MMD) and syndrome (MMS). In the pediatric age group clinical presentation is mainly cerebral ischemia. We present the diagnostic work up and management of newly diagnosed children referred to our moyamoya center.

Method and patient selection: Twenty-six newly diagnosed MM children were referred and managed during March 2011 and December 2013 (mean age 8 years, range 1–17 years). Twenty-four underwent multiple cerebral revascularizations following diagnostic work-up.

Results: Diagnostic workup included: clinical-neurological evaluation along with child development/cognition testing, 6-vessel cerebral angiography, MRI-MRA and a H215O-PET scan with Diamox challenge. The MMS presentations were: neurofibromatosis, renal artery stenosis, possible Noonan syndrome, fibromuscular dysplasia, trisomy 21. Headache and transient ischemic attacks were common presenting symptoms. Bilateral strokes were seen mostly in children under 5 years of age. Unilateral angiopathy was seen in four children. Twenty-four children showed bilaterally decreased perfusion reserves on Diamox-H215O-PET in anterior cerebral artery (ACA) and/or middle cerebral artery (MCA) and/or posterior cerebral artery (PCA) territories. Depending on symptomatology, extent of angiopathy and territorial perfusion reserve deficits multiple cerebral revascularizations were performed. Follow up at 6 months–1 year and then regularly up to puberty continues. The first 15 children remain stroke free at 6 months post surgery.

Conclusions: Moyamoya angiopathy in Europe is emphasized. Meticulous diagnostic work-up followed by targeted surgical revascularization in the setting of a dedicated pediatric center is crucial for good clinical outcome.

Disclosure: Nothing to disclose.

EP2107

Detection of patent foramen ovale in patients with ischemic stroke

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Introduction: Emboli from the venous system can cross the PFO through a right-to-left shunt (RLS) and thus leading to a stroke. To detect PFO, transesophageal echocardiography (TEE) is the standard method but has many critical complications. Transcranial Doppler ultrasonography (TCD) is more economical and non-invasive method than TEE. We compare the results of TCD and TEE in ischemic stroke for detection of RLS to identify the diagnostic value of TCD.

Methods: 220 patients for ischemic stroke who performed both TCD and TEE were enrolled. Presence of risk factors for ischemic stroke were investigated. The sensitivity and specificity of TCD method were calculated. The number of High intensity transient signal (HITS) on TCD monitor was counted during the patient keeping Valsalva maneuver. The number of HITS on TEE during 5 cardiac cycles was also counted. PFO positive group detected by TCD ($n = 190$) were divided into subgroups. Sensitivity and specificity were calculated at different cutoffs of TCD method.

Results: The mean age was 61.2 years. There were 139 male and 81 female and 66 patients were less than 55 years (30 %). Proven PFO by TEE were also detected by TCD with sensitivity (86.5 %), specificity (14.2 %) and the positive predictive value (81 %). AUC value was 0.608, so TCD was confirmed as a good screening test ($p = 0.030$).

Conclusions: Our results demonstrated that TCD is highly sensitive method and especially in subgroups above grade IV.

Disclosure: Nothing to disclose.

EP2108

Cytokine response to diet and exercise affects atheromatous matrix metalloproteinase-2/9 activity in mice

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Introduction: Atheromatous matrix-metalloprotease (MMP) activity is related to plaque rupture and thromboembolic stroke. We tried to identify the principal circulating factors that modulate atheromatous MMP-2/9 activity in response to diet and exercise.

Methods: Apolipoprotein-E knock-out mice ($n = 56$) with pre-existing plaque, fed either Western diet (WD) or normal diet (ND), underwent either 10-week treadmill exercise or not. In vivo atheromatous MMP activity was visualized using molecular imaging with an MMP-2/9 activatable near-infrared-fluorescent probe. We measured atherosclerosis-related cytokines, lipid levels, visceral fat, and correlated these outcome measures to atheromatous MMP activity.

Results: Body weight, visceral fat, and plaque size were all higher in WD-fed animals than in ND-fed animals. Exercise training did not significantly affect these parameters in either WD-fed animals or ND-fed animals. However, atheromatous MMP activity was different: ND animals with and without exercise had similar low MMP activities, WD animals without exercise had high MMP activity, and WD animals with exercise had reduced levels of MMP activity, close to the levels of ND animals. Factor analysis and path analysis showed that soluble vascular cell adhesion molecule (sVCAM)-1 was directly positively related to atheromatous MMP activity. Adiponectin was indirectly negatively related to atheromatous MMP activity by way of sVCAM-1. Resistin was indirectly positively related to atheromatous MMP activity by way of sVCAM-1. In addition, visceral fat amount was indirectly positively associated with atheromatous MMP activity.

Conclusions: Diet and exercise affects atheromatous MMP activity by modulating the systemic inflammatory milieu, with sVCAM-1, resistin, and adiponectin closely interacting with each other.

Disclosure: Nothing to disclose.

EP2109

Aspiration thrombolysis with reperfusion catheter of the Penumbra system for treatment of acute posterior circulation ischemic stroke

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Introduction: To assess the feasibility and results of aspiration thrombolysis using reperfusion catheter of the Penumbra system for the treatment of acute ischemic stroke in posterior circulation.

Methods: 127 consecutive patients within 6 h from ischemic symptom onset, during a period of 48 months (Dec 2009–Dec 2013), treated by a standardized protocol using the reperfusion catheter of the Penumbra system without the separator for thrombus aspiration were reviewed. We included those with acute ischemic stroke in posterior circulation ($n = 20$) with mean age 66 years (54–77), 11 females, 9 males. We performed balloon-assisted angioplasty or stent-assisted angioplasty in four patients which thrombotic occlusion was detected. The location of occlusions, Thrombolysis in Cerebral Infarction (TICI) score, post-thrombolysis hemorrhage or malignant edema and clinical outcome (initial National Institute of Health Stroke Scale [NIHSS], 3-month modified Rankin scale [mRS]) were evaluated.

Results: The Thrombolysis in Cerebral Infarction (TICI) grade 2 or 3 was observed in 48 patients (17/20, 85 %). Symptomatic intracranial and intra-ventricular hemorrhage was developed in one patient (1/20). The median initial NIHSS scores showed 17.2(2–39). At 3 months, good outcome was noted in 7 of 20 patients (35 %, mRS 0-2).

Conclusions: In posterior circulation stroke, mechanical thrombolysis using aspiration thrombolysis using reperfusion catheter of the Penumbra system is safe and effective in achieving recanalization with good long-term outcome.

Disclosure: Nothing to disclose.

EP2110

Abstract withdrawn

EP2111

Surgical treatment of superficial CNS siderosis must be definitive and on time, yet is only rarely achieved

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Introduction: In superficial CNS siderosis subpial hemosiderin deposits of the brain and spinal cord accumulate because of chronic subarachnoidal hemorrhage, leading to progressive cerebellar ataxia, sensory deafness and, eventually, cognitive decline. The elimination of the bleeding source is the only causative treatment. However, knowledge about the natural course and response to treatment remains scarce.

Methods: We therefore present our experience with one female and eight male patients (median age 49.5 years, range 29–74 years).

Results: A possible bleeding etiology was identified in all patients. Five patients had a definitive acquired bleeding: Three had road traffic accidents leading to brachial plexus, respectively, cervicothoracic nerve root avulsions, one patient had an odontoid fracture during childhood and another patient had been operated upon for a medulloblastoma. Mean delay from injury to first clinical symptoms was 20 ± 10 years (SD). Four patients had congenital bleeding sources, including spinal arachnoid cysts ($n = 3$) and a congenital brain malformation ($n = 1$). One patient had both a possible congenital (thoracic arachnoid cyst) and acquired bleeding source (surgery for pediatric brain tumor). Neuroimaging revealed potentially excisable lesions in 5 patients (56 %). Definite surgical excision with postsurgical clearance of CSF bleeding derivates was achieved in 2 patients (22 %); yet, symptom progression was halted in just one patient.

Conclusions: Although identification of the bleeding etiology is generally possible in patients with superficial CNS siderosis, definitive surgical removal of the bleeding source is achieved only rarely, and even then, patients may deteriorate, probably because hemosiderin-associated neurodegeneration becomes irreversible with time.

Disclosure: Nothing to disclose.

EP2112

Central but not peripheral pulse pressure predicts lost of disability-adjusted life years in patients with acute ischemic stroke

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Introduction: Stroke is the leading cause of disability and of one the major causes of death. The aim of our study was to determine whether peripheral or central pressure parameters are associated with lost of disability-adjusted life years (DALY).

Methods: In our study we enrolled 114 patients admitted to the Department of Neurology (Gdańsk) due to acute ischemic stroke. Peripheral and central blood pressure were measured using oscillometric sphygmomanometer and applanation tonometry, respectively. The lost of DALY is the sum of years lost due to premature mortality and years lost due to disability. The association between lost of DALY (both for mRS at day 7 and 30 after stroke) and mean blood pressure (MBP), peripheral blood pressure parameters (systolic, pSBP; diastolic; and pulse pressure), central blood pressure parameters (systolic; and pulse pressure, AoPP) was investigated using regression analysis.

Results: In regression analysis only AoPP was related with lost of DALY. The higher AoPP was associated with lower lost of DALY (coefficient of regression for AoPP for mRS at day 7 and at day 30 was -0.1886 and -0.2020, respectively, and both $P = 0.04$).

The association remains significant after adjustment for gender, stroke severity, body mass index, history of hypertension, pSBP and MBP (coefficient of regression for AoPP for mRS at day 7 and at day 30 was -0.7859 and -0.3847, respectively, and both $P = 0.03$).

Conclusions: Central but not peripheral blood pressure may be an independent predictor of years lost due to premature death and disability in patients after ischemic stroke.

Disclosure: Nothing to disclose.

EP2113

Biomarkers of platelet activation and plasmatic coagulation in patients with acute and chronic cerebrovascular diseases—a pilot case control study

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Introduction: In animal stroke models distinct members of the plasmatic coagulation cascade (e.g. factor (F) XI and FXII, von Willebrand factor (VWF)) as well as platelet surface molecules (PSM, e.g. glycoprotein (GP)Ib and GPIIb/IIIa) are crucially involved in the development of the ischemic lesion. However, their pathophysiological relevance in humans still awaits clarification as does their potential use as biomarkers and therapeutic targets in cerebrovascular diseases. Thus, we wanted to characterize their regulation in patients with acute ischemic stroke (AIS) or transitoric ischemic attack (TIA), chronic cerebrovascular disease (CCD) and healthy volunteers (HV). Furthermore, we aimed to identify potential predictors of biomarker levels.

Methods: 115 patients with AIS/TIA, 117 patients with CCD and 104 HV were included in this case–control study. Blood was collected at days 0, 1 and 3 in patients with AIS or TIA and once in CCD patients and HV. Blood coagulation factors and platelet activation markers were measured and correlated with demographical and clinical parameters.

Results: Patients with AIS/TIA (200 ± 95 %, $p < 0.001$) and CCD (158 ± 46 %) had significantly higher VWF levels than HV (113 ± 36 %, $p < 0.001$). Stroke severity, age and sex independently influenced the levels of VWF ($p < 0.05$). No differences were found for any other coagulation marker.

Conclusion: VWF is upregulated in AIS/TIA patients, which is in line with preclinical studies and results from other groups. VWF might become a suitable biomarker and/or drug target in ischemic brain disease.

Disclosure: Nothing to disclose.

EP2114

Pharmacological stroke prevention in elderly people with atrial fibrillation in Poland

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Introduction: Atrial fibrillation (AF) is one of the most important cardiovascular risk factors, especially in the elderly. The aim of the study was to evaluate the frequency of pharmacological stroke prevention among older people with AF in Poland.

Methods: The study was based on data collected during the implementation of a multicentre research project called PolSenior which concerned people older than 65 years.

Results: The study group consisted of 4,979 people (mean age: 79.35 ± 8.69 years). Among them, there were 875 patients (18.7 %) with documented history of AF. Pharmacological prevention was used by 498 (56.9 %) older people with AF; OAPs by 386 (45.3 %), OACs by 117 (13.4 %), and dual therapy by 15 (1.7 %). The $CHADS_2$ score was calculated in 679 people (lack of data in 196 cases). Among the respondents with 0 points (n = 33), 7 persons (21.2 %) were treated (only with OAPs). Among the respondents with 1 point (n = 138), 47 persons (34.1 %) used OAPs and 14 persons (10.1 %) used OACs. Among the respondents with 2 or more points (n = 508), 254 persons (50 %) received OAPs and 76 persons (15 %) OACs. The most often used drug was aspirin. Acenocoumarol was more often used than warfarin. New OACs were not used at all.

Conclusions: Our study determined the frequency of pharmacological prevention among elderly people with AF in Poland. We found that OACs are applied too rarely in this group of patients. Educational programs should be developed among general practitioners concerning current recommendations for pharmacological cardiovascular prevention.

Disclosure: Nothing to disclose.

EP2115

A novel mutation in KRIT1 gene associated with familial cerebral cavernous malformations

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Introduction: Cerebral cavernous malformations (CCMs) are vascular malformations that may affect any part of the central nervous system. This condition has been associated with heterozygous mutations in CCM1/KRIT1, CCM2/malcavernin and CCM3/PDCD10 genes.

Methods: We performed clinical, instrumental and molecular studies in a novel Italian pedigree displaying multiple CCMs. CCM1, CCM2 and CCM3 coding exons and flanking intronic regions were PCR-amplified and directly sequenced.

Results: Among seven family members carrying CCMs three were asymptomatic, three suffered from cerebral haemorrhage and one experienced seizures. CCM1 sequence analysis disclosed a novel heterozygous nucleotide substitution (c.263-10A>G) in intron 3 in the proband and in his mother. The variant was absent in 340 Italian control chromosomes. To test the effects of the variant on CCM1 transcript, RNA was retro transcribed and cDNA was used as template in RT-PCRs.

Conclusions: CCM1 encodes for a protein that binds to integrin cytoplasmatic domain-associated protein-1 alpha (ICAP1alpha) and plays a critical role in cell proliferation. This protein is required for integrity of endothelial junctions maintenance and may play a role in microtubule targeting. Molecular studies in mutation carriers demonstrated that the novel c.263-10A>G mutation creates an abnormal acceptor splice site with partial retention of intron 3 leading to a premature termination codon within CCM1 reading frame resulting in the loss of transcript through nonsense-mediated mRNA decay. These findings support the pathogenicity of c.263-10A>G mutation and its involvement in cerebral cavernous malformation pathogenesis.

Disclosure: Nothing to disclose.

Child and developmental neurology 1

EP2116

Mucopolysaccharidosis type III: Tunisian experience

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Introduction: Mucopolysaccharidosis III (MPS III) or Sanfilippo syndrome is a rare and misdiagnosed lysosomal storage disorder characterized by cognitive decline, a distinct behavioral disturbances and relatively mild somatic disease. The aim of this study was to present clinical and neuroimaging features of MPS III in a Tunisian series.

Methods: Eleven children with biochemically confirmed MPS III were followed up (2005–2013). Clinical and neuroimaging features were analyzed.

Results: Eleven children (3 males and 8 females) were included. Mean age was 12.9 years (5–21). Mean age at onset was 3 years (0–4.7). Mean age at diagnosis was 9.9 years (4–18). Main clinical features were: developmental and/or speech delay (10/11), developmental and/or speech regression (7/11), cognitive decline (6/11), behavioral abnormalities (11/11) with predominance of agitation (9/11), hyperactivity (7/11), irritability (6/11), aggressivity (4/11) and autistic-like behavior (3/11). Somatic features were relatively mild with delayed appearance: dysmorphic features (11/11), hepatomegaly (7/11), splenomegaly (3/11), deafness (4/11). Brain MRI performed in seven patients was normal in one patient and showed cerebral atrophy and periventricular signal abnormalities in six patients.

Conclusions: The diagnosis of MPS III should be evoked in children with developmental or speech delay and/or behavioral abnormalities. Early diagnosis is important in this devastating, progressive disorder, for genetic counseling and development of potential therapeutic options.

Disclosure: Nothing to disclose.

EP2117

Ring chromosome 15 in a family diagnosed as neurofibromatosis

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Introduction: Neurofibromatosis type I (NF1) is characterized by café au lait spots, fibromatous tumors of the skin and there is an increased susceptibility to tumor development. NF1 is an autosomal dominant disorder with an incidence of about 1 in 3,000.

Less than 50 patients with ring chromosome 15 syndrome have been reported up to now. Most cases occur sporadic. The transmission of a ring from a mother to a child has been reported twice.

Methods: An infant was diagnosed as NF1 due to multiple café au lait spots. His mother had some spots and hemihypertrophy of a leg.

Results: Chromosomal analysis, array comparative genomic hybridization and targeted High Throughput Sequencing revealed the genetic cause of their symptomatology.

Conclusion: To our knowledge, this is the third time a maternally transmitted ring chromosome 15 has been described. Ring chromosome 15 has been reported to cause café au lait spots and may be confused with NF1 especially when there are family members with similar symptomatology.

Different genetic investigations may be of importance even in seemingly straightforward clinical NF cases.

Disclosure: Nothing to disclose.

EP2118

Mosaic ring chromosome 18 in a child with mental retardation and delayed speech

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Introduction: In ring chromosome 18 [r(18)] one or both ends of chromosome 18 are lost and joined forming a ring-shaped figure. Thus, r(18) patients can show features of 18q- and/or 18p- syndrome, depending on the size of the 18p and 18q deleted regions.

R(18) is characterized by developmental delay, mental retardation, facial dysmorphisms and major abnormalities. Mosaic r(18) cases are more seldom and usually have more subtle clinical findings.

Methods: A male infant with microcephaly and delayed speech was genetically investigated.

Results: Chromosomal analysis and array comparative genomic hybridization (aCGH) revealed the r(18) mosaicism, the size of the deletions and the breakpoints.

Conclusion: Genotype phenotype correlation in mosaic r(18) syndrome have rarely been described, 12 times in literature, and the exact size of the deletions have only been described twice before.

Clear breakpoint delineations are necessary for genotype - phenotype correlations and for delineating the related neurocognitive and behavioral aspects.

Disclosure: Nothing to disclose.

EP2119

Neuroprotective effects of *N*-acetyl-L-cysteine in human oligodendrocyte progenitor cells and in neonatal rats with hypoxic-ischemic encephalopathy

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Introduction: Hypoxic-ischemic encephalopathy (HIE) is one of the most devastating neurological diseases in children exhibiting diverse neurobehavioral symptoms. Previous studies on the candidate compounds attained from neuronal culture displayed controversial results in animal models or in humans. Since oligodendrocyte progenitor cells (OPCs) are the target cells of demyelinating HIE, it was expected that compounds displaying protective activity against hypoxic cytotoxicity in OPCs would be effective in animal models.

Methods: Human OPCs (F3.Olig2) were incubated with various concentrations of *N*-acetyl-L-cysteine (NAC) and potassium cyanide, and the cytoprotective effects of NAC were assessed by MTT and apoptosis assays. Male rats were subjected to hypoxia–ischemia surgery at postnatal day 7 (PND7), intraperioneally administered with NAC (100 mg/kg) once a day, and their physical functions were measured at PND20, 30 and 40. To evaluate the integrity of host myelins, brain sections were stained with Luxol fast blue and antibodies to myelin basic protein.

Results: NAC decreased potassium cyanide cytotoxicity of F3.Olig2 cells in MTT assay, and especially suppressed apoptosis by regulating Bcl2 and p-ERK. NAC administration recovered motor functions such as the using ratio of forelimb contralateral to the injured brain, locomotor activity, and rota-rod performance of HIE animals. It was also confirmed that NAC attenuated demyelination in the corpus callosum, a white matter region vulnerable to HIE.

Conclusions: The results indicate that NAC exerts neuroprotective effects in vitro and in vivo by preserving OPCs, via regulation of anti-apoptotic signaling.

Disclosure: Nothing to disclose.

EP2120

High frequency of additional cerebral involvement in adrenomyeloneuropathy (AMN)

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Introduction: X-linked Adrenoleukodystrophy (X-ALD) is an inherited disorder of peroxisomal metabolism associated with mutations in the ABCD1 gene, resulting in damage to central and peripheral nervous system and endocrine organs. Adrenomyeloneuropathy (AMN) was considered a relatively mild phenotype with only incidental additional cerebral demyelination. However, in 2001 it was reported that 13/68 male patients with AMN (19.1 %) developed additional brain involvement during a follow-up interval of 9,5 $\pm$ 5,5 years. We studied the frequency of additional cerebral demyelination in AMN patients in the Netherlands.

Methods: Consecutive AMN patients without cerebral demyelination from the Dutch X-ALD cohort, seen between January 1, 1992, and January 1, 1999, were included. Primary endpoints were demonstration of brain involvement, death, or the end of our study. Three levels of certainty were used to classify cerebral demyelination; confirmation by MR-Imaging, detailed information from treating physicians, or information obtained from their families. Results were compared with a study carried out in 2001, using the differences and their 95 % confidence intervals.

Results: Seventeen out of 27 AMN patients (63 %) developed additional cerebral demyelination 10.2 $\pm$ 6.9 years after onset of myelo(neuro)pathy. Mean survival was 3.4 $\pm$ 2.9 years. Additional brain involvement was higher in the Dutch AMN patients (difference 44 %, 95 % CI 0.23–0.64).

Conclusions: Additional cerebral demyelination in AMN may be even more frequent than previously reported. Survival is just as poor as in Childhood Cerebral ALD. Therapies that can halt relentlessly progressive cerebral demyelination in these patients are needed.

Disclosure: Nothing to disclose.

EP2121

How evolutionary anthropology informs the evolution of inhibitory interneurons in the cerebral neocortex

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Introduction: Inhibitory interneurons (INS) play a role in postnatal brain development, increasing signaling to maintain balance between excitatory/inhibitory in cortex networks; balance is imperative to generate behaviorally-relevant patterns.

Methods: This paper explores inhibitory INS' evolution/their significance in cerebral-neocortex development.

Results: Energy metabolism sets humans apart from primates, maintaining neural tissue's high cost: evolutionary increases in synaptic signaling/connectivity/glial cells/glial:neuron unexpected 46 % greater density, $p < 0.001$. INS' energy efficiency exceeds excitatory neurons': 85 % energy consumption associated with excitatory glutamate recycling, using both glycolytic/glycogenolytic processes, only glycolytic ATP for INS' synaptic cleft recycling.

Key in evolution's INS' origins is recruitment of other mechanisms for primates' cortices' greater number/diversity: lampreys' (450 Mya) INS' circuits devoid of sense organs/pallium/geniculate eminence (GE); gnathostomes' (350 Mya) INS' tangential migration from GE to pallium, highly conserved; INS' competence to enter neocortex subventricular zone (SVZ) established in amniotes (310 Mya); competence to enter cortical plate from GE, mammalian unique (185–210 Mya). 40 Mya primates' INS' number/diversity/complexity increased more than excitatory neurons': a pre-existing mechanism's boosting, a bipartite process: INS' progenitors migrating radially.

Relaxed phylogenetic brain/body constraints to a behavioral evolutionary shift was adaptive force for anthropoid primates' social acumen. An extrinsic supply neuromodulators for behavioral flexibility, dopamine (DA), acetylcholine (ACh), serotonin (5-HT) with slower/longer neuromodulation altered INS' terminal axon patterns; humans'/chimps' axonal density increased as DA/5-HT/ACh "coils"/"clusters" for plasticity; a subtle human evolutionary shift favored V/VI cortex layers' increased innervation, $p < 0.05$.

Conclusions: Evolutionary ancient INS are vitally important to brain function as local integrators of cerebral neocortex activity and… to our preeminent human identity.

Disclosure: Nothing to disclose.

EP2122

Systemic juvenile lupus erythematosus long lasting remission of severe neurological symptoms after treatment with Rituximab

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Introduction: Systemic lupus erythematosus (SLE) has a much higher incidence in Asian and African populations than in western countries. Up to 50 % of patients suffer from neuropsychiatric symptoms of different pathogenesis.

Case presentation: We report a 13-year-old girl who was diagnosed with SLE with rheumatic symptoms. She rapidly developed confusion, focal epileptic seizures with secondary generalization and left sided hemiparesis combined with high fever and tachycardia. Initial showed right hemispheric cortical dwi-positive lesions in the MCA territory. During the following 8 weeks extensive progression of MRI lesions to subcortical regions in both hemispheres with additional microbleeds could be demonstrated, no arterial occlusion, no typical vasculitic changes, no meningeal enhancement. CSF was without significant pathology. Aggressive treatment with high dose corticosteroids and iv Immunoglobulin G was started, followed by one cycle of iv cyclophosphamide and plasma exchange. The patient deteriorated with respiratory failure, increase of liver enzymes, severe thrombopenia and anemia, colitis and secondary infectious complications. After stabilization of vital functions and weaning from the respirator Rituximab was given with no side effect. The patient recovered tremendously without any persistent motor dysfunction, she was able to resume schooling and has no neuropsychological deficits except occasional headache and fatigue. A second dose of Rituximab was applicated 6 months later after an increase of CD 20 lymphocytes. Under a low dose corticosteroid treatment the patient has been free of new somatic and neuropsychiatric SLE manifestation since 2 years.

Conclusion: Rituximab was well tolerated and longterm effective in this case of juvenile SLE with life threatening cerebral lupus vasculopathy. Further studies have to establish the therapeutic significance of Rituximab in severe neuropsychiatric Lupus.

Disclosure: Nothing to disclose.

EP2123

Stereotypies as a marker of autism severity

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Introduction: The new classification of autism spectrum disorder on DSM-V emphasizes the importance of the severity of this condition. Stereotypies have been related with the severity of autism, but few studies analysed the association between them. The aim of this study was to explore the association between the frequency and type of stereotypies and autism severity scores and comorbidities.

Methods: A series of consecutive patients from a paediatric neurology clinic with ASD and stereotypies were selected. The diagnosis of ASD was based on ADOS and ADI-R scales, and DSM-V criteria. Severity was obtained from ADOS and DSM-V criteria. Standardized video recording of the patients were obtained with consent. Two independent researchers performed the classification.

Results: We evaluated 15 autistic patients, 80 % males, with a median age of 7.6 years (3.8–15.7). The median intelligence quotient (IQ) or general development quotient (GDQ) was 45 (32–68) and 51 (32–81), respectively. The ADOS median severity score was 7 (7–10). The median number of motor stereotypies per 10 min was 6 (2–20) and 87 % of patients presented also visual or vocal stereotypies. The frequency of motor stereotypies increased with ADOS severity score ($p = 0.028$), social communication DSM-V severity score ($p = 0.025$), absence of intelligible speech ($p = 0.029$) and lower IQ ($p = 0.035$).

Conclusions: This study suggests that motor stereotypies are more frequent on autistic patients with more severe autism and lower IQ. This highlights the necessity of understanding the neurobiology of stereotypies and the nature of their relation with ASD.

Disclosure: Nothing to disclose.

EP2124

A diffusion tensor MRI study of pediatric patients with severe non-traumatic brain injury

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Introduction: We applied DT MRI to analyze damage to the supra- and infra-tentorial districts in pediatric patients with vegetative state (VS) or minimally conscious state (MCS) and their correlations with clinical scales of disease severity.

Methods: Seven pediatric patients in a VS and six in a MCS, suffering from severe acquired brain injury due to non-traumatic origin and ten pediatric healthy controls underwent a DT MRI scan and patients were assessed using the Glasgow Coma Scale and Disability Rating Scale. We obtained fractional anisotropy (FA), mean (MD), axial (AD) and radial diffusivities (RD) from the corpus callosum (CC), inferior (ICP), middle (MCP), and superior (SCP) cerebellar peduncles.

Results: Compared to controls, patients had lower FA of the CC and SCP, and higher MD, AD and RD of the CC and cerebellar peduncles. Compared to acute patients, those in the chronic stage had lower FA and higher MD, AD and RD of the anterior part of the MCP. Differences of FA, MD and RD between supra- vs. infra-tentorial compartments differentiated patients from controls. Furthermore, the difference of FA between supra- vs. infra- tentorial compartments distinguished VS from MCS patients ($p < 0.01$). Significant correlations were found between DT MRI indexes and clinical scales (r ranging from -0.77 to 0.73).

Conclusions: In pediatric patients with VS/MCS due to non-traumatic origin, the severity of clinical disability correlates with structural damage to both infratentorial and the long-range cortico-cortical tracts, suggesting that global, rather than focal damage, contributes to the clinical severity of these patients.

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EP2125

Leukoencephalopathies in inborn errors of metabolism: the Tunisian experience

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Introduction: Leukoencephalopathies (LE) in inborn errors of metabolism (IEM) are common. They are due to primary defect of myelination or to metabolite toxicity toward myelin. Diagnostic approach may be complex. The aims of our study were to describe clinical and radiological characteristics and to determine main etiologies of LE with IEM.

Methods: A prospective study (2004–2013) included patients with LE and IEM. All patients had cerebral MRI. White matter abnormalities were analyzed, and correlated to clinical and electrophysiological findings. Biochemical tests were performed according to the presumed etiology.

Results: Fifty-five patients (24 males, 31 females) were included. LE was classified into demyelination (decreased T1 signal) (30/55) and hypomyelination (normal T1 signal) (25/55). In the demyelination group, the main clinical features were psychomotor milestones loss (21/30) and peripheral neuropathy (17/30). Lysosomal storage diseases were diagnosed in 21/30 cases with predominance of metachromatic leukodystrophy (10/30). The hypomyelination group presented often with psychomotor delay (17/25). The main etiology was respiratory chain defect (9/25).

Conclusions: Analysis of MRI patterns of LE is a diagnostic clue to orientate biochemical tests of IEM. A structured and multidisciplinary diagnostic approach is crucial to identify etiologies and to allow genetic counseling.

Disclosure: Nothing to disclose.

EP2126

PEDOT-PSS modified silk electrode for neural activity measurement

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A poly(3,4-ethylenedioxythiophene)-poly(styrenesulfonate) (PEDOT-PSS) is one of the implantable conductive polymer candidates for improving the biocompatibility of the electrode. Our previous results using a PEDOT-PSS modified microelectrode array (PPM-MEA) indicated continuous monitoring of neural cell development and network formation. We also reported the differentiation conditions of neural stem cells (NSCs) from rat embryo striatum could be monitored with this electrode array.

Here we report the formation of flexible electrodes using silk fiber for implantable electrode. Polymerization of the fiber with the conductive polymer indicated higher biocompatibility and allowed us for longer measurement. Brain neural activities of mouse and chick were measured with this electrode for more than 6 months. Flexible characteristics of the electrode would be important for stable contacts to neurons. Stimulation experiments with this electrode will be reported.

As the PEDOT-PSS modified silk electrode is a soft and biocompatible measurement method, the usage of this electrode could be a useful tool not only for implantable and stable activity monitoring, such as primary evaluation of physiological conditions of the neurons, but also for the reconstruction of neural pathway.

Disclosure: Nothing to disclose.

EP2127

Childhood neuroferritinopathy caused by novel mutation in the PLA2G6 gene: better prognosis? Case report of a family

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Introduction: Childhood neurodegeneration with brain iron accumulation (NBIA) presents with heterogenous clinical manifestation. We describe a family, where progressive neurological symptoms affected three girls with autosomal recessive inheritance. The aim of our investigations was to classify the genetical

background of NBIA. Genetic tests revealed novel mutation in PLA2G6 gene.

Methods and patients: We report a Caucasian family with three affected girls out of five children. Two of the patients were identical twins and their younger sister. Earliest symptoms presented at the age of 2–3 years as gait disturbance, speech difficulties, followed by mental deterioration, cerebellar ataxia, pyramidal involvement. All of them developed bulbar dysfunction, vertical gaze palsy combined with saccadic eye movements. Symptoms showed continuous progression. All of the patients became wheel-chair dependent.

Results: PANK2 and PLA2G6 gene mutation were tested in one of the twins. There was no pathologic mutation of PANK2, but heterozygous variants in exon 13 of the PLA2G6 gene were detected. One of the mutations (c.1798C>T p.R600W), is known as probably disease-causing, the other variant (c.1864C>T p.P622S) can lead to moderate differences between proline and serine. These abnormalities can be concluded as the cause NBIA in the investigated family. Seggregation analysis revealed that father and the healthy young brother are heterozygous for R600 W mutation while mother and the unaffected sister are heterozygous for P622S mutation.

Conclusions: Genetic tests revealed previously unreported heterozygous variants in exon 13 of the PLA2G6 gene without pathogenic mutation of PANK2, leading to better prognosis than previously reported variants.

Disclosure: Nothing to disclose.

Multiple sclerosis and related disorders 2

EP2128

Alemtuzumab as rescue therapy in a cohort of 15 aggressive multiple sclerosis patients previously treated by Mitoxantrone: an observational study

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Introduction: Alemtuzumab is superior to Interferon-beta-1a in relapsing remitting Multiple Sclerosis (RRMS) but expose to autoimmune side-effects. We aimed to describe safety and neurological impact of Alemtuzumab as last-line rescue therapy in aggressive MS patients previously treated by Mitoxantrone (MITOX).

Methods: From June 2004 to June 2012, 13 patients received Alemtuzumab 20 mg/day and 2 received 12 mg/day for 5 days. EDSS, relapses, secondary progression were prospectively assessed at 12 and 6 months before treatment, at baseline, 1 month after therapy and every 3 months; TSH, Platelets, white blood cell counts and proteinuria were monitored.

Results: In January 2014, mean follow-up was 5.8 years. 8 Secondary Progressive (SP) and 7 RRMS patients had a mean age of 39.9 and 30.1 years, respectively, at Alemtuzumab start. MS duration was 13.6 and 8.3 years, respectively. The year before Alemtuzumab: EDSS worsened by 1.02 and 1.86 point; Annual Relapse Rate was 0.75 and 3.15 and new gadolinium enhancing lesions raised 2 to 30. MITOX was administered up to 2.7 years before Alemtuzumab (mean cumulative dose 123 mg/m^2). Previous treatment consisted of Natalizumab (2), Methotrexate (5), Azathioprine (4), Cyclophosphamide (2), Fingolimod (1). Two patients developed Grave's disease and one hypothyroidism. Out of eight SPMS, five improved and remained stable (to 21 months–5 years); two remained stable (to 17 months–7 years); one worsened. Out of seven RRMS, six improved (EDSS 4–1 point) and remained stable (1–6 years). two patients were retreated (28–40 months).

Conclusion: Alemtuzumab controls aggressive RRMS despite previous use of MITOX.

Disclosure: Nothing to disclose.

EP2129

Gender effects in the treatment of multiple sclerosis with interferon-beta

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Introduction: Gender influences incidence and disease course of multiple sclerosis (MS).

Objectives: To determine whether male and female MS patients respond differently to Interferon-beta (IFN-beta) in terms of reduction number of of relapses.

Methods: We included all 2033 patients with relapsing-remitting MS who started treatment with IFN-beta from 1996 to 2003, identified from the nationwide and complete Multiple Sclerosis Treatment Registry. We defined neutralizing antibody (NAb)-positive and -negative periods in the single patient by the results of the Nab-tests, taken at regular scheduled intervals. Patients served as their own controls and relapse counts were compared between Nab negative and Nab positive periods, added up for all periods and for all patients. NAb-positivity under IFN-beta treatment was regarded as a proxy for no treatment.

Results: NAbs significantly abrogate the IFN-beta treatment efficacy in both genders. Women had higher relapse rates than men in NAb-positive and-negative periods. The all over female: male relapse rate ratio irrespective of NAb status was 1.47 (95 %CI; 1.28–1.68). The NAb-positive/negative relapse rate ratio was 1.39 in males and 1.49 in females. In a generalized linear Poisson models analysis with relapse counts as response variable the main effects NAbs, sex, age at treatment start, and number of relapses in 2 years before treatment start were strongly significant, but interaction between sex and NAb status proved statistically insignificant, $p = 0.30$.

Conclusions: As NAbs influenced the on-treatment relapse rates strongly in both sexes but without statistical significant difference, there is no indication of different effects of IFN-beta in men or women with relapsing-remitting MS.

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EP2130

Predicting early conversion to multiple sclerosis in patients with clinically isolated syndromes: the importance of an integrated modeling of risk factors

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Introduction: The early identification of patients at high risk of developing MS represents the main purpose of diagnostic criteria and of clinicians in everyday clinical practice.The aim of this study is to investigate risk factors for early development of clinically definite MS (CDMS) in patients with clinically isolated syndromes (CIS).

Methods: Patients admitted to our Department within 3 months from CIS onset were included. We evaluated baseline clinical, brain MRI, multimodal evoked potentials (EPs),Vitamin D and CSF data and assessed their prognostic value for early development of CDMS.

Results: 227 CIS patients have been identified: 21 patients (9 %) developed CDMS at 6 months, 43 (19 %) at 12 months, 71 (31 %) at 24 months and 120 (52.9 %) during the entire follow-up (6.82 years SD 2.78).In a multivariate logistic regression model,a high EPs score increased the risk of a relapse at 6 months (OR:1.74; 95 % CIs: 1.49–15.93); the risk of CDMS at 12 and 24 months was related to the presence of CSF oligoclonal bands (OBs) [respectively: OR 3.1 (1.04–7.98) and OR 3.57 (1.27–11.98)]. A high number (>9 T2) of lesions at baseline brain MRI was the most important prognostic factor for the development of MS in the long term [OR 5.7 (2.09–12.77)].

Conclusion: The concurrent presence of CSF OBs,a high number of T2 lesions and a high EPs score at baseline was associated with a CDMS rate of 40 % at 12 months ($p < 0.01$).The integration of all risk factors at clinical presentation is thus important for an accurate estimate of absolute risk of early clinical relapse.

Disclosure: V. Martinelli has received personal compensation for activities with Biogen Dompe, Merck Serono, Bayer Schering, Teva and Sanofi Aventis as a speaker. G. Dalla Costa, G. Di Maggio, L. Moiola, M. Rodegher and B. Colombo have nothing to declare. L. Leocani and R. Furlan have nothing to declare. M. Filippi has received honoraria for lectures and travel expenses and consulting fees as an investigator in previous and current treatment trials from Teva, Merck Serono, Bayer Schering Pharma AG, Biogen-Dompe and Genmab, and has received research support from Teva, Merck Serono, Bayer Schering Pharma, Biogen-Dompe and Genmab. G. Comi has received compensation for consulting services and/or speaking activities from Bayer Schering Pharma AG, Serono Symposia International Foundation, Merck Serono International, Teva, Sanofi-Aventis and Biogen Dompe.

EP2131

Prolonged-release fampridine treatment and walking ability and balance in patients with multiple sclerosis: results of the randomized, double-blind MOBILE study

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Introduction: Walking impairment negatively impacts quality of life in multiple sclerosis (MS). PR-fampridine tablet (dalfampridine extended-release in US) is the only agent currently approved to improve walking in MS.

Methods: MOBILE was a 24-week, randomized, double-blind, multicentre, placebo-controlled study. Patients (18–70 years) with progressive or relapsing-remitting MS and EDSS score of 4–7 were treated with PR-fampridine 10-mg tablets or placebo twice daily. Efficacy endpoints included change from baseline in the 12-item MS walking scale (MSWS-12), Timed Up and Go Test (TUG), Berg Balance Scale (BBS), 29-item MS impact scale (MSIS-29), and EuroQol (EQ-5D-5L). Post-hoc statistical testing compared multiple thresholds of improvement between treatment groups for each of MSWS-12 and TUG using a logistic regression, adjusted for baseline.

Results: 132 subjects were randomized to treatment; baseline patient characteristics and demographics were comparable between groups. A higher proportion of subjects randomized to PR-fampridine vs placebo experienced clinically meaningful improvements over 24 weeks from baseline on the MSWS-12 ($\geq$8 point mean improvement): 48.5 vs. 28.1 % ($P = 0.015$); and TUG speed ($\geq$15 % mean improvement): 47.1 vs. 30.2 % ($P = 0.026$), respectively. PR-fampridine treatment versus placebo also resulted in early and consistent improvements from baseline on the BBS (median 2.93 vs. 1.71 points) and MSIS-29 physical subscale (median -4.96 vs -2.19 points). Safety findings were similar to previous studies.

Conclusions: PR-fampridine treatment resulted in sustained, clinically meaningful improvements in walking ability and balance. These findings extend prior Phase 3 results by including a longer treatment period and a broader range of objective and patient-reported measures of walking ability.

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EP2132

Activation-induced cell death and intracellular modulation of apoptosis in T lymphocytes of primary progressive and relapsing-remitting multiple sclerosis patients

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Introduction: Failure to eliminate auto-reactive T lymphocytes (TL) by activation-induced cell death (AICD) and other apoptosis mechanisms has been involved in the pathogenesis of multiple sclerosis (MS). However, differences in the apoptotic response of TL from different clinical forms of MS remain unknown.

Objectives: To evaluate AICD, Fas, caspase 3 and 19 apoptosis-related genes expression in peripheral blood mononuclear cells

(PBMC) from primary progressive (PP) and relapsing-remitting (RR) MS patients, and healthy controls (HC).

Methods: PBMCs were obtained from 13 HC, 23 RRMS (17 in remission and 6 in relapse) and 13 PPMS patients. Fas expression and AICD were evaluated in TL by flow cytometry (FC). AICD was induced using phytohaemagglutinin. Caspase 3 expression was assessed by western blot and genetic expression by RT-qPCR.

Results: AICD and Fas expression were decreased in TL from RRMS patients compared to HC ($p < 0.05$). Activation of caspase 3 was impaired in MS patients. PUMA (pro-apoptotic) expression was reduced in RRMS in remission compared to HC ($p < 0.01$). BID (pro-apoptotic) was overexpressed in RRMS in remission compared to PPMS while FLIP-L (anti-apoptotic) was overexpressed in PPMS compared to RRMS ($p < 0.01$ and 0.05).

Conclusion: The reduction of Fas expression and caspase 3 activation could partially account for the impairment of AICD observed in TL from RRMS patients. Transcriptional differences observed point to an anti-apoptotic status in PPMS patients. Altogether, these results suggest that AICD is important in the pathogenesis of RRMS, while the dysregulation of other apoptosis pathways could play a role in PPMS.

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EP2133

Efficacy of L-carnitine in the treatment of fatigue in multiple sclerosis (FACTSEP)

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Introduction: So far, no placebo-controlled randomized study has been conducted to provide a reliable estimation of Carnitine effect in the treatment of fatigue in patients with multiple sclerosis (MS).

Methods: A randomized placebo-controlled multicenter double-blind crossover study was designed comparing L-carnitine treatment (2 g oral solution, twice daily) versus placebo. Over a total of 9 months period, two three months periods with trial treatment were separated by a wash-out period of 3 months. ClinicalTrials.gov Identifier: NCT01149525. Eligible MS patients were affected of fatigue for more than 3 months with global score on Modified Fatigue Impact Scale (MFIS) > 45. The primary outcome measure was the global score on the 21 item Modified Fatigue Impact Scale (MFIS, translated and validated in French). Secondary outcome measures included the Fatigue Severity Scale (FSS), Fatigue Visual Analogic Scale (VAS), physical dimension scale of MFIS, and the MS Quality Of Life scale SEP 59 derived from the MSQOL-54, validated in French.

Results: Fifty-nine patients were randomized to receive first L-carnitine treatment or placebo. Mean age was 45, 74 % were women, and median EDSS was 3.0. At inclusion mean MFIS score was 71.3 % (standard deviation [SD] 15.5) and mean FSS was 6.1 (SD 0.8). Adherence to study treatments was good and no significant unexpected adverse event was reported throughout the study.

Conclusions: This is the first placebo-controlled double-blind randomized study comparing the efficacy of L-carnitine for the treatment of fatigue in Multiple Sclerosis. Main final end-point results will be available for presentation at the meeting.

Disclosure: This study is sponsored by academic French health institutions (Programme Hospitalier de Recherche Clinique) and has also received support from Sigma-Tau and Biogen-Idec.

EP2134

Structural MRI correlates of cognitive impairment in patients with multiple sclerosis: a Multicenter study

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Introduction: To apply a voxel-wise analysis to high-resolution T1-weighted and diffusion tensor (DT) MRI scans to assess the structural correlates of cognitive dysfunction in multiple sclerosis (MS) patients and their validity in a multicenter setting.

Methods: Brain dual-echo, 3D T1-weighted, and DT MRI sequences were collected from 62 relapsing-remitting MS patients and 65 healthy controls (HC) from seven European centers. Patients with $\geq$ 2 abnormal neuropsychological tests at the Rao's battery were considered cognitively impaired (CI). The distribution of gray matter (GM) and white matter (WM) atrophy and microstructural WM damage were assessed using voxel-wise approaches.

Results: No group*x*center interaction was found for T2-hyperintense, T1-hypointense lesion volume, GM and WM volumes, whereas

significant interaction for GM and WM DT MRI metrics was found. Twenty-three MS patients were CI. Compared to cognitively preserved (CP), CI patients had higher T2 and T1 lesion volume, and atrophy of the brain, WM, GM and deep GM nuclei. From DT MRI analysis, intrinsic damage within T2 lesions, but not damage to the WM and GM, was more severe in CI *vs* CP patients. Using voxel-based morphometry, compared to CP patients and HC, CI patients had atrophy of the thalami, hippocampi, several fronto-parietal GM regions and the posterior corpus callosum (CC). At the level of the CC, CI patients also had lower fractional anisotropy.

Conclusions: The application of voxel-wise methods to define the regional distribution of brain damage in a multicenter setting in MS patients is feasible and contributes to better characterize disease manifestations.

Disclosure: Nothing to disclose.

EP2135

Forceps minor damage and co-occurrence of depression and fatigue in multiple sclerosis

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Objective: Using diffusion tensor (DT) MRI, we analysed the architectural integrity of the brain white matter (WM) from a large cohort of MS patients to identify the structural substrates of the concomitant presence of depression and fatigue.

Methods: Brain dual-echo, 3D T1-weighted and DT MRI scans were acquired from 147 MS patients and 90 gender and age-matched healthy controls (HC). Patients were stratified by the presence of depression (92 depressed [D], 55 non depressed [nD]) and fatigue (81 fatigued [F], 66 non fatigued [nF]). Sixty-five patients had co-occurrence of D and F (DF). Whole-brain voxel-wise comparisons of WM DT MRI abnormalities were performed using tract-based spatial statistics (TBSS). Tract-specific analyses were run in brain WM tracts using standard-space templates.

Results: Whole-brain voxel-wise analysis yielded no significant differences between the different patient' subgroups. At tract-specific analysis, DF patients had reduced fractional anisotropy (FA) of the forceps minor. Reduced FA of the right anterior thalamic radiation and right uncinate fasciculus was found in F-MS *vs* nF-MS patients after correcting for depression. No significant differences were found between D vs nD-MS patients, after correcting for fatigue.

Conclusions: MS patients with co-occurrence of D and F share a more severe microstructural involvement of the forceps minor compared to patients without these symptoms. Abnormalities of the anterior thalamic radiation and uncinate fasciculus are linked to fatigue. This study provides evidence for a partially overlapping damage to frontal and fronto-temporal pathways underlying D and F in MS.

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EP2136

Cognitive reserve in multiple sclerosis modulates hippocampal functional connectivity and protects from memory deficits

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Introduction: We assessed the interaction between cognitive reserve, memory impairment and hippocampal resting state (RS) functional connectivity (FC) in MS.

Methods: RS fMRI, dual-echo and 3D T1-weighted scans were obtained from 87 MS patients and 49 matched healthy controls. A cognitive reserve index (CRI) was calculated including education, premorbid leisure activity and IQ. Patients were classified in memory impaired (MI) and memory preserved (MP) based on their performance at memory tests of the Rao's battery. Between-group differences of hippocampal RS FC and correlations between RS FC *vs* clinical, conventional MRI and neuropsychological/CRI variables were assessed using random-effect analyses.

Results: Twenty-two patients had MI. Hippocampal atrophy did not differ between MI and MP patients. The analyses of the R and L hippocampus gave the same results, we report those obtained from the R one. Compared to controls and MP patients, MI patients had reduced hippocampal RS FC with the bilateral caudate nucleus, L superior parietal lobule and bilateral superior frontal gyrus; compared to the other two groups MP patients had increased RS FC with the R cerebellum and R orbital gyrus. Higher CRI was related to higher RS FC with the L orbital gyrus. The association between hippocampal RS FC and memory in MS patients was not influenced by global cognitive status, EDSS and whole brain volume, several correlations were detected with hippocampal volume and T2 lesion volume.

Conclusions: Cognitive reserve contributes to protect from memory decline in MS by modulating hippocampal functional integrity.

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EP2137

Central cerebellar white matter contributes to motor coordination deficits in multiple sclerosis

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Introduction: Cerebellar atrophy is evident even in early stages of multiple sclerosis (MS), and cerebellar volumes are one of the most important predictors of diagnosis and disability in the disease. Atlas-based segmentation of the cerebellum to anatomically define its lobules could contribute largely to the localization of functionally diverse pathologies in MS. Here we investigated the associations between motor and cognitive impairment and atrophy in cerebellar subregions in MS.

Methods: Ninety-one individuals with relapse-onset MS underwent structural MRI and performed multiple sclerosis functional composite. Lobular gray matter and central cerebellar white matter (corpus medullare) segmentation was performed on lesion-filled T1-weighted images using the MAGeT Brain algorithm (Chakravarty et al. 2013), a modified multi-atlas segmentation framework that performs bootstrapping based on the dataset being studied to refine automatic segmentations. All cerebellar volumes were adjusted for intracranial volume based on regression models derived from twenty healthy individuals' scans. Correlation between test scores and cerebellar volumes were assessed using GLM, with age and gender as covariates.

Results: Kurtzke functional cerebellar score ($F_{1,87} = 11.22$,$p = 0.001$) and 9-hole-peg-test ($F_{1,87} = 12.11$,$p = 0.001$) were negatively correlated with cerebellar corpus medullare volume. Scores of 25-foot-walk and paced-auditory-serial-addition-test showed no significant correlation with either cerebellar gray matter or white matter volumes.

Conclusion: These findings suggest that central cerebellar white matter volume may prove useful as a surrogate biomarker for motor disabilities in MS. Further, this study supports feasibility and utility of a multi-atlas segmentation algorithm (MAGeT brain) for cerebellar volumetry in MS patients, which could be used as secondary endpoints in clinical trials.

Disclosure: Nothing to disclose.

EP2138

SlanDC as a target of laquinimod induced effects on innate immune system of MS patients

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Background: Laquinimod is an oral drug for the treatment of relapsing remitting multiple sclerosis (MS). The mechanism of action is not completely understood. Effects of treatment were demonstrated on central nervous system and the peripheral innate immune system.

Methods: As part of the MTD trial LAQ101 MS patients were treated with increasing doses of laquinimod (0.6–2.7 mg). Immune cell phenotypes were analyzed by FACS before and after 4 weeks of daily laquinimod administration with focus on innate immune cell populations. Some patients were analyzed weekly. Additionally a functional analysis was done.

Results: We could demonstrate a significant decrease of frequencies of slanDC (0.30–0.08 %, $p < 0.0001$) and other DC populations after 4 weeks of laquinimod treatment, while others like monocytes were unaffected (6.9–7.6 %). Weekly analysis showed a quick drop of DCs already in the first week. There was a dose-dependent modulation of certain DC populations, which was significant for slanDCs (slope, $p < 0.0001$). Functional analysis demonstrated a decrease of different activation markers after ex vivo stimulation with LPS or R848, which were more pronounced for slanDC than monocytes.

Conclusions: We could demonstrate significant dose-dependent, ex vivo effects of laquinimod with special focus on the innate immune system. The effects are early detectable already after 1 week of treatment. Moreover we could show functional effects by laquinimod treatment. The mechanism and functional impact of these effects need further investigations.

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EP2139

The effect of prolonged-release fampridine treatment on health-related quality of life outcomes after 1 year: results from the ENABLE study

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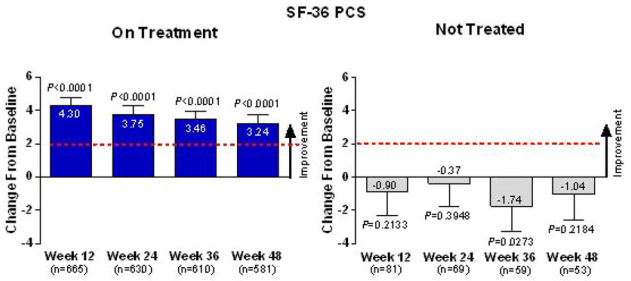
Introduction: Walking impairment negatively impacts health-related quality of life (HRQoL) in multiple sclerosis (MS). Prolonged-release (PR) fampridine tablet (dalfampridine extended release in US) improves walking in MS patients.

Methods: ENABLE was an open-label, 48-week, multicentre, observational study. The objective was to evaluate the effects of PR-fampridine 10 mg twice daily on HRQoL. Clinical response to treatment was defined as any improvement in the Timed 25-Foot Walk at weeks 2 and 4, and any improvement in the MS Walking Scale (MSWS-12) at week 4. Patients with clinical response at week 4 remained on PR-fampridine treatment for the remaining 44 weeks. The primary endpoint was change from baseline in the SF-36 physical component summary (PCS) at weeks 12, 24, 36, and 48 in patients on treatment. Disability status was measured by Disease Steps scale ranging from 'normal' to 'confined to wheelchair'.

Results: Baseline patient characteristics and demographics were comparable between groups. At week 4, 707/901 (78.5 %) patients demonstrated clinical benefit and remained on treatment. PR-fampridine treatment was associated with significant and clinically meaningful improvements in SF-36 PCS (all timepoints; $P < 0.0001$) from baseline (Fig. 1). Significant improvements from baseline were also observed in other HRQoL measures. Among patients on PR-fampridine treatment who had both disease step assessments, 536/592 (90.5 %) demonstrated stable or improved disability status from baseline to week 48.



Graph is mean change from baseline and 95% confidence interval. P values are Wilcoxon signed rank test compared with baseline. Red line: minimal clinically important difference (MCID) = 2 points.

Conclusions: PR-fampridine was associated with HRQoL benefits, observed as early as 12 weeks after treatment initiation, and maintained through 48-weeks. Majority of patients on treatment demonstrated stable or improved disability status throughout the study.

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EP2140

Multiple sclerosis in Iceland from 1900 to 2000: the natural history in a total population

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Introduction: We report symptomatology and natural history of all patients with MS in Iceland in 1900–2000.

Methods: Patients were collected through two total population studies and long term registration. EDSS was used to score disability.

Results: 529 patients (356 women, 173 men) were included. 74.7 % had RRMS at onset (77.0 % women, 69.9 % men), 15.7 % had RPMS (14,3 % women, 18.5 % men) and 9.6 % PPMS (8.7 % women, 11.6 % men). Age at onset was significantly higher for men ($t = -2{,}417$, $df = 521$, $p = 0.016$) and also for PPMS compared with PRMS and RRMS (35.1, 28.2 and 27.0 years, respectively, $F = 21{,}031$, $df = 2$, $p = 0.000$). Tventy six percent of patients with RRMS at onset converted to SPMS in the observation period. Time to secondary progression was 41.8 ± 2.10 years for women and 30.4 ± 2.16 years for men (Log rank = 6,598, $df = 1$, $p = 0.01$). Time from onset to moderate disability (EDSS 3–6) was 34.5 years for RRMS and 7.0 years for the progressive types, PPMS and RPMS (Log rank = 366.02, $df = 1$, $p = 0.000$). Time to severe disability (EDSS 7+) was 48,2 years for the RRMS and 16.4 years for the progressive types (Log rank = 226,11, $df = 1$, $p = 0.000$). Time to moderate and severe disability was significantly associated with age at onset but not affected by sex or presenting symptoms. Time to moderate ($p = 0.036$) and severe ($p = 0.021$) disability was significantly shorter for men than for women.

Conclusion: The clinical course of MS in Iceland is more benign than reported in many studies. Age at onset and male sex are risk factors for more severe clinical course.

Disclosure: Nothing to disclose.

EP2141

Progression to disability milestones in multiple sclerosis patients treated with natalizumab in the clinical practice setting

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Introduction: TOP is an ongoing, global, open-label, 10-year prospective study of relapsing-remitting MS patients treated with natalizumab.

Methods: Analyses included patients with ≥2 years of data. Confirmed disability progression was defined as an increase in Expanded Disability Status Scale (EDSS) score of ≥1.0 point or ≥2.0 points, sustained for 6 months. Rates of confirmed progression to milestone EDSS scores were also evaluated.

Results: As of May 2013, 2,588 patients with available baseline EDSS scores had completed ≥2 years of study, receiving a median (range) of 35.5 (4.0–82.0) natalizumab infusions; 1,080 of 3,679 potential 2-year completers (29 %) had discontinued treatment. At baseline, mean EDSS score was 3.4. Overall, 11.7 % and 3.4 % of patients had sustained EDSS score increases of ≥1.0 point and ≥2.0 points, respectively. Of 698 patients with baseline EDSS scores of 0.0–2.0, 7.7 % had confirmed progression to scores >=3.0. Rates of confirmed EDSS progression to scores ≥4.0 were 7.9 % in patients with baseline scores of 0.0–3.0 (n = 1,244) and 12.3 % in patients with baseline scores of 2.0–3.0 (n = 546). Rates of confirmed EDSS progression to scores ≥6.0 were 2.7 % in patients with baseline scores of 0.0–5.0 (n = 2167) and 5.7 % in patients with baseline scores of 3.0–5.0 (n = 923). Progression rates will also be examined among patients who discontinued treatment before and after 2 years.

Conclusions: Rates of progression to significant disability milestones were low during 2 years of natalizumab treatment. Longer-term evaluation of EDSS progression independent of relapse occurrence is warranted to confirm these results and to further assess secondary disease progression.

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Muscle and neuromuscular junction diseases

EP2142

Isolated ocular distribution in double seronegative myasthenia with low density receptor-related protein 4 antibodies: a case series

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Introduction: Antibodies targeting low density receptor-related protein 4 (LRP4), have been recently detected in patients with double seronegative myasthenia gravis (MG). The clinical phenotype of this particular subgroup of patients has not been clearly elucidated.

Case series: We present clinical and laboratory findings concerning three cases of double seronegative MG patients with LRP4 antibodies. A total of two females and one male patient of Caucasian origin were admitted to our Department with intermittent diplopia and eyelid ptosis. Symptoms had a fluctuating course and worsened during the day. Clinical examination did not reveal weakness in limb, axial, facial and tongue muscles. Deep tendon reflexes were elicited normal without signs of pyramidal tract involvement. Pharyngeal reflexes were preserved. Thorough blood tests and screening for systemic autoimmune diseases were unrevealing. Brain MRI and CT of the mediastinum were unremarkable. Serological tests for acetylcholine receptor antibodies and muscle specific kinase receptor antibodies were negative. Patients serum was also tested for antibodies against LRP4 using a cell-based assay. The results were positive. Repetitive nerve stimulation and single fiber electromyography confirmed the diagnosis of myasthenia gravis. All patients responded adequately to pyridostigmine. After 6 months two of them remained free of symptoms. The remaining patient had substantial resolution of her symptoms after the addition of prednisolone.

Conclusions: Our double seronagative patients with LRP4 antibodies share a common phenotype, characterized by ocular distribution, mild or moderate severity and favorable response to pyridostigmine.

Disclosure: Nothing to disclose.

EP2143

Distal myosin heavy chain-7 (thumb) myopathy due to the novel transition c.5566G>A with heterogeneous cardiac involvement

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Introduction: Myosin-heavy-chain (MYH7)-myopathy manifests clinically with a distal, scapuloperoneal, limb-girdle (proximal), or axial distribution and may involve the respiratory muscles. In the majority of the cases the heart is affected, ranging from relaxation impairment to dilative cardiomyopathy with ventricular arrhythmias. Progression of cardiac involvement and earlier onset in successive generations has not been reported in MYH7-myopathy.

Methods: Case study.

Results: In a five-generation family MYH7-myopathy manifested with late-onset, distal > proximal myopathy and variable degree of cardiac involvement. The index patient developed myopathy from age 49 years with anginal chest pain. Her mother presented with a similar phenotype but had only developed myocardial relaxation impairment. The daughter of the index patient had only mild distal myopathy but presented with left ventricular hypertrabeculation/noncompaction and required an implantable cardioverter defibrillator (ICD) because of ventricular arrhythmias since age 37 years. Her daughter was diagnosed with dilated cardiomyopathy at infancy, without overt skeletal muscle disease. MYH7-myopathy in the presented family was due to the novel mutation c.1566G>A in the MYH7 gene.

Conclusions: There is cardiac involvement in MYH7-myopathy, and cardiac affection in MYH7-myopathy is highly variable between the generations ranging from relaxation abnormality to noncompaction, ventricular arrhythmias, and dilated cardiomyopathy. While manifestations and progression of MYH7-myopathy may be mild, cardiac disease in MYH7-myopathy may be highly variable and progress with successive generations.

Disclosure: Nothing to disclose.

EP2144

Carnitine deficiency, a spectrum disorder: case series and histopathological and ultrastructural characterization

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Introduction: The brain must first oxidize ketone derivatives of acetyl CoA and acetoacetyl CoA produced by hepatic β-oxidation of fatty acids before they can be used as an energy source. To achieve this, the "carnitine shuttle" facilitates the transfer of long-chain fatty acids from the cytoplasm across the inner mitochondrial membrane into the mitochondrial matrix for β-oxidation in muscle, liver and cardiac tissues. The shuttle consists of three enzymes (carnitine palmitoyltransferase 1, carnitine acylcarnitine translocase, carnitine palmitoyltransferase 2), and organic cation transporter type 2 (OCTN2). A deficiency in any of these components leads to carnitine deficiency, with a wide spectrum of presentations, and creates a diagnostic challenge for clinicians.

Methods: Case series of 6 patients with carnitine deficiency (age range 1.5–53 years).

Results: Neurological manifestations included hypotonia, burning pain, decreased endurance, sensory deficits, developmental delay, stiffness, poor coordination and muscle weakness. All cases had low serum carnitine levels. In one case, a new variant of the gene responsible for primary carnitine deficiency (SLC22A) was found. Two cases had abnormal muscle biopsies. Two cases had suspected primary carnitine deficiency, one had secondary carnitine deficiency and the other three were not clear. In all the six cases, neurological symptoms improved after initiation of carnitine supplementation.

Conclusions: Our case series highlights the wide spectrum of neurological complaints in patients with carnitine deficiency. Our

report also underscores the importance of including carnitine deficiency in the differential diagnosis for many neurological signs and symptoms so that treatment can be initiated if appropriate.

Disclosure: Nothing to disclose.

EP2145

Late onset myasthenia gravis: what is specific about it?

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Introduction: Myasthenia gravis (MG) is heterogenous regarding clinical features, age at onset, thymus pathology and different autoantibodies. Recognition of clinical subtypes is essential in management and prognosis of the disease.

Aim: To analyze if late onset MG (LOMG, onset >50 years) has specific features compared to early onset form (EOMG, onset <50 years).

Methods: 338 LOMG patients were treated in our Clinic from 2002 until 2010. This group was compared with 189 patients with EOMG from the MG Belgrade registry.

Results: Male predominance (1.7:1) was observed in LOMG, and female predominance in EOMG (2.8:1). Anti-AChR antibodies were more common in LOMG (90.3 vs. 79.7 %; $p < 0.05$). The presence of MuSK antibodies was similar in both groups of seronegative patients (18.5 % in EOMG vs. 20 % in LOMG; $p > 0.05$). Severity of the disease was similar in EOMG and LOMG group ($p > 0.05$). Pure ocular form was more common in LOMG group (21.0 vs. 10.6 %; $p < 0.01$). Thymoma was equally present in LOMG and EOMG patients (13.2 vs. 14.5 %; $p > 0.05$), while hyperplasia was more common in EOMG group (63.0 vs. 5.6 %; $p < 0.01$). Other autoimmune disorders were found in 22.2 % of EOMG and in 8.9 % of LOMG patients ($p < 0.01$), while malignancies were present with similar frequencies in both groups (8.0 % in LOMG vs. 5.3 % in EOMG; $p > 0.05$).

Conclusions: Male predominance, low incidence of thymus hyperplasia, higher frequency of AChR antibodies, pure ocular form and lower frequency of autoimmune disorders suggest that LOMG is a different entity of this disease.

Disclosure: Nothing to disclose.

EP2146

Design of a confirmatory phase 3, multicentre, randomized, double-blind, placebo-controlled study of ataluren in patients with nonsense mutation Duchenne muscular dystrophy

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Introduction: In ~13 % of patients, Duchenne muscular dystrophy (DMD) is caused by a nonsense mutation (nm) in the dystrophin gene. Ataluren is an investigational oral drug designed to promote ribosomal read-through of premature stop codons in mRNA, leading to production of full-length, functional protein. We describe an ongoing confirmatory phase 3 placebo-controlled study designed to assess the efficacy and safety of ataluren 40 mg/kg/day in boys with nmDMD. The design of this study reflects lessons learned from prior studies and targets a study population to best show a treatment effect over 48 weeks.

Methods: All patients have a confirmed nonsense mutation in the dystrophin gene, are 7–16 years of age, are receiving a stable dose of corticosteroids, and have a screening 6-min walk distance (6MWD) ≥ 150 metres but below the protocol-specified %-predicted threshold. Overall, 220 patients were randomized in a 1:1 ratio to placebo or ataluren. The primary endpoint is 6MWD after 48 weeks. Secondary efficacy measures include timed function tests, quality of life, North Star Ambulatory Assessment, and patient/parent-reported disease-related symptoms and activities of daily living.

Results: In a retrospective subgroup analysis of patients in the phase 2b trial of ataluren in nmDMD who met the current study criteria, the difference between ataluren 40 mg/kg/day (administered as 10, 10, 20 mg/kg tid; $n = 30$) vs placebo ($n = 31$) in mean change in 6MWD over 48 weeks was approximately 50 m.

Conclusions: This study is designed to confirm the treatment effect of ataluren seen in the phase 2b ataluren trial.

Disclosure: JB, AR, RS, GLE, MH and SWP are all employees of PTC Therapeutics, Inc., which has developed ataluren.

EP2147

EUROMAC: disease registry for McArdle disease and other pure muscle glycogenolytic disorders presenting with exercise intolerance

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Introduction: The European Union has funded the development of a new disease registry for McArdle disease and other rare glycogenolytic disorders presenting with exercise intolerance. The scope of the project is to identify as many patients as possible across all European countries and to collect important natural history and epidemiological data.

Methods: EUROMAC is a new European network which currently has 20 partners from 7 European countries and includes collaborators from Turkey and the USA. The registry will be accessed directly by patients via the EUROMAC website and aims to recruit as many patients as possible from all European countries. A database will be developed of diagnostic laboratories and specialist clinics in Europe

which will be made freely available via the website. Patient support groups will also be involved.

Results: The EUROMAC consortium aims to improve genetic diagnosis by signposting relevant diagnostic laboratories. Standards of care will be developed, together with a plan to develop outcome measures for large multi-centre clinical trials. The project will incorporate public participation and aims to improve access to patient support bodies across Europe. Data on natural history and epidemiology of patients living in Europe will be analysed.

Conclusion: the EUROMAC is an European registry for McArdle disease and other rare glycogenolytic disorders. We seek to recruit as many European partners as possible and welcome collaborators and volunteers both from health services and patient support organisations.

Apply online: http://euromacregistry.eu/info@euromacregistry.eu +(34) 934 894 054.

Disclosure: Euromac is funded by the European Commission's Directorate General for Health and Consumers under contract no. 2012 12 14.

EP2148

Muscle MRI of scapular girdle in Facioscapulohumeral muscular dystrophy (FSHD)

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Introduction: In Facioscapulohumeral muscular dystrophy (FSHD), the upper girdle is early involved and often difficult to assess only relying on physical examination. Our aim was to evaluate the pattern and degree of involvement of upper girdle muscles in FSHD compared with other muscle diseases with scapular girdle impairment.

Methods: We propose an MRI protocol evaluating neck and upper girdle muscles. A large cohort of consecutive symptomatic FSHD patients and patients affected by muscular dystrophies and myopathies with prominent upper girdle involvement underwent this protocol.

Results: The trapezius and serratus anterior were the most and earliest affected muscles in FSHD, whilst spinati and subscapularis were consistently spared even in late disease stages. Asymmetry and hyperintensities on short-tau inversion recovery (STIR) sequences were common features. The overall involvement appears to be disease-specific in FSHD as it significantly differed from that encountered in the other myopathies.

Conclusions: The detailed knowledge of single muscle involvement provides useful information for correctly evaluating patients' motor function and to set a baseline for natural history studies. Upper girdle imaging can also be used as an additional tool helpful in supporting the diagnosis of FSHD in unclear situations, and may contribute with hints on the currently largely unknown molecular pathogenesis of this disease.

Disclosure: Nothing to disclose.

EP2149

Heterogeneity of muscle and CNS involvement in Steinert's disease (DM1): what does link behaviour to brain imaging?

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Introduction: Myotonic dystrophy is a genetic and multisystemic disorder due to polynucleotide expansions being only partially reliable to predict phenotypic expression. Beyond muscular involvement DM1 phenotype can be characterized by functional/morphological brain abnormalities to different extents. From a neuropsychological point of view executive and visuo-spatial dysfunctions, mood and personality impairments are reported.

Methods: 40 subjects with established clinical-genetic diagnosis, underwent a complete neurological assessment, including psychological interview and neuropsychological evaluation. Main caregiver underwent patient's Quality-of-life interview. A subgroup of 15 patients underwent brain MRI investigation.

Results: We found reduced scores in neuropsychological tests for frontal functions (61 %) and visuo-spatial impairments (66 %); interestingly verbal abilities were rather preserved(80 %). Behaviour was characterized by mixed mood conditions (anxiety, depression, apathy) and by variable sets of pathological personality traits, even though without fulfilling diagnostic criteria for major psychiatric disorder according to DSM-IV. Patient's and main caregiver's reports showed internal discrepancies(63 %), with patients tending to denial some aspects of their condition. Brain imaging revealed involvement of the white matter in frontal (53 %), parietal (27 %) and temporal (73 %) lobes. Statistical analysis showed significant relationships between reduced spatial memory performances and temporal lobe white matter changes (Fisher-Exact-Test $p < 0.05$).

Conclusions: Our study indicates that CNS involvement in DM1 is an heterogeneous condition characterized by cognitive/psychopathological dysfunctions; this could be a prominent feature in DM1, leading to an increased burden in management. White matter lesions are common in DM1 patients independently from CTG-repeat-expansion and disease-duration. CNS disorders could have significant relationships with white matter lesions and should be investigated since the early phases of illness.

Disclosure: Nothing to disclose.

EP2150

Increased prevalence of malignancy in adult mitochondrial disorders

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Introduction: There are indications that patients with a mitochondrial disorder (MID) develop more frequently malignomas or benign tumours than the general population. Aims of the study were to find out if the prevalence of tumours is actually increased in MID-patients and which of the malignomas or benign tumours are the most frequent.

Methods: Retrospectively evaluated were the charts of MID-patients for the presence of malign or benign tumours. MID was diagnosed according to the modified Walker-criteria.

Results: Among 475 MID-patients screened for tumours, at least a single malignoma was found in 65 patients (13.7 %), and at least a single benign tumour in 35 patients (7.4 %). Among those with malignancy, 22 were men and 43 female. Among those with a malignancy 1 had definite MID, 9 probable MID, and 55 possible MID. The most common of the malignancies was breast cancer, followed by dermatological, gynecological, and gastrointestinal malignancies. The most frequent of the benign tumours was lipoma,

followed by pituitary adenoma, meningiomas, carcinoids, and suprarenal adenomas. Compared to the general population, the prevalence of malignancies and of benign tumours was markedly increased. The female preponderance was explained by the frequent maternal inheritance of MIDs.

Conclusions: Adult patients with a MID, particularly females, carry an increased risk to develop a malignancy or a benign tumour. Since malignancy is an important determinant for their outcome, these patients should be more accurately screened for neoplasms, not to overlook the point, at which an effective treatment can no longer be provided.

Disclosure: Nothing to disclose.

EP2151

Quantitative grip force assessment of muscular weakness in myasthenia gravis

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Introduction: Muscular weakness in myasthenia gravis (MG) is commonly assessed using Quantitative Myasthenia Gravis Score (QMG). More objective and quantitative measures of muscular weakness may complement the use of clinical scales and might detect subclinical affection of muscles. We hypothesized that muscular weakness in patients with MG can be objectively quantified with non-invasive grip force tasks and that pathological findings correlate with disease severity as measured by the QMG.

Methods: This was a prospective study investigating patients with confirmed diagnosis of MG. All data was compared to healthy controls (HC). Subjects and HC were asked to lift a device (250 and 500 g) equipped with an electromagnetic sensor that measured three-dimensional changes in position and orientation. These were used to calculate position index coefficient (PI-C) and orientation index (OI-C) as measures for involuntary movements due to muscular weakness.

Results: 40 patients with MG (55.7 years, 42.5 % female, mean QMG 7.2) were included. PI-C and OI-C were significantly increased in MG patients for the 500 g device in the dominant and non-dominant hand. Subgroup analysis showed that patients with ocular myasthenia gravis (OMG) showed significantly higher values for the PI-C and OI-C in the non-dominant hand compared to HC. No correlation between QMG and grip force performance was found.

Conclusion: Quantitative Grip Force Assessment may be a useful objective tool for measuring muscular weakness in MG and seems to detect subclinical generalized muscle weakness in patients with OMG. Used as endpoint, it might increase the sensitivity and power of future clinical trials.

Disclosure: Nothing to disclose.

EP2152

Early diagnosis and early treatment in LOPD: when asymptomatic patients should be treated

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Pompe disease is a lysosomal disorder caused by GAA deficiency. Late Onset Pompe Disease (LOPD) is characterized by progressive muscle weakness and/or respiratory failure but, sometimes, only by an asymptomatic hyperCKemia. It has been suggested that an early diagnosis is fundamental for a timely ERT start to maximize its efficacy. According to the current guidelines, ERT is recommended for patients clinically defined or in presymptomatic patients with detectable muscle weakness or reduction in respiratory parameters on clinical examination.

Objective: To discuss about current treatment guidelines for LOPD, focusing on early diagnosis.

In a recent high risk population study (LOPED study), involving 17 Neuromuscular Italian Centers, we were able to diagnose 17 new LOPD patients out of 1051 patient with suspected neuromuscular disorders. Among those patients, 35 % manifested with asymptomatic hyperCKemia, 59 % with hyperCKemia and limb girdle muscle weakness (LGMW) and 6 % only with LGMW. The median time from onset of symptoms to diagnosis was 7.7 years. ERT has been initiated in 11 patients: 8 out of the 11 showed LGMW with hyperckemia whereas other 3 evidenced hyperCKemia without clinical symptoms but muscle morphology showed severe muscle damage and muscle MRI in proximal muscles revealed an sclero-adipose substitution.

Our study demonstrated that 35 % of patients apparently with asymptomatic hyperCKemia showed a combination of clinical, morphological and neuroradiological data that suggesting to start ERT early. This study suggests that current treatment guidelines should be carefully updated.

Disclosure: Nothing to disclose.

EP2153

Clinical and genetic features of Calpainopathies in Saudi Arabia

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Objectives: Characterization of phenotypic, pathological, radiological and genetic findings in 8 Saudi Arabian families with Calpainopathies, limb girdle muscular dystrophy type2A (LGMD2A).

Methods: Review of clinical, radiological, immunohistochemistry and neurophysiological findings in patients with limb girdle muscular dystrophy (LGMD) in a tertiary care referral center in Saudi Arabia. Screening for mutation in Calpain (CAPN3) gene were done.

Results: 64 families with LGMD2 were studied, 8 families (12 %) had the LGMD2A phenotype, 21 patients (6 male, 15 female). The main age of onset was 15 (Range 9-35). Average age of Goweŕs sign is 2 years after onset and was noted in more than 80 % patients. Initial symptoms were lower limb weakness, inability climbing stairs

and gait disturbance in majority of patients. Asymmetry was noted in 30 % of patients, loss of ambulation was observed in 80 % within 6–8 years after onset. Radiological and histopathological studies confirmed these findings, Six novel mutations in CAPN3 gene were identified in 8 families (g.IV55+1 G>A in 2 families, Glu104X in 1 family, Gly480Arg in 1 family, c.2334_2335 1200 in 1 family, c.1076C>T in 1 family, c.c.2242C>T in 1 family).

Conclusion: The prevalence of LGMD2A is around 12 % of our LGMD cohort. The clinical details are variables and consistent with other reports from different ethnic groups. Of interest, most of the families are Bedouin in origin (Nomads). Genetically, all identified mutations were novel and will add to the spectrum of all CAPN known mutations.

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EP2154

Evaluation of the *trail* mediated apoptotic pathway in myasthenia gravis patients with thymic abnormalities

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Introduction: Myasthenia Gravis (MG) is accompanied by follicular thymic hyperplasia in 40–70 % of cases, and by thymoma in 10–15 %. TRAIL is a TNF family member, with a claimed role in negative selection of thymocytes in thymus. Yet the results are controversial. Alterations in the expression levels of TRAIL ligand and receptors and their inhibitors is significant in terms of evaluating different roles exerted by TRAIL, including apoptosis, in various tissues.

Methods: We investigated expression levels of TRAIL apoptotic ligand and receptors, and the antiapoptotic NFkB molecule immunohistochemically, in 22 MG patients with thymoma, 5 MG patients with thymic hyperplasia, and in 10 normal thymic tissue samples. Apoptotic cell counts were detected by TUNEL.

Results: Expression levels of DR4 and DR5 death receptors, and DcR2 decoy receptor were significantly higher in thymoma, while DR5 was increased in thymic hyperplasia compared to normal thymus. Furthermore, no detectable levels of active NFkB was evident in normal or abnormal thymus. Apoptotic cell count in normal thymus correlated with TRAIL expression.

Conclusions: Our results are compatible with an active apoptotic pathway for TRAIL in normal thymus and thymic hyperplasia, in terms of low decoy receptor levels, and absence of NFkB activation. Decoy receptors may be increased in thymoma as a protection from infiltration. Correlation of apoptotic cell count in normal thymus with TRAIL levels may suggest a possible role for TRAIL in thymic atrophy. These results, when combined with functional and in vivo tests, will be informative on applicability of a possible "TRAIL-mediated medical thymectomy".

Disclosure: Nothing to disclose.

EP2155

Myotonic dystrophy type 1 with myasthenia gravis: is this a by chance association?

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Introduction: Myotonic dystrophy type1 (DM1) is an inherited muscle disease characterized by muscle weakness, myotonia and, within the multisystem involvement, the occurrence of immunological disorders. We describe three unrelated DM1 cases in which DM1 was associated with myasthenia gravis.

Case descriptions:

First case: 60-year-old male with diagnosis of DM1 since the age of 30 years. At the age of 56 he presented a rapid decline of clinical conditions, in particular in worsening of respiratory insufficiency, severe fatiguability in daily activities and appearance of left eyelid ptosis. Acetylcholine receptor antibody serum titre resulted positive and thoracic CT detected the presence of thymoma, confirming the diagnosis of thymomatous myasthenia.

Second case: 71-year-old male, affected by a mild form of DM1, complaining for some months of a sub-acute onset of dropped head and respiratory difficulties. Further investigations confirmed the diagnosis of myasthenia gravis associated with thymoma. In both cases the thymoma was removed surgically, with subsequent improvement of clinical conditions.

Third case: 33-year-old male coming to our attention for 2-year history of handgrip myotonia and progressive nasal voice and presence, in his family pedigree, of an affected sister with occurrence of an otherwise typical ocular myasthenia with increased levels of acetylcholine receptor antibodies.

Conclusions: The rare but not exceptional occurrence of myasthenia gravis in DM1 is to be considered to correctly manage these at some extent clinically overlapping disorders. It remains to be elucidated which pathogenic mechanisms underlie possible autoimmune comorbidities in DM1 in the frame of a syndromic appearance or just a coincidence.

Disclosure: Nothing to disclose.

Neurogenetics 1

EP2156

Genetic risk factors in patients with acute ischemic stroke: the role of PPARG and IL-6

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Background: Ischemic stroke is multifactorial disease which include interaction among various genetic and environmental factors.

Objective: The aim of present study was to estimate possible associations of two analysed gene, peroxisome proliferator activated receptor-gamma (PPARG) and interleukin-6 (IL-6) and their gene variability on ischemic stroke development in patient group.

Methods: Study included 301 subjects (114 patients and 187 healthy controls). Data on patients presenting with acute ischemic stroke, their earlier medical history and modifiable risk factors: (hypertension, hyperlipidaemia, high body mass, cigarette smoking, physical activity), were prospectively collected from January 2008 until January 2012. Genotyping was performed using PCR–RFLP based methods.

Results: According to the results of comparisons of individual genotype against others, genotypes PPARG CC ($p < 0.001$), IL-6 -174 GC ($p < 0.001$,) were statistically more frequent in the patient's group. Patients had significantly higher BMI, higher blood pressure, and higher level of total cholesterol, LDL, triglycerides, lowered

level of HDL, and elevated level of CRP. Study patient's group recorded a higher proportion of men, and participants with a positive family history on cerebrovascular disease than in control group. Statistically significant association in patient group was found between IL-6 genotypes and levels of C reactive protein ($\div^2 = 9.728$; df = 2; P = 0.009; ö = 0,292). Elevated C-reactive protein was most common among patients with IL-6 174 GC genotype (p = 0.009).

Conclusion: PPARG CC and IL-6 174 GC gene polymorphism variants could be susceptibility factors for ischemic stroke development in patient group, particularly in males, in presence of hypertension and elevated CRP levels.

Disclosure: Nothing to disclose.

EP2157

Double trouble: ataxia with oculomotor apraxia type 1 in a Leber's hereditary optic neuropathy pedigree

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Introduction: Leber's hereditary optic neuropathy (LHON) is a rare mitochondrial disorder caused in >90 % of cases by one of three mutations in the mitochondrial (mt)DNA (G3460A, G11778A, or T14484C). The phenotype of LHON is usually characterized by isolated bilateral visual loss. Rare cases of other neurologic symptoms in LHON have been designated as LHON plus, LHON overlap or Leigh-like syndromes in LHON.

Patient and methods: An 8-year-old German girl presented to our institute with progressive cerebellar signs and learning disability from the age of 6 years. She had no visual problems but four maternal family members were affected by LHON, harbouring the homoplasmic mtDNA mutation G11778A. On examination, the girl showed marked gait and limb ataxia, oculomotor apraxia, dystonia, chorea, hyporeflexia and foot deformities (pes cavus, pes equinus). The MRI showed cerebellar atrophy and signs of hippocampal atrophy. Visual acuity, fundoscopy and visual evoked potentials were normal. Although protean neurologic symptoms have been described in rare cases of LHON plus, the phenotype in our patient led us to the strong suspicion of ataxia with oculomotor apraxia type 1 (AOA1).

Results: Genetic testing revealed the pathogenic homozygous mutation c.837G>A, p.Trp279x in the aprataxin gene, causing AOA1.

Conclusions: Extended genetic testing leads to an increasing number of double trouble cases. The identification of a mutation in a certain syndrome should not be taken as proof of causality. Some older case reports in the literature (including LHON plus, LHON overlap and Leigh-like syndromes in LHON) may be erroneous due to overlooked double trouble.

Disclosure: Nothing to disclose.

EP2158

Mast syndrome in the first non-Amish kindred caused by a homozygous stop mutation in *SPG21*

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Introduction: Mast syndrome is also known as autosomal recessive hereditary spastic paraplegia-21. To date, only a single mutation in *SPG21*, also known as *ACP33*, has been identified in an extended Amish pedigree. Age of onset ranged from childhood to the 4th decade. Clinical features include dementia, cerebellar, and extrapyramidal signs as well as psychiatric abnormalities.

Case report: We report on a 48-year-old man of Caucasian origin first presenting with progressive gait disturbance at age 40 years. Subsequently, slurred speech and severe cognitive impairment developed. On examination, the patient showed cerebellar signs with gait ataxia and dysarthria as well as lower-limb spasticity and vertical gaze palsy. Visual acuity D/S was 0.5 and fundoscopy revealed a pigmentary retinopathy. A 51-year-old sister suffered from spastic tetraparesis with multiple contractures and has been bedridden since age 39 years. Gait disturbance and cognitive decline had slowly progressed since her early thirties but she had already experienced psychotic symptoms at age 25 years.

Results: Exome sequencing identified a novel homozygous *SPG21* mutation, c.118T>C (p.Arg40*), predicting a premature truncation of >80 % of the protein. Sanger sequencing confirmed the mutation in the homozygous state in both affected siblings while the mother and two healthy sisters were heterozygous carriers. The loss-of-function character and matching phenotype strongly argue for a disease-causing role of mutant *SPG21* in our patients.

Conclusions: We report the first cases of Mast syndrome in the non-Amish population. This family expands the phenotypic spectrum of Mast syndrome as retinopathy and gaze palsy have not been described before.

Disclosure: Nothing to disclose.

EP2159

POLR3A-mutations revealed by whole-exome sequencing in two patients with unusual findings in brain MRI

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Introduction: *POLR3A* is considered a housekeeping gene and is expressed ubiquitously. Both *POLR3A* and *POLR3B* encode catalytic subunits of RNA polymerase III (Pol III). Recently, pathogenic biallelic mutations in either *POLR3A* or *POLR3B* have been described as the genetic cause for Pol III-related leukodystrophies.

Patients and methods: We describe two male patients with recessive-type mutations in *POLR3A* revealed by exome sequencing. A 28-year-old patient presented with progressive gait disturbance, severe dysarthria, dysphagia, dysmorphic features and pronounced cognitive impairment. First symptoms appeared at the age of 10. His older sister showed a similar albeit milder phenotype. An unrelated 17-year-old patient showed first symptoms with intermittent fever attacks at the age of 9 months which continue to occur occasionally. A progressive gait disturbance and dysarthria are present since early childhood. The patient also presented with dystonia, cognitive impairment, several spots of alopecia and oligodontia.

Results: Pol III-related leukodystrophies are autosomal recessive disorders which present with a heterogeneous clinical syndrome including movement disorders, abnormal dentition and signs of hypomyelination on brain MRI. We describe two patients with motor dysfunction observed in both and abnormal dentition seen in one of the patients. On brain MRI, no features of white matter

hypomyelination or cerebellar atrophy could be seen but both showed signal alterations and atrophy of the basal ganglia. There was no laboratory evidence of a metabolic disorder. A muscle biopsy performed in one of the patients revealed no pathological findings.

Conclusion: *POLR3A* mutations may not always be associated with leukodystrophy.

Disclosure: Nothing to disclose.

EP2160
Clinical and genetic features of anoctaminopathies in Saudi Arabia

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Objectives: Characterization of phenotypic and genetic findings in two families with Anoctaminopathies, limb girdle muscular dystrophy type2L (LGMD2L).

Methods: We performed a mutation analysis in Anoctamin5 (ANO5) gene in patients diagnosed with LGMD in a tertiary care hospital in Saudi Arabia.

Results: All cases of LGMD from the neuromuscular registry (2000–2013) in a tertiary care hospital were recruited. All gene responsible for LGMD 2 were screened. Out of 56 families with LGMD2, we identified 2 families (3.6 %) with anoctaminopathy.

In the first family, mild asymmetrical calf muscles weakness and atrophy was first noted at age 39. CK level was >10× normal. Muscle biopsy showed necrotizing myopathic changes. MRI legs showed fatty involution without loss of volume involving the gastrocnemius and soleus muscles in asymmetrical fashion. Minimal disease progression was noted over 18 years of follow up. A novel ANO5 Gene mutation Arg58Trp was found.

In the second family, a male presented at age of 41 with asymptomatic hyperCkemia and intermittent dyspnea. Over 10 years of follow up he became disabled with muscle cramp, myoglobinuria and difficulty ambulating. Homozygous deletion of 11.9 Kb encompassing exon 13–exon 17 was found in ANO5 gene. Full cardiac investigation were normal in both patients.

Conclusion: The prevalence of LGMD2L is around 3.6 % in Saudi Arabian native LGMD cohort. Slowly progressive, late onset and asymmetrical weakness were the salient features in these two families. The genetic findings were novel and will add to the spectrum of all ANO5 known mutations.

Disclosure: Nothing to disclose.

EP2161
Hereditary spastic paraplegias in Hungary—genetic diagnostic improved by next generation sequencing

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Introduction: Hereditary spastic paraplegias (HSP) are a clinically and genetically heterogeneous group of neurodegenerative diseases. There are altogether more than 50 known SPG genes causing HSP. Differentiating between the different genes is hard, because there is imperfect correlation between clinical classification and genetic types of HSP. Our aim is to determine the frequencies of different SPG gene mutations among hungarian HSP patients.

Methods: All patient with suspected HSP were seen by a specialist in neurology. In the genetic diagnostic we perform a two step test. In the first step SPG3A and SPG4 genes are analysed with Sanger sequencing. If there is no pathogenic mutation in SPG3A and SPG4, we continue with whole exome sequencing. Results are validated with Sanger sequencing.

Results: At this point we diagnosed 51 patient with possible HSP (28 male, 23 female). Complicating symptoms were present at 24 patients. Sanger sequencing of both SPG3A and SPG4 was done at 21 patient. Sanger sequencing revealed SPG4 in eight cases, but no SPG3A mutation was detected. One patient, by whom previously muscle biopsy was performed, carries pathogenic mutation in the SPG7 gene. Nine patient went through whole exome sequencing. Whole exome sequencing revealed the cause of the spastic paraplegia in further six patient (SPG11 in two patients, SPG5A in one patient, SPG7 in one patient, X-linked SPG1 in one patient, and possible adrenomyeloneuropathy in one patient).

Conclusions: Next generation sequencing significantly improves genetic diagnostic in HSP, although there are cases which were not solved yet by this method.

Disclosure: Nothing to disclose.

EP2162
Whole exome sequencing analysis in recessive hereditary spastic paraplegia patients from Turkey

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Introduction: Hereditary Spastic Paraplegia (HSP) is an inherited, rare, neurodegenerative disorder. It is characterized with lower limb spasticity and progressive weakness. In 'complicated' HSP, additional neurological and non-neurological symptoms are observed. HSP inheritance can be autosomal dominant, autosomal recessive, or X-linked. Twenty-three genes and nine loci are associated with autosomal recessive form of HSP (ARHSP).

Methods: DNA sample of one patient from each of six ARHSP families were exome sequenced (WES). The data is filtered and candidate variations are determined. Segregation analyses were performed in the families to confirm that the variation is responsible for the HSP phenotype. Control samples from Turkey were also screened to exclude the possibility that they can be polymorphic variations.

Results: Mutations in two known HSP genes were identified. The first one was the c.325_326insTGTC insertion in ALS2 gene in family H59, and the second one was the c.4321C>T (p. A1394X) variation in Spastizin gene (SPG15) in family H61. Spastizin is the second most commonly mutated gene in ARHSP with thin corpus callosum that is also observed in our patient. Four families were found to be negative for mutations in known HSP genes. However, candidate genes were determined in two of these families for which segregation analysis is being performed. The remaining two families have promising WES data to identify novel HSP genes.

Conclusions: Exome sequencing unravelled pathogenic mutations in two among the six families implicating further genetic

heterogeneity of ARHSP and will possibly lead to identification of novel genes in families from Turkey.

Disclosure: Nothing to disclose.

EP2163

Exome sequencing vs phenotype directed gene screening in CMT patients from Turkey

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Introduction: Charcot-Marie-Tooth (CMT) disease is an inherited peripheral neuropathy and an excellent candidate to be analyzed by exome sequencing because of its locus heterogeneity.

Methods: Seventeen Turkish CMT patients were exome sequenced and the data were filtered to identify causative mutations. In the second part of the study, eight other Turkish CMT patients were screened for mutations in the GDAP1, GJB1, MPZ, NDRG1 and PMP22 genes that have been targeted based on clinical observations.

Results: The data revealed two novel variations in MFN2 gene as well as a novel splicing variant in *GJB1*. Previously identified mutations in AARS and DNM2 genes were found to be causative in two other families. All were confirmed by Sanger sequencing and segregation analysis. Novel variations identified in DNM2, LRSAM, FGD4 and KIF1B genes should be validated among family members and in controls. Six variations that have been previously reported as SNPs and one novel variation were observed in all seventeen patients. Screening of CMT genes in eight other patients based on clinical data revealed a novel mutation in *PMP22*. The presence of the founder p.R148X mutation in *NDRG1* was also confirmed in two affected brothers.

Conclusions: Identification of causative variations in five among seventeen families by exome sequencing implicates that it is a promising alternative approach for disease-causing variation identification. However, screening of selected gene or genes based on ethnicity and clinical data is still useful in genetic diagnosis of the disease.

Disclosure: J.R.L. is a paid consultant for Athena Diagnostics, has stock ownership in 23andMe and Ion Torrent Systems, and is a co-inventor on multiple US and European patents related to molecular diagnostics for inherited neuropathies, eye diseases, and bacterial genomic fingerprinting.

EP2164

A novel *NSD1* mutation in Sotos syndrome with constriction of vena cava

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Introduction: Sotos syndrome, first described in 1964, is characterized by typical facial appearance, overgrowth (height and/or head circumference ≥2 SD above the mean), and sometimes other features such as learning disability behavioral problems, congenital cardiac anomalies, neonatal jaundice, renal anomalies, scoliosis, and seizures.

The occurrence of Sotos syndrome is 1 in 10,000 to 1 in 14,000 newborns. However, many cases are assumed to be undiagnosed.

Methods: Genetic analyses including karyotype, array comparative genomic hybridization and exome high throughput sequencing (HTS) was performed in a two-year-old girl with an unknown syndrome.

Results: HTS analysis revealed a novel *de novo* nonsense mutation in the *NSD1* gene.

Her facial appearance was consistent with Sotos syndrome whereas her associated balloon dilated vena cava inferior constriction has not previously been assigned to Sotos syndrome.

Conclusion: We describe a novel *NSD1* nonsense mutation causing Sotos syndrome. To our knowledge, this is the first time a Sotos patient has presented with a vena cava constriction.

Disclosure: Nothing to disclose.

EP2165

CYP7B1 screening in multiple sclerosis patients shows association among new variants, pyramidal signs and autoimmune disease

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Introduction: Autosomal recessive spastic paraplegia type 5 (SPG5) is due to mutations in the CYP7B1 gene, encoding for the cytochrome P450-7B1, responsible for oxysterols 7α-hydroxylation. Oxysterol/cholestenoic acids pool plays a role in motor neuron survival and immune response. SPG5 is characterized by white matter abnormalities at brain resonance imaging (MRI). In view of clinical presentation and MRI findings, multiple sclerosis (MS) is a possible differential diagnosis of SPG5.

Methods: One hundred and seventeen MS patients with clinical spastic paraplegia or possible autosomal recessive transmission were selected for the mutational screening.

Results: Forty-three patients had primary progressive, 26 relapsing remitting, 26 secondary progressive, and 22 relapsing progressive MS clinical course. No CYP7B1 homozygous mutations were identified. Two novel variants and one pathogenic mutation were found at heterozygous state.

Conclusions: The two novel variants cosegregated with pyramidal signs and autoimmune diseases suggesting that they might be susceptibility factors. Reduced cytochrome P450-7B1 enzymatic activity could alter the balance among neurotoxic and neuroprotective oxysterols promoting motor neuron degeneration and/or immune response.

Disclosure: Nothing to disclose.

EP2166

Circulating miRNAs as potential biomarkers in primary progressive aphasia

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Introduction: Changes in miRNA levels are characteristic of many neurodegenerative diseases. Various miRNA are enriched in different brain areas. The main aim of this study was to evaluate the distribution of extracellular miRNAs in serum samples from logopenic, semantic and agrammatic variant of Primary Progressive Aphasia (PPA) patients.

Methods: Cell free circulating miRNAs were isolated from 400 µl of serum using mirVana Paris kit. C. The miRNA wide analysis was performed by SABioscience miScript miRNA PCR arrays containing 84 miRNAs most commonly reported to be differentially upregulated in serum in a discovery sample of three logopenic, three semantic and three agrammatic PPA patients and four healthy age-matched controls. *C. elegans* miRNA cel-miR-39 (synthetic RNA oligonucleotides), added to each denatured sample, was used for sample-to-sample normalization. Best hits will be validated via real time PCR in a larger population.

Results: Statistically significant decreased levels of hsa-miR-17-3p, hsa-miR-27a-3p, hsa-miR-29a-3p were observed in logopenic patient compared to controls ($p < 0.05$); statistically significant decreased levels of hsa-miR-125b-5p were observed in agrammatic patients compared to controls ($p < 0.05$). In semantic patients, a trend toward dowregulation of hsa-miR-574-3p and of hsa-miR-145-5p was observed.

Conclusions: According to these results, downregulation of different miRNA can reflect specific brain area atrophy patterns in different PPA subtypes. miRNA down-regulation could determine an over-expression of target genes likely involved in the PPA pathogenesis. Extracellular miRNAs, along with other markers, could represent non-invasive and relatively inexpensive peripheral biomarkers for early diagnosis of PPA.

Disclosure: Nothing to disclose.

EP2167

The influence of the catechol-*O*-methyltransferase gene polymorphism on the occurrence of dyskinesia in patients with Parkinson's disease in Serbian population

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Introduction: Differences in catechol-*O*-methyltransferase (COMT) activity and genotype may determine individual variations in the therapeutic response to levodopa or Parkinson's disease (PD) susceptibility. Catechol-*O*-methyltransferase is an enzyme that inactivates catecholamines, including levodopa. An amino acid change (Val-108-Met) in the COMT protein has been found to result in a change from high to low enzyme activity. This substitution is linked to low COMT enzyme activity and is designated the L (low activity) allele, in contrast to the H (high activity) allele. Given that genetic factors may be involved in the occurrence of the adverse effects of chronic levodopa therapy in PD patients, we measured the wave in which the met/val substitution may affect the appearance of dyskinesia.

Methods: We had genotyped 120 patients with PD from an existing hospital database of Parkinsonian patients ($n = 120$, primarily Serbian origin) by using polymerase chain reaction (PCR) amplification and digestion by the restriction enzyme NlaIII.

Results: Since individuals with the G/G genotype have three to fourfold higher activity of the COMT enzyme than those with the A/A genotype, it has been hypothesized that COMT polymorphism might affect levodopa metabolism. Comparison of the allele frequencies revealed that homozygous for the low-activity allele was also significantly more in PD patients with dyskinesia in comparison with those without dyskinesia ($p = 0.042$, odds ratio $= 3.20$).

Conclusions: Our results may help understand the mechanism that cause motor complications of levodopa therapy in PD patients.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 4

EP2201

Profile of triggers and cerebrovascular risk factors in 321 patients with transient global amnesia (TGA)

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Introduction: The pathogenetic mechanisms causing transient global amnesia (TGA) remain elusive. Various aetiologies have been proposed, amongst are vascular causes, a migrainous phenomenon, cortical spreading depression, metabolic disturbance and epilepsy. Remarkably, cerebrovascular risk factors (CVRF) are not believed to be associated with TGA. Thus, we wanted to characterize the profile of CVRF in a large cohort of patients with TGA.

Methods: We performed a retrospective study of patients with TGA (from 1/2003 until 1/2009) according to the criteria by Hodges and Warlow (1990). The analysis included potential triggers and CVRF including arterial hypertension, obesity, hyperlipidaemia, diabetes, smoking and carotid stenosis over 50 %.

Results: A total of 321 patients (female 65 %) were studied, mean age was 64 years (range 18–86).

Triggers were present in 31 %. Most frequent were physical (20 %) and psychological (8 %) triggers.

The most common CVRF was arterial hypertension (58 %), followed by hyperlipidaemia (42 %), diabetes (8 %), smoking (3 %), carotid stenosis over 50 % (3 %) and obesity (2 %). One CRVF was present in 41 %, 2 in 31 %, 3 in 3 %, and 4 in 1 %.

Conclusions: Our data indicate the presence of CVRF in a subgroup of patients with TGA. While TGA is considered a benign, self-limited syndrome, this cohort may be prone to future cerebrovascular events. Further studies are required to evaluate long-term prognosis based on the profile of atherosclerotic risk factors.

Disclosure: Nothing to disclose.

EP2202

Clinical, cognitive and neuroimaging features differentiating vascular from degenerative mild cognitive impairment. Results from a nested case–control study

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Introduction: Mild cognitive impairment (MCI) can be subsided by vascular or atrophic brain lesions. Clinical and neuroimaging markers selective of the two conditions are still incompletely determined, mostly because of the definitions and potential confounders. We investigated factors differentiating degenerative (deg-MCI) from vascular MCI (vas-MCI).

Methods: Using a nested case–control design we identified from two larger prospective registries two groups of 30 patients with vas-MCI or deg-MCI. Both groups had been assessed by a clinical, neuropsychological, laboratory and neuroimaging protocol.

Results: Familiar dementia was prevalent in deg-MCI group (67 % vs 33 %, $p = .019$), while hypercholesterolemia (13 % vs 67 %, $p < .001$), stroke (3 % vs 37 %, $p = .002$), migraine (23 % vs 53 %, $p = .033$), psychiatric disorders (40 % vs 73 %, $p = .018$), gait disorders (10 % vs 70 %, $p < .001$), and urinary disturbances (20 % vs 50 %, $p = .029$) were more common in the vas-MCI group. Logistic regression showed an independent association between story recall test and deg-MCI ($p = .003$), and depression severity with vas-MCI ($p = .045$). On MRI lacunar infarcts ($p = .001$) are associated with vas-MCI, while global atrophy ($p = .001$) and enlarged perivascular spaces (EPSV) in hippocampus and centrum semiovale with deg-MCI ($p = .001$ respectively). We found no difference in distribution of Apolipoprotein E gene polymorphisms analysis (27 % vas-MCI vs 33 % deg-MCI).

Conclusions: Few selective markers may discriminate vas-MCI and deg-MCI, as impaired episodic memory and depressive disturbances on clinical grounds, lacunar infarcts, global atrophy and EPSV on brain imaging grounds. If confirmed from larger series, this information may be useful to the setting of clinic-functional screening of patients with different MCI types.

Disclosure: Nothing to disclose.

EP2203

LDL subclasses in ischemic stroke: a risk factor?

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Introduction: Elevated low density lipoprotein (LDL) plasma concentration is a primary risk factor in the development of atherosclerosis. By polyacrylamide gel electrophoresis methods, seven LDL subclasses were identified. Small dense LDL (sdLDL) is the main subclass responsible for development of the atherosclerotic process. In this study, the relationship between ischemic stroke and LDL subclasses was investigated.

Materials and methods: In one year period, consecutive 110 ischemic stroke patients who were classified according to TOAST classification as cardioembolism ($n = 40$), large-artery atherosclerosis ($n = 40$) and small-vessel occlusion ($n = 30$) and 60 healthy controls were included to this study. LDL subclasses were established by Lipoprint system polyacrylamide disc gel electrophoresis.

Results: The ischemic stroke group consisted of 61.8 % ($n = 68$) males and 38.2 % ($n = 42$) females and mean age was 66.7 ± 12.0 years. The mean age of the control group was 61.2 ± 4.2 years and 50 % ($n = 30$) were male, 50 % ($n = 30$) female. The LDL-2, LDL-3 and LDL-4 subclasses were significantly higher in the ischemic stroke group compared to the control group ($p < 0.05$). There were no statistically significant differences between the LDL-1 levels of ischemic stroke and the control groups ($p > 0.05$). Also, there were no significant differences between levels of LDL subclasses of cardioembolism, large-artery atherosclerosis and small-vessel occlusion subgroups ($p > 0.05$).

Conclusion: sdLDL is an established risk factor for ischemic heart diseases, similarly LDL subclasses are higher in ischemic stroke patients. The examination of LDL subclasses may influence the treatment strategy and prognosis in ischemic stroke.

Disclosure: Nothing to disclose.

EP2204

Evaluated serum levels of brain-derived neurotrophic factor (BDNF) in acute ischemic stroke

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Introduction: Neurotrophic factors are important molecules in recovery process of stroke patients. Brain-derived neurotrophic factor (BDNF) replies for proliferation, differentiation, structural and functional stability, viability of neurons. The aim of the study was to find relationships between serum levels of BDNF and clinical characteristics of patients with ischemic stroke.

Methods: We measured serum levels of BDNF in patients with acute ischemic stroke ($n = 39$) within 24 h from symptom onset, in patients with clinically stable cerebrovascular disease ($n = 28$) and in healthy controls ($n = 26$). Intensity of neurological impairment was estimated by the NIH Stroke Scale, kinesthetic praxis—by the Denckla tests, cognitive impairment—by the Mini-Mental State Examination and the Frontal Assessment Battery, depression level—by the Beck Depression Inventory.

Results: The serum levels of BDNF were significantly lower in acute stroke patients as compared to patients with clinically stable cerebrovascular disease and healthy controls. The serum levels of BDNF were also lower in patients with clinically stable cerebrovascular disease in comparison to healthy controls. The serum levels of BDNF in acute stroke patients were strongly correlated with the NIH Stroke Scale ($p < 0.01$) on admission and kinesthetic praxis disorders ($p < 0.05$), degree of cognitive impairment ($p < 0.01$), depression level ($p < 0.01$) at days 30 and 60 after stroke.

Conclusions: The received data may be important for individualization of diagnostics and therapeutic interventions in patients with acute ischemic stroke.

Disclosure: Nothing to disclose.

EP2205

Cerebral venous sinus thrombosis: an analysis of 46 patients

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Introduction: Cerebral venous sinüs thrombosis (CVT) is seen infrequently than arterial stroke and effects every age group. Onset and process is variable and prognosis is usually good, but early development of coma and intracranial hemorrhage leads to bad prognosis.

Methods: In our retrospective study, it's aimed to search neurological deficits, etiological factors, localization and prognosis of the 46 patients who are hospitalized with the diagnosis of cerebral venous thrombosis in Neurology Clinics of Bezmi Alem Valide Sultan Vakıf Gureba and Okmeydanı Education and Research Hospitals.

Results: Of 46 patients (30 women, 16 men) mean age was 39 + 12.29. 22 patients in subacute and 20 patients in acute stage admitted to our clinics.The most frequent symptom was headache (69.6 %) and the most seen neurological sign was papilledema (56.5 %). 13 patients had hemorrhagic infarct, 6 had ischemic infarct, 24 had no parenchymal lesion,1 had epidural abscess and 2

subarachnoid hemorrhage. 16 had isolated sinus thrombosis, the most commonly affected sinus in isolated or combined sinus thrombosis is transverse sinus (n = 37). No etiological reasons were found in 11 patients, 17 had one, 18 had more than one reason. The predisposing factors were infections (n = 8), puerperium(n = 5), oral contraceptive pills (n = 7), hereditary thrombophilia (n = 21), Behçet's Disease (n = 2), ulcerative colitis (n = 1) and head injury (n = 1).

Conclusions: CVT needs highly clinical suspicion. Early treatment reduces the risk of exitus and severe disability. CVT should be remembered in the differential diagnosis of headaches of unknown etiology.

Disclosure: Nothing to disclose.

EP2206

Thrombolysis with alteplase for acute ischemic stroke in octogenarians in Croatia

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Introduction: According to the Croatian licence alteplase is not to be used for treatment of acute ischemic stroke in octogenarians. Main concern in this patients group is post-thrombolytic intracranial haemorrhage.

Objective: To assess baseline and clinical outcome details in octogenarians compared to younger stroke patients treated with intravenous alteplase.

Methods: Data on patients treated with alteplase within 4.5 h from stroke onset were prospectively collected from January 2008 until November 2013. Patients were categorized in two groups, younger and older than 80. Baseline and outcome details between groups were compared.

Results: 260 patients were included in this study, 140 male and 120 female, mean age 69 ± 11.5 (range 28–90). There were 19.6 % (51) octogenarians; 13 % of male patients and 28 % of female patients. 23.5 % (12) octogenarians and 15.8 % (33) younger patients had "time-to-treatment" longer than 3 h. There was no statistically significant relationship between age and previous history of hypertension; modified Rankin Score at admission or post-thrombolytic intracranial haemorrhage. "Time-to-treatment" >3 h was not related to post-thrombolytic intracranial haemorrhage in any group. Results indicate that there was statistically significant relationship between age and mortality (Pearson Chi Square = 21.3, $p < 0.001$), indicating that the mortality rate is higher in octogenarians. Patient age and atrial fibrillation are statistically significant related (Pearson Chi Square = 17.9, $p < 0.001$), indicating that the FA is more likely in older patients.

Conclusions: Among patient who receive thrombolytic therapy for ischemic stroke the octogenarians have greater risk of death but not of post-thrombolytic intracranial haemorrhage.

Disclosure: Nothing to disclose.

EP2207

Cardiac troponin T changes in acute ischemic stroke

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Introduction: Elevation of cardiac troponin T (cTnT) in serum reflects myocardial injury, but it was also observed in other conditions with cardiac injury including acute ischemic stroke. The objective was to identify the relationship between elevated cTnT and stroke severity, location and outcome.

Methods: cTnT levels were prospectively performed in 385 patients with different subtypes of acute ischemic stroke admitted in NICU within 72 h of onset, as TOAST criteria. The patients were divided into two groups: an elevated cTnT (group 1) (n = 42) and a normal cTnT (group 2) (n = 343). The short-term prognosis was assessed by 30-days modified Rankin Scale responder analysis and the NIHSS. Serum cTnT levels were determined using a high sensitive Troponin T assay (Roche Elecsys Troponin, Mannheim, Germany), cut-off value at 0.01 ng/mL. Statistical analysis was performed.

Results: Serum cTnT level was elevated in 10.91 % (42/385) of patients. cTnT positivity on admission is an independent and powerful prognosis predictor in acute ischemic stroke. It was observed more frequent insular lobe involvement in elevated cTnT group (17/42) (31 %) than in group 2 (55/343) (16 %) ($p = 0.040$). Stroke severity was greater in elevated cTnT group. The outcome was worse in elevated cTnT group as compared to group 2 (13/43) (30.95 %) vs. (68/343) (19.82 %) ($p = 0.013$).

Conclusions: cTnT in acute ischemic stroke is a marker of stroke severity, of insular lobe lesion and of prognosis prediction. cTnT is a highly specific and sensitive marker of myocardial damage in acute ischemic stroke due to insular lesion that induces disturbances of autonomic balance.

Disclosure: Nothing to disclose.

EP2208

Imagistic and clinical correlations in progressive ischemic stroke

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Introduction: Progressive ischemic stroke (PIS) represents a particularly form of stroke with a worsening clinical course, more specific an alteration of the neurostatus with consecutive examinations.

Methods: The studied group consisted in 51 patients. Based on the clinical and imagistic criteria they were diagnosed with PIS. Considering the time elapsed from the debut to the aggravation of the neurological symptoms, patients were divided in early worsening of the neurological status (24–36 h since the debut of the stroke) and late worsening of the neurological status (36 h up to 1 week). The methods used to assess the patient's neurostatus were the NIH stroke scale and notable changes in the neurological deficits. Complementary lab tests and neuro-imaging -computed tomography (CT) and magnetic resonance were performed also. Risk factors, affected arterial territory, associated neurological deficits, extracerebral complications and the aspect of the cerebral lesions in the CT performed at hospital admittance, were analyzed as well.

Results: Out of all ischemic strokes in our clinic, 4.70 % have been PIS. Motor deficits were the most frequent neurological signs(88.23 %). Hypertension was the first incriminated risk factor (94.1 %), followed by diabetes mellitus (29.41 %), hypercholesterolemia (28.29 %) and atrial fibrillation (23.52 %). In 17.64 % it has

been noticed early hypodense brain lesions. Early worsening of the neurological status was present at 47.05 % and the rest of 52.94 % had a late worsening.

Conclusions: The progression of the ischemic strokes is a multifactorial, dynamic process, probably triggered by intracerebral events, followed by systemic events.

Disclosure: Nothing to disclose.

EP2209

Lipoprotein-associated phospholipase A2 as a vascular-specific inflammatory enzyme related to plaque vulnerability is an independent predictive marker of ischaemic stroke and coronary heart disease

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Introduction: Inflammation plays important role in plaque vulnerability. Lipoprotein-associated phosholipase A2 (LP-PLA2) hydrolyses oxidized phospholipids (generated in atherosclerotic plaques by oxidative stress) and produces lyso-phosphatidylcholine and oxidized fatty acids which are strong attractants for monocytes and macrophages. The inflammatory progression reduces fibrotic cap of plaque and increases a rupture-proneness of plague. The increased serum level of LP-PLA2 is perspective predictive marker of ischaemic stroke and myocardial infarction.

Methods: Material consists of 436 subjects divided in 4 subgroups.

1. Ischaemic stroke (IS)($n = 171$), mean age 69 ± 11 years, men 52 %.

2. Coronary artery disease (CAD)($n = 87$), mean age 70 ± 9 years, men 32 %.

3. Arterial hypertension (AH)($n = 124$), mean age 60 ± 10 years, men 46 %, healthy controls(C)($n = 56$), mean age 47 ± 13 years, men 55 %.

In all subjects: Neurological and cardiological examinations, IS confirmed by CT/MRI, SPECT, battery of biochemical/haematological investigations, LP-PLA2 using ELISA, intima-media thickness (IMT) using ultrasonography by radio-frequency data analysis, augmentin index (Alx) and pulse wave velocity (PWV) using aplanation tonometry, Alx and PWV are indices of arterial stiffness. Statistical software STATISTICA Base Cz Version10, Kruskal–Wallis test, linear regression and Pearson correlation coefficient.

Results: The study showed statistically higher values all followed parameters in IS, CAD, AH comparing to C ($p < 0.01$–0.0001). Close correlation between LP-PLA2 and IMT, arterial stiffness was documented in all followed groups.

Conclusions: Our results documented significant changes in LP-PLA2,IMT and arterial stiffness in all followed groups (IS, CAD, AH) comparing to C. The measurement of LP-PLA2, IMT and arterial stiffness are very useful parameters for assessing cerebrovascular and cardiovascular risk. They represent significant prognostic power to ascertain subjects with increased risk for onset of cerebrovascular and cardiovascular events.

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Disclosure: Nothing to disclose.

EP2210

Tumour mimic due to an anatomical variant - bilateral anterior cerebral artery and Heubner's artery territory infarction

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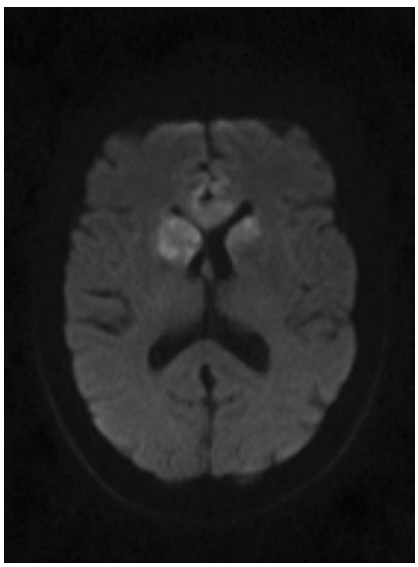
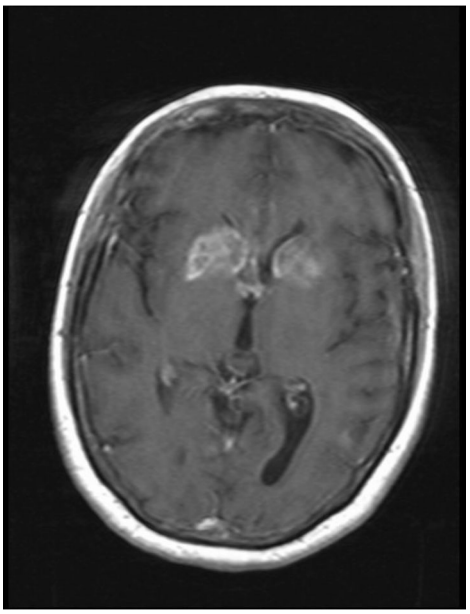
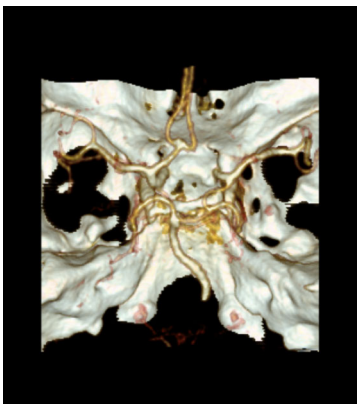
Introduction: Bihemispherical lesions that infiltrate the corpus callosum and enhance with Gadolinium generally have a poor prognosis. Butterfly glioma and central nervous system lymphoma are the two most common causes that can present with this type of lesions on MR-imaging. However, more benign options should not be ignored.

Case report: A 56-year-old woman presented at the Emergency Room with an acute abulia and aimless, involuntary movements of the right arm. After this abated somewhat, she displayed a persisting change of personality; she remained indifferent and detached. MR FLAIR T2 sequences of the brain showed bilateral hyperintensity in the genu of the corpus callosum, caudate nuclei, anterior limb of the internal capsule, lentiform nuclei; with strong enhancement on T1 sequences after intravenous injection of Gadolinium.

Methods: Additional diffusion-weighted images were suggestive of recent ischemia. CTA of the circle of Willis demonstrated an anatomical variant—the right A1 segment was absent. Follow up MRI after 1 month showed lessening of Gadolinium enhancement.







Conclusions: Bilateral ACA and Heubner's artery infarction can appear as a tumour on MR imaging. In patients who present with an acute onset of symptoms, a vascular etiology should be considered. In these cases CTA or MRA can demonstrate the absence or hypoplasia of one A1 segment as an anatomical variant.

Disclosure: Nothing to disclose.

EP2211

Abstract withdrawn

EP2212

The evaluation of aggregation activity of platelets in patients with ischemic stroke after i.v. thrombolysis and its influence on reocclusion after successful recanalization therapy

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Introduction: The i.v. thrombolysis is effective in selected patients with acute ischemic stroke (IS). However there is high percent of reocclusion after successful recanalization therapy. The mechanisms of reocclusion and ways for its prevention are unclear.

Methods: 60 patients (42 males; age 61 ± 11 years, mean NIHSS 14 ± 4) with IS were treated with i.v. rt-PA thrombolysis according to ESO recommendations. The recanalization and early reocclusion rates documented by MR angiography were 51.7 % and 22.6 %. 60 patients with IS (39 males; age 64 ± 12 years; mean NIHSS 12 ± 4) were included in the control group. We evaluated the ADP-induced (ADP-A) and adrenalin-induced (Adr-A) platelets' aggregation 24 h after stroke onset.

Results: The ADP-A and Adr-A in patients after i.v. thrombolysis were 39.6 ± 8.8 % and 42.6 ± 11.5 %, greater than in patients of control group where ADP-A and Adr-A were 29.1 ± 9.7 % and 28.5 ± 12.3 % ($p < 0.05$). The ADP-A and Adr-A in patients after i.v. thrombolysis with reocclusion were 45.9 ± 10.5 % and 47.1 ± 14.2 %, greater than in patients without reocclusion where ADP-A and Adr-A were 36.2 ± 9.3 % and 39.5 ± 10.2 % ($p < 0.05$).

Conclusions: We demonstrated the increase of platelets' aggregation activity in patients after i.v. thrombolysis compared to control as well as in patients with reocclusion compared to those without reocclusion after i.v. thrombolysis. This may reflect the platelets' activation after thrombolysis. Additional data is needed to prove the necessity for antiplatelet therapy earlier than 24 h after i.v. thrombolysis.

Disclosure: Nothing to disclose.

EP2213

Endovascular treatment of acute basilar artery occlusion

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Introduction: The most effective therapeutic approach in management of acute basilar artery occlusion (BAO) has not been established yet. The aim was to evaluate safety and efficacy of multimodal endovascular treatment (EVT) of acute BAO, including bridging therapy (intravenous thrombolysis [IVT] with subsequent EVT).

Methods: In the retrospective study, the set consisted of 62 BAO patients (46 males; mean age 58.7 ± 12.5 years) with radiologically confirmed BAO. Following data was collected: baseline characteristics, risk factors, pre-event antithrombotic treatment, neurological deficit at time of treatment, time to therapy, recanalization rate (with successful recanalization defined as Thrombolysis in Cerebral Infarction score 2–3), post-treatment imaging findings. 30-day and 90-day outcome was assessed using modified Rankin scale (mRS) with good clinical outcome defined as 0–3 points.

Results: Successful recanalization was achieved in 91.9 % patients. Stepwise binary logistic regression analysis identified presence of arterial hypertension (OR = 0.121, 95 % CI: 0.028–0.531; p = 0.005) and treatment type—the use of bridging therapy (OR = 6.64, 95 % CI: 1.56–28.1; p = 0.01) as significant independent predictors of good 30-day outcome and, time from symptoms onset to treatment (OR = 0.714, 95 % CI: 0.543–0.939; p = 0.016)) as significant independent predictor of good 90-day outcome.

Conclusions: Data in this series showed that multimodal EVT was an effective recanalization method of acute BAO. Bridging therapy was associated with better 30-day clinical outcome. EVT should be started as soon as possible after IVT and not considered only as a rescue strategy. Supported by IGA MH CR grants NT/11046-6/2010, NT/11386-5/2010, NT/13498-4/2012, and by the grant project CZ.1.05/2.1.00/01.0030.

Disclosure: Nothing to disclose.

EP2214

Symptomatic cerebral fat embolism: long-term follow-up

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Introduction: Symptomatic cerebral fat embolism (CFE) is a rare complication after traumatic injury or orthopaedic surgery. It may present with an altered state of consciousness, various neurological signs and is diagnostically challenging. Data about long-term follow-up are missing so far.

Methods: After identifying nine patients with CFE in the medical records and revising the clinical signs and the diagnostic process we performed a telephone interview targeting clinical course after discharge, neurological impairment and quality of life at present, using the Barthel Index.

Results: All nine patients showed severe neurological deficits in the beginning, including disturbance of consciousness from somnolence to coma. On follow-up 3–58 month after the insult two patients had died. The other patients had either recovered completely or showed only minor neurological deficits after rehabilitation even in cases with initial coma. They were nearly independent in daily life and needed only minimal assistance.

Conclusions: The prognosis of CFE can vary. Most patients had a good outcome after long-term follow-up. We conclude that patients with an unexplained coma after traumatic injury or orthopaedic surgery a diffusion-weighted MRI needs to be performed to find the pattern of disseminated hyperintense lesions in the white matter that are associated with CFE.

Disclosure: Nothing to disclose.

EP2215

Inracranial varicella zoster virus vasculopathy manifesting as transient ischaemic attacks

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Introduction: Intracranial vasculopathy associated with varicella zoster virus (VZV) infection is a rare cause of transient ischaemic attacks (TIA's) after Ramsay-Hunt syndrome, with ipsilateral cerebral hemisphere most often affected.

Case report: A 62 year-old male without vascular risk factors had Waldenstrom macroglobulinemia since 2010. In February 2013, while being on chemotherapy, he developed a left Ramsay-Hunt, treated with acyclovir. In August 2013, he presented repeated transient episodes of right motor deficits over 2 weeks, suggestive of TIA's. Brain DWI MRI revealed several acute ischemic lesions in the left middle cerebral artery (MCA) territory (small cortical frontal and parietal lesions, lenticular and caudate nucleus); angio-MRI showed a severe proximal left MCA stenosis; blood analysis, cervical vessels ultrasonography, 24 h Holter, transthoracic echocardiography, HIV, hepatitis and syphilis serologies were normal; CSF revealed 6 cells/mm^3 and PCR for VZV was positive. The patient was treated with acyclovir (10 mg/kg/day) for 21 days and prednisolone (1 mg/kg/day) for 5 days. He had no new focal signs during admission. He was discharged on valacyclovir, and had no further symptoms during the follow-up. Serial assessments with transcranial Doppler and repeated angio-MRI showed maintenance of MCA stenosis. Repeated CSF analysis showed 2 cells/mm^3 and PCR for VZV was negative.

Conclusions: VZV vasculopathy is rare but must be considered in the differential diagnosis of patients with cerebral vascular events, particularly if immunocompromised. This case of VZV vasculopathy has also the particularity of involvement of a large intracranial artery, while involvement of both large and small arteries is the most common presentation.

Disclosure: Nothing to disclose.

Clinical neurophysiology

EP2216

Navigated repetitive transcranial magnetic stimulation in treatment of spasticity

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Introduction: Our aim is to assess the efficacy of different types of navigated repetitive transcranial magnetic stimulation (rTMS) in modulating lower limb spasticity.

Methods: Fifteen patients (10 males, 5 females, mean age 46 ± 8.6 years) with secondary progressive multiple sclerosis and lower spastic paraparesis received 10 sessions rTMS over the motor hotspot of the tibialis anterior muscle in the primary motor cortex

with 80 % of motor threshold [ten patients underwent intermittent theta burst stimulation (iTBS) (frequency 30 Hz, burst frequency 5 Hz, number of pulses 3, number of bursts 10, total number of pulses 30), five patients high-frequency rTMS (10 Hz)]. We assessed Modified Ashworth Scale (MAS), Modified Fatique Impact Scale 2 (MFIS 2), Expanded disability status scale (EDSS), Kurtzke Functional Systems Score (FSS) and Spasticity Subjective Evaluation Scale (SSES), before and at the end of rTMS session, 2 and 12 weeks after.

Results: Both iTBS and high-frequency rTMS sessions significantly reduced MAS (3.0 [3.0; 3.0] before; 2.0 [1,0; 2,0] after; $p = 0.01$); MFIS 2 and SSES scores. We haven't defined any significant difference between our groups. These effects were persisting for 2 weeks after the end of the stimulation protocol in all patients and remained at the same level in a half of them in 3 months.

Conclusions: Our results indicate evident efficacy of both types of rTMS in treatment of severe spasticity. We currently move forward and include more patients with spasticity caused by variable range of disorders.

Disclosure: Nothing to disclose.

EP2217

Use of excitatory deep repetitive transcranial magnetic stimulation with the H-coil to improve motor planning in Parkinson's disease: evidence from sensorimotor rhythms event-related desynchronization

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Introduction: To investigate the clinical and neurophysiological effects of a combined prefrontal-primary motor cortex repetitive transcranial magnetic stimulation (rTMS) in Parkinson's disease (PD) using the H-coil.

Methods: Twenty patients (3F; 63 ± 9 years old; PD duration: 6 ± 3 years) were included and underwent 12 deep rTMS sessions in 4 weeks. Excitatory 10 Hz rTMS was applied over M1 contralateral to the patient's worse side (WS) and over the bilateral prefrontal cortices. Motor control was assessed before and after deep rTMS, OFF medication, using clinical (UPDRSIII, lateralized scores, timed arm tapping, and Nine-Hole Peg Test) and neurophysiological measurements (Event-Related Desynchronization (ERD) of the mu and beta sensorimotor rhythms during self-paced WS wrist extensions).

Results: No drop-outs or adverse events were recorded. Our results showed that UPDRSIII (global and subscores) and timed tests significantly improved after treatment ($p < 0.001$). Mu and beta ERD latency onsets were also significantly increased after treatment (Mu: −1,237 ± 177 ms before, and −2,024 ± 215 ms after; beta: −1,247 ± 151 ms before, and −2,229 ± 179 ms after; $p < 0.01$).

Conclusions: Deep rTMS is a safe treatment that improved motor symptoms and modulated the cerebral activity related to motor planning. The delayed mu and beta ERD shows that deep rTMS facilitated the activity of hypofunctioning cortico-striato-thalamo-cortical circuits, probably through dopamine release. This study highlights the importance of the H-coil for rTMS in PD, and the importance of repeating the sessions for more than 2 weeks. Further placebo-controlled, randomized studies are needed to assess the therapeutic efficacy deep rTMS and its consequences on cortical motor control.

Disclosure: Nothing to disclose.

EP2218

Use of sLORETA to investigate cortico-thalamo-cortical impairments in normoacoustic tinnitus sufferers

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Introduction: This electroencephalographic (EEG) study aimed to study and localize resting-state activity, auditory and cognitive evoke-related potentials (ERPs) in normoacoustic tinnitus sufferers.

Methods: 17 medication-free normoacoustic subjects with chronic, unilateral high-pitched tinnitus (6F, mean age 43.6 ± 9.8 years, mean disease duration 22 ± 35 months) underwent resting-state EEG (29 scalp electrodes, 5 min eyes opened, 5 min eyes closed) and auditory oddball paradigm (80 % 1,000 Hz frequent stimuli, 20 % rare stimuli at 2,000 Hz) for ERPs analyses (N1, P2 and P300). Cortical 3D distribution of current source density (CSD) of EEG data was computed with sLORETA. Results were compared with 17 healthy controls (9F, mean age ± SD 45.7 ± 15.1 years) and correlated with psychoacoustic measures.

Results: Eyes opened, patients had lower sources of alpha2 (10.5–12 Hz), beta2 (18.5–21 Hz) and beta3 (21.5–30 Hz) rhythms in the left inferior parietal lobule. Eyes closed, patients had decreased alpha2 sources in the left inferior temporal and post-central gyri, and low gamma sources in the left middle temporal gyrus. Such decreased activity did not correlate with patients' clinical features. N1 had shorter latencies in patients for both rare and frequent stimuli. P2 had shorter latencies only for the rare condition. P300 did not differ between groups. SLORETA showed decreased sources of ERPs in the left inferior temporal gyrus in patients.

Conclusions: We showed a cortico-thalamo-cortical involvement in normoacoustic tinnitus patients. Decreased CSD and shorter ERP latencies suggest a hyperexcitability of the thalamo-cortical circuits involving the left inferior temporal and parietal lobules.

Disclosure: Nothing to disclose.

EP2219

Evaluation of brainstem involvement in multiple sclerosis

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Objectives: The aim of the present study was to determine the optimum method to detect brainstem lesions in patients with MS.

Methods: 72 patients with the diagnosis of relapsing-remitting MS according to the revised McDonald's criteria were prospectively included in the study. Expanded Disability Status Scale (EDSS) score and brainstem functional system score (BSFS) (part of the EDSS evaluating brainstem symptomatology) were calculated. MRI was performed on 1.5T and T1, T2, PD and FLAIR sequences were analyzed for presence of brainstem lesions. Auditory evoked potentials (AEP) and ocular and cervical vestibular evoked myogenic

potentials (oVEMP and cVEMP) were performed according to the standardized protocol.

Results: From 72 patients, 18 (25 %) had clinical involvement of the brainstem. MRI showed brainstem involvement in 29 (40 %) patients. Of the neurophysiological tests, AEP showed pathological result in 16 (22 %) patients, oVEMP in 36 (50 %) patients, cVEMP in 18 (25 %) patients, and VEMP (combination of oVEMP and cVEMP) in 45 (63 %) patients. VEMP detected brainstem lesions in higher percentage than clinical examination, MRI and AEP, which was statistically significant (<0.0001, 0.012 and <0.0001, respectively).

Conclusions: Results of the present study have shown that VEMPs are the best method to detect brainstem lesions in multiple sclerosis and that they detect them significantly better than clinical examination, AEP or MRI.

Disclosure: Nothing to disclose.

EP2220

Corticospinal reserve predicts walking improvement to deep rTMS with H-coil in people with progressive multiple sclerosis

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Introduction: Walking impairment affect up to 85 % of subjects with multiple sclerosis, impacting on quality of life. High-frequency repetitive transcranial magnetic stimulation (rTMS) enhances corticospinal plasticity, potentially favouring effects of neurorehabilitation. The H-coil allows deeper magnetic fields compared with traditional stimulators. In a preliminary study, we found that rTMS with H-coil enhances improvement in walking after neurorehabilitation. We aimed at replicating the study and at combining results with those of the previous study in order to explore correlations with baseline features.

Methods: We randomized 20 patients with progressive MS into real ($n = 10$) and sham-placebo rTMS ($n = 10$), who underwent 11 stimulation sessions. Walking speed (10 mt test) and endurance (2 and 6 min Test) were assessed at baseline and at the end of treatment, as well as modified Ashworth Scale (MAS), VAS for spasticity and pain, Fatigue Severity Scale, EDSS, MS walking scale-12, PASAT and NHPT.

Results: Compared with sham, real rTMS group had a significant improvement in 10MWT and Ashworth, confirming data from a previous pilot study. When pooling data with the latter study, a strong correlation with clinical improvement in walking tests was found exclusively in the real group.

Conclusions: Resting-motor-threshold (RMT) results from the combination of corticospinal excitability and of the amount of corticomotor fibers available for conduction. While rTMS mainly acts on the former mechanism, the latter is a limiting factor in the presence of corticospinal damage. In this condition, RMT could be considered as a therapeutic reserve index, being predictive of therapeutic response to corticospinal neuromodulation.

Disclosure: Nothing to disclose.

EP2221

Prolonged peri-ictal clinical-EEG alterations in patients with PCDH19 mutation

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Purpose: Protocadherin coding gene (PCDH19) is a major gene in female patients with infantile onset epilepsy, associated with variable degree of mental retardation and autistic features with obsessive/hyperactive traits. PCHD-19-related epilepsy is characterized by febrile and afebrile cluster of seizures with prominent involvement of the fronto-temporal regions; status epilepticus can occasionally occur. We aim to provide further electroclinical insight about the clinical EEG features of the seizures cluster in benign forms of PCDH19-related epilepsy.

Methods: We selected patients with drug resistant PCHD19-related epilepsy, without severe mental retardation or severe psychiatric features. The patients underwent video-EEG-recordings, clinical ± neuropsychological evaluation at their baseline, during and after the cluster of seizures.

Results: 10 patients has been selected. All of them had mild cognitive impairment, normal EEG at baseline and recurrent clusters of a few brief seizures (1-3 days) associated with variable degrees of cognitive/behavioural alterations persisting for days to weeks after seizures clusters.

Long-lasting peri-ictal video-EEG recordings were obtained in 6/10 patients; 6/6 had prolonged peri/post-ictal EEG slowing (days to weeks) and 3/6 subjects also had multifocal spikes/slow waves, in 1 case associated with multifocal jerks and in 1 case with several subtle morpheic motor seizures.

Conclusions: Most PCDH19 patients share peculiar neuropsychological profile and ictal electro-clinical features suggesting both an ictal involvement and a more persistent impairment of the fronto-temporal limbic structures.

In our patients, we documented furthermore the frequent recurrence of more prolonged clinical-EEG alterations, associated to the typical seizures clusters, possibly reflecting a fronto-limbic status-like condition.

Disclosure: Nothing to disclose.

EP2222

The evaluation of the A wave detected patients in an electrophysiology laboratory

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Introduction: A waves are present in at least one nerve in 5 % of the clinically asymptomatic subjects; this is about 65 % in subjects with polyneuropathy. In this study we evaluated the patients with detected A waves according to their diseases and electrophysiologic data.

Methods: The patients referred to our EMG laboratory in Istanbul Education and Research Hospital between January 2010 and September 2013 were evaluated retrospectively. EMG and nerve conduction studies of patients with A waves detected in F wave studies were selected and classified according to their results.

Results: Data from 64 patients were obtained from their clinical records and electrophysiological tests. 41 patients were polyneuropathy (64.06 %), 7 patients were lombar spinal pathology (10.94 %) and 2 had normal electrophysiological data (3.12 %). Forty nine of the patients diagnosed with polyneuropathy were at the early stage and pre-diagnosed as Guillain–Barre syndrome. Twelve patients were diagnosed as motor demyelinating, 21 were sensorymotor demiyelinating, 8 were sensorymotor axonal and 8 were sensorymotor mixed type polyneuropathy. Two of the other polyneuropathy patients were multifocal motor polyneuropathy, one hereditary polyneuropathy, one chronic inflammatory demyelinating polyneuropathy, one diabetic polyneuropathy and the last one was *n*-hexane polyneuropathy. Spinal

pathologies were L5 and S1 radiculopathies, lombar trauma and spina bifida.

Conclusions: A waves can be seen in normal subjects and anterior root pathologies but mostly in polyneuropathies especially in the acquired polyneuropathies. They must be recognized well, differentiated from F waves and their presentation must alarm clinicians as an early sign of an acquired polyneuropathy.

Disclosure: Nothing to disclose.

EP2223

Tongue somatosensory evoked potentials: evaluation of the brainstem involvement in patients with early multiple sclerosis

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Objectives: The aim of this study was to determine the efficacy of tongue somatosensory evoked potentials (tSSEP) in evaluation of brainstem involvement in patients with early multiple sclerosis (MS).

Methods: tSSEP was performed on ten healthy volunteers and 29 patients with first clinical episode of a demyelinating event suggestive of MS. Obtained data were compared between the two groups, and tSSEP findings of MS patients were correlated with clinical and MRI data.

Results: MS patients had statistically significant prolongation of N1, P1 and N2 latencies on the left side compared with healthy controls (17.8 ± 3.5 vs 15.2 ± 1.3, $p = 0.004$; 23.9 ± 3.3 vs. 20.8 ± 1.0, $p = 0$; 29.9 ± 4.2 vs. 26.7 ± 2, $p = 0.01$, respectively) and P1 and N2 on the right side (23.8 ± 3.5 vs. 20.8 ± 1.3, $p = 0.04$; 30.3 ± 3.8 vs. 27.3 ± 1.9, $p = 0.01$, respectively).Out of the 29 MS patients 8 (28 %) had clinically evident involvement of the brainstem and 19 (66 %) had brainstem lesions demonstrated on brain MRI. There was 20 MS patients with prolonged latencies of tSSEP on either side no clinical signs of brainstem dysfunction and this difference was statistically significant ($p < 0.0001$). As well, tSSEP detected brainstem lesions in higher percentage than MR, reaching statistical significance ($p < 0.039$).

Conclusions: tSSEP is an efficient method for evaluating the afferent trigeminal pathway in patients with early multiple sclerosis, more sensitive than clinical evaluation and radiological imaging in the detection of brainstem lesion.

Disclosure: Nothing to disclose.

EP2224

Abnormal subclinical thermal sensory perception in 3 cases of ciguatera intoxication

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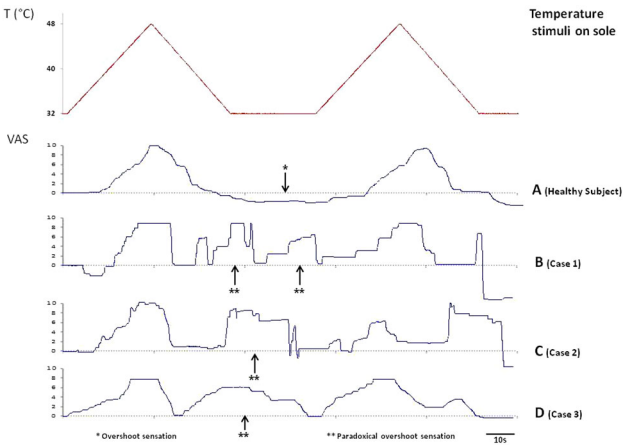
Introduction: The most striking expression of ciguatera intoxication is paradoxical perception of thermal sensation. We used a recently described psychophysical testing to examine the thermal perception abnormalities in three patients with such intoxication.

Methods: Three female patients (named B,C and D, in the figure, aged 35–38 years) presented gastrointestinal and neurological symptoms after ingestion of Caribbean fish. They reported paresthesias and abnormal temperature sensation for weeks, although had no such complaints at neurophysiological evaluation. We applied temperature stimuli consisting on slow increase or decrease of temperature (0.5°/s) from 32 °C to heat or cold pain. Subjects asked to do continued (dynamic) expression of their sensation through an electronic visual analog-scale (VAS) device. Healthy volunteers (one example named A in figure), show overshoot sensation after heat or cold pain (figure*; Medici et al. 2013). We also studied nerve conduction in sural and median nerves (NCS), sympathetic sudomotor skin responses (SSR), contact-heat-evoked-potentials (CHEPs) and quantitative sensory testing (QST).

Results: Patients had normal neurological examination, NCS, SSR, CHEPs and QST (except for one patient who had abnormally enhanced sensory threshold for cold and heat to stimuli to the feet). However, no overshoot cold sensation was observed in any of them, after heat pain in the feet. Instead, they showed a paradoxical large and long-lasting heat sensation, particularly in sole (Figure).



Conclusions: The abnormal behaviour of our patients after heat pain stimuli may reflect the disturbances on thermal perception, frequently observed during ciguatera poisoning. Small nerve fibers dysfunction can be reliably evidenced employing dynamic psychophysical testing.

Disclosure: Nothing to disclose.

EP2225

Open label pilot study of urethral injections of botulinum toxin to treat women in urinary retention due to Fowler's syndrome

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Introduction: Urinary retention is uncommon in women, and one cause is a primary disorder of urethral sphincter relaxation (Fowler's Syndrome). This aim of this study was to assess the efficacy and

safety of urethral sphincter injections of botulinum toxin in women with Fowler's Syndrome. Methods: In this open label pilot study, ten women with mean age 40.2 years(25–65) with a primary disorder of urethral sphincter relaxation (elevated UPP, sphincter volume and abnormal EMG) presenting with obstructed voiding (n = 5) or in complete urinary retention (n = 5) were recruited from a single tertiary referral centre. Symptoms were assessed using the IPSS questionnaire, urinary flow and post-void residual volume. After 2 % lidocaine injection, 100 U of onabotulinum toxin type A was injected into the striated urethral sphincter, divided on either side, under EMG guidance. Patients were reviewed at week 1, 4 and 10 post-treatment and symptoms were reassessed. The UPP was repeated at week 4.

Results: Three out of five women showed a 50 % improvement in flow rate. Four out of five women in complete retention could void spontaneously, with a mean flow rate of 11.4 ml/s at week 10. Six patients discontinued catheterisation at week 10. The mean static UPP improved from 113 (86–139) to 92.2 (66–151) cmH_2O at baseline. No serious side effects were reported. Seven out of ten women opted for repeat injections.

Conclusions: Botulinum toxin injections into the striated urethral sphincter are associated with clinically meaningful improvement in voiding parameters representing a safe and reasonable outpatient treatment for those with retention/obstructed voiding awaiting sacral neuromodulation.

Disclosure: Funding: Funding: an unrestricted educational grant from Allergan. National Health Service Research Ethics Committee approval by NHNN and ION joint REC Clinical Trial: Yes Registration Number: EUDRACT 2008-004858-33 RCT: No Subjects: HUMAN Ethics Committee: NATIONAL HOSPITAL FOR NEUROLOGY AND NEUROSURGERY and INSTITUTE OF NEUROLOGY JOINT RESEARCH ETHICS COMMITTEE Helsinki: Yes Informed Consent: Yes.

EP2226

Forehead sympathetic skin responses in determining autonomic involvement in Parkinson's disease

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Introduction: Sympathetic skin responses (SSR) and R–R interval variation (RRIV) are simple and reliable electrophysiological markers of autonomic nervous system (ANS) involvement in Parkinson's disease (PD). There is growing evidence to suggest varying degrees of autonomic involvement in different body parts in PD. The purpose of this study was to evaluate SSR of forehead and demonstrate any differences with SSR of upper and lower extremities in determining ANS involvement in patients with PD.

Methods: Twenty early stage, 20 advanced stage idiopathic PD patients and 20 healthy controls participated in this study. SSR of forehead, hands and feet, RRIV, orthostatic hypotension, QT intervals and dysautonomic symptoms were evaluated.

Results: Absent forehead SSR was determined unilaterally in 4, bilaterally in 7 early stage patients, and unilaterally in 4, bilaterally in 8 advanced stage PD patients (p = 0.000). However, absent extremity SSR was determined in at least 1 extremity of 3 advanced stage PD patients, and none of the early stage PD patients. No difference was noted in RRIV at rest between the three groups (p = 0.218); whereas RRIV at deep hyperventilation was lower in both early and advanced PD patients compared to controls (p = 0.014, p = 0.002, respectively).

Conclusion: We suggest that forehead SSR might be more sensitive than extremity SSR in determining ANS dysfunction particularly in the early stage of PD. Further research and biopsy studies should be performed on forehead SSR to support the role of this simple and noninvasive electrophysiologic examination as a diagnostic tool in autonomic involvement of early stage PD patients.

Disclosure: Nothing to disclose.

EP2227

Newly developed Waldenstrom's macroglobulinemia during immunomodulatory treatment for chronic inflammatory demyelinating polyneuropathy with antibodies against myelin-associated glycoprotein (MAG) and sulfatide

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Waldenstrom's macroglobulinemia (WM) newly developed in a patient with chronic inflammatory demyelinating polyneuropathy (CIDP) with antibodies against myelin-associated glycoprotein (MAG) and sulfatide who was undergoing treatment with intravenous immunoglobulins (iv-IG).

WM patients can develop polyneuropathies and few have anti-MAG and/or anti-sulfatide antibodies. Anti-MAG antibodies (4 % of WM) are associated with sensorimotor axon loss and demyelination and anti-sulfatide (5 % of WM) with sensory axonal loss. Rarely, both antibodies can be present, with a more severe phenotype.

Anti-MAG anti-sulfatide CIDP can present independently, not associated with WM.

There are no reports to date of patients with anti-MAG anti-sulfatide CIDP whom developed WM during immunomodulatory treatment with iv-IG. In addition, Rituxan has not been proven beneficial, as it has been previously reported for anti-MAG CIDP.

Seventy-six-year-old right-handed man presented with persistent numbness in his left foot, 3 months following artificial disc placement in his lumbar spine. No weakness reported, only sensory symptoms. No radicular signs on exam nor impingement on spine images. Serum anti-MAG and anti-sulfatide antibodies were elevated. NCS/EMG studies revealed CIDP with prolonged distal motor latencies. Patient underwent chronic therapy with iv-IG, which stabilized his symptoms. After six years of treatment, he newly developed WM. Subsequent Rituxan infusions did not improve his clinical picture nor NCS/EMG findings.

WM can newly develop in an autoimmune setting, such as anti-MAG and anti-sulfatide CIDP undergoing iv-IG treatment. This may reflect a possible induction of pathological B cell clone proliferation. Rituxan infusions did not improve the clinical symptoms nor NCS/EMG features of demyelination.

Disclosure: Nothing to disclose.

EP2228

Long-term evolution of EEG in Unverricht-Lundborg disease

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Introduction: EEG features Unverricht Lundborg Disease (ULD) is characterized by an alteration of the background rhythm (BR), paroxysmal abnormalities and photoparoxysmal response.

Objective: To evaluate the EEG features of patients with ULD.

Methods: We included 17 ULD patients confirmed genetically and having more than 15 years duration of disease progression at the time of inclusion. This study was conducted between 2005 and 2013. EEGs

were recorded at inclusion, 2 years and 5 years of follow-up. We divided our study population into 2 groups according to the activity of the disease (group 1: unstabilized patients with epileptic seizure and group 2: stabilized patients without seizure).

Results: 47 EEG were included. The mean duration of follow up was 26.5 ± 6.9 years. The average BR was 8.2 c/s. BR was normal in 30 records (64 %), slow in 17 (36 %). Epileptic abnormalities were found in 22 EEGs (47 %): generalized in 20, focused in 2, amplified by hyperventilation in 4 and photoparoxysmal response in 4. 18 EEG records in group 1 showed slow BR in 14 cases and generalized spike and wave discharges in 16. Concomitant myoclonus was recorded in 11 records. Photoparoxysmal response was found in 4 cases. 29 EEG records in group 2 showed normal BR in 27 records and generalized spike and waves discharges in 6.

Conclusions: This study shows that the progressive disappearance of EEG abnormalities in ULD is rather due to the treatment than a gradual spontaneous tendency to decrease over the years. EEG features in ULD depends on clinical stabilization.

Disclosure: Nothing to disclose.

EP2229

Transcranial direct current stimulation for seizure control in patients with Lennox–Gastaut Syndrome

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Introduction: Lennox–Gastaut Syndrome (LGS) is a relatively frequent and heterogeneous epileptic encephalopathy associated with several types of seizures with anti-epileptic drug resistance. Transcranial direct current stimulation (t-DCS) is a non-invasive and safe method tried in drug-resistant epilepsies. Our aim was to investigate the effect of t-DCS on the seizures of LGS patients.

Methods: Twelve patients (mean age 15.5; 6 males), diagnosed as LGS with their typical clinical and electroencephalographic (EEG) findings, were included after the signed consent of their legal guardians. All patients received anodal and cathodal stimulation (2 mA for 30 min on 3 consecutive days, with amplitude modulation at 12 Hz). Five patients also received sham stimulation (60 s stimulation gradually decreased in 15 s).

Results: Only two patients had more than 50 % decreases in their seizure frequencies by cathodal stimulation. However, sham stimulation of these two patients did not show any change in seizure frequency. One of them had type-1 lissencephaly and the other had normal magnetic resonance imaging (MRI) findings. Both had prominent focal EEG findings in comparison to non-responders. Longest positive effect of t-DCS lasted 1 month. On the other hand, anodal stimulation was not effective. No adverse effect has been reported.

Conclusions: Although our series was small, it can be suggested that cathodal t-DCS may be effective in selected patients with significant focal EEG findings despite a devastating epileptic syndrome. Anodal t-DCS is not effective for improving seizure outcome among LGS patients. Further studies with large series of patients are needed.

Disclosure: Nothing to disclose.

EP2230

Evaluation of the effect of modafinil on cognitive functions in patients with idiopathic hypersomnia with P300

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Introduction: Modafinil is a well-tolerated psychostimulant drug with low addictive potential that is used to treat patients with narcolepsy and other excessive sleepiness. Whereas favorable effects of modafinil on cognitive functions have been shown in a large number of studies, there are very limited number of reports presenting the effects of modafinil electrophysiologically. The aim of this study was to investigate the effects of modafinil on auditory p300 latency and amplitude electrophysiologically.

Methods: Eighteen patients (age range: 16-48) with a diagnosis of Idiopathic Hypersomnia (IH) were included in the present study. As a standard treatment, 200 mg/day modafinil was administered to each patient. P300 auditory test was performed for each patient before and at the end of 1 week of modafinil treatment.

Results: After 1 week of modafinil treatment, mean P300 latencies (at all electrode sites) were significantly lower than the latencies before the treatment (*P* values for Fz, Cz and Pz recording sites were 0.039, 0.002 and 0.004, respectively). An increase in the P300 amplitudes was detected only at Fz recording site, but not at Cz or Pz recording sites. (*P* values for Fz, Cz and Pz recording sites were 0.014, 0.100 and 0.05, respectively).

Conclusions: One week of modafinil treatment improved the cognitive performance, alertness and executive functions in IH patients. Our findings obtained electrophysiologically provide further confirmation for previous reports in which modafinil has been shown to exert favorable effects on cognitive performance, alertness and executive functions.

Disclosure: Nothing to disclose.

EP2231

Gastrocneumius Hoffmann-reflex in the diagnosis of various neurological diseases: correlation with clinical features

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Introduction: The Hoffmann reflex (H-reflex) is commonly used in the diagnosis of radiculopathies, but it has been investigated in many conditions. Although H-reflex technique seems simple there are some limitations to its interpretation. The aim of this study was to analyze gastrocneumius H-reflex parameters in various neurological diseases and investigate their correlation with clinical manifestation and final diagnosis.

Methods: H-reflex was done bilaterally from gastrocneumius medialis muscles in prone position. Peak to peak amplitudes of

M-wave and H-reflex, latency and H_{max}/M_{max} ratio were recorded. The data was supplemented by other electrophysiological parameters (for n.tibialis, n. peroneus and n.suralis), results of neurological examination and neurovisualization, and, if necessary, laboratory findings.

Results: 134 patients were studied (59 with S1 radiculopathies, 34 with disorder of central nervous system, 27 with polyneuropathies, 6 with peroneal neuropathies, 8 with sciatic neuropathy*). The S1* radiculopathies could be well confirmed in 50 (84.7 %) patients (low H_{max}/M_{max} ratio (6.7 ± 0.6) with prolonged latency), but 24 patients had decreased ratio also contralaterally without clinical manifestation there. The central nervous disorder could be confirmed in 22 (64.7 %) of 34 patients which had high H_{max}/M_{max} ratio (50.7 ± 3.6) with normal latency. In 12 patients (33.3 %) the electrophysiological results were controversial. H-reflex was helpful in 26 patients (96.3 %) with polyneuropathies, where the affection of proximal fibers was observed in 21 patients. H-reflex was helpful in sciatic *n*europathy and differential diagnosis of peroneal neuropathies.

Conclusions: Gastrocneumius H-reflex is a good diagnostic tool but caution must be exercised in the assessment of its results.

Disclosure: Nothing to disclose.

Epilepsy 1

EP2232

Prognosis of idiopathic generalized epilepsies patients with at least 10 years follow up and predictors of at least 5 years remission off medication

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Purpose: The idiopathic generalized epilepsies (IGEs) constitute nearly a third of all epilepsies. The aim of this study was to analyze long-term outcome in patients with IGE and predictors of at least 5 years seizure remission off medication.

Method: In this retrospective cohort study, we analyzed seizure outcome in 65 patients who had IGE with follow up for at least 10 years at single epilepsy center in Egypt.

Results: After a mean follow up of 13 years, 47 (72 %) of the patients remained free of seizures for at least 5 years throughout the duration of follow up. Among the seizure free patients, 38 (81 %) were taking AEDs and 9 (19 %) were off medication for at least 5 years. Among the nine patients with at least 5 years seizure remission off medication during the follow up period, none had epilepsy with GTCs only, seven patients were females, seven patients had more than 50 % normal EEGs of all EEGs done during follow up period, eight patients were on monotherapy low dose, one patient had sleep deprivation as precipitating factor for seizures. None of nine patients had three seizure types.

Conclusion: A significant proportion of the patients with IGE with at least follow up 10 years achieved at least 5 years seizure freedom. Good predictors for at least 5 years seizure remission off medication were female gender, normal EEGs more than 50 %, low dose monotherapy while bad predictors were epilepsy with GTCs only, three seizure types and sleep as precipitating factor.

Disclosure: Nothing to disclose.

EP2233

What do 'they' perceive about epilepsy?

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Introduction: Studies showed that epilepsy is one of the poorly understood diseases among public. We purposed to investigate the social attitude to epilepsy and perceived stigma of epilepsy among patients.

Methods: The study was approved by the Local Ethics Committee and designed as a cross-sectional, descriptive study. Participants consisted patients with various types of seizures, were randomly chosen from the epilepsy outpatient clinic. A questionnaire was developed and consisted of items about negative attitudes and perceived stigmatization.

Results: Of the 330 patients with epilepsy, mean age was 29.05 ± 11.31 years (range 13–74), 64.8 % were female and 35.2 % were male. See Table 1 for respondent demographics. The questions related to stigmatization showed that 41.8 % of patients felt different from other people without epilepsy. 39.9 % of the married patients with epilepsy who were diagnosed before their marriage stated that they did not tell about the disease to their partners before. Furthermore, 48.0 % of patients who had epilepsy during their education stated that their teachers and friends did not know about their illness. 37.4 % stated that they hided their illness at their work-place. 44.6 % had difficulty in finding job because of disease.

Conclusions: Studies showed that people from general public are not very knowledgeable about epilepsy. This leads to prejudice, stigmatization and inaccurate treatment. We would like to show the attitudes toward epilepsy and how it affects the lives of people with epilepsy.

Disclosure: Nothing to disclose.

EP2234

P-glycoprotein (Pgp) overactivity in pharmacoresistant epilepsy patients with focal cortical dysplasia compared to healthy controls measured using (*R*)-[^{11}C]verapamil PET and the Pgp inhibitor Tariquidar

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Introduction: Focal cortical dysplasia (FCD) is a common cause of pharmacoresistant epilepsy. P-glycoprotein (Pgp) expression was observed in reactive astrocytes in FCD, suggesting that overactivity at the blood–brain-barrier prevents antiepileptic drugs from entering target sites [1]. Recently, we could detect in vivo evidence for Pgp overactivity in the sclerotic hippocampus using positron emission tomography (PET) and the Pgp substrate (*R*)-[C-11]verapamil (VPM) together with the Pgp inhibitor Tariquidar (TQD) [2]. Here, we report the application of this methodology to three patients with FCD and pharmacoresistant epilepsy.

Methods: Three pharmacoresistant FCD patients (2 male, age 24–62 years) and 13 healthy controls (7 male, age 35–55 yeas) underwent VPM PET scans before and after TQD. Parametric maps of VPM-K_1, the plasma-to-brain transport rate constant, were generated for voxel-based analysis using SPM8. We hypothesize that VPM uptake at baseline and VPM increases after TQD would be reduced in brain areas with Pgp overacitivity in pharmacoresistant FCD.

Results: Compared individually against the group of 13 controls, all three FCD patients had reduced VPM-K_1 at baseline and reduced VPM-K_1 increases after TQD, both in close proximity to the area of FCD identified by MRI and the reduction also extended further to other cortical regions ($p < 0.01$).

Conclusions: Reduced VPM-K_1 at baseline and reduced increases in VPM-K_1 after TQD support Pgp overactivity in pharmacoresistant FCD patients not limited to epileptogenic areas, but also extending to other cortical regions, suggesting widespread abnormalities in FCD.

References:

[1] Sisodiya et al., Brain, 2002. 125:22–31.

[2] Feldmann et al., Lancet Neurol., 2013. 12: 777–785.

Disclosure: Nothing to disclose.

EP2235

Self-management education for adults with poorly controlled epILEpsy (SMILE): a randomised controlled trial protocol

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Introduction: Teaching people with epilepsy to identify and manage seizure triggers, implement strategies to remember to take antiepileptic drugs, implement precautions to minimize risks during seizures, tell others what to do during a seizure and learn what to do during recovery may lead to better self-management. No teaching programme exists for adults with epilepsy in the UK although a number of surveys have shown patients want more information.

Methods: This is a multicentre, pragmatic, parallel group randomised controlled trial to evaluate the effectiveness and cost-effectiveness of a two-day Self-Management education for epILEpsy (SMILE UK), which was originally developed in Germany (MOSES).Four hundred and twenty eight adult patients who attended specialist epilepsy outpatient clinics at 15 NHS participating sites in the previous 12 months and who fulfil other eligibility criteria will be randomised to receive the intervention (SMILE (UK) course with treatment as usual- TAU) or to have TAU only (control). The primary outcome is the effect on patient reported quality of life. Secondary outcomes are seizure frequency and psychological distress (anxiety and depression), perceived impact of epilepsy, adherence to medication, management of adverse effects from medication, and improved self-efficacy in management (mastery/control) of epilepsy. Within the trial there will also be a nested qualitative study to explore users' views of the intervention, including barriers to participation and the perceived benefits of the intervention. The cost-effectiveness of the intervention will also be assessed.

Results: Teachers have been recruited and the intervention piloted.

Conclusions: The full RCT is now underway.

Disclosure: Nothing to disclose.

EP2236

EEG as a prognostic tool for classic absence

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Introduction: The main purpose of this paper is to offer some guidance to expect the prognosis of typical absence from the EEG.

Methods: This was an observational study conducted from July 2006 to July 2012. Data of 42 newly diagnosed patients with typical absence seizures was collected retrospectively and analyzed.

Results: The mean time until seizure and EEG control for those with +ve 3 Hz. SWC during routine EEG recording was (9.9 ± 14.4) months. While the mean total follow up period for all cases were (19.3 ± 20.5). 100 % of patients with +ve 3 Hz. SWC during the third minute and after HV were controlled and 80 % of the overall no. of controlled patients in this study was found during third minute HV (p value = 0.049). The majority of the controlled patients with 3 Hz. SWC after HV and during second minute or third minute HV was prescribed only monotherapy.

Conclusions: Prognosis of typical absence was good yet the presence of the 3 Hz. SWC with late onset either during the third minute HV or even after had a better prognosis as regard; All of this group were controlled, monotherapy was used to control the majority of patients with late onset 3 Hz. SWC. These data was only significant for the association between the 3 Hz SWC and the percentage of control of absence seizures during the third minute HV (80 %) [p value = 0.049]. A multicenter study should be done in the nearby future.

Disclosure: Nothing to disclose.

EP2237

Abstract withdrawn

EP2238

Comparative effectiveness of the antiepileptic drugs (AEDs) levetiracetam, valproate and carbamazepine among patients aged 60 years and over with newly diagnosed epilepsy

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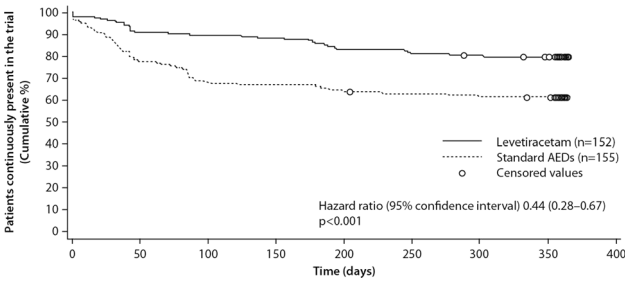
Introduction: The efficacy and safety of levetiracetam (LEV) were compared with those of the standard AEDs valproate (VPA) and carbamazepine (CBZ) among patients aged ≥60 years in a post hoc analysis of KOMET trial data (Trinka E, et al. J Neurol Neurosurg Psychiatry 2013).

Methods: Patients with ≥2 unprovoked seizures in the previous 2 years or ≥1 in the previous 6 months participated in this open-label, 52-week trial. Physicians chose CBZ as first-line treatment for patients with presumed focal and VPA for those with presumed generalised/unclassifiable epilepsy. Patients were randomised to CBZ/VPA or LEV with time to treatment withdrawal as primary outcome.

Results: 155 patients (aged ≥60 years; 103 focal, 52 non-focal) were treated with standard AEDs and 152 with LEV (104 focal, 48 non-focal). Time to treatment withdrawal was significantly longer for LEV compared with standard AEDs: HR (95 % CI) 0.44 (0.28–0.67), $p < 0.001$. Treatment withdrawal rates were numerically lower with LEV compared with standard AEDs at 6 (14.5 % vs 34.2 %) and 12 months (20.4 % vs 38.7 %). Time to first seizure [HR (95 % CI) 0.92 (0.63-1.35)], and seizure-freedom rates at 6 (65.6 % vs 62.9 %) and 12 months (61.8 % vs 59.1 %) were similar with LEV or standard AEDs. LEV-treated patients had a longer time to withdrawal due to adverse events [HR (95 % CI) 0.36 (0.20–0.62)] and there were fewer overall withdrawals due to AEs (11.2 % vs 26.5 %) suggesting better tolerability of LEV compared with standard AEDs.

Conclusions: LEV is an effective treatment option for elderly individuals with new-onset epilepsy.



[Time to treatment withdrawal-LEV vs standard AEDs]

Disclosure: UCB sponsored. All authors are employees of UCB Pharma.

EP2239

Non-expert use of quantitative EEG displays for seizure detection in the adult neuro-intensive care unit

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Introduction: Non-convulsive status epilepticus (NCSE) can only be recognized by continuous video-EEG in the neurological intensive care unit (NICU). Quantitative EEG display methods like amplitude integrated EEG (aEEG) and density spectral array (DSA) have been developed to facilitate EEG interpretation and may even be used by non-experts. We investigated whether these methods could be used by NICU personnel for seizure identification.

Methods: Ten patients with NCSE and ten control subjects without seizures were enrolled. EEG recordings of all patients were converted to aEEG and DSA, displayed simultaneously without conventional EEG. Two physicians and two nurses, who were trained for seizure recognition with both methods, analyzed the visual displays individually and marked seizure timings. Their results were compared statistically with those of the electroencephalographer.

Results: Participants analyzed 615 h of EEG data with 700 seizures. Overall, 63 % of the seizures were recognized by all, 15.6 % by three, 11.6 % by two, 8.3 % by one rater and only 1.5 % were missed by all of them. A cyclic pattern of seizures facilitated recognition, whereas bilateral independent seizures were more likely to be missed when compared with focal unilateral or generalized seizures. False positive rates were 1 per 2 h in the study and 1 per 6 h in the control groups. Interrater agreement was high ($k = 0.79$–0.81, $p < 0.001$). There was no difference in performance between physicians and nurses.

Conclusions: NICU personnel can be trained for seizure recognition using the digital EEG trend analysis methods. This may lead to early identification and treatment of NCSE.

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EP2240

Targeting hyperphosphorylated tau is a disease-modifying treatment in a post-status epilepticus rat model of temporal lobe epilepsy

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Introduction: To investigate whether treatment with sodium selenate, a drug that reduces the pathological hyperphosphorylation of tau by increasing protein phosphatase 2A (PP2A) activity, would reduce spontaneous seizures, neurodegeneration and glial activation in a post-status epilepticus (SE) rat model of temporal lobe epilepsy (TLE).

Methods: After 4 h of SE induced by systemic kainic acid (KA) injections, or control-saline injections, young-adult male Wistar rats ($n = 9$/group) were given continuous sodium selenate treatment (1 mg/kg/day), with a subcutaneous osmotic mini-pump for 2 months. In-vivo MRI and MRS was used to assess neuronal damage and glia activation 1 month post-injury. Video-EEG recording was used to evaluate the seizure frequency and duration both during the treatment and after the treatment. Molecular tests were used to assess levels of hyperphosphorylated tau and related pathologies.

Results: During the treatment, the post-SE rats with saline treatment got 1.4 seizures/day, and selenate treatment could reduce the frequency to 0.1 seizures/day. After the drug washout, the effect was sustained (8.6 seizures/day in saline group vs. 2.6 seizures/day in selenate group). Selenate treatment also decreased the neurodegeneration and glial activation reflected by MRS imaging and further confirmed by immunofluorescence imaging. The selenate treatment also reduced the volume of ventricles and increased the volume of hippocampus in post-SE rats.

Conclusions: Sodium selenate treatment can reduce spontaneous seizures and biomarkers for neurodegeneration and glial activation in a post-SE rat model of TLE.

Disclosure: Nothing to disclose.

EP2241

Dystrophin expression in an animal model for temporal lobe epilepsy

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Introduction: Duchenne muscular dystrophy is a genetic disorder caused by alterations in the dystrophin gene. Aside from progressive muscular degeneration, Duchenne muscular dystrophy is also associated with cognitive deficits such as impairment in expressive language, working memory, and attention. Moreover, recent

literature showed that the prevalence of epilepsy is higher in boys with Duchenne muscular dystrophy, suggesting that a lack of dystrophin may result in increased seizure susceptibility. We aimed to determine whether increased seizure susceptibility also results in an alteration in dystrophin expression within the central nervous system.

Methods: We evaluated dystrophin expression in adult amygdala kindled rats by analyzing dystrophin expression by Western blot and by immunofluorescence in several brain regions.

Results: Immunoblotting demonstrated that the various isoforms of dystrophin, including some of the isoforms that are present in skeletal muscle, are expressed differently in the hippocampus, cortex, and cerebellum of amygdala kindled rats. Dystrophin appeared to co-localize with both astrocytes and endothelial cells. Dystrophin was also expressed in Purkinje cells, where it was mainly localized within the membrane of both the soma and the dendrites.

Conclusions: In short, dystrophin is ubiquitously expressed in the brains of amygdala kindled rats.

Disclosure: Nothing to disclose.

EP2242

Abstract withdrawn

EP2243

Epilepsy impairs long-term functional outcome after different stroke subtypes

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Introduction: To determine the influence of post-stroke epilepsy on long-term functional outcome in stroke survivors.

Methods: This study is a prospective cohort study among 140 stroke survivors with a first-ever TIA, ischemic stroke, or intracerebral hemorrhagic (ICH) stroke, aged 18–90 years. After a mean follow-up of 10 years, we performed a follow-up assessment that included an evaluation for post-stroke epilepsy and functional outcome. Odds ratios for poor outcome on the modified Rankin Scale (mRS) (score > 2) and Instrumental Activities of Daily Living (IADL) (score < 8) were calculated using logistic regression analysis.

Results: One hundred twelve patients (80 %) with ischemic stroke, 4 patients (2.8 %) with TIA, and 28 patients (20 %) with ICH developed post-stroke epilepsy. Ischemic stroke patients with epilepsy more often had a poor functional outcome than those without, both on the mRS and IADL (mRS score > 2: 24.5 % vs. 9.2 %, $p = 0.001$; IADL < 8: 28.8 % vs. 14.6 %, $p = 0.02$). In this case, epilepsy occurred in 24.5 % of patients with cardioembolic stroke. Epilepsy was not related to functional outcome in patients with TIA and ICH. Multiple regression analysis revealed that epilepsy was an independent predictor of poor functional outcome after ischemic stroke assessed by mRS (mRS score > 2: odds ratio 4.02, 95 % confidence interval 1.33–8.60). In contrast, there was no such relation for IADL.

Conclusions: Epilepsy after stroke is a common problem that negatively affects functional outcome, even more than 10 years after ischemic stroke.

Disclosure: Epilepsy after stroke is a common problem that negatively affects functional outcome, even more than 10 years after ischemic stroke.

EP2244

Abstract withdrawn

EP2245

Epilepsies of child and adolescent

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Epilepsy is a public health problem in Senegal, with a prevalence of 8.3—14/1,000. It mainly affects children.

The objective of this work is to study the biographical aspects, phenotypic and evolutionary of epilepsy in a cohort of children in Senegal.

Patients and methods: This is a retrospective chart review of children with epilepsy followed up regularly at Fann University Hospital and Childreńs Hospital Albert Royer, July 2003 to December 2010. Inclusion criteria were: epilepsy aged under 16 years, regularly monitored for at least 3 years, with appropriate treatment, effective dose, with good adherence.

Results: We collected 522 children, aged 3 months to 16 years, with a sex ratio of 1.7 in favor of boys. The epilepsy was idiopathic in 57 % of children and non-idiopathic in 43 % of patients. Etiological factors were dominated by parental consanguinity, abnormal pregnancy and childbirth, infections of the central nervous system. In the group of idiopathic epilepsies not, the signs associated with epilepsy were language disorders (15.70 %), behavior (15 %) and motor deficits (10.32 %). 22.41 % of school children had learning difficulties sometimes leading to repetition or school exclusion.

Conclusions: The fight against epilepsy in Senegal implies an effective prevention policy which necessarily improving the socio-health and the fight against infections. This is the challenge of the Senegalese league against epilepsy.

Disclosure: Nothing to disclose.

EP2246

Concerns and questions with respect to epilepsy, antiepileptic drug (AED) treatment and pregnancy experiences from the German Pregnancy Registry (GRAP)

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Introduction: The German Registry of Antiepileptic Drugs and Pregnancy (GRAP) participates in the European Pregnancy Registry (EURAP) and offers nationwide free consultation service via mail or phone. The starting point of this study was the EURAP-NL (The Netherlands) report from 2012. We evaluated the German database.

Methods: We retrospectively analyzed all incoming questions that were addressed via email to GRAP by women with epilepsy, their relatives or physicians within a 4 year period (April 2009–April 2013). A total number of 106 inquiries were included. Characteristics of questioners, question topics, AED treatment regimes and timing of inquiry relative to the pregnancy were evaluated.

Results: The majority of questions were addressed by epilepsy patients (51.9 %, $n = 55$), followed by healthcare professionals (45.3 %, $n = 48$), in particular neurologists (34 %, $n = 36$). The three most common topics were related to congenital malformation risks associated with AEDs, AED treatment adjustments during pregnancy and demand of additional information material besides current guidelines. The most frequently AEDs mentioned were levetiracetam ($n = 40$), lamotrigine

(n = 39) and valproate (n = 18). More than half of the inquiries were asked outside the pregnancy period (51.2 %, n = 44).

Conclusions: This study showed similar to experiences in the Netherlands that there is an immense need of additional information for women with epilepsy and their physicians. Our results may help to detect information deficits in purpose to develop new guidelines for healthcare providers and establish further information and counselling materials for women with epilepsy.

Disclosure: Nothing to disclose.

Neuro-epidemiology; Neurorehabilitation

EP2247

Risk of cancer in relatives to patients with myotonic dystrophy: a population based cohort study

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Introduction: Myotonic Dystrophies (DM) are autosomal dominantly inherited neuromuscular disorders caused by unstable nucleotide repeat expansions. DM and cancer have been associated, but the pathogenesis behind the association remains unclear. It could relate to derived effects of the DM genotype or to a common underlying *trans*-acting genetic factor which might increase the risk of both cancer and enhanced mitotic repeat expansions. In the latter case, an increased risk of cancer would be expected also in non-DM relatives to DM patients. To elucidate this, we conducted a population based cohort study investigating risk of cancer in relatives to DM patients.

Methods: DM was identified using the National Danish Patient Registry and results of genetic testing. Information on cancer was obtained from the Danish Cancer Registry. We established a cohort of 5,757,565 individuals with at least one relative using the Danish Family Relations Database based on kinship-links in the Danish Civil Registration System. Familial aggregation of cancer was evaluated by (incidence) rate ratios (RRs) comparing the rate of cancer among relatives to patients with DM from 1977 to 2010 (exposed), with the rate of cancer among persons with a relative of the same type, but without DM (non-exposed).

Results: In first degree relatives to individuals with DM the adjusted RR of cancer overall was 0.89 (0.71–1.12) and 0.68 (0.37–1.12) before age 50 and 0.96 (0.74–1.23) at age 50 or older, respectively.

Conclusions: The present study does not support an increased risk of cancer in non-DM relatives to DM patients.

Disclosure: The study was supported by grants from the University of Copenhagen, the Lundbeck Foundation and the Danish Cancer Society.

EP2248

The prevalence of multiple sclerosis in Northern Portugal: results from a multisource population-based study

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Introduction: The prevalence of Multiple Sclerosis (MS) has been increasing worldwide and the north–south gradient of prevalence is becoming less evident on the Northern hemisphere. A population-based study performed 15 years ago in Portugal reported a lower prevalence estimate than the average for Western Europe. The aim of this study is to estimate the prevalence of MS in a well-defined geographical region of Northern Portugal (Entre Douro-e-Vouga).

Methods: Multiple overlapping sources were used to ascertain all cases from the reference population: records from hospitals in the region and the neighbouring regions; diagnostic databases of primary care physicians; and applications for social security disability benefits. The prevalence date was 1st of January 2013 and the reference population 274,859 inhabitants. Patient's neurologists were contacted to confirm a positive diagnosis based on MacDonald criteria and to retrieve clinical information.

Results: A total of 161 patients were identified after eliminating duplicates. The female to male ratio was 1.8:1 and the median age at onset was 30.0 (IQR 24.0; 39.0). Relapsing remitting forms accounted for 65 % of patients, secondary progressive for 21 % and primary progressive for 13 %. The prevalence was estimated in 58.6 patients per 100,000 (95 % CI, 49.9–68.4).

Conclusions: In this study we report a higher prevalence of MS than what had been previously described in Portugal, but still far from the values recently reported in other southern European countries.

Disclosure: Nothing to disclose.

EP2249

The effectiveness of the vestibular rehabilitation on the posturographic platform with biofeedback training of patients with dizziness and imbalance

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Introduction: The development of the rehabilitation methods of patients with vertigo and imbalance is one of the most pressing problems. The vestibular rehabilitation on the posturographic platform with biofeedback training can be an effective rehabilitation mean of the patients with dizziness and imbalance of various genesis.

Methods: The investigated group included 60 patients with vertigo and imbalance, who participated in the programme of rehabilitation on the posturographic platform with biofeedback training consisting of 10 repetitions, was performed every day 5 days a week. The patients aged 25–75 years. 40 % of patients were with unilateral vestibular loss, 28 % of patients were with multifactorial disequilibrium of the elderly, 5 % of patients were with transient ischemic attacks, 27 % of patients were with of phobic postural vertigo.

Results: A statistically significant improvement of the balance according to computer stabilometry was observed after the rehabilitation programme on the posturographic platform.

Conclusions: The use of the rehabilitation programme on the posturographic platform with biofeedback training is an effective method of vestibular rehabilitation of patients with dizziness and imbalance.

Disclosure: Nothing to disclose.

EP2250

Primary brain tumours incidence in Georgia: a 3-year prospective population-based study

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Introduction: In March 2009 a prospective population-based study was started in Georgia to define the incidence and describe other epidemiological data of malignant and non-malignant primary brain tumours.

Methods: Information from treatment facilities and diagnostic neuroimaging services was regularly collected by our representatives and stored in a cancer reporting form. Further verification was performed to ensure the completeness of data and absence of duplication.

Results: 1476 incident cases were indentified during a period of 3 years with the overall incidence rate of 10.48 per 100,000 person-years, age-standardised (AS) to the year 2000 US population. Non-malignant tumours constituted 62 % of all cases. There was a clear female preponderance in sex distribution (58 vs. 42 %, $p < 0.001$). Among individual histology types AS incidence rates were highest for meningioma (2.58/100,000), pituitary adenoma (1.38/100,000) and glioblastoma (0.49/100,000). The AS incidence rates were higher among females than males for all primary brain tumours (10.62 vs. 9.06/100,000) as well as for individual histologies except for glioblastoma, several other neuroepithelial and germ cell tumours.

Conclusions: Differences in rate values compared with 2004–2005 Central Brain Tumor Registry of the United States data may be explained by a higher percentage of unclassified tumours (38.5 %) in our study. Distribution of tumours by histology and sex was overall in line with published CBTRUS statistics.

Disclosure: Nothing to disclose.

EP2251

Neurological emergencies in an interdisciplinary University based Emergency Department

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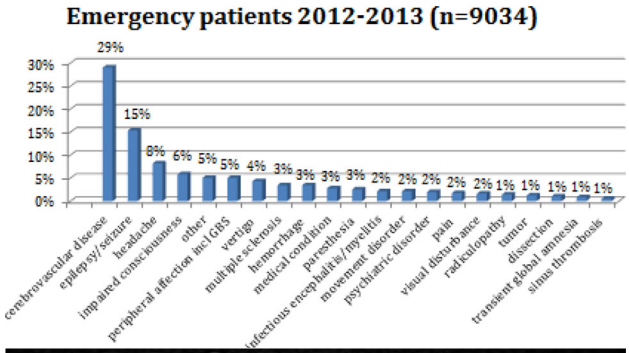
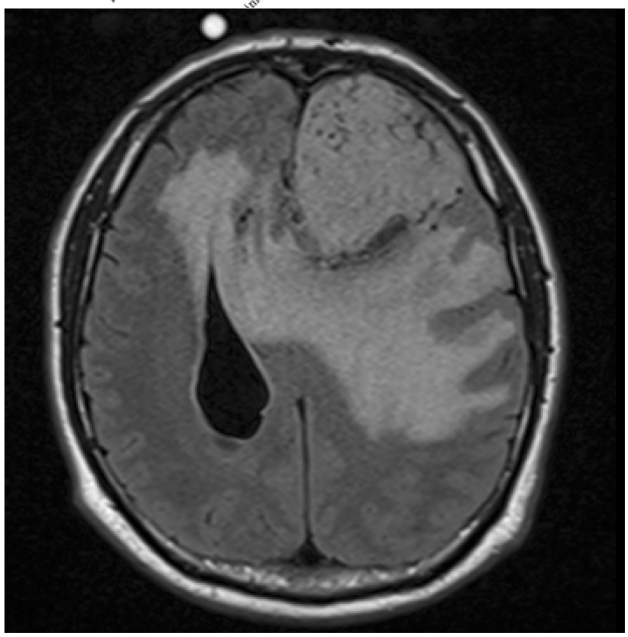
Introduction: Neurological emergencies are associated with high morbidity and mortality. Given the rapid improvement in diagnostic and therapeutic options, especially in stroke patients, immediate and accurate diagnosis and initiation of treatment is crucial to improve patients' outcome. We prospectively assessed the numbers and the spectrum of neurological diseases seen by neurologists in an interdisciplinary University based Emergency Department (iUED) in order to calculate the manpower necessary for a 24 h neurological service. In previous studies cerebrovascular diseases, epilepsy and headache accounted for 50 % of all emergencies, seen by neurologists.

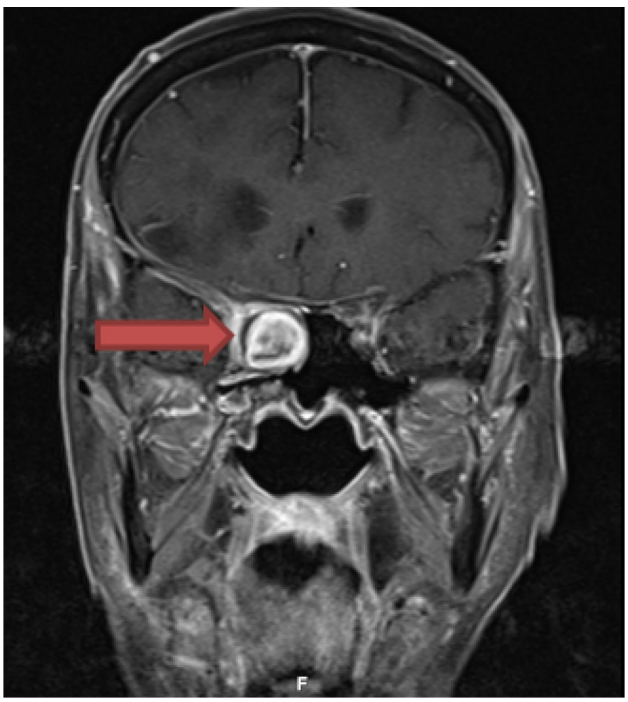
Methods: The Bernese Department of Emergency Medicine is an iUED providing a 24-h service with emergency physicians, neurologists and other specialists as needed. The University Hospital Bern (Inselspital) covers a catchment area of about 300'000 inhabitants. We prospectively analyzed all admissions to the iUED who required neurological assessment from January 2012 to December 2013. The 2 most challenging clinical cases are presented in the appendix.

Results: We assessed 9,034 patients (female 47 %, mean age 56.2 ± 20.2.). Cerebrovascular disease (CVD), including acute ischemic stroke and transient ischemic attacks, was the most common diagnosis (2,816/29 %), followed by epilepsy/seizures (1,386/15 %), headache (739/8 %) and impaired consciousness (528/6 %). Neurological emergencies increased from 2,612 consultation in 2009 to 4,871 in 2013.

Conclusions: Stroke is still the most important disease, seen by neurologists in a large iUED, followed by seizures and headache. As the number of neurological emergency consultations substantially increased in the past decade this study emphasizes the importance of a 24-h-neurological service within an iUED.







Disclosure: Nothing to disclose.

EP2252

The effect of functional electrical stimulation on gait parameters in stroke survivors

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Introduction: Stroke frequently causes persistent disability. Functional electrical stimulation (FES) based neuroprostheses are used to improve gait in neurological patients, but it could also have a therapeutical effect.

Methods: 107 subjects with chronic hemiparesis were distributed in 3 groups: "active FES" (67 subjects), "passive FES" (20 subjects), classical treatment (20 patients).

An ODFS III^{TM} (Odstock Medical, UK) device was used. The rehabilitation programme consisted in nine consecutive sessions (30 min daily), different for each group.

The ''active FES" group used the device during gait, to generate synchronized dorsiflexion of the foot during take off and flight phases of gait; "passive FES" patients used the device while resting to generate repeated dorsiflexion (but not in connection with gait); the "classical treatment" group has been performing gait training (with guidance but without any instrumental approach).

Speed, stride length and walking effort were measured on a 25 m course - for active FES patients both with the stimulator (assisted gait) and without it.

Results: Speed and stride length significantly increased in all FES groups, with better performance of active training (both assisted and nonassisted gait) versus passive FES patients ($p < 0.005$). Energy consumption (reflected by the physiological cost index) decreased for active FES patients both during assisted ($p < 0.001$) and unassisted gait ($p = 0.001$) but not in the passive FES and "no FES" treatment groups.

Conclusions: FES gait training generated a significant supplementary improvement of gait parameters compared to classical gait rehabilitation, even in short term use, in both assisted/nonassisted gait.

Disclosure: Nothing to disclose.

EP2253

Effects of action observation therapy on functional brain plasticity in healthy adult individuals

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Introduction: To assess the effect of an action observation therapy (AOT) training in healthy subjects on functional plasticity of the motor network and the mirror neuron system.

Methods: Thirty-six, right-handed, healthy subjects without any particular manual ability were randomized in 2 groups: "AOT" group watched videos that represented daily-life actions, "environmental" group watched videos of different landscapes. fMRI was acquired at baseline (T0) and after 2 weeks of training (W2), while the subjects manipulated six complex objects alternated to a sphere, with both hands. At both timepoints, functional measures testing manual dexterity were assessed. fMRI analysis was performed with the SPM8 software.

Results: After treatment, during right-hand manipulation, the "AOT" group showed an increased activation of the left inferior parietal lobule and right postcentral gyrus, which correlated with a better motor performance at functional clinical scales of the right hand. Compared to the "environmental" group, the "AOT" group had an increased activation of several frontal regions, including the inferior frontal gyrus (IFG), and left cerebellum during right- and left-hand manipulation. They also showed an increased activation of the right thalamus during left-hand manipulation. A reduced activity of the right middle temporal gyrus was observed in the "AOT" group after treatment and compared to the "environmental" group. In the "AOT" group, the increased activity of the right IFG was significantly correlated with improvement in finger tapping after treatment.

Conclusions: AOT promotes increased activity of brain areas of the motor network and MNS, which facilitates functional motor improvement.

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EP2254

Patient reported outcome measures for spasticity: comparison of psychometric properties and correlation with clinician assessment

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Introduction: Spasticity can be assessed by clinicians, typically using the Ashworth Scale, or by a range of patient reported outcome measures (PROMS). The characteristics of these PROMS have not previously been compared, nor their correlations with clinician assessments analysed.

Methods: MEDLINE, Embase, and PsycINFO databases were searched using keywords 'spasticity', 'self-reported', 'patient-based', followed by individual searches using the names of identified scales. Data on the correlation, validity and reliability were extracted from the studies.

Results: 53/1,010 studies met inclusion criteria. 7 self-reported scales for spasticity were identified: visual analogue scales (VAS)/numerical rating scale (NRS), Penn Spasm Frequency Scale (PSFS), Performance Scale Spasticity Subscale, Multiple Sclerosis Spasticity Scale-88, Patient Reported Impact of Spasticity Measure, Spinal Cord Injury—Spasticity Evaluation Tool, Self-Report Spasticity Scale. Overall, poor to moderate correlations were found between clinician assessment, mainly using the Ashworth Scale, and patient outcome measures for spasticity ($r = 0.24$–0.7).

Conclusions: VAS and PSFS have high clinical utility, but content validity is low and the scales are ordinal. The remaining measures have higher content validity and can provide interval measures, however data on other psychometric properties is lacking. Clinician

assessment may measure only a part of the patient's spasticity experience, hence the use of PROMS in spasticity assessment is encouraged. Further research is needed on the comprehensive assessment of spasticity.

Disclosure: Nothing to disclose.

EP2255

Morbidity and mortality of stroke in teaching hospital of Tlemcen (Algeria) 12 years of registration (2001–2012)

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Introduction: The aim of this study is to examine morbidity and mortality of stroke in department of neurology at teaching hospital of Tlemcen (west Algeria).

Methods: All patients admitted to hospital for stroke during 2001–2012 is included in descriptive study; the assessment is based on mortality during 28 days after the attack.

Results: A total, 5053 patients were included with an annual average of 421 patients, a sex ratio 0.7 and average of age 66.32 CI95 %: 65.88–66.76 years, for women 66.12 CI95 % : 65.5–66.7 years and men 67.9 CI95 %: 66.2–69.5 years, the typology of stroke is ischemia (71.5 %), hemorrhagic (26.3 %) and mixed (2.2 %), 15.4 % (n = 782) of patients had died, a sex ratio equal 0.78 and an average of age 69.87 CI95 %: 68.92–70.82 years, for women 69.6 CI95 %: 68.3–71.02 years, and men 70.16 CI95 %: 68.89–71.44 years, the typology of stroke is ischemia (40 %), hemorrhagic (26.3 %) and mixed (7.5 %), a logistic regression showed the following risk factors, hemorrhagic (OR = 2.1 CI95 % 1.7–2.5), age $\geq$ 65 years (OR = 1.87 CI95 % 1.6–2.2) and mixed (OR = 1.86 CI95 % 1.1–3.3). assessing trends in incidence and frequency of stroke mortality shows the stability of incidence and decreasing of mortality ($r = -0.91$, $p < 10\text{-}3$, $r^2 = 0.84$). The incidence of stroke in Tlemcen province was less them of developed countries respected the gradient between two regions but was close than developing countries, stroke attacks affect the younger population.

Conclusions: Stroke a problem of public health needed implantation of a strategy of control and patient management Based on etiologic studies.

Disclosure: Nothing to disclose.

EP2256

The effect of single session bi-cephalic transcranial direct current stimulation on gait performance in sub-acute stroke

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Introduction: Non-invasive brain stimulation with transcranial direct current stimulation (tDCS) modulates cortical excitability and improves upper limb motor performance when applied to chronic stroke patients. Whether tDCS can influence gait function in sub-acute stroke patients is unknown.

Methods: We evaluated the effect of single session, bi-cephalic tDCS on gait performance in 14 subacute patients with stroke involving the cerebral hemisphere (2–8 weeks post-stroke) in a double-blinded, sham-controlled study. Patients were randomly allocated to receive either active (n = 7) or sham (n = 7) tDCS. The anodal electrode was placed on the scalp over the ipsilesional lower limb primary motor cortex and the cathode was placed over the contralesional leg motor cortex. Gait performance was measured using the Timed Up and Go test and the Tinetti Balance and Gait index before and after active or sham tDCS.

Results: The tDCS group were significantly quicker in the Timed Up and Go test in the tDCS group, compared to the sham group ($p = 0.018$). The Tinetti Balance and Gait index was not different between groups ($p = 0.897$).

Conclusions: This is the first study to examine the effects of tDCS on gait in stroke patients in the sub-acute stage. Active tDCS improved gait performance (Timed Up and Go) in stroke patients, despite no changes to limb biomechanics of the hemiparetic side (Tinetti balance and Gait index), as compared to sham stimulation. These results suggest that tDCS could be used as a therapeutic adjunct for gait rehabilitation following stroke.

Disclosure: Nothing to disclose.

EP2257

Mortality by stroke subtype illustrates improvement in stroke care in Poland from 1999 to 2010

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Introduction: Substantial transformation occurred in Poland over the last two decades. Both socioeconomic and demographic makeover impacted health care system. Cardiovascular diseases mortality started declining in Poland from early 1990s but cerebrovascular diseases (CVD) mortality 10 years later. Stroke care has been rapidly developing from about 2000. According to diverse CVD etiology we investigated patterns in mortality by stroke subtype from 1999 to 2010.

Methods: We estimated age adjusted mortality rates for men and women based on death certificate data. The mortality curves were plotted for cerebrovascular diseases (CVD), cerebral infarction (CI), intracerebral hemorrhage (IH), subarachnoid hemorrhage (SAH) and not specified stroke as haemorrhage or infarction (NSS).

Results: Overall CVD mortality rates declined by 33 % in men and 40 % in women. CI mortality remained almost unchanged but IH mortality declined by 20 % in men and 38 % in women. Mortality from SAH declined accordingly by 19 % and 12 %. The most significant decline was seen in NSS mortality, 63 % in men and 66 % in women. NSS was recognized as a cause of death in 18280 cases in 1999 (43 % of all CVD deaths) but in 8897 cases in 2010 (25 % of all CVD deaths).

Conclusions: Substantial decline in CVD mortality in Poland from 1999 to 2010 was found. The number of death cases related to NSS decreased by 50 % almost certainly due to improved diagnostic standard resulting in better identification of stroke subtypes.

Disclosure: Nothing to disclose.

EP2258

Stroke mortality has ultimately declined in Poland

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Introduction: Stroke mortality was declining in most western Europe whereas in Poland was continuously increasing in the second half of twentieth century. Moreover Polish population was continuously

aging from mid 1980s what may surge both stroke incidence and mortality. The aim of the study was to explore trends in mortality from stroke and cardiovascular diseases in Poland from 1976 until 2010.

Methods: Statistical data based on death certificates were gathered from Central Statistical Office. Annual age standardized (world standard) mortality rates for cerebrovascular diseases (CVD), cardiovascular diseases (CD), ischemic heart disease (IHD) and atherosclerotic disease (ASD) from 1976 to 2010 were calculated. Men and female trends were plotted separately.

Results: Stroke mortality in Poland was increasing from 1976 until 1999 reaching 91/100,000 in men and 71/100,000 in women. Continuous decline was observed thereafter down to 60/100,000 in men and 43/100,000 in women in 2010. Similar pattern was seen for IHD but CD and ASD mortality started declining about a decade earlier. After switching ICD-9 to ICD-10 classification in 1997 CVD and IHD mortality rates suddenly increased but ASD mortality rate significantly dropped while gradual declining trend in CV mortality was sustained.

Conclusions: Despite aging of the population stroke mortality started declining in Poland at last almost a decade after cardiovascular disease but similar to ischemic heart disease mortality. Stroke mortality in Poland is still considerably higher then in western European countries. Death certificate data before 1997 may be biased by misclassifications of vascular death causes.

Disclosure: Nothing to disclose.

EP2259

A meta-analysis of incidence and standardized mortality rates in multiple sclerosis

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Introduction: Patients with MS have an increased mortality in comparison to the general population. Available data on excess mortality are conflicting, and MS mortality has not been addressed in relation to changes in survival in the general population. We studied changes in survival of MS patients over the last decades by the means of a meta-analysis of longitudinal mortality studies on cohorts of MS patients using Standardized Mortality Rates (SMR).

Methods: Medline, Embase and the Cochrane Library up to December 2013 were searched using the keywords "Multiple Sclerosis" and "standardised mortality" or "standardized mortality". Inclusion criteria were: availability of data on the number of deaths; mean/median patient follow-up; SMRs. Incidence mortality rate (IMR) was calculated. Natural logarithm of the IMRs and SMRs were pooled by inverse-variance weighting. Available SMRs for causes of death were processed.

Results: 10 studies and 1 unpublished data from our centre were included (24,213 patients with 6,669 deaths). Pooled overall SMR was 2.5 (95 %CI 2.3–2.8). SMR was 2.27 (95 %CI 2.03–2.55) for males and 2.85 (95 %CI 2.57–3.16) for females. When compared to general population, there was no decrease over time in the overall SMRs in any of the genders. Mortality due to cardio-vascular diseases and suicide, but not cancer, were significantly increased in MS patients (24 and 98 %, respectively).

Conclusions: The excess MS mortality has not changed over the past decades. Female patients with MS have survival disadvantage compared to the males. Cardio-vascular conditions and suicide appear as principal causes of death in MS patients.

Disclosure: Nothing to disclose.

EP2260

The efficiency of mirror therapy on drop foot in patients with multiple sclerosis

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Introduction: The aim of the study was to investigate the efficiency of mirror therapy on drop foot in 26 with patients Multiple Sclerosis (MS) who met the inclusion criteria were randomly divided in two groups after their EDSS scores were evaluated by neurologists for their functional states and their MMT for their cognitive states. Bilateral ankle exercises were performed in addition to NMES therapy with a mirror in the mirror group ($n = 13$) while they were performed without a mirror in the control group ($n = 13$). The duration of the therapy was 1 h, 3 days a week in the hospital with NMES and 2 days at home without NMES. Exercise therapy was continued at home until week 12.

Methods: The range of motion of the ankle (electrogoniometer), ankle angular velocity, muscle strength of dorsiflexor (dynamometer), muscle tone of plantar flexor muscles (MAS), ankle proprioception, 25 feet walking velocity, duration of stair climb test, mobility (RMI), ambulation states (FAS), functionality (FIM) were measured at the beginning, after the treatment in sixth and twelfth weeks.

Results: More positive improvements were obtained in the mirror group than in the control group in terms of ankle range of motion, angular velocity, muscle strength, muscle tone, proprioception, 25 feet walking velocity, duration of stair climb test, functionality, mobility and ambulation.

Conclusions: Our study showed that the results of bilateral ankle exercises done with a mirror in addition of NMES therapy are superior to the ankle exercises performed without a mirror.

Disclosure: Nothing to disclose.

EP2261

Link between helicobacter pylori infection and idiopathic Parkinson disease

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Objectives: It has been postulated gastrointestinal infection with helicobacter pylori play a role in developing Parkinson's disease and both diseases share certain characteristics, such as familial aggregation and association with water sources. The purpose of this study was to investigate the relationship between Helicobacter pylori infection and idiopathic parkinson disease (IPD) by using Helicobacter pylori serological test.

Methods: Eighty four patients with IPD and 81 healthy controls were included in this study. Immunoglobulin (Ig) G concentrations were determined by enzyme-linked immunoadsorbent assay (ELISA) in patients with IPD and controls. Chi square and Mann–Whitney U tests were used for statistical analysis.

Results: Positive serum *H. pylori* IgG antibody was detected in 88 % (74 of 84) of the patients vs. 77 % (57 of 81) of the controls ($p < 0.005$). Age, sex, habitat and drinking water supply were similar in both groups.

Conclusions: There is a significant association between Helicobacter pylori IgG seropositivity and IPD. Although *H. pylori* infection may be an important factor in initiating or exacerbating IPD, it may not represent the sole cause of the disease.

Disclosure: Nothing to disclose.

Spinal cord and root disorders; Peripheral nerve disorders

EP2262

Correlation of electromyography and magnetic resonance imaging findings in the diagnosis of radiculopathy

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Introduction: Electromyography (EMG) and magnetic resonance imaging (MRI) are the main diagnostic tools in radiculopathy. The aim of the study was to classify and correlate MRI and EMG findings in diagnosis of suspicious cervical or lumbosacral radiculopathy.

Study design: Retrospective.

Methods: We reviewed 346 patients, with complaints of numbness and pain in the neck and back for at least 8 weeks, referred from neurology and neurosurgery outpatient clinics to our neurophysiology lab between 2011 June and 2013 May. Patients with diabetes mellitus, previous disc or spine operation, polyneuropathy and spinal cord diseases as tumor, infection or syrinxs were excluded. Patients who were investigated with both neuroimaging and neurophysiological studies, in those who had normal nerve conduction results and had no motor deficits were included. MRI findings were classified in four groups as degenerative abnormalities, bulging disc, protrusion and nerve root compression. EMG findings were classified also in four groups as denervation, re-innervation, chronic neurogenic changes and normal. Root compression disclosed by MRI and abnormal EMG results were considered as positive findings for radiculopathy.

Results: We studied 66 patients. Mean age was 52.15 ± 12.07. Total of 37(56.1 %) were female, 29(43.9 %) were male and 43 % was cervical, 57 % was lumbosacral radiculopathy. We determined 27.27 % MRI positive and 16.69 % EMG negative results. Positive predictive value is higher for MRI (94.44 versus 32.08 %) and negative predictive value is higher for EMG (92.31 versus 25 %).

Conclusions: In the present study EMG is more sensitive than MRI, but MRI is more specific than EMG.

Disclosure: Nothing to disclose.

EP2263

Prevalence and imaging characteristics of asymptomatic and symptomatic spondylotic cervical spinal cord compression

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Introduction: Magnetic resonance imaging (MRI) is able to detect spondylotic cervical cord compression that could cause cervical spondylotic myelopathy (CSM) but could also remain asymptomatic ("asymptomatic spondylotic cervical cord compression"—ASCCC). Diffusion tensor imaging (DTI) parameters was shown to differentiate between CSM and ASCCC.The aim was to estimate the prevalence and MR parameters of both ASCCC and CSM in a general population above the age of forty.

Methods: Eighty-nine randomly chosen healthy volunteers, recruited irrespective of the presence of signs of CSM, 50 women and 39 men, aged 65 (median), 40–80 (range) years participated in the study. All underwent MRI examination on a 1.5 T device using standard images and diffusion tensor imaging (DTI) at the C5/6 level or at a level of maximum compression and at C2/3 as a reference. Subject with MRI signs of cervical cord compression were subsequently examined clinically.

Results: MRI signs of cervical cord compression were found in 50 individuals (56.2 %). Focal impingement was present in 9 cases (10.1 %), and wide compression in 41 subjects (46.1 %). The T2 hyperintensity was present in two subjects. DTI parameters showed no significant difference between subgroups with and without signs of compression. Clinical signs of symptomatic CSM were found in two cases (2.2 %).

Conclusions: Prevalence of spondylotic cervical cord compression in the fifth–eighth decades is higher than previously reported. Most compressions are asymptomatic and are not associated with hyperintensities and significant changes in DTI parameters. The predictive significance of different types of compression remains to be established.

Disclosure: Nothing to disclose.

EP2264

Non-traumatic spinal cord disorders at the Neuro-ICU 2001–2013: aetiology, reasons for admission and mortality

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Introduction: Most recent studies indicate that non-traumatic spinal cord disorders have surpassed the number of traumatic spinal cord injuries. Their causes and outcomes are variable, and there is limited knowledge on acute clinical worsening and requirement for neurocritical care. Here, we aimed to study the relative frequencies of aetiologies, reasons for admission and mortality at the Neuro-ICU.

Methods: A retrospective chart review of patients admitted to the Neuro-ICU during a 12-year period at a tertiary care centre. Definitions for aetiologies of non-traumatic spinal cord disorders were taken from New and Marshall (Spinal Cord, 2013).

Results: We identified 73 patients (51 % female), mean age was 62.2 year (22–90).

The most frequent aetiologies were infection (28.7 %), inflammatory/autoimmune disorders (17.8 %), motor neuron disease (16.4 %), vascular disorders (16.4 %), followed by neoplastic (8.2 %), vertebral column degenerative (6.8 %) and genetic disorders (5.5 %).

The most common reasons for Neuro-ICU admission were paresis (41.1 %), respiratory distress (27.4 %) and decreased level of consciousness (12.3 %), followed by sepsis/multiple organ failure (11.0 %), pain (5.5 %) and seizures (2.7 %).

The overall mortality rate was 23 %, no gender differences were found. The top three underlying etiologies were motor neuron disease (29.4 %), vascular disorders (23.5 %) and infections (17.6 %).

Conclusions: Neuro-ICU admission for non-traumatic spinal cord disorders is characterized by a broad range of aetiologies and reasons for deterioration. Many patients are in critical conditions, as reflected

by the high fatality rate. Further studies are needed to broaden the knowledge of neurocritical care and predictors of unfavourable outcome.

Disclosure: Nothing to disclose.

EP2265

Medical conditions and outcomes after traumatic spinal cord injury in Estonia

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Objective: To evaluate health conditions and outcomes in the chronic phase of traumatic spinal cord injury (TSCI) in Estonia.

Design: Prospective, population-based study.

Patients and methods: One hundred and three patients with TSCI filled a follow-up questionnaire and the subjects were also individually interviewed and clinically evaluated. The patients assessed their own quality of life using the International Spinal Cord Injury Quality of Life Basic Data Set.

Results: There were 90 men and 13 women (mean age 36.6 ± 12.8 years). The mean time since TSCI was 1,800 ± 1,414 days (min 370, max 5,475 days). The majority of individuals reported themselves satisfied with their psychological condition (7.1 ± 2.5), but were less contented with their physical health (5.8 ± 2.2) or life in general (6.4 ± 2.0) ($p < 0.001$).

The most frequently reported problems were spasticity (51 %), pain (42 %) and bladder problems (42 %). Pain was more frequent among patients with lower (thoracic or lumbar) and incomplete TSCI ($p = 0.03$), whereas spasticity was dominated as a problem among patients with cervical trauma ($p < 0.001$).

Fifty-two percent of patients reported neuropathic or musculoskeletal pain after TSCI compared to 14 % before the trauma ($p < 0.001$). The intensity of pain (Visual Analogue Scale) was negatively correlated with the self-rating of physical health ($p = 0.005$).

Conclusion: Patients with TSCI report that their psychological health is good. Pain and spasticity are the most often mentioned problems that need to be dealt with in order to improve their life in general.

Disclosure: Nothing to disclose.

EP2266

Modulation of cortical activity in patients with chronic spinal cord injury treated by intrathecal baclofen: a pilot fMRI study

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Introduction: Spasticity is a disabling symptom of upper motor neuron syndrome in spinal cord injury (SCI) which can be solved in severe cases by intrathecal baclofen (ITB). The aim of this study was to assess brain activation after continuous ITB delivery during simple motor tasks evaluated by functional magnetic resonance imaging (fMRI).

Methods: Two subjects (27- and 35-year-old males) with chronic posttraumatic cervical spinal cord injury at C4-5 level were studied by 1.5 T fMRI with three tasks employed:

1. finger-tapping and mental movement simulating,
2. finger taping and
3. foot flexion.

Tasks were performed before and 12 weeks after ITB pump implantation. Analysis was processed in SPM8 using the FWE corrected threshold ($p < 0.05$). Spasticity was assessed by modified Ashworth scale (MAS).

Results: ITB treatment profoundly decreased limb spasticity in both subjects. Before-ITB pump implantation fMRI showed weak activations in all tasks. Post-ITB tasks extensively raised activation in the motor system network, namely the primary sensorimotor cortex and supplementary motor area.

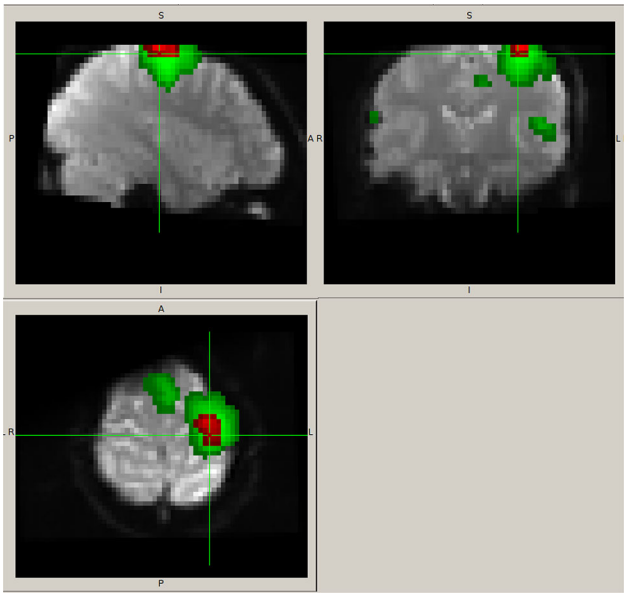

Figure shows comparison of fMRI activations in one subject prior (red) and after ITB treatment (green).

Conclusions: Continuous ITB administration relieving spasticity in SCI patients was associated with increased activation of sensorimotor cortex. We suggest that ITB may cause distant functional reorganization of motor network at cortical level.

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Disclosure: Nothing to disclose.

EP2267

Anti-TNF alpha-induced neuropathies

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Introduction: Our aim was to determine the type and frequency of peripheral neuropathy in patients with inflammatory disorders (ID) taking anti-TNF alpha agents.

Methods: We retrospectively ascertained neuropathy in a cohort of patients having in common ID, use of anti-TNF alpha agents, and peripheral neuropathy (PN) between 2000 and 2012.

Results: We identified 10 patients among 19,500 EMG exams over 13 years corresponding to inclusion criteria; and systematically reviewed the clinical features, laboratory studies, electrophysiological findings, and histopathological changes.

Among the patients, 6 were males, 4 had bowel ID and 6 arthritis.

Five had a focal or multifocal peripheral neuropathy: one had erythromelalgia at the digits of her left hand; two had a non-compressive, inflammatory, radiculopathy; two had neuropathy with persistent conduction block (one localized proximally on the femoral nerve, the other at the peroneal head).

Five patients developed a generalized, non length-dependent, neuropathy: two had a sensory variant of GBS; one a Lewis–Sumner syndrome; one a CIDP-like neuropathy; another a motor type of Guillain–Barré syndrome.

All patients improved following discontinuation of anti-TNF alpha agents and introduction of immunomodulatory or immunosuppressant agents, except for the CIDP like neuropathy that eventually revealed a CMT neuropathy.

Conclusions: Our rare anti-TNF alpha-induced neuropathies were surprisingly heterogeneous in their clinical manifestations (onset, pattern, type) and were seen during initial or maintenance therapy periods. No true peripheral nerve toxicity (i.e., dependent on cumulative dose) was identified. Early recognition of these neuropathies has management (targeted immunotherapy) and prognostic (mostly favorable) implications.

Disclosure: Nothing to disclose.

EP2268

Various manifestations of the peripheral nervous system after bariatric surgery

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Introduction: Sleeve gastrectomy is a safe and effective fast growing weight loss surgery option. Nevertheless complications are not rare.

Methods: To present five patients who developed sensorimotor symptoms after sleeve gastrectomy.

Results: Five patients were referred to the Neurological Department of Papageorgiou General Hospital, because of weakness, sensory symptoms and gait disorders a few (2–5) months after sleeve gastrectomy for morbid obesity.

The first patient was diagnosed with axonal sensorimotor polyneuropathy due to thiamine and folic acid (FA) deficiency.

The second patient presented with drop foot and numbness on the right leg. Neurophysiological assessment revealed ipsilateral peroneal neuropathy.

The third patient developed gait disorder and bilateral drop foot due to axonal sensorimotor polyneuropathy with prominent bilateral peroneal neuropathy and FA deficiency.

The fourth patient presented with marked difficulty in rising and walking due to proximal leg weakness. FA deficiency was revealed.

The fifth patient developed disabling flaccid paraparesis 10 days after a febrile diarrhoeic syndrome. Prominent clinical and neurophysiological deterioration occurred during the first days after hospitalisation despite full vitamin supplementation. Identical oligoclonal bands were present in serum and cerebrospinal fluid. High titer of Widal anti-S.parat. B–H antibodies and FA deficiency were found. Neurophysiological assessment was consistent with acute inflammatory axonal polyneuropathy and treatment with plasmapheresis was successful.

Conclusions: Sleeve gastrectomy can cause serious sensorimotor complications due to mononeuropathy or polyneuropathy, attributed to malabsorption of the B-complex vitamins. Although neurological manifestations are almost always complications of the bariatric surgery, they may also be attributed to comorbid conditions.

Disclosure: Nothing to disclose.

EP2269

Spinal cord infarction with fibrocartilagenous embolism in Japan: a single-centre prospective study

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Introduction: Spinal cord infarction (SCI) is a rare vascular disorder that accounts for 1 % of all strokes. Neither the etiology nor any definitive treatment for SCI has yet been established. Recent studies have shown vertebral diseases, such as fibrocartilagenous embolism (FCE), to be related to the pathogenesis of some cases of SCIs. However, SCIs with FCE have not yet been reported in Japan. Aim of this study is to clarify the prevalence and characteristics of FCE in Japan.

Methods: We prospectively recruited the patients with acute SCI from September 2010 to December 2013. Ischemia of the spinal cord was confirmed by diffusion weighted MRI, and myelitis cases of any etiology were excluded. The distribution of the ischemic lesions was classified using Novy's method (2006). Mateen's criteria (2011) were used to diagnose FCE without biopsy or necropsy. Functional severity was assessed using the American Spinal Injury Association Impairment Scale (AIS).

Results: In 2,047 patients with stroke admitted during the period, we identified ten cases with SCI. At baseline, five were AIS A or B, seven were wheel-chair-bound, and eight had dysuria. Three were diagnosed to have SCI with FCE. Ischemic lesions with FCE demonstrated either anterior or posterior spinal artery pattern. The disability levels were similar between FCE and non-FCE.

Conclusions: FCE was involved in more than 10 % of SCI patients in Japan. Our next question is to identify optimal methods for treating both FCE and non-FCE to improve the outcome of SCI cases.

Disclosure: Nothing to disclose.

EP2270

Non-tuberculous spondylodiscitis: etiology, diagnosis, risk factors and management

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Introduction: Spondylodiscitis is an infection of the intervertebral disc and the adjacent vertebral bodies. Spinal infections are uncommon. The diagnosis is often delayed due to the rarity of the disease.

Methods: We analysed retrospectively the clinical characteristics of patients with non-tuberculous spondylodiscitis who were admitted and treated in our clinic. The period of the study is 3 years.

Results: The clinical features of 21 patients were analysed. *Mycobacterium tuberculosis* was excluded as an etiological agent in all of them by specific tests. Fifteen(15) of patients with non-tuberculous spondylodiscitis were men(71.4 %), all of our patients had back pain, 13 of them (61.9 %) had fever on the onset of the disease. The inflammatory markers were increased in 18 patients (85.7 %), anemia was demonstrated in 13 patients (61.9 %), 11 patients were with diabetes mellitus (52.3 %), 4 patients were with concomitant oncological disease (19 %). Etiological factor was identified in 14 patients (66.7 %). SAPHO (synovitis, acne, pustulosis, hyperostosis, osteitis) syndrome was diagnosed in one patient. Three patients were surgically treated. Intravenous application of antibiotics was administrated to the other 18 patients. The diagnosis was performed by MRT in all patients.

Conclusions: The main risk factors identified in our study is the concomitant diabetes mellitus. *Staphylococcus aureus* is the most

frequent pathogen in non-tuberculous cases. The combination antibiotic therapy is highly effective.

Disclosure: Nothing to disclose.

EP2271

Falls in independent ambulatory individuals with spinal cord injury who walked with and without a walking device

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Introduction: Patients with spinal cord injury (SCI) encounter sensorimotor impairments that reduce mobility that subsequently increases risk of falls. Some studies reported that using a walking device can reduce risk of fall whereas some study contrarily indicated that using a walking device increases a risk of fall. Thus, this study prospectively assessed incidence of falls over 6 months in ambulatory individuals with SCI who walked with and without a walking device.

Methods: Eighty-nine ambulatory subjects with SCI were interviewed and assessed for their baseline data and prospectively interviewed to gather fall data every week for 6 months using a fall questionnaire.

Results: Approximately, 39–40 % of device users and non-device users with SCI experienced falls during 6 months. Most of the falls occurred while walking within the house and its immediate surroundings. Subjects reported the lower limb muscle weakness, environmental hazards, slippery floor, and obstacle on the floor were major causes of falls.

After falls, two subjects required medical attention due to patellar and sternum fractures.

Conclusions: The findings indicated that the incidence of falls in ambulatory individuals with SCI was approximately the same. However, the falls were likely occurred in the house and its immediate surroundings. Thus the improvement for functional ability in their own environments is crucial to minimize risk of falls.

Disclosure: The Improvement of Physical Performance and Quality of Life (IPQ) Research Group, Khon Kaen University, Thailand.

EP2272

Walking devices in patients with spinal cord injury

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Introduction: There is a trend toward a decreased length of rehabilitation for patients with spinal cord injury (SCI). It is likely that the patients cannot achieve an optimal level of ability at the time of discharge, and this may increase the need of a walking device for daily activities.

Study design: A cross-sectional study.

Objectives: To explore types of walking device used in independent ambulatory patients with SCI.

Setting: A tertiary rehabilitation center and community hospitals, Thailand.

Methods: The data of 195 independent ambulatory patients with SCI were interviewed for customary walking device used.

Results: More than half of the subjects (64 %) walked with a walking device in which most of them used a standard walker (45 %), followed by a single-tip cane (11 %) and bilateral crutches (8 %), respectively.

Conclusion: More than half of ambulatory subjects with SCI needed a walking device, particularly a standard walker, for daily walking. However, the findings were derived from subjective information of the subjects. A further study that explores for functional ability relating to the requirement of a walking device may help to confirm the findings.

Disclosure: Nothing to disclose.

EP2273

Functional assessments for predicting multiple falls in independent ambulatory patients with spinal cord injury

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Introduction: Fall is an important problem in patients with spinal cord injury (SCI). However, there is no evidence on the use of functional tests to predict risk of falls in these individuals. Thus this study compared ability of the Berg balance scale (BBS), Time up and go test (TUGT), 10-m walk test (10MWT), Functional reach test (FRT), step test, and Five time sit to stand test (FTSST) to predict risk of multiple falls in patients with SCI.

Methods: Eighty-three independent ambulatory patients with SCI were evaluated for their functional abilities and monitored fall data prospectively for 6 months.

Results: After 6 months follow up, 23 subjects experienced multiple falls (range 2–11 times). Findings of the study indicated that the FRT was the best tool to predict multiple falls in patients with SCI (cutoff score = 20 cm, 73 % sensitivity, 55 % specificity and area under the receiver characteristic curve = 0.64).

Conclusions: The FRT was the best tool to predict risk of multiple falls in patients with SCI. However, the FRT had low specificity (55 %), and subjects who could reach less than 20 cm still faced with a high risk of falls. Thus the FRT may be suitable as a screening tool to predict multiple falls and a comprehensive assessment to predict falls is still needed.

Disclosure: The Improvement of Physical Performance and Quality of Life (IPQ) Research Group, Khon Kaen University, Khon Kaen, Thailand.

EP2274

Neurological and neurosurgical treatment of adult patients with Chiari malformation

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Introduction: The best surgical tactics in Chiari malformation not established yet. We follow up the group of patients which firstly

were treated conservatively and after some period were operated on.

Methods: The results of supervision and surgical treatment of 93 patients with various kinds of Chiari malformation, which were operated in 2000–2013 in Institute of Neurosurgery were analyzed. Among 93 patients Chiari malformation 0 is marked at 5 patients, Chiari malformation I at 57, Chiari malformation 1.5 at 16, Chiari malformation II at 13 patients, Chiari malformation III has not been marked, Chiari malformation IV is marked at 2 patients. For that period we consistently applied three different variants of surgical tactics depending on type of Chiari malformation.

Results: Control MRI was performed from 12 days until 9 years after operation. The average terms of supervision was 3,7 years, the longest period was 9 years. The follow up data was received at all 93 patients. After operation the neurological semiology has been in details appreciated, we used Chicago Chiari Outcome Scale (CCOS) for results evaluation. Improvement was achieved in 62 patients, unchanged were 25 patients and worsened 5 patients.

Conclusions: The choice of treatment in decompensate Chiary malformation patients is surgical treatment. For achievement of the best result, surgical treatment should be directed on: suboccipital decompression, restoration of cerebrospinal fluid outflow in cranio-vertebral junction, increase volume of a posterior fossa.

Disclosure: Nothing to disclose.

Child and developmental neurology 2

EP3101

Multiple sclerosis in Tunisian children

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Introduction: Multiple sclerosis (MS) is an inflammatory disorder of the central nervous system commonly diagnosed in adult. It is being recognized increasingly in children. The objective of this study was to report epidemiological, clinical features and effect of disease modifying therapies (DMT) in a series of Tunisian patients with pediatric MS.

Methods: Retrospective study (2005–2014) was conducted in 10 children with relapsing-remitting MS (according to 2010 Mc Donald criteria) followed up in our department. Epidemiological, clinical data and DMT effects were analyzed.

Results: There were 3 males and 7 females [mean age was 15.9 years (5–20 years)]. Mean age at onset was 11.9 years (3–17 years). Mean follow-up period was 3.8 years. Three patients were followed up for type 1 diabetes that preceded the first demyelinating event. Optic neuritis and motor dysfunction were the most common presenting features. ADEM-like presentations were noted in two patients. Interferon (INF) β 1a and INF β 1b were respectively prescribed in seven and three cases. All patients received INF after their second demyelinating attack. They showed a decrease of their annualized relapse rate without any intolerance symptoms. However, a disease progression was noted in one patient in spite of a full medication adherence.

Conclusions: Our findings, although based on a small case series of patients, suggest that diagnosis of MS is still challenging in children younger than 12 years who usually have ADEM-like presentations. Early treatment with IFN beta-1 has been found to be safe and beneficial for Tunisian children with MS.

Disclosure: Nothing to disclose.

EP3102

Obstructive sleep apnea syndrome in children - importance of polysomnography

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Introduction: The syndrome of obstructive sleep apnea (OSA) is a frequent, albeit under-diagnosed condition in children, which may lead to substantial morbidity if left untreated. The purpose of the present study was to investigate the night sleep structure in children with OSA using polysomnography (PSG) method.

Methods: 18 male children (mean age 10.0 years) with clinical manifestation of OSA were investigated. All children appeared to have tonsillar hypertrophy found by laryngological examination. All of them underwent a PSG and the main sleep parameters were calculated in all cases.

Results: According to the PSG report, the main criteria of the sleep study were the following: sleep latency 10 min, REM 22 %, II stage 42 %, III stage 11 %, respiratory arousal 11 %, saturation 96 %, desaturation index 1, snoring index 38, apnea index 1–2. In particular, the episodes of central (Central Apnea CA) and obstructive apnea (OA) were observed with low indexes (CA Index 1.5–2.5; OA Index 0.2–0.6) in all cases, mainly plagued with EEG-arousals, snore-arousals and LM-arousals.

Conclusions:

1. Investigation of night sleep by using PSG can help researchers to reveal variability of sleep architecture during the different clinical presentation of OSA in children.
2. PSG study in those children did not establish a clear relationship between tonsillar hypertrophy and frequency of apnea episodes.
3. PSG can help sleep specialists in distinguishing OSA from benign snoring.

Disclosure: Nothing to disclose.

EP3103

Hypomelanisis of Ito: diagnostic based clinical criteria

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Introduction: Hypomelanisis of Ito is a rare neurocutaneous disorder characterised by hypopigmented skin lesions appearing in linear distribution on any body part. Chromosomal mosaicism and sporadic mutations are the causes of Hypomelanosis of Ito, but the identity of a specific gene has not been confirmed.

Case study: We present a child 2.5-year-old with sharply marked hypomelanosis on the back and diffuse in a few other areas. On the front left side towards axillary region there is a linear depigmentation. The child has atopic dermatitis and poor development of teeth, with a palatal abscess and dental indication for extraction of all teeth. His fundus is pale and gray. He has mental retardation, pharmacoresistant epilepsy, cortical malformation and delayed myelinization as seen on MR. His speech is delayed and his behaviour is in the autistic spectrum. He has an extremely low value of sodium which we cannot attribute to SIADH, renal loss, or increased intake of fluids. He has been evaluated metabolically (organic and amino acids, biotinidase) and all tests are within normal ranges. The skin biopsy is unremarkable, most likely a mosaicism.

Conclusion: Although there are 40 or 100 or more different states of mosaicism, diagnosis is based on clinical criteria, especialy unique distribution of hypopigmented lesions coupled with pharmacoresistent epilepsy and cortical dysplasia with delayed myelination. Our

patient is most likely a "pigmentary mosaic of the Ito type." In the near future, exome sequencing may help elucidate the molecular basis of many cases of so-called Hypomelanosis of Ito.

Disclosure: Nothing to disclose.

EP3104

An health technology assessment protocol in child: pediatric neuromuscular ultrasound normative data

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Introduction: Neuromuscular diseases, mainly the pediatric ones, are clinically heterogeneous, progressive and disabling, often requiring invasive, uncomfortable and expensive investigations. The ultrasonographic evaluation of neuromuscular diseases is a highly specific and sensitive first level screening-tool. It is non-invasive, painless, safe, inexpensive, easy and quickly to perform, characterized by high spatial and temporal resolution. The knowledge of physiological maturative ultrasound neuromuscular modifications is essential to correctly interpret pathological changes, to direct the differential diagnosis and guide focused II level diagnostic choices. We collected both quantitative and qualitative pediatric normative data, by a neuromuscular ultrasound (NMUS) Health-Technology-Assessment (HTA) study.

Methods: In 120 healthy children shared in 5 age groups.

(1) 2–5;
(2) 6–8;
(3) 9–11;
(4) 12–14;
(5) 15–16 years; M65–F55).

We have performed a NMUS wide protocol for the first time including bilaterally distal and proximal muscles of upper (Forearm Flexors, Biceps brachii, Flexor carpi radialis) and lower limbs (Anterior Tibial, Long Toe Extensor, Soleus, Medial and Lateral Gastrocnemius, Rectus Femoris, Vastus Intermedius) and nerves (Median, Ulnar, Sural) evaluating muscular thickness, echogenicity and pennation and nerveś perimeter and area.

Results: The muscular echogenicity of I–II groups was lower than III–IV–V ones. Muscular thickness increased with age and BMI, expecially between IV and V groups. No significative differences were found between males and females.

Conclusions: In clinically heterogeneous pediatric neuromuscular diseases, neuromuscular ultrasound (NMUS) is an informative, easy, non invasive screening tool that, predicting presence-absence of neuromuscular disease, can help prioritise subsequent invasive investigations, guide the therapeutic rehabilitation path with restrained cost and with a minor management-duty for the care-giver.

Disclosure: Nothing to disclose.

EP3105

Patterns of ankle dorsiflexion through gait cycle in children with idiopathic toe walking

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Introduction: Idiopathic toe walking (ITW) encompasses a wide range of gait variations with abnormal foot contact. Instrumented gait analysis is used to define how far these patterns are from normal gait. We aimed to outline ankle dorsiflexion patterns in ITW children.

Methods: Ankle dorsiflexion curves through 100 % of gait cycle were extracted from 4-5 left/right gait cycles in 10 ITW clinically diagnosed school-aged children. 97 (48 left/49 right) curves were treated for hierarchical clustering analysis using dynamic time warping unnormalized distance as dissimilarity measure and average as grouping criterium. ITW curves were then compared with ankle dorsiflexion 145 curves from 30 non ITW school-aged controls.

Results: 3 patterns of ITW curves are defined. Ankle dorsiflexion through gait cycle in pattern A is similar to the one shown in the non ITW group. Pattern B gathers curves in which ankle dorsiflexion curve is parallel to normal but overall ankle plantar flexion values are increased throughout the gait cycle (particularly in mid- and terminal stance). Pattern C groups curves with toe strikes at initial contact and decreased values in dorsiflexion through stance, leading to earlier foot clearance. ITW children use one (11/20 limbs), two (7/20 limbs) or even three (2/20 limbs) of these patterns to walk. Left and right gait cycles of a single patient may differ in ankle flexion pattern.

Conclusions: ITW children use different ankle dorsiflexion patterns to walk. Usually two different patterns can be used by one child. With-in patient variability should be carefully controlled in treatment studies.

Disclosure: Nothing to disclose.

EP3106

Heterozygote mutation in POLR3A and AIMP1 genes in patient with hypomyelinating leukodystrophy

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Introduction: Leukodystrophies are a heterogeneous group of inherited neurodegenerative disorders, mutations in POLR3A and AIMP1 genes were recently reported to cause clinically overlapping hypomyelinating leukodystrophy phenotypes.

Case description: We describe a 3 year-old girl with hypomyelination leukodystrophy. She was born from non-consanguineous parents; the pregnancy and delivery were uneventful. She presented severe static psychomotor developmental delay and growth failure from the birth, spastic tetraparesis, axial hypotonia, late teeth eruption and hypodontia. Work-up of inborn errors of metabolism was normal. MRI at the age of 10 months showed diffuse hypomyelination, reduction of NAA and elevation of choline peak on spectroscopy. VEP and SEVP were normal, EEG showed focal left occipital epileptiform activity. Heterozygous missense mutation c.4112A>G (p.Asn1371Ser) was found in exon 31 of gen POLR3A, which related with hypomyelinating leucodystrophy type 7. Also c.592C>T (p.Pro198Ser) mutation in exon 5 of gene AIMP1 in heterozygote was found, which related with hypomyelinating leukodystrophy type 3.

Conclusions: Mutation p.Asn1371Ser of gen POLR3A has not been described before in the database of the project of 1000 genomes.

We did not find any other mutation in the same gene. Mutation p.Pro198Ser of gene AIMP1 has not been described before. As we found only a unique mutation in two different genes in recessive condition we could not identify the molecular origin of the patient's clinical phenotype. However mutation located in the intronic part of the gene could perhaps explain the clinical phenotype of the patient. Further studies are needed to characterize the nature of these mutations.

Disclosure: Nothing to disclose.

EP3107

Long-term outcome in patients with West syndrome: an out-patient clinical study

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Introduction: West syndrome (WS) is an epileptic encephalopathy consisting of infantile spasms, developmental involvement and hypsarrhythmia. This study analyses the long-term development of our patients with WS.

Method: The patients were followed in the neurology clinic of Cerrahpaşa Medical Faculty for at least 3 years. Demographic features, clinical and laboratory data were registered. Three groups were formed depending on the severity of the neurological picture and as; A: Independent, mentally active; B: Supported, socially active; C: Severely handicapped. Three other groups were determined according to the state of epilepsy: I: Epilepsy +/treatment +; II: Epilepsy controlled/treatment +; III: No epilepsy/no treatment.

Results: A total of 109 patients were enrolled in the study. Etiological groups were as symptomatic (99), cryptogenic (9) and idiopathic (1). Parental consanguinity was present in 30, positive family history for febrile seizures or epilepsy in 17 patients. According to the latest evaluation 7 patients were deceased, 9 patients were in group A, 63 patients in group B and 30 patients were in group C. Six patients were in group III, 50 patients in group II and 46 patients in group I. Main parameters with significant negative impact on the course of WS in our patients were presence of symptomatic etiology, partial seizures before the onset of spasms and the younger age at onset of epileptic seizures other than spasms.

Conclusion: Although WS is a condition with severe detrimental consequences, approximately half of the patient population may achieve decent standards of social living.

Disclosure: Nothing to disclose.

EP3108

Juvenile migraine and cutaneous cephalic allodynia: a clinical study

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Introduction: In the past years, several studies have underlined the importance of Allodynia during cephalalgic attacks for the comprehension of migraine physiopathological mechanisms, as for its treatment. Nevertheless, there are only two studies about allodynia in the pediatric population, both undertaken in small groups. The aim of this study was to evaluate the prevalence of Allodynia during cephalalgic attacks in a juvenile population with primary headaches and to study the correlation between allodynia and other main symptoms of migraine.

Methods: A short questionnaire on allodynia was administered to all children seen in a 2 years period and diagnosed with primary headache. Chi square and t-tests were used to compare nominal and continuous variables. Odds ratio, calculated by means of a logistic regression analysis, has been used as measure of association of CAS and migraine characteristics.

Results: 230 children suffering from primary headache (105 males, 125 females, age 4-17 years) have been enrolled: 202 children were affected by migraine, 28 (12.2 %) by other primary headaches; migraineurs significantly complained allodynia (37 versus 0 %). Pain increased by physical activity (OR 2.0, 95 % CI 1.0, 3.8), patient showed phonophobia (OR 2.3, 95 % CI 1.0, 5.1) and nausea (OR 1.9, 95 % CI 1.0, 3.7).

Conclusions: According to our data Allodynia is common during pediatric migraine attacks. The associations between allodynia and physical activity, nausea and phonophobia, even if not described in any precedent studies on pediatric population, are supported by several studies on adult population and they imply specific physiopathological mechanisms.

Disclosure: I would like to participate at the tournament of young neurologist.

EP3109

Screening for psychopathological comorbidity with Strengths and Difficulties Questionnaire (SDQ) assessment in adolescent migraine and tension-type headache

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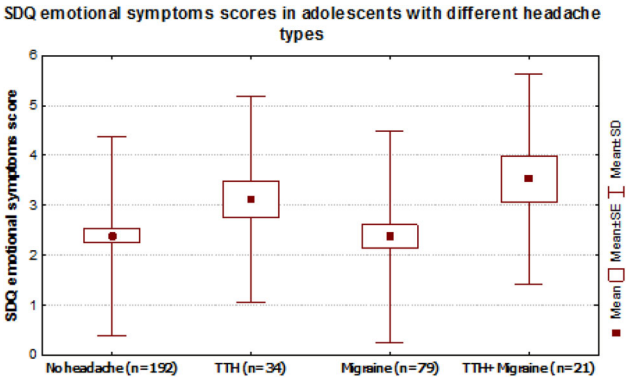
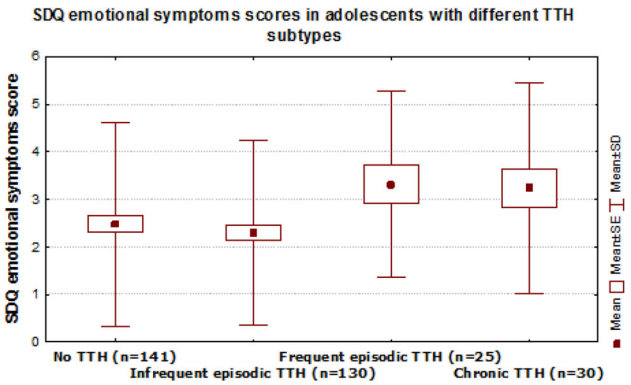
Introduction: The SDQ is a brief psychopathological screening tool that has been recommended for the detection and classification of psychosocial problems in adolescents. Data regarding the SDQ assessment in adolescent headache are limited.

Methods: 326 adolescents aged 12–18 years were examined by trained neurologist to diagnose the headache types. Based on ICHD-II criteria, a classification of migraine and clinical relevant tension-type headache (TTH, including the subtypes "frequent episodic TTH, chronic TTH"), and mixed type of headache (in subjects fulfilling the diagnostic criteria for both probable migraine and probable TTH) were given. Clinically irrelevant "infrequent episodic TTH" was assessed as "no headache" for the main analysis. Adolescents were tested with self report version of SDQ questionnaires. Kruskal–Wallis test was used.

Results: We have found a strong positive association between TTH presence and SDQ emotional symptoms score (Kruskal–Wallis test $p < 0.021$, fig. 1). No differences have been found in conduct problems, peer problem, and prosocial behaviour scores, as well as, SDQ total difficulties score.



Additional analysis has shown that only "frequent episodic TTH" and "chronic TTH", but not "infrequent episodic TTH", were associated with SDQ emotional symptoms score (Kruskal–Wallis test $p < 0.023$, fig. 2). No differences have been found between TTH subtypes and other SDQ scores.



Conclusions: Thus, frequent episodic and chronic TTH, but not infrequent episodic TTH or migraine, are strongly associated with psychopathological comorbidity such as emotional problems. We suggest that such subtypes of headache diagnostics and treatment in adolescents should include estimation and treatment of their mental health status.

Disclosure: Nothing to disclose.

EP3110

Gender differences in the association between iron deficiency markers (ferritin, soluble transferrin receptor) and adolescent recurrent headache

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Introduction: Several psychological and neurological conditions have been described as connected to iron deficiency, such as fatigue, weakness, irritability, pica, and restless leg syndrome. However, adolescent recurrent headache has not been studied well in this relation, although the iron deficiency prevalence is high in this age.

Methods: Two adolescents groups (aged 12–18 years, otherwise healthy with normal hemoglobin level) were selected: with recurrent headache (1 or more headaches episodes per week over the past 3 months) and without headache (no more than one headache episodes per month over the past 3 months). Serum concentrations of ferritin and soluble transferrin receptor (sTfR) were estimated with ELISA kits. Two-tailed exact Fisher test was used.

Results: We have found the strong positive association between recurrent headache and low serum ferritin concentration (<12 μg/l) in adolescent boys only, but not in girls (Tab. 1).

Table 1
Serum ferritin level < 12 μg/l and recurrent headache in adolescent boys and girls

GENDER	Ferritin concentration < 12 μg/l		p (two-tailed exact Fisher test)
	No headache (n=71)	1 or more headaches episodes per week over the past 3 months (n=40)	
Male (n=46)	17.7 %	50.0 %	0.052
Female (n=65)	24.3 %	14.3 %	0.365

This tendency was the same when had used the other cutoff point for the ferritin lowering estimation <20 μg/l (Tab. 2), but it disappeared when we had used the cutoff point as 30 μg/l.

Table 2
Serum ferritin level < 20 μg/l and recurrent headache in adolescent boys and girls

GENDER	Ferritin concentration < 20 μg/l		p (two-tailed exact Fisher test)
	No headache (n=71)	1 or more headaches episodes per week over the past 3 months (n=40)	
Male (n=46)	29.4 %	66.7 %	0.038
Female (n=65)	48,7 %	21,4 %	0.037

We have found no distinctions in sTfR level in accordance of presence/absence of headache and gender.

Conclusions: Low serum ferritin level is associated with recurrent headache in adolescent boys but not in girls. We suppose that the different iron deficiency pathophysiology can mask such tendency in adolescent girls. Probably, due the low erythropoietic activity in headache boys and/or low diagnostic accuracy we have found no distinctions in sTfR levels.

Disclosure: Nothing to disclose.

EP3111

Intellectual ability in Duchenne muscular dystrophy and dystrophin gene mutation location

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Introduction: Duchenne muscular dystrophy (DMD) is the most common form of muscular dystrophy during childhood. Frequently observed non-progressive cognitive disability in DMD patients is caused by mutation in dystrophin gene (*DMD*) gene. In this study, we aim to determine association between intelligence level and *DMD* mutation location among our patients with DMD.

Methods: Forty one male DMD patients, aged 3–16 years, were recruited at the Clinic for Neurology and Psychiatry for Children and Youth in Belgrade. All patients had defined *DMD* mutation (MLPA or PCR) and cognitive status assessment (Brunet-Lezine scale, Vineland-Doll scale, Wechsler Intelligence Scale for Children or Wechsler Adult Intelligence Scale).

Results: Between 37 patients with estimated intelligence quotient (FSIQ), six patients (16.22 %) had borderline intelligence, while seven patients (18.92 %) were intellectually impaired. The FSIQ was not statistically significantly associated with structural site of mutation within *DMD*. However, intellectual ability was statistically significantly associated with groups of *DMD* isoforms. Mutations affecting expression of Dp140, Dp71 and Dp40 have been associated with higher frequency and severe cognitive impairment in DMD.

Conclusions: Classification of mutation based on the altered *DMD* isoforms explained variation in intellectual ability with effect of cumulative loss of *DMD* isoforms and important role of Dp140, Dp71 and Dp40 on FSIQ.

Disclosure: Nothing to disclose.

EP3112

Chemical exposure and nutritional deficiency induced pregnancy outcomes and neuropsychiatry development of children in India

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Introduction: Developing fetuses and infants are exquisitely sensitive to environmental chemicals which may disrupt the specific developmental processes and cause neurodevelopmental disabilities. At any stage during brain development alteration or disruption in the process imposed by environmental toxins and deficiency of iodine may affect its functioning leading to behavioral and functional abnormalities. The present study considers the environmental as well as nutritional factors to associate the changes, if any, in the developing children and fetus.

Methods:

1. Detailed history about any antecedent medical facts was collected from all women, the necessary clinical examination was done in them. To understand the intendependence of neuropsychiatric development and life style factors on human development.
2. Determination of maternal thyroid function at the end of each trimester by estimation of total T3 (TT3), total T4 (TT4), free T3 (FT3), FT4, and TSH levels.
3. Collection of urine samples for estimation of urinary iodine excretion (UIE).
4. Affect of socialization on the development of children.

Results: Exposure to a number of chemicals may adversely affect child development through altered endocrine function. Variations in the urinary iodine excretion during pregnancy were recorded demonstrating physiological adaptation allowing energy conservation.

Conclusions: Iodine is an important requirement during pregnancy as it effects the formation of thyroid and thus affects neurodevelopment of foetus directly.

Environmental factors and life style plays a very significant role in the neuropsychiatric behavior of children.

The study is in progress to relate the effect of toxicants & pesticides with neurodevelopment of children in tribal areas.

Disclosure: Nothing to disclose.

Cognitive neurology/neuropsychology

EP3113

Mapping alexithymia: how the brain identifies, processes and talks about emotions

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Introduction: Alexithymia is a personality construct characterized by a continuum spectrum of difficulties in identifying, interpreting and communicating feelings. Aim of this study is to provide a brain model of physiological activation, processing and communication of emotions, and to investigate the association between alexithymia and brain functionality in these three conditions.

Methods: Nineteen healthy young subjects underwent the TAS-20 scale and a functional MRI (fMRI) scan. The 2 × 3 fMRI design included 2 conditions (neutral-N and negative emotional-NE) and 3 tasks: physiological activation (film watching), processing (judgment of felt emotion pleasantness/intensity), and preparation for emotion communication (felt emotion report). In each task, one-sample t-tests and multiple regressions were performed to investigate differences between N and NE conditions and the relationships between the NE fMRI signal and TAS-20 scores.

Results: Three subjects were alexithymic according to TAS-20. Compared to N, NE condition showed: a greater recruitment of the anterior and middle cingulum, superior frontal cortex, and supplementary motor area during the activation task; an additional activity of the precuneus and middle frontal cortex during processing; an additional involvement of the occipital associative cortices for communication. In the three tasks, all the regions were less activated with increasing values of TAS-20.

Conclusions: The brain emotional system includes cognitive and sensorimotor regions responsible for emotional awareness and body sensations, parietal and frontal regions for recalling and processing emotional memories, and cortical associative regions to organize emotional material for communication. Alexithymia is associated with a reduced recruitment of each part of this complex system.

Disclosure: Nothing to disclose.

EP3114

Reaction time to incidents as a function of age and neurological disease: preliminary findings from a large driving simulator experiment

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Introduction: Reaction time (RT) of the driver in unexpected incidents is an important component of accident probability, yet it is difficult to investigate during on-road driving. Herein, we present initial findings from RT performance of neurology patients and healthy controls of different ages in two driving simulation environments: Rural and Urban, in order to examine the factors influencing RT. The research is part of a larger project funded by the National Strategic Reference Framework (NSRF 2007-13, O.P. "Thales"), aiming at integrating subject variables with driving environments/conditions in a driving simulator experiment.

Methods: *Participants*: Thus far, 87 drivers participated: 49 controls, 14 mild cognitive impairment (MCI) patients, 13 mild dementia patients (with different diagnoses), and 11 Parkinson's disease (PD) patients. *Measures*: RT in unexpected incidents in the two driving environments.

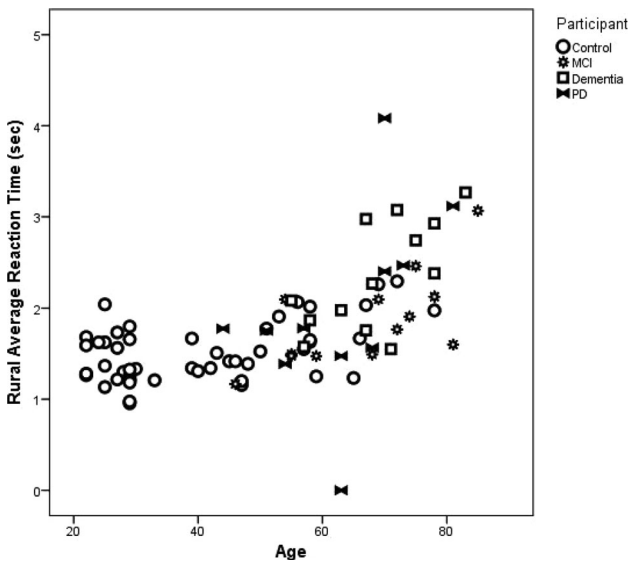
Results: Univariate analyses of variance with group as fixed variable and age as covariate showed that RT was affected by age but not by group in both environments. Contrasts of each patient group with the control group showed that dementia patients were slower than controls in the Rural environment ($p = .053$). Small samples precluded analyses by gender.

Table 1. Performance of the participants groups in the two driving conditions

Condition	Variable	**Controls** (n=49) ± *SD*	**MCI** (n=14) ± *SD*	**Dementia** (n=13) ± *SD*	**PD** (n=11) ± *SD*
Rural	Age	40.78 ± 15.91 22-78	67.00 ± 11.59 46-85	68.62 ± 8.71 55-83	63.09 ± 10.81 44-81
	Gender	W=23 M=26	W=4 M=10	W=3 M=10	W=0 M=11
	Reaction time (sec)	1.51 ± 0.32	1.86 ± 0.49	2.34 ± 0.60	1.98 ± 1.05
		Controls (n=45) ± *SD*	**MCI** (n=12) ± *SD*	**Dementia** (n=9) ± *SD*	**PD** (n=5) ± *SD*
Urban	Gender	W=21 M=24	W=2 M=10	W=1 M=8	W=0 M=5
	Reaction time (sec)	1.32 ± 0.38	1.57 ± 0.40	1.69 ± 0.50	1.58 ± 0.35

Table 2. Univariate analyses of variance of performance in the two driving conditions

Condition	Variable	Age	Participant type
Rural	Reaction time (sec)	$F(1, 82) = 19.72$, $p < .0001$, $\eta_p^2 = .19$	$F(3, 82) = 2.24$, *ns*
Urban	Reaction time (sec)	$F(1, 66) = 8.51$, $p < .01$, $\eta_p^2 = .11$	$F(3, 66) = 0.19$, *ns*



Conclusions: Initial findings show that dementia patients are slower to react in unexpected incidents in the Rural environment, possibly because of higher speed than in the Urban environment. A driver's diagnosis does not suffice for predicting RT performance; the contribution of other subject variables (e.g., gender, driving experience) and neuropsychological measures to driving performance will be explored in future analyses with larger samples.

Disclosure: Nothing to disclose.

EP3115

Discriminative ability of the "Parkinson's disease: cognitive functional rating scale" in cognitive impairment profiles different from Parkinson's disease

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Introduction: The "Parkinson's Disease-Cognitive Functional Rating Scale" (PD-CFRS) was recently validated as a useful instrument to explore the impact that cognitive decline in Parkinson's disease (PD) exerts on functional aspects of daily living. It is presently unknown whether the instrument captures similar construct in other conditions associated to cognitive impairment (CI).

Methods: In addition to the PD-CFRS, 200 patients received a comprehensive cognitive assessment (MMSE, MoCA, PD-CRS and MDRS-2). Thirty-one mild cognitive impairment (MCI)-amnestic patients (32 %), 33 MCI-multidomain (34 %) and 33 PD-MCI (34 %) completed the non-demented group. Dementia group consists on 35 Alzheimer (AD) patients (34 %), 34 with vascular dementia (VD) (33 %) and 34 PD with dementia (PDD) (33 %). The Blessed Dementia Scale (BDS) and the Global Deterioration Scale (GDS) were used as functional "gold standards". Coefficients of variation, logistic regression, effect-size analysis and ROC curves measured the PD-CFRS discriminative ability between conditions.

Results: The PD-CFRS presented high concurrent validity with the BDS (ICC = 0.828) and elevated correlation levels with all functional and cognitive scores (for all $p < 0.001$). ROC curve analysis [AUC = 0.992; 95 %CI: 0.984–0.999] showing a PD-CFRS cut-off score of ≥9 [(SEN = 0.942; SPE = 0.948] for detecting functional impairment in dementia. A similar cut-off (≥9) resulted when excluding PD patients (AUC = 0.997; SEN = 0.986; SPE = 0.969). Cohen's $d > 2.60$ (≤10 % overlap) between MCI and dementia subgroups indicate an irrelevant interference between PD-CFRS scores.

Conclusions: The discriminative properties in diagnostics other than PD suggested that the PD-CFRS is an excellent tool to evaluate functional aspects in the transition from MCI to dementia.

Disclosure: Nothing to disclose.

EP3116

Cortical blindness with residual face perception: a case of facial blindsight

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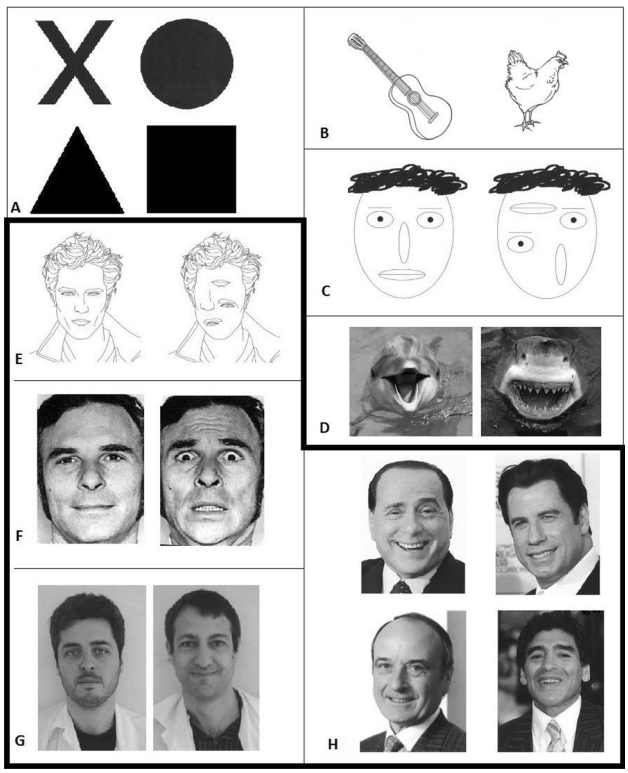
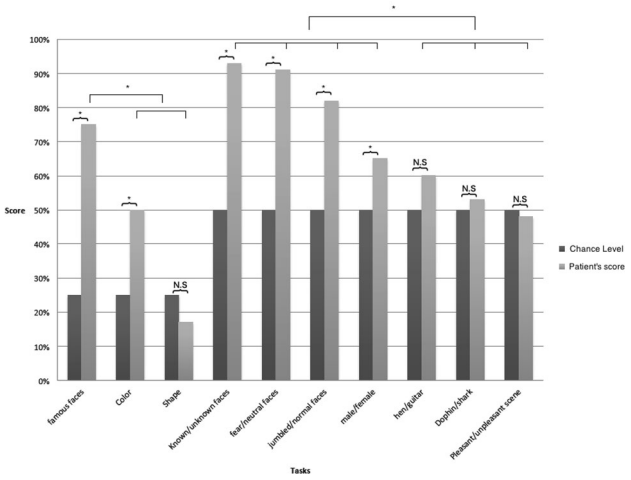
Introduction: Blindsight refers to unconscious residual visual abilities despite destruction of visual cortex. Such capabilities have been described in several patients for color and shape discrimination, facial emotion recognition or navigation skills.

Methods: Here we present A.M., a patient suffering from partial cortical blindness (he presents only small degrees of brightness perception) with residual abilities in face processing. We designed forced choice tasks to test form perception (Figure 1A–B), color perception, face perception (Figure 1C, E, G, H), and emotion perception (Figure 1D, F).



Results: A.M. presents the remarkable capacity to distinguish between jumbled/normal faces, known/unknown faces and famous people's categories even if he isn't able to recognize or even describe them. In contrast, he performs at chance for form and color discrimination. Results of visual assessment are summarized in Figure 2.



Conclusion: This case confirms that face processing involves distinct neural system from object recognition and suggests that it could occur without complete awareness through a subcortical pathway independent of the primary visual cortex.

Disclosure: Nothing to disclose.

EP3117

Neuropsychological assessment in SCA36: '*Costa da Morte*' ataxia

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Introduction: SCA36 is a recently described spinocerebellar ataxia (SCA), caused by an intronic GGCCTG repeat expansion in NOP56, relatively frequent among Galician patients with ataxia. In addition to cerebellar manifestations, motor neuron symptoms and sensorineural hearing loss are additional features of SCA36. Although cognitive impairment in patients with different SCAs is variable, prefrontal dysfunction is common to all subtypes. Our aim was to explore cognitive and affective areas in SCA36.

Methods: We evaluated 15 SCA36 patients (9 women, 6 men, mean age 62.7 ± 14.4 years), from 'Costa da Morte', a coastal region in Northwestern Spain. All study subjects had a genetically confirmed NOP56 expansion and variable severity of motor dysfunction measured through the SARA scale. The following tests were used for the study: Frontal Assessment Battery (FAB), to measured frontal and executive functions; Mini-Mental State Examination (MMSE) for general cognitive performance and Geriatric Depression Scale (GDS) to detect the presence of affective problems.

Results: The mean score obtained with the FAB was 12.1 ± 3.9, while MMSE results were 24.8 ± 4.4 and GDS score ranged 14 ± 8.2

Conclusions: Although preliminary, these results indicate that in SCA36 there is mild cognitive impairment as disease progresses, however dementia is uncommon. In concordance to what is observed in other SCAs, SCA36 patients show a variable degree of frontal-executive deficit. Special attention should be paid to affective aspects and mood, that are also frequently altered. Sensorineural hearing impairment, characteristic of SCA36, hampers the application of some neuropsychological tests.

Disclosure: Nothing to disclose.

EP3118

Cognitive impairment in multiple sclerosis patients: validity of a computerized cognitive screening battery

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Objective: To investigate the pattern of cognitive impairment in relapsing-remitting multiple sclerosis (RRMS) and secondary progressive multiple sclerosis (SPMS) patients, using a computerized battery.

Methods: RRMS patients (N = 50), SPMS patients (N = 30) and healthy controls (N = 31) were assessed by a computerized neuropsychological battery (Central Nervous System Vital Signs, CNS VS), Trail Making Test (TMT) A, B, semantic and phonological verbal fluency tasks.

Results: The overall prevalence of cognitive dysfunction was 53.75 %, while frequency of cognitive dysfunction was 38 % for RRMS and 80 % for SPMS patients. Comparison of performance between groups demonstrated that RRMS patients differed from controls with large effect size on reaction time, medium effect size on TMT A and small effect size on TMT B, phonological verbal fluency task, composite memory, psychomotor speed and cognitive flexibility. SPMS patients differed from controls in all neuropsychological measures (except complex attention) with large effect sizes on TMT A, B, phonological verbal fluency task, composite memory, psychomotor speed, reaction time and cognitive flexibility. Between patient groups (RRMS and SPMS), medium effect sizes were present on TMT B and psychomotor speed, while small effect sizes were present on composite memory and processing speed.

Conclusion: CNS VS appears to be sensitive in detecting cognitive impairment in RRMS and SPMS patients. Significant impairment in episodic memory, executive function and processing speed was detected, with gradual increment of the frequency as disease progresses.

Disclosure: Nothing to disclose.

EP3119

Theory of mind in multiple sclerosis

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Introduction: Social behaviour and interaction is strongly linked to the ability to understand the minds of others and their feelings. Theory of Mind (ToM) is defined as the capability to make inferences about mental states of other individuals. Social Cognition allows to understand the mind of others, acting according such information and process. Our aim is to evaluate and assess the ToM in patients of Multiple Sclerosis (MS).

Methods: We studied 38 patients of Relapsing Remitting Multiple Sclerosis (RRMS) with EDSS of 2 (or less) utilizing the Test of Eyes Expression (Baron Cohen, 2001), Facial Affect Recognition and the Faux Pas Test.

Neuropsychiatric and Cognitive profiles were studied with standard batteries for MS.

A healthy control group of 38 individuals, was paired according age, gender, education and intellectual level.

Results: MS patients were significantly impaired in ToM Test, specially in the facial affect recognition (mainly decoding emotions of anger and fear) and in social behaviour related personal interaction (faux pas). These results had no correlation with cognitive performances or other variables linked to disease (EDSS, evolution time, treatment) in our group of patients.

Conclusions: Our findings suggest that Social Cognition and ToM are disrupted functions in RRMS patients, and are no related with neuropsychological deficits.

This compromise (deficits in emotional decoding, inference of mental states of other individuals, ability to perceive otheŕs feelings) could contribute to increase the psychosocial burden of our patients, increasing disability in MS.

Disclosure: Nothing to disclose.

EP3120

Behavioral dysexecutive disorders in Huntington's disease

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Dysexecutive symptoms such as apathy, impulsivity and distractibility have been reported on clinical ground in HD. However previous studies have assessed dysexecutive behavioral disorders using clinical interview or nonspecific questionnaires incorporating other features resulting in highly variable evaluation with poorly defined performance indices. This study aimed to assess dysexecutive behavioral abnormalities in HD, using a validated instrument, the Behavioral Dysexecutive Syndrome Inventory (BDSI)[1].

14 patients (mean age: 55.5 years; SD 12.4; range: 34–73; mean duration: 8.7 years; SD = 7; range 2–30; mean MMSE score: 25; SD = 3.4) with clinically diagnosed and genetically confirmed HD, were included. The assessment of depressive symptoms (Montgomery Asberg Depression Scale) showed a mild depression in 7 patients.

The BDSI is a highly structured caregiver based interview which rates frequency and severity of 12 dysexecutive disturbances (global hypoactivity with apathy, hyperactivity, irritability-impulsivity, euphoria, perseverative behavior; environmental dependency, social behavior disorders).The analysis of individual performance was performed using cutoff scores at the 5 % level using normative data obtained in 96 controls1.

The prevalence of behavioral dysexecutive syndrome was high (50 %; 95 %CI: 24–76). The behavioral profile was characterized by the prominence of irritability (50 %), hyperactivity (43 %), apathy (29 %), disinterest (22 %) and difficulties for anticipation (14 %).

This study based on the BDSI revealed in HD that behavioral dysexecutive disorders are: (1) frequent with a prevalence of 50 %, (2) characterized by a specific profile with the prominence of irritability and hyperactivity (3) whereas the hypoactivity-apathy disorders were less frequent contrary to most other degenerative disorders.

[1] Godefroy O, Ann Neurol. 2010

Disclosure: Nothing to disclose.

EP3121

A voxel based morphometric study to investigate volume differences in regional gray matter between patients associated with different subtypes of vascular cognitive impairment

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Introduction: Voxel-based morphometry (VBM) was used to investigate volume differences in regional gray matter between patients suffered from mild cognitive impairment associated with periventricular white matter hyperintensities(PWMH)and strategic single-infarct (SSI).

Methods: 14 patients with PWMH, 10 patients with SSI after 6-month poststroke time window and 16 healthy controls were included in this experiment. Participants were neuropsychologically tested to characterize cognitive function in seven domains: orientation, attention, working memory, language, visuospatial ability, psychomotor speed, and memory. Magnetic Resonance Imaging scans were acquired and whole brain regional differences in gray matter volume between three groups were examined with VBM. Two-sample T-test models were used to assess the contribution of demographic variables, stroke-related variables, and voxel-based morphometry results to classification of cognitive impairment group membership.

Results: SSI and PWMH showed significant volume difference in regional gray matter. Significant gray matter volume reductions mostly in the bilateral temporal lobes were found in PWMH, compared with SSI. Decreased gray matter density in the left prefrontal areas could also be seen in PWMH.

Conclusions: These findings suggest that grey matter atrophy in temporal cortical and prefrontal regions are of particular relevance to PWMH-related cognitive decline, from a morphological point of view. Characteristics of gray matter atrophy in PWMH which is similar to degenerative disease prompt that merger or secondary neurodegenerative changes in the vascular cognitive impairment subtypes can not be ruled out.

Disclosure: Nothing to disclose.

EP3122

Cerebral microbleeds and cognitive impairment in neurodegenerative and cerebrovascular diseases

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Introduction: We hypothesize that cerebral microbleeds (CMBs) influence in cognitive decline. Their presence and localization might be an additional criteria for diagnosis of dementia. Previous study demonstrated that patients with DLB (dementia with Lewy bodies) have more CMBs than patients with AD (Alzheimer disease).

Methods: We studied 120 outpatients with cognitive decline older than 65 years. MRI was performed on MR tomograph 1.5 Tesla. CMBs were analyzed using microbleeds anatomical rating scale (MARS). Neuropsychological battery included Montreal Cognitive Assessment scale (MoCA), Addenbrooke's Cognitive Examination (ACE-R), Clock Drawing Test, fluency test and the visual memory test (SCT).

Results: We did not found cortical CMBs in patients with DLB in most cases (78 %). Multiple (more than three cortical) CMBs were observed in two DLB cases only and might be considered as sporadic CAA (cerebral amyloid angiopathy). The most CMBs were observed in patients with AD + VaD (Vascular dementia) (73 %) compared to AD + DLB (11 %). CMBs were associated with worse memory and visuospatial functional domains and the total ACE-R score in AD + DLB groups in comparison with DLB negative CMBs group ($p < 0.05$).

Conclusions: We hypothesize that vascular pathological process is an universal factor which contributes to neurodegeneration irrespective of the type of dementia. CMBs might be a more sensitive indicator of the severity and clinical significance of cerebrovascular disease than the severity of leukoaraiosis. Multiple CMBs might represent an independent factor of cognitive decline. We guess that the vascular changes in LBD observed in Alzheimer's involvement component that requires additional pathological studies.

Disclosure: Nothing to disclose.

Epilepsy 2

EP3123

An inventory on deceased infantile spasms patients

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Introduction: The premature death rate for patients with Infantile Spasms (IS) ranges from 5 to 31 %. Nearly a third of the deaths are reported to be before age 3 and 61 % occurred at/or before age 10 years.

Methods: Among a total of 210 patients seen at least once in our IS out-patient clinic of neurology department, in Cerrahpaşa Medical Faculty, data of a total of 37 patients with premature death are examined. Personal and familial medical information, birth history, type of spasms, age at onset of spasms, pre-existing developmental condition, presence of partial seizures, video-EEG characteristics and cranial MRI findings (cMRI) are evaluated.

Results: Male to female ratio was 23/14. Sixteen pair of parents of 37 patients (43 %) were consanguinous. Follow-up time was 2 months–12 years. Age of death ranged between 7 months and 9 years. Thirty-six patients (97 %) had pre-morbid developmental delay. All patients had symptomatic IS. Perinatal asphyxia was the most frequent condition among the antecedent events with a rate of 19/37 (51 %). Most frequent cMRI findings were diffuse cortical-subcortical atrophy in 13 patients (35 %) and extensive subcortical involvement in 5 patients (14 %).. Specific reason for death could be detected in only nine patients, six of which happened during respiratory tract infections.

Conclusions: The most severe cases resulting with premature death among patients with IS are found to be associated with symptomatic etiology and with extensive cortical and subcortical lesions. High incidence of death during respiratory infections should warn the clinician to be cautious about immune incompetency in those cases.

Disclosure: Nothing to disclose.

EP3124

Antiepileptic drugs and apolipoproteins: toward an assessment of vascular risk

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Introduction: The use of antiepileptic drugs is highly prevalent, often chronic, with frequent polytherapy and usually aiming to an overall young population. Notwithstanding, epilepsy has been associated with an increased overall vascular risk, including stroke. Furthermore,

commonly used drugs, such as valproate and carbamazepine, may alter certain markers of vascular risk. This study aims to evaluate their effect on plasma apolipoproteins as markers of vascular risk.

Methods: We selected 94 patients without major known vascular risks, nor nutritional or metabolic abnormalities, from our hospital 2,012 outpatient epilepsy list. Clinical and analytical data was obtained from electronic medical records based on apolipoproteins assay (N = 264). SPSS Statistics 20 (IBM, 2011) was used for statistical analysis according to data characteristics and an alpha level of .05.

Results: Compared to other treatments, taking carbamazepine was associated with higher levels of apolipoprotein A-I ($U = 837.5$, $p = .044$, $r = .21$), particularly among women [$t(59) = -2.421$; $p = .019$; r = .30], while taking valproate was associated with lower levels ($U = 805$; $p = .024$; r = .23). Accordingly, taking carbamazepine was associated with higher apolipoprotein A-I compared to taking valproate ($U = 423$; $p = .017$; $r = .28$), also among women [$t(44) = 2.721$; $p = .009$; $r = .37$]. Though some drug overlapping was observed, no statistically significant positive associations ($p > .05$) were found.

Conclusions: The results concord with previous studies and suggest a potential effect of commonly used antiepileptic drugs on vascular risk among young and otherwise overall healthy adults. Proper clinical studies may provide better insight on this matter and yield guidelines for vascular protection.

Disclosure: Nothing to disclose.

EP3125

Etiology of "refractory epilepsies" cases in the long term video-EEG monitoring (LTM) unit

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Introduction: Refractory epilepsy constitutes for the approximately 30 % of all cases of epilepsy. In most cases is associated with structural lesion of the brain, and should be regarded as a candidate to the surgical treatment. Patient with refractory epilepsy should undergo complex evaluation in order to find out the underlying cause of epilepsy. We present analysis of etiology of the 91 cases of "refractory epilepsy" referred to long term video-EEG monitoring unit within 6 months.

Methods: All of the patients underwnt long term video-EEG monitoring, clinical and neuropsychological evaluation as well as epilepsy devoted MRI protocol. The classification of the epilepsies were done according to the ILAE recommendations.

Results: 31 patients (34 %) admitted to the LTM unit have had non-epileptic seizures from which 13 cases (14 %) were diagnosed as PNES (psychogenic non-epileptic seizures), 18 patients have had other paroxysmal events. Of the 60 cases of the epilepsy 12 (20 %) were classified as primary generalized epilepsies probably of genetic or unknown etiology. 48 cases of epilepsies have had seizures with focal semiology. 17 (35,4 %) cases of epilepsies with focal seizures semiology were MRI negative. In 31 (64.5 %) cases the underlying structural lesion was found.

Conclusions: Despite the progress in the diagnostic process of epilepsy there are still approximately one third of misdiagnosed cases of "refractory epilepsy". Our data suggest that all patients with "refractory epilepsy" should undergo thorough complex evaluation for the exclusion of epilepsy and in order to indentify possible candidates for the epilepsy surgery.

Disclosure: Nothing to disclose.

EP3126

Prescribing patterns of antiepileptic drugs and interaction risk in general practice

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Introduction: The aims of this study were: to analyze the prescribing pattern of newer and older antiepileptic drugs (AEDs); to assess the exposure to potential drug-interactions in a general practice setting.

Methods: On a population of 150,000 individuals we identified patients who received AED prescriptions during 2005–2011. One-year prevalence and incidence of use and global AEDs consumption were calculated. The risk of drug interactions was calculated as overlapping days between the exposition days of AEDs and interacting drugs.

Results: Prevalence of older AED use slightly increased during the study period, while a strong increase of newer AED use was observed until 2006, followed by a deep fall in 2011. Among older AEDs, phenobarbital and valproate were the most widely used in 2011, accounting for 21.2 and 16.2 % of total AED consumption. In the same year, oxcarbazepine and lamotrigine were the most used new AEDs (10.9 % and 10.8 % respectively), while gabapentin and pregabalin exhibited the higher incidence of use. The main indication of use was epileptic disorders for older AEDs and neuropathic pain for newer AEDs. A high number of patients treated with older AEDs, received co-prescription at clinically relevant interaction risk. Among newer AEDs, topiramate showed the highest annual rate of possible interactions.

Conclusion: Significant differences were shown in the prescribing pattern of newer and older AEDs. A not negligible patients exposition to potential clinically relevant drug-interactions was shown. The co-prescription of drugs at risk of interaction with AEDs should be evaluated with caution or avoided, if possible.

Disclosure: Nothing to disclose.

EP3127

Ictal extrapyramidal motor symptoms in temporal lobe epilepsy

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Introduction: The basal ganglia form circuits with the frontal and temporal neocortices. Dystonic limb posturing and gyratory movements are established ictal extrapyramidal motor symptoms (EPMS). Order and duration of new ictal EPMS were investigated to elucidate seizure propagation pathways in frontal- (FLE) and temporal lobe epilepsy (TLE).

Methods: Videos of 38 patients with medically refractory TLE or FLE referred to the epilepsy monitoring unit at the Department of Neurology, Medical University of Innsbruck between 01.01.2001 and 01.08.2002 were analysed for the ictal EPMS dystonia with tremor and tonic extension after figure-4-sign (TEAF4).

Results: An aura preceded more often TLE than FLE seizures (p = 0.000). Dystonia (p = 0.002) or seizure propagation from dystonia to version (p = 0.038) were predominantly observed in seizures with temporal lobe origin. Forced blinking (p = 0.034) and making a grimace (p = 0.002) were exclusively documented in seizures with frontal lobe origin. An immobile limb (p = 0.028), dystonia with

tremor ($p = 0.012$) and TEAF4 ($p = 0.014$) were exclusively documented in seizures with temporal lobe origin. Preferred seizure propagation pathways exclusively documented in seizures with temporal lobe origin were aura to head turn ($p = 0.028$) or dystonia to a generalized seizure ($p = 0.005$).

Conclusions: Ictal dystonia, tremor and TEAF4 were exclusively documented in our TLE subgroup. The basal ganglia seem to be an important propagation pathway as documented by the different semiological signs following dystonia in TLE, but not in FLE.

More prospective studies are required to elucidate basal ganglia involvement in seizure propagation pathways and establish ictal EPMS as semiological signs with distinct localizing value.

Disclosure: Nothing to disclose.

EP3128

Analysis of gene expression NRN1 in patients with epilepsy with aCGH microarray DNA methods

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Introduction: Work includes comparing the level of gene expression NRN 1 in patients with epilepsy N = 30 (10 with temporal lobe, 10 with frontal lobe and 10 with idiopathic epilepsy) and control group (patients with no clinical history of seizures) N = 30. The NRN1, neuritin 1 gene encodes neuritin-1, a GPI-anchored neuronal protein that functions extracellularly to modulate neurite outgrowth.

Methods: The study group was consisted of 30 patients with a diagnosis of epilepsy (10 with temporal lobe, 10 with frontal lobe and 10 with idiopathic epilepsy). The control group were patients matched for sex and age, with no clinical history of epilepsy, not taking antiepileptic drugs. The material consisted of peripheral blood lymphocytes. From lymphocytes was isolated the genetic material. RNA was extracted and hybridized to the array and RT-PCR. The method, that we used was cDNA microarrays type "Human Whole Genome DNA Microarray" by Biote21 AGILENT ALL HUMAN FEATURES. NIA Analysis Software were used. Hierarchical-clustering gene selection was made centered correlation (distance measure and single linkage). Using the method of TR-PCR we have confirmed the result for the genes with the largest increase or decrease of the transcript in the study group versus control group.

Results: We received increased expression in all group (all groups vs. control group 10,006 times) and the most hyperexpression (12,707 times) in the temporal lobe epilepsy group. FDR = 0.2763.

Conclusions: Statistically significant hyperexpression gene NRN 1 in all groups of epilepsies.

The largest hyper expression in temporal lobe epilepsy group.

Disclosure: Nothing to disclose.

EP3129

Stigma scale of epilepsy

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Objective: To draw attention this common psychosocial problem associated with epilepsy which is stigmatization. We aimed to present results of stigma scale of epilepsy (Dr. Li Li Min and colleagues' scale from Brazil).

Methods: The subject were divided in three groups:

1. Patients from the epilepsy Outpatients Clinic of the Şişli Hamidiye Etfal Education and Resource Hospital.
2. Patients' families.
3. People in community.

The Stigma Scale of Epilepsy (SSE) contains 5 questions with 24 item, each with a four-point scale: 1 not at all, 2 a little, 3 a lot, 4 totally. In addition, the Beck Depression Scale (BDS), Hamilton Anxiety Scale (HAS), Short Functionality Scale (SFS). All subjects were gave informed consent. First the question was read and then the subject wrote down the answers. The form was the same for all the subjects.

Results: We interviewed 80 subjects (32 patients, 25 their family and 23 people in the community). The SSE score of patients, family and in the community that believe that PWE are stigmatized or rejected is higher than the SSE scores of who don't believe it.Although there was strong correlation high SSE scores and poor functionality; there wasn't any correlation with SSE and DDS, HAS, age of epilepsy onset, time of epilepsy, education and social class.

Conclusions: Prejudice and discrimination are often worse than the seizures themselves in terms of impact on daily life of people with epilepsy and their family. The understanding of the aspect of epilepsy is important to reduce the burden of epilepsy.

Disclosure: Nothing to disclose.

EP3130

Spreading depression enhances the rate of neurogenesis in the rat hippocampus and dentate gyrus

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Introduction: Spreading depression (SD) known by transient loss of spontaneous and evoked neuronal activity and changes in ionic, metabolic and hemodynamic characteristics of the brain. Neuronal damage followed by SD, supposed to have a dramatic impression on SD-derived pathologic conditions. We aimed to determine whether SD is able to stimulate persistent neurogenesis.

Methods: Wistar rats (60–80 g) randomly chosen and 3 M KCl injected for induction of SD. Four weeks after the first injection, all rats were decapitated and the brains removed. The density of mitotic cells, divided cells, and new neurons in the pyramidal cell layer of hippocampal CA1 and CA3 and granular cell layer of dentate gyrus was assessed. We also detect the DNA during the S phase using bromodeoxyuridine (BrdU).

Results: A remarkable increase occurred in the number of BrdU-labeled cells in hippocampal region, detected by immunohistochemistry method. The density of mitotic cells, divided cells, and new neurons in hippocampal CA1 and CA3 and granular cell layer of dentate gyrus also increased.

Conclusions: We conclude that SD potentiates to trigger persistent neurogenesis in rat hippocampus.

Disclosure: Nothing to disclose.

EP3131

Abstract withdrawn

EP3132

Dentatorubral pallidoluysiana atrophy: study of a Portuguese family

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Introduction: Dentatorubral pallidoluysiana atrophy (DRPLA) is a rare neurodegenerative disorder. The juvenile type is often diagnosed as progressive myoclonus epilepsy (PME), whereas the adult type exhibits a Huntington-like phenotype.

Methods: To describe a Portuguese ancestor's family with DRPLA and prominent genetic anticipation.

Results: Patient IV-4 A 22-year-old woman presented with an 8-year-old onset history of cognitive decline and recurrent complex partial and generalized tonic–clonic seizures, associated with trains of massive stimulus-induced myoclonic jerks since the age of 16 and further cerebellar ataxia. Molecular analysis was negative for PME autossomal recessive causes. The patient died at 32 from medical complications.

Patient IV-5 (proband): A 32-year-old woman presented with cognitive decline, behavior disturbances and progressive myoclonic epilepsy, with recurrent generalized tonic–clonic seizures following trains of bilateral massive myoclonus, since the age of 10. Further, she developed progressive cerebellar ataxia, since the age of 18, and bilateral upper limb choreic movements, since the age of 30.

Interictal EEG revealed, in both, a generalized slow background activity and predominantly posterior epileptiform activity, with bilaterally synchronous spike and spike-wave discharges. The DRPLA diagnosis was established in patient IV-5 (63 CAG repeats in atrophin-1 gene), after their 64-year-old father (III-6) began to develop mild gait ataxia, dysarthria and cervical dystonia.

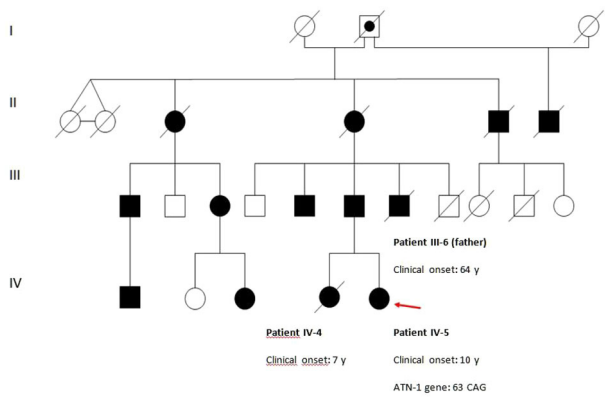

Fig. 1 Pedigree of the family with DRPLA. A prominent anticipation with a reduction in age at clinical onset of 57 years. The solid symbols represent affected patients and the open symbols represent unaffected members.

Conclusions: Despite extremely rare in non-Japanese population, DRPLA is the second most prevalent autosomal dominant ataxia in Portugal. In patients presenting PME, the diagnosis mainstay relies on the identification of an autosomal dominant pattern in inheritance, which may be misrecognized due to the genetic anticipation.

Disclosure: Nothing to disclose.

EP3133

SF-36 metric as a diagnostic aid for conversion disorder

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Introduction: SF-36 metric is widely used for quantifying the Quality of Life (QoL) and country specific normative data are available. In this study, QoL perceptions of patients suffering from epilepsy and Conversion Disorder related to Psychogenic Non-Epileptic Seizures (Cd-PNES) are compared using SF-36 and the efficacy of using SF-36 to identify cases of Cd-PNES is investigated.

Methods: 124 epileptic and 24 Cd-PNES patients filled the SF-36 questionnaire. SF-36 country normalised scores for physical and mental oriented dimensions as well as calculated Physical Health Composite (PHC), Mental Health Composite (MHC) outcomes were statistically compared and their cross-correlations evaluated.

Results: PHC scores of epileptics were similar to healthy population values but Role Physical and General Health dimensional scores were lower (all $p \cong 0$) by ½ standard deviation (SD); Cd-PNES patients had lower PHC and physical dimension scores by ½ SD (all $p \cong 0$). While female epileptics MHC scores were one s.d. below normal with all mental dimensions being negatively affected (all $p \cong 0$), Cd-PNES patients MHC scores were >2 SD below normal ($p \cong 0$) further underscoring by 1 SD epileptic patients for all mental except Social Function dimensions ($p \cong 0$). Correlation between PHC and MHC scores was absent ($r^2 < 0.02$) in epileptics but inversely present in Cd-PNES patients ($r^2 = 0.42$, $p \cong 0$). The average of PHC and MHC scores was found to have sensitivity >80 % and specificity >83 % in discriminating Cd-PNES cases from epileptics.

Conclusions: SF-36 metric may be helpful as a simple diagnostic aid for discriminating Cd-PNES from epilepsy.

Disclosure: Nothing to disclose.

EP3134

Epilepsy and sexual function in epileptic patients in mono and polytherapy

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Introduction: Aim of this study was to assess sexual dysfunction in men and women with epilepsy treated with AEDs of old and new generation, in mono and polytherapy.

Methods: Twenty-two epileptic patients (13M, 9F) aged from 22 to 60 and from 32 to 50 years, respectively, and 24 healthy subjects (13M, 11F) of the same age, were administered the Arizona Sexual Experience Scale (ASEX) and the Beck Depression Inventory (BDI) to assess the sexuality and depression, and were taken blood samples for determination of: TT, E2, SHBG, DHEAS, FSH, LH, T, cortisol, Δ4, with the calculation of the FAI. The statistical analysis was performed with ANOVA and simple regression tests.

Results: Statistically significant increases ($p \leq 0.03$) in the total ASEX score in patients treated with AEDs, compared with controls, were found; in particular in achieving and maintaining of erection ($p \leq 0.008$), in the satisfaction received from the orgasm ($p \leq 0.02$), which indirectly reflect increases of SHBG ($p \leq 0.02$) and FSH ($p \leq 0.03$), and decrease of DHEAS ($p \leq 0.008$) and FAI ($p \leq 0.01$) in male subjects. In female subjects the comparison of the scores of ASEX with hormonal profile, in patients and controls, did not reveal any significant difference.

Conclusions: In male subjects, the comparison of the scores of ASEX between patients and controls shows an impairment of sexual

function, according to hormone profile (SHBG, FSH, DHEAS, and FAI), which indirectly indicates an overall reduction in free testosterone levels (TF).

Disclosure: Nothing to disclose.

EP3135
Historical criteria that distinguish seizures from syncope: external validation of screening questionnaire

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Introduction: Aim of our work is to perform external validation of the screening questionnaire, proposed by Sheldon et al. 2002, designed to distinguish seizure from syncope based on historical criteria.

Methods: Alongside to the standard clinical observation, screening questionnaire with nine historical questions was performed in all patients evaluated due to transient loss of consciousness. Score results were compared to final diagnosis based on detailed neurology, electrophysiology and cardiology assessment. Analyses were performed with and without inclusion of additional clinical variables, using multiple regression models. Discrimination values were tested with classification tables and receiver-operator characteristic (ROC) analysis. Calibration characteristics were tested with Hosmer–Lemeshow Chi square statistic.

Results: From July 2013 to December 2013, 65 patients have been evaluated due to transient loss of consciousness. Final diagnosis of epileptic seizures has made in 52 patients (23M, 29F) and syncope in 13 patients (10M, 3F). Patients with epileptic seizures have been significantly younger (median 36.5 years, IQR 23–65.5) than patients with syncope (median 59, IQR 50–65). However, only screening questionnaire score has significant effect in multivariate logistic regression model (OR 60.6). Screening questionnaire correctly classified 87.69 % patients with sensitivity 86.54 % and specificity 92.13 %. Area under ROC curve was 0.89, and Hosmer–Lemeshow c^2 (8) = 12.97, p = 0.1130.

Conclusions: Screening questionnaire based on historical criteria could be useful additional tool for differentiate seizure from syncope. Regarding the pretest probability, questionnaire's overall gain in diagnostic accuracy is moderate. Potential improvement for the use in the tertiary academic centers could be considered in future studies.

Disclosure: Nothing to disclose.

EP3136
Epilepsy surgery including clinical evaluation with invasive monitoring

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Background: Partial epilepsies (PE) are the most frequent cause of refractory seizures. Surgical treatment requires identification of the epileptogenic zone (EZ) as well as the possibility of its safe removal.

Objectives: Audit benefits and risks of surgery after EZ identification with invasive video-EEG monitoring in refractory PE.

Methods: Retrospective design. Patients who have undergone epilepsy surgery in two steps, between August 2012 and August 2013. First approach included video-EEG monitoring with intracranial electrodes. Second time consisted in removal of those electrodes and resection of the EZ.

Results: Twenty-one patients, 31 procedures. Eight (mean age 26, five-50) underwent two times surgery. Pre-surgical investigation included brain CT and MRI, ictal and inter-ictal SPECT, SISCOM, brain PET, scalp EEG, video-EEG monitoring with surface electrodes, electrocorticography and brain mapping, neuropsychological tests, Wada test and psychiatric evaluation. Five patients had seizures on a weekly basis and three had them daily. All were polymedicated, average, with three anticonvulsive drugs. They presented different etiologies for the epilepsy and surgery has been decided on an individual basis. Two patients had surgical complications, meningitis and limb paresis. Half presented compatible pathology with presurgical hypothesis: three cases of dysplasia, one ganglioglioma. Six patients were seizure-free after surgery. Two maintained the same frequency. All with follow-up in Neurology and Neurosurgery appointments.

Conclusion: Two-step epilepsy surgery arises when noninvasive monitoring, including multiple approaches, is not enough for EZ identification. In our series, this strategy allowed a significant improvement of clinical status and quality of life.

Disclosure: Nothing to disclose.

Neuro-oncology

EP3137
Prognosis of oligodendroglial tumours: a PET C11 methionin, molecular and long term clinical study

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Introduction: Survival of patients with oligodendroglioma varies widely from few months to decades. Establishing prognostic factors is important for their management. PET (Positron Emission Tomography) with C11 methionin provides information about oligodendrogliomas metabolism and aggressiveness. More recently, molecular biology with IDH 1 (isocitrate dehydrogenase) mutation and 1p–19q co-deletion was a major step forward in oligodendrogliomas prognostic evaluation.

Objectives: The objective of this study was to determine the prognostic value of initial PET C11 methionin (Ratio maximum: Rmax), IDH1 mutation and 1p-19q co-deletion in a series of patients with oligodendroglial tumours.

Method: Thirty-four patients were included in this retrospective, monocentric study. Survival analyses were done with Kaplan–Meier method and Cox model with univariate and multivariate analyses to take into account clinical prognostic factors.

Results: In univariate analyses, extent of resection (p = 0.02), WHO grade II (p = 0.016), IDH1 mutation (p = 0.003), 1p-19q co-deletion (p = 0.007) and low Rmax (p = 0.018) were associated with longer progression free survival. On overall survival, age (p = 0.002), IDH1 mutation (p < 0.001), 1p-19q (p = 0.006) and low Rmax (p = 0.01) were associated with longer survival. In multivariate analyses, extent of resection, WHO grade II and IDH1 mutation were associated with longer progression free survival. Only IDH1 (p < 0.001) and age (p = 0.024) were independent prognostic factors for overall survival.

Discussion: In addition to clinical factors, PET with C11 methionin and IDH1 mutation provide information on oligodendrogliomas prognosis. However, only IDH1 mutation has a strong and independent prognostic impact in this study.

Disclosure: Nothing to disclose.

EP3138

Mechanisms of lung tumour cell adhesion to human brain microvascular endothelial cells (HBMECs) during cerebral metastasis formation

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Introduction: Adhesion of circulating primary lung tumour cells to the endothelium of brain microvasculature is a crucial step in cerebral metastasis formation. This may be mediated by endothelial adhesion molecules binding to their counter ligands and receptors on the tumour cells; interactions that are potentially facilitated by the presence of specific molecules in the tumour microenvironment. We have shown previously that pro-metastatic factors, vascular endothelial growth factor (VEGF) and tumour necrosis factor-alpha (TNF-α), secreted by A549 and SK-MES-1 lung tumour cells increased both the expression of HBMEC adhesion molecule E-selectin and the adhesion of lung tumour cells to HBMEC monolayers. We have now examined: (1) the lung tumour counter ligands/receptors that bind to E-selectin; and (2) whether inhibiting the E-selectin axis affects endothelial cell/lung tumour adhesion.

Methods: Tumour cell ligands/receptors were examined by flow cytometry. Adhesion of lung tumour cells to HBMECs was assessed at a physiological shear stress of 1 dyn/cm^2. Specifically HBMECs were pre-treated with 200 pg/ml VEGF or 160 pg/ml TNF-α and lung cancer cells were then flowed over the monolayer ± anti-E-selectin antibody.

Results: Sialyl Lewis X (sLeX) was the predominant antigen expressed in both A549 and SK-MES-1 cells. Inhibition of sLeX binding to E-selectin using E-selectin antibody significantly reduced A549 adhesion to HBMECs induced by VEGF (from 272 ± 74.1 to 105 ± 58 %) and TNF-α (206 ± 108.7 to 108 ± 7.8 %). Similar attenuation of SK-MES-1 adhesion was also observed.

Conclusion: Tumour-secreted factors enhance adhesion of lung tumour cells to HBMECs via sLex/E-selectin binding, thereby potentially facilitating metastasis formation.

Disclosure: Nothing to disclose.

EP3139

Primary natural killer/T-cell lymphoma presenting as leptomeningeal disease

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Introduction: Primary central nervous system natural killer/T-cell lymphoma (primary-CNS-NK/TCL) is a rare non-Hodgkin's lymphoma. To our knowledge, only five patients have been described previously, all of whom were male, with brain parenchymal involvement and previous Epstein-Barr virus infection, it has never been reported to present as leptomeningeal disease as our case. Our objective is to report a rare case of primary-CNS-NK/TCL presenting as leptomeningeal disease and to share our diagnostic/therapeutic approach to this rare disease.

Methods: We report a rare case of primary-CNS-NK/TCL presenting as leptomeningeal disease. The patient was diagnosed and treated at The University of Texas MD Anderson Cancer Center in June 2013. She consented to the publication of her laboratory results and imaging studies for educational purposes.

Results: The patient presented with multiple cranial neuropathies and gait ataxia. Brain and spinal cord magnetic resonance imaging demonstrated leptomeningeal enhancement of the cerebellar folia/vermis, and spinal cord dura, but no brain parenchymal disease. Cerebrospinal fluid (CSF) revealed atypical lymphoma cells of NK/T-cell lineage by flow cytometric immunophenotyping. Molecular analysis using real-time quantitative polymerase chain reaction did not detect Epstein–Barr virus DNA in the lymphoma cells. Bone marrow biopsy revealed no morphologic, flow cytometric, or immunohistochemical evidence of B-, T- or NK-cell lymphoma. The patient was given systemic chemotherapy with high-dose methotrexate, vincristine, and procarbazine, along with intrathecal therapy with cytarabine. The patient showed clinicoradiographic improvement and CSF cytology became negative.

Conclusion: This case highlights an atypical presentation of primary-CNS-NK/TCL with a potentially successful treatment regimen.

Disclosure: Nothing to disclose.

EP3140

Cytoplasmic iron deposition is associated with the expression of oxidative DNA damage marker in meningiomas

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Objectives: Angiomatous meningiomas are rare meningioma subtypes, which are characterized by abundant vessels. We encountered 2 cases of newly diagnosed angiomatous meningiomas exhibiting tumor cells with brown pigments, which were histochemically proven to be iron.

Methods: In an attempt to understand its pathological significance, we assessed this unusual finding in representatives for each grade of meningiomas (total 51 cases) and immunoexpression of transferrin receptor (CD71) and the oxidative DNA damage marker, 8-hydroxy-2′-deoxyguanosine (8-OHdG).

Results: Iron deposition in the tumor cells was observed in 8/15 (53 %) of angiomatous meningioma cases, 2/6 (33 %) of microcystic meningiomas, and 2/20 (10 %) of meningothelial meningiomas, which included clustered microvessels, but not in fibrous, atypical, or anaplastic meningiomas ($P = 0.001$). Cytoplasmic CD71 expression was largely negative in angiomatous meningioma cases, but positive in meningothelial and high-grade meningiomas, suggesting that the transferrin-dependent iron transporter was involved in iron uptake in meningiomas. Nuclear expression of 8-OHdG was observed in > 50 % of the 15/15 angiomatous meningioma cases and was associated with the presence of regressive histopathological findings such as hyalinized vessels and cystic changes. In addition, the fraction of iron-containing tumor cells was correlated to those expressing 8-OHdG ($P = 0.005$).

Conclusions: Our finding indicates that cytoplasmic iron deposition in the tumor cells is characteristic of highly vascularized benign meningiomas and related to increased oxidative DNA damage markers.

Disclosure: Nothing to disclose.

EP3141

Psychological patterns of patients with recurrent brain tumour

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Introduction: Patients with brain tumor are rarely assessed for quality of life and psychological variables and even fewer studies have investigated these features in patients with a recurrence of brain tumors. The aim of the present study was to investigate the reaction to the illness of patients with recurrent brain tumors.

Methods: We enrolled 81 patients with recurrent CNS tumors. Multidimensional aspects of quality of life were assessed through "Functional Assessment of Cancer Therapy-Brain"; "Hospital Anxiety and Depression Scale" and "Psychological Distress Inventory". Karnofsky Performance Status was used to evaluate patients' functional status.

Results: The distress of our sample was significantly lower than distress reported in patients affected by other cancer types. All mean Fact-Br sub-scale scores were significantly lower in patients as compared with normative data. There were significantly lower scores in our sample for functional well-being and for social/family well-being than a sample of patients with primary brain tumors. Unexpectedly, emotional well-being mean score was significantly higher in our recurrence sample than in patients with primary brain tumors. The anxiety seems not to be influenced by relapse diagnosis, depression instead was significantly higher than normative data.

Conclusions: The recurrence of a brain tumor can have a major impact on patients condition and their psychological response than KPS levels. The dissociation between patients judgment on their quality of life (bad excepted for emotional) and their reported distress (low) is the most intriguing finding, suggesting highly preserved coping strategies in emotional sphere despite intact judgment and disease awareness.

Disclosure: Nothing to disclose.

EP3142

What about caregivers of brain tumor patients? Focus on psychological reactions to the illness

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Introduction: Caregivers of brain tumor patients often provide care to a family member, with a potentially short terminal disease trajectory and that may experience severe functional, cognitive and psychological sequelae. Very little is known about quality of life and well-being in caregivers of patients with brain tumors.

Methods: Participants consisted of 100 caregivers of patients with brain tumors admitted at our Neuro-oncology Unit. The questionnaires used were: Hospital Anxiety and Depression Scale (HADS), 36-Item Short-Form Health Survey (SF-36), Caregiver Reaction Assessment Scale (CRA).

Results: This study reported that, on average, caregivers of patients with brain tumors live with a clinically significant reduction in their quality of life, as compared with the general population. This reduction in quality of life concerned mainly their Mental Health. They experienced also a higher level of anxiety (mean = 10.94, S.D. = 4.06) and depression symptoms (mean = 7.25, S.D = 3.99). Further, the caregivers' burden appears mainly in their ability and energy to provide care and in their financial strain. However, these caregivers presented a positive physical reaction to their relative's illness and a positive impact on self-esteem.

Conclusions: This study highlights levels of anxiety and depression significantly high in caregivers of brain tumor patients. Since tumor grade does not significantly affect caregivers' quality of life, it would mean that a diagnosis of a brain tumor leads to a life in which the perception of "incurable disease" prevails, as compared with "high- or low-grade disease".

This context suggests a comprehensive approach, possibly with psychological and practical support, to help the affected family.

Disclosure: Nothing to disclose.

EP3143

Quality of life and recovery of disease in meningioma patients: a longitudinal study

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Introduction: Meningiomas account for about 35 % of all primary intracranial tumors influencing both survival and neurological functions. This suggests the importance to take into consideration postoperative Health-related quality of life (HRQOL) issues.

Objective: We aimed to describe HRQOL issues after surgery in meningioma patients using specific validated rating scales.

Materials and methods: Eighty-two meningioma patients were enrolled before craniotomy or cerebral-biopsy and assessed at first and second follow-up(6 months and between 12 and 18 months respectively).Mini-Mental State Examination (MMSE) was administered to assess cognitive deterioration. European Cooperative Oncology Group (ECOG) scale was used to evaluate performance status, to assess disease progression, and how the disease affects patients' daily-living abilities and determine appropriate treatment and prognosis. Performance was evaluated using five-point Likert scale.

Results: The time elapsed between diagnosis and intervention does not influence patients' HRQOL. The presence of post-operative complications determines an increase of depression in subjects at both 6 and 12 months. All patients who did not have postoperative complications, at 12 months after surgery, got back to previous life habits restoring their precious psycho-physical-social condition. The presence of post-operative complications with consequent permanent deficits, suggests the need to provide a specific support for these patients in order to promote a better HRQOL.

Conclusion: The HRQOL after surgery seems to be influenced by many factors: in particular the resolution of preoperative symptoms seems to be an important positive prognostic factor. Moreover, at 12 months we found a statistically significant relationship between MMSE low scores and the time elapsed between diagnosis and surgery.

Disclosure: Nothing to disclose.

EP3144

Haematological toxicity of Valproic acid versus levetiracetam in patients with glioblastoma multiforme undergoing concomitant radio-chemotherapy

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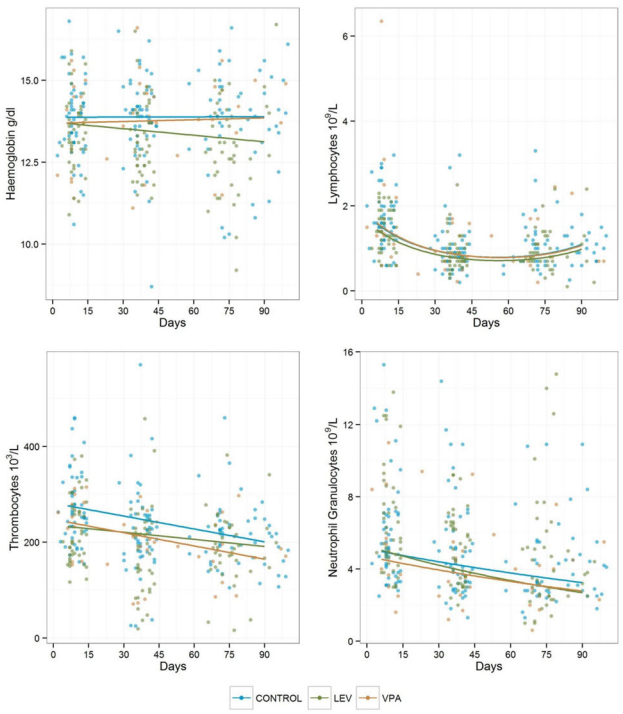
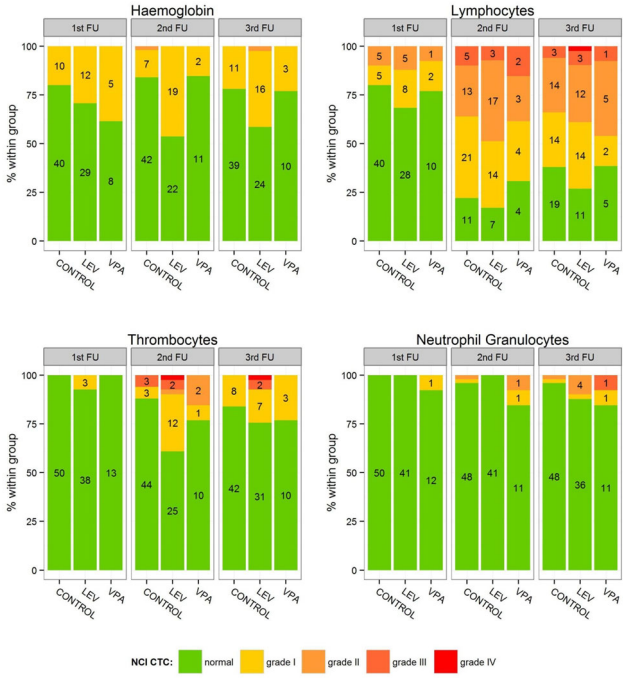
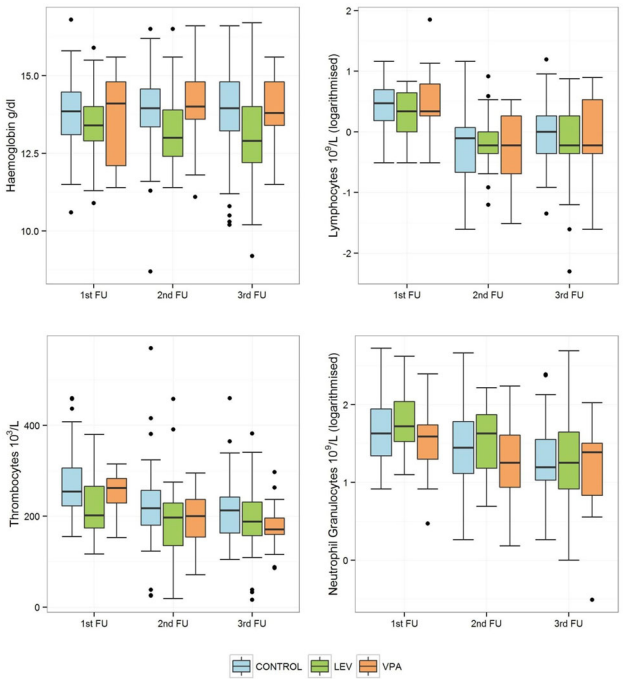
Introduction: Patients with glioblastoma multiforme (GBM) and symptomatic seizures are in need of a sufficient antiepileptic treatment. Haematological toxicity is a limiting side effect of both, first line radio-chemotherapy with temozolomide (TMZ) and co-medication with antiepileptic drugs. Valproic acid (VPA) and levetiracetam (LEV) are considered favourable agents in brain tumor patients with seizures, but are commonly reported to induce haematological side effects on their own. We hypothesized, that antiepileptic treatment with these agents has no impact on haematological side effects during radio-chemotherapy in the first line setting.

Methods: We included 104 patients from two neuro-oncologic centres with GBM and standard radio-chemotherapy in a retrospective cohort trial. Patients were divided according to their antiepileptic treatment with either VPA, LEV or without antiepileptic drug therapy (control group). Declines in haemoglobin levels and absolute blood cell counts for neutrophil granulocytes, lymphocytes and thrombocytes were analyzed twice during concomitant and once during adjuvant phase. A comparison between the examined groups was performed, using a linear mixed model.

Results: Neutrophil granulocytes, lymphocytes and thrombocytes significantly decreased over time in all three groups (all $p = < 0.012$), but there was no significant difference between the compared groups. A significant decline in haemoglobin was observed in the LEV treated group ($p = 0.044$), but did not differ between the compared groups.







Conclusions: As a novel finding, this study demonstrates that co-medication either with VPA or LEV in GBM patients undergoing first line radio-chemotherapy with TMZ has no additional impact on medium-term haematological toxicity.

Disclosure: Nothing to disclose.

EP3145

Leptomeningeal carcinomatosis: a 5-year case series at Centro Hospitalar Entre o Douro e Vouga: Northern Portugal

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Introduction: Leptomeningeal carcinomatosis (LCM) is an uncommon but devastating neurological complication of systemic cancer. Breast cancer and small cell lung cancer are the most frequent tumours associated with LCM. Global incidence is estimated in 0.8–8 % of all patients with cancer.

Methods: We performed a retrospective analysis of medical records from all patients with diagnosis of LCM, for the past 5 years.

Results: A total of eight patients (six women) were included. Median age at LMC diagnosis was 57 years (34–80).

Four patients had breast cancer diagnosis, two had lung cancer, one had malignant plasmacytoma and one had endometrial cancer.

Only in one patient LMC was the first manifestation of cancer; the overall mean time of diagnosis of LMC was 30.6 months (0–108).

Three patients presented with cranial nerve palsy, two patients with rapid progressive cognitive decline, two patients had seizures and one presented with isolated headache.

Meningeal contrast enhancement on MRI was found in seven patients and brain metastases in four patients.

Positive CSF cytology for malignant cells was found in only two patients.

Median survival after the diagnosis of LCM: 50 days (15–420). Two patients had survival time superior to 12 months.

Conclusions: Breast and lung cancer were the most frequent primary tumours in our series, as usually described in literature. + Positive CSF cytology for malignant cells was marginally lower to other case series. One-year survival was higher to previously described, considering that two patients survived for more than 1 year.

Disclosure: Nothing to disclose.

EP3146

Limbic encephalitis anti-Ma2, thymoma and myasthenia gravis

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Introduction: Limbic encephalitis associated with thymoma has been rarely described and associated with antibodies anti-Hu, anti-CV2 and anti-voltage-gated-potassium-channel.

Case report: A 65-year-old woman was diagnosed with thymoma while she was undergoing etiological investigation of myasthenia gravis (anti-acetylcholine receptors > 80 nmol/L). A month after partial resection of thymoma type AB and locally invasive, she developed visual hallucinations, delirium, heteroaggression, disorientation, memory impairment and hyperphagia. Neurological examination revealed memory, attention, orientation, calculation and abstraction impairments and release of primitive reflexes. CSF and Brain-MRI were unremarkable. Serial EEGs showed slow fronto-temporal activity mainly on the right and centro-parietal epileptic foci. SPECT showed left parieto-temporal hypoactivity. Brain-PET revealed parieto-temporal-occipital hypometabolism. Anti-Ma2 antibody was identified in the serum. Considering the coexistence of limbic encephalitis and anti-Ma2 antibody she underwent extensive search to rule out another malignancy (full body CT, mammary ecography/mammography, upper gastrointestinal endoscopy, thyroid ecography and full body PET) which was negative. There was no significant clinical response to treatment with immunoglobulin, corticosteroids and sodium valproate.

Conclusion: The association between limbic encephalitis, thymoma and myasthenia gravis is rare. It has been described in cases with a positive anti-CV2/CRMP5 (1 report) and anti-VGKC (1 report) antibodies, or cases where an antibody was not identified. This is the first report of a positive anti-Ma2 antibody limbic encephalitis associated with thymoma and myasthenia gravis.

Disclosure: Nothing to disclose.

EP3147

MRI negative meningeal myelomatosis with bilateral abducens nerve palsy and response to intrathecal chemotherapy

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Introduction: Leptomeningeal involvement (LMI) in Multiple Myeloma (MM) is extremely rare. We report a patient with MM presenting with bilateral abducens nerve palsy, responding to intrathecal chemotherapy (ITC).

Methods: Single case report.

Results: A 66-year-old patient presented with a lambda-light chain MM. Four cycles of bortezomib/doxorubicin were given, followed by autologous stem cell transplantation. A complete remission was achieved. 5 months later he relapsed and received 3 cycles of the DTP-PACE scheme. Two months later a PET-CT showed multiple osseous lesions, but no skull involvement.

20 months after the hematological diagnosis the patient developed vertigo, headache and a bilateral abducens nerve palsy. CCT and MRI were normal, no meningeal enhancement was found.

The CSF was pleocytotic, protein was elevated, glucose was normal. The plasma cells were atypical. They were classified as neoplastic and CD45+ and expressed the aberrant phenotype CD 19-56+.

ITC with methotrexate and cytarabin was given 4 times. Additionally systemic chemotherapy was given. The CNS symptoms responded to therapy.

3 months later he had an intrathoracal relapse. The CSF was normal. The cranial MRI showed only an osseous lesion in the petrous pyramid. The patient is currently still alive surviving LMI for 7 months.

Conclusions: LMI in MM is rare and often combined with osseous lesions of the base of the skull and meningeal enhancement in MRI. In our case these associated signs were absent and the diagnosis was made on the positive cytology. Despite positive response to ITC survival is limited to 3–6 months.

Disclosure: Nothing to disclose.

EP3148

Optimal glioblastoma treatment in elderly patients: a systematic review

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Introduction: Glioblastoma (GBM) is the most common primary brain tumour in adults and the incidence steadily increases with age. The diagnostic rate doubles in the age group between 65 and 84 years and survival is significantly reduced than younger. Moreover there is not an established standard of care: the role of surgery and radio-chemotherapy remain controversial.

Objective: We assess the scientific literature to define the optimal treatment for older patients that improves survival without compromising quality-of-life (QoL).

Materials and methods: Three recent phase III randomized controlled trials, and five prospective-retrospective uncontrolled phase II trials were identified. A total of 1187 GBM elderly patients, median age 72.4, were enrolled in order to receive: standard radiotherapy (RT) vs hypofractionated-RT vs 6 cycles of chemotherapy (CHT) with temozolomide (TMZ) or standard postsurgical involved-filed RT vs 100 mg/m^2 TMZ on days 1–7, 1 week-on 1 week-off or supportive-care alone vs supportive-care alone in combination with RT. Phase II studies dealt with CHT with TMZ in two cases, radio-chemotherapy by Stupp in two cases and only one study compared radio-chemotherapy vs RT alone. The primary end point was overall survival(OS) in all studies.

Results and conclusion: Our review did not show a statistically significant superiority of a particular treatment, but demonstrates that all therapeutic decision, both chemo and/or radiotherapy, could improve OS of elderly patients with good Karnofsy-Performance-Status (KPS) rather than palliative care (6.7 months-vs-3.8 months). In particular hypofractionated-RT plus TMZ chemotherapy may be the best way to treat patients with KPS $\geq$70 %. In patients with a poor KPS, RT could be a reasonable choice. A meta-analysis on collected data, will be performed.

Disclosure: Nothing to disclose.

Neuro-ophthalmology/-otology

EP3149

Cortical modulation of vestibulo-ocular reflexes as revealed with tDCS (transcranial direct current stimulation)

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Introduction: Recently, transcranial direct current stimulation (tDCS) has been shown to modulate cortical vestibular function (Kyriakareli et al. Neuroreport 2013; Arshad et al. Brain Stimul 2014). Given that this technique has shown potential to treat balance disorders (e.g. leucoaraiosis; Kaski et al. Neurorehabil Neural Repair 2013) there is a need to understand the mechanisms involved in tDCS-mediated vestibular modulation. We postulate that tDCS modulation of vestibulo-ocular reflexes (VOR) is mediated by activation of VOR suppression mechanisms (VORS).

Methods: Horizontal eye movements were measured in 6 healthy right handed subjects using electro-oculography, during full field optokinetic stimulation (40°/s), rotational VOR and VORS (0.25 Hz, 40°/s) and pursuit at two frequencies of 0.1 Hz and 0.4 Hz. Conditions were counterbalanced using a Latin square design. TDCS was applied over posterior parietal cortex for 15 min at 1.5 mA. Each subject underwent three experimental sessions, one with the anode over P4 and the cathode over P3, reverse in the second session with third sham controlled session.

Results: No significant difference was found between right or left anodal TDCS conditions in pursuit frequency at 0.1 Hz ($p = 0.28$) or 0.4 Hz($p = 0.29$), with VOR ($p = 0.86$) or OKN ($p = 0.64$). However, VOR suppression showed a significant effect in the right anode condition ($p < 0.04$, single-tailed paired samples t-test).

Conclusion: This data provide support for the hypothesis that bilateral stimulation of parietal cortex selectively modulates VOR suppression by top down modulation. The lack of significant impact on pursuit eye movements suggests a degree of dissociation between cortical pursuit and VORS mechanisms.

Disclosure: Nothing to disclose.

EP3150

Comparing iatrogenic canal switch in benign paroxysmal positional vertigo: Semont versus Epley maneuver

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Introduction: Semont (SM) and Epley maneuvers (EM) are a well established effective and safe treatment of posterior canal benign paroxysmal positional vertigo (BPPV). However, data comparing SM and EM regarding maneuver induced canal switch are lacking.

Methods: We prospectively investigated 102 consecutive posterior canal BPPV patients after application of the Semont or the Epley maneuver and looked for the appearance of ipsilateral horizontal or anterior canal BPPV symptoms.

Results: Although treatment success was similar for SM and EM (67 and 76 % respectively) there was a significant difference in posterior-to-horizontal canal switch rates. In particular, 4 of 51 patients (7.8 %) of the EM group converted to the geotropic type of horizontal canal BPPV, whereas none of the 51 SM patients exhibited a canal switch. All four patients were cleared with a single barbecue maneuver. Posterior-to-anterior canal conversions were not observed in our sample.

Conclusions: Despite the relatively small sample, our data suggest a small but significant difference in canal switch rate between EM and SM, which could be partly explained by the higher number of maneuver steps during which the head is in the dependent position throughout the EM.

Disclosure: Nothing to disclose.

EP3151

Apogeotropic central positional nystagmus: characteristics and mechanisms

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Introduction: This study aimed to determine the pattern and associating neuro-otological characteristics of apogeotropic central

positional nystagmus (apogeotropic CPN) in comparison to apogeotropic nystagmus from cupulolithiatic horizontal canal benign paroxysmal positional vertigo (apogeotropic BPPV). In addition, we try to discover the mechanism of apogeotropic CPN by lesion analysis and mathematical modeling.

Methods: Twenty seven patients with apogeotropic CPN and 20 patients with apogeotropic BPPV underwent recording of spontaneous nystagmus while sitting and supine and position-triggered apogeotropic nystagmus in the ear-down position. We measured the gravitation-induced nystagmus (GIN) by subtracting the intensity of spontaneous nystagmus while supine from that of apogeotropic nystagmus in the ear-down position to either side.

Results: The intensity of spontaneous nystagmus was similar between the sitting and supine positions in the apogeotropic CPN group, but greater in the supine position in the apogeotropic BPPV group. In both groups, the apogeotropic nystagmus was greater when it was in the direction of the spontaneous nystagmus while supine. The intensity of GIN was symmetrical between the sides in the apogeotropic CPN group, but markedly asymmetrical in the apogeotropic BPPV group. Lesion analysis and mathematical modeling suggest that nodulus, uvula, and tonsil produce tilt estimation error in velocity-storage circuit.

Conclusions: Lesions involving the nodulus, uvula, and probably the tonsil may produce erroneous tilt estimation and apogeotropic GIN. The apogeotropic CPN appears to result from summation of the spontaneous nystagmus while supine and symmetrical apogeotropic GIN in ear down position produced by erroneous tilt estimator.

Disclosure: Dr. J-S Kim received research support from SK Chemicals, Co. Ltd.; Dr. S. Glasauer receives research support from the German Research Foundation (DFG) and the German Federal Ministry of Education and Research (BMBF) and is a shareholder of EyeSeeTec GmbH.

EP3152

Involvement of the retinal nerve fiber layer (RNFL) in early Alzheimer's disease: evidence from optical coherence tomography

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Introduction: Visual symptoms can often be detected in Alzheimer's disease (AD). Such deficits find their neuropathologic basis in amyloid beta (Ab) deposits in visual cortex and retina. Optical coherence tomography (OCT) is a non-invasive imaging technology that provides high-resolution cross-sectional images of RNFL. It is still a matter of debate whether RNFL is reduced in AD. The aim of our study was to investigate the difference of RNFL thickness between AD subjects and healthy controls (HC), and to evaluate if RNFL thickness may be correlated with disease duration, neuropsychological data and cerebrospinal fluid (CSF) biomarkers.

Methods: We recruited 76 subjects, including 53 patients with mild/moderate untreated AD (33 F, 71.5 ± 6.6 years) and 23 HC (12 F, 66.7 ± 7.4 years). Examination was performed using spectral domain OCT. For statistical analysis the significance level was set at $p \leq 0.05$.

Results: We found a significant RNFL thinning, both global and selective for each quadrant in AD compared to HC ($p = 0.05$): average 92.09 ± 9.8 vs 98.18 ± 5.9 μm; superior quadrant 112.5 ± 17.3 μm vs 121.4 ± 12.5 μm; inferior quadrant 119 ± 16.5 μm vs 125.86 ± 10 μm; temporal quadrant 67.29 ± 12 μm vs 71.41 ± 12.2 μm; nasal quadrant 69.46 ± 12.2 vs 73.97 ± 12.7 μm. However, RNFL thickness was not correlated with disease duration, MMSE or CSF biomarkers.

Conclusions: Our data support that neurodegeneration involving distal optic nerve pathways may occur in AD. Further studies are granted aimed at investigating the usefulness of OCT as a biomarker in early diagnosis of AD, in addition to brain MRI, PET and CSF.

Disclosure: Nothing to disclose.

EP3153

Value of structural MRI and neurophysiology in the diagnosis of vestibular paroxysmia

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Introduction: Vestibular paroxysmia (VP) is defined as neurovascular compression (NVC) syndrome of the eighth cranial nerve (N.VIII) similar to trigeminal neuralgia (1,2,3). The aim of the current study was twofold, first, to assess the value of MRI for detecting a NVC and second, to analyse the significance of audiovestibular testing.

Methods: 20 VP patients and 20 patients with trigeminal neuralgia as controls were examined. All participants underwent standardized MRI to detect NVC. Moreover, extensive audiovestibular testing including subjective visual vertical (SVV), fundus photographs, video-oculography, cervical vestibular evoked myogenic potentials (cVEMP), caloric and acoustic testing was performed.

Results: NVC could be detected in every VP patient resulting in a diagnostic sensitivity and specificity of 100 and 65 %. The compressing vessel was the AICA in 15 (75 %), the PICA in one (5 %), a vein in two (10 %) and the vertebral artery in two cases (10 %, VA). Audiovestibular testing revealed normal results in five patients (25 %), a unilateral loss of audiovestibular function in nine patients (45 %) and audiovestibular results with signs of reduced as well as increased function within the same nerve in six patients (30 %). The 20 controls had 7 (35 %) asymptomatic NVC (5 AICA, 1 PICA, 1 vein).

Conclusions: Neurophysiological testing in combination with MRI allows a reliable diagnosis of VP. The combination of both methods enables an identification of the affected side and a differentiation between deficit syndromes or increased excitability of N. VIII.

1. Brandt, Dieterich 1994a2. Brandt, Dieterich 1994b3. Hüfner et al., 2009

Disclosure: Nothing to disclose.

EP3154

Abstract withdrawn

EP3155

Unilateral inferior cerebellar peduncular lesion

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Introduction: The inferior cerebellar peduncle (ICP) connects the medulla oblongata with the cerebellum. The ICP carries many types of input and output fibers that are concerned with integrating proprioceptive sensory information and motor vestibular function, but the clinical characteristics of ICP lesion have not been previously investigated.

Methods: Nineteen patients with unilateral ICP lesion were recruited from two Neurology Clinics of University Hospitals. All patients underwent complete and standardized neurotological evaluation including nystagmus, head impulse test, subjective visual vertical, ocular torsion, bithermal caloric tests, and pure tone audiometry.

Results: All patients showed abnormal ocular tilt reaction (OTR); nine with contralesional side and ten with ipsilesional side. Of the nine patients with contralesional OTR, four had an isolated ICP lesion in low pons or rostral medulla, and the other five had an additional lesion in superior cerebellar peduncle, and cerebellum. Most patients showed ipsilesional nystagmus, profound falling to the ipsilesional side, normal head impulse and bithermal caloric tests. Remarkably, the direction of OTR and falling was dissociated in most patients. Whereas, ten patients with ipsilesional OTR had a ICP lesion in the lateral medulla, and showed ipsilesional falling, which always corresponded to the direction of OTR.

Conclusions: The present study demonstrated two distinct vestibular signs in unilateral ICP lesion according to the lesion level. Directional dissociation of body lateropulsion and OTR may be a distinctive sign of unilateral ICP lesion in pontine ICP lesion, which indicates that neural pathways responsible for head and body coordination may run inversely at ICP level.

Disclosure: Nothing to disclose.

EP3156

Study of correlation between scale for the assessment and rating of ataxia, ocular movements and clinical items in spinocerebellar ataxia type 3

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Introduction: Different alterations in ocular movements have been described in spinocerebellar ataxia type 3 (SCA3). The aim of this study is analyse the correlation between the ocular movements and the items of the scale for the assessment and rating of ataxia (SARA) and some clinical data.

Methods: Horizontal saccades, horizontal smooth pursuit, optokinetic nistagmus, velocity step tests and rotation vestibular test were evaluated in 16 patients with SCA3 by Synapsys®. We calculated the Spearman's correlation coefficient between ocular movement parameters, SARA items and clinical variables (sex, years of evolution, and age at the evaluation) were calculated and it was expressed by a social network.

Results: A poor correlation between the SARA items and ocular movements parameters is shown (the velocity of right horizontal saccades is significantly correlated in a negative way with gait, right finger chase and stance, and velocity of left horizontal saccades is correlated with right and left finger chase in a negative way too). The correlation with clinical variables are not strong either (right smooth pursuit is correlated in a negative way with evolution and age. Velocity of right horizontal saccades is associated in a negative way with evolution).

Conclusions: Eye movements' alterations and cerebellar signs measured by the SARA scale are different modules of the SCA3 spectrum of affection. In contrast with cerebellar signs, eye movement alterations are not closely correlated with sex and years of evolution.

Disclosure: Nothing to disclose.

EP3157

Gait characteristics of patients with downbeat nystagmus syndrome

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Introduction: Downbeat nystagmus (DBN) is a common form of acquired fixation nystagmus with key symptoms of oscillopsia and gait disturbance. Gait disturbance could be a result of impaired visual feedback due to the involuntary oscillations. Alternatively, a malfunction of cerebellar locomotor control might be involved, since DBN is considered a vestibulocerebellar disorder.

Methods: Investigation of walking in 50 DBN patients and 50 healthy controls (HS) using a pressure sensitive carpet (GAITRite®). The patient cohort comprised subjects with only ocular motor signs (DBN) and subjects with an additional limb ataxia (DBN+). Gait investigation comprised different walking speeds and walking with eyes closed.

Results: In DBN, gait velocity was reduced ($p < 0.001$) with a reduced stride length ($p < 0.001$), increased base of support ($p < 0.05$) and increased double support ($p < 0.001$). Walking with eyes closed led to significant gait changes in both HS and DBN. These changes were more pronounced in DBN patients ($p < 0.001$). Speed-dependency of gait variability revealed significant differences between the subgroups of DBN and DBN+ ($p < 0.05$).

Conclusions: The gait of patients with DBN is impaired due to a disturbed balance control. (II) Impaired visual control caused by involuntary ocular oscillations cannot sufficiently explain the gait disorder. (III) Analysis of gait variability allows distinguishing DBN from DBN+: Patients with DBN only show a speed dependency of gait variability similar to that of patients with afferent vestibular deficits. In DBN+, gait variability resembles the pattern found in cerebellar ataxia.

Disclosure: Nothing to disclose.

EP3158

The neuroanatomical correlates of vestibular adaptation in ballet dancers

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Introduction: Sensory input evokes low-order reflexes and higher-order perceptual responses. Vestibular stimulation elicits vestibular-ocular reflex (VOR) and self-motion perception (e.g. vertigo) whose response durations are normally equal. Adaptation to repeated whole-body rotations, e.g. ballet training, is known to reduce vestibular responses. We investigated the neuroanatomical correlates of vestibular perceptuo-reflex adaptation in ballet dancers and controls.

Methods: We measured the vestibular reflex and vestibular perceptual responses following whole body step rotations in the dark in dancers and rowers (all female, right-handed). All subjects underwent structural brain MRI in a separate session allowing us to make comparisons between brain structure and vestibular function.

Results: Dancers' vestibular-reflex and vestibular-perceptual responses to whole-body yaw-plane step rotations were: (i) briefer (ii) and uncorrelated (controls' reflex and perception were correlated). Voxel-based morphometry showed a selective grey matter (GM) reduction in dancerś vestibular-cerebellum correlating with ballet experience. Dancers' vestibular-cerebellar GM density reduction was related to shorter perceptual responses (i.e. positively correlated) but longer VOR duration (negatively correlated). Contrastingly, controlś vestibular-cerebellar GM density negatively correlated with perception and VOR. Diffusion-tensor imaging showed that cerebral cortex white matter (WM) microstructure correlated with vestibular perception but only in controls.

Conclusions: In summary, dancers display vestibular perceptuo-reflex dissociation with the neuronatomical correlate localised to the vestibular-cerebellum. Controlś robust vestibular perception correlated with a cortical WM network conspicuously absent in dancers. Since primary vestibular afferents synapse in the vestibular-cerebellum, we speculate that a cerebellar gating of perceptual signals to cortical regions mediates the training-related attenuation of vestibular perception and perceptuo-reflex uncoupling.

Disclosure: Nothing to disclose.

EP3159

Predictors of development of chronic vestibular insufficiency after vestibular neuritis

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Objectives: To evaluate the role of clinical parameters, MRI and ocular VEMP (oVEMP) and cervical VEMP (cVEMP) as predictors of development of chronic vestibular insufficiency after vestibular neuritis.

Methods: Twenty six patients with vestibular neuritis were included: 15 patients (58 %) showed complete clinical recovery, 11 (41 %) were diagnosed with the syndrome of chronic vestibular insufficiency. Clinical parameters (vomiting, nystagmus, postural stability, nausea) were assessed at the diagnosis. MRI was performed within 3 months and VEMP within 6 days and at 1 year after the initial presentation. The amplitude asymmetry ratio (AR) was calculated using the following formula: AR = ((healthy side − affected side)/(healthy side + affected side) × 100).

Results: Of all studied parameters, only chronic white matter supratentorial lesions present on brain MRI negatively correlated with clinical recovery (Phi coefficient −0.637, $p = 0.001$). The logistic regression analysis showed that positive brain MRI and older age reduced odds for clinical recovery. There was no correlation between clinical recovery and oVEMP AR recovery between groups ($p = 0.781$). Seven patients showed improvement and 19 showed worsening on oVEMP AR after 1-year follow-up. Model for predicting the outcome of clinical recovery using asymmetry score recovery, as an independent variable, was not statistically significant.

Conclusions: Older age and chronic white matter lesions on brain MRI are positive predictors of development of chronic vestibular insufficiency after vestibular neuritis. VEMP are not useful in predicting the development of chronic vestibular insufficiency.

Disclosure: Nothing to disclose.

EP3160

Cogan-I-syndrome and pregnancy

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Introduction: Cogan-I-Syndrome is a rare autoimmunological disease defined by the triad of non-syphilitic interstitial keratitis, cochlear and vestibular dysfunction (1). We now present two young women and the course of Cogan-I-Syndrome during pregnancy.

Case 1 In this 34-year-old woman Cogan-I-Syndrome was diagnosed 3 months prior to pregnancy. Using high dose steroids (1000 mg/day prednisolone for 5 days), vertigo and ocular inflammation could be rapidly terminated. During the first trimester, the symptoms reoccurred requiring oral steroid treatment (80 mg/day prednisolone).

Case 2 In this 37-year-old woman Cogan-I-Syndrome became clinically present 8 weeks after labor. Since the symptoms could not be controlled by steroid treatment (initially 1,000 mg/day prednisolone for 5 days followed by oral prednisolone) the therapy was augmented by azathioprine.

Conclusion: We present two women with onset and relapse of Cogan-I-Syndrome in close correlation to pregnancy. In case 1 the disease activity relapsed within the first pregnancy trimester. In case 2 the disease had its onset shortly after labour. There are only three further reports on Cogan-I-Syndrome during pregnancy (2–4), and one woman showed a worsening of the disease during pregnancy. Further data is needed in order to decide whether pregnancy can be viewed as a possible trigger mechanism for Cogan-I-Syndrome or if these three out of five known cases must be considered as coincidental.

References
1: Norton, Cogan, 1959
2: Deliveliotou et al., 2007
3: Bakalianou et al., 2008
4: Currie et al., 2009

Disclosure: Nothing to disclose.

EP3161

Optical coherence tomography and transorbital echography study in patients with neuromyelitis optica

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Introduction: Optical coherence tomography (OCT) is a simple non-invasive technique to quantify the thickness of retinal nerve fiber layer (RNFL) and macular volume. Transorbital duplex echography (TDE) can also measure the optic nerve (ON) diameter.

The objectives are to study the optic nerve by OCT and TDE in neuromyelitis optica (NMO) and NMO related disorders (NMORD) and to evaluate the relationship between OCT and TDE and clinical parameters.

Methods: Patients underwent a neurological and ophthalmological evaluation including visual acuity, funduscopic examination and optical coherence tomography (OCT, Cirrus). Retinal nerve fiber layer thickness (RNFL), macular volume (MV), and ganglionar cells layer (GC) were measured. TDE in both eyes was also performed and the ON diameter measured. A control group of 25 healthy subjects was also evaluated with TDE.

Results: Ten patients with NMO and NMORD with a mean EDSS of 3.0 were recruited, 7 eyes were affected by optic neuritis. The RNFL was decreased (85.28 ± 15 μm), temporal and nasal sector were most affected; CG was also reduced (75.06 ± 14.03). ON diameter was similar (3.55 ± 0.64 mm) to the control group. When we divided the patients among patients with optic neuritis and non-optic neuritis, we found significant differences in the RNFL, GC and ON diameter between both groups. The RNFL only correlated with the number of optic neuritis. However, the ON diameter was associated significantly with EDSS and evolution time.

Conclusions: OCT parameters are useful to detect optic neuritis in NMO/NMORD patients in comparison with TDE but transorbital echography correlated better with clinical parameters.

Disclosure: Nothing to disclose.

EP3162

Pedunculopontine nucleus DBS modulates visual-vestibular integration

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Introduction: Gait dysfunction in Parkinson's disease responds poorly to STN (subthalamic nucleus) stimulation. The pedunculopotine nucleus (PPN) may improve gait in PD and recent primate work shows PPN-vestibular reactivity. Could PPN-related gait improvement in PD relate to improved vestibular sensory function?

Methods: Four PD patients with simultaneously implanted bilateral PPN and STN electrodes and eight healthy age matched controls were tested on: (1) vestibular perceptual thresholds while subjects were seated in the dark in a Barany chair; (2) postural sway with lights on with eyes open (EO) and lights off with eyes closed (EC).

Results: When PPN stimulation was off, patients had worse vestibular perceptual thresholds ($t(10) = -2.355$, $p = 0.040$) than controls. On PPN stimulation, thresholds marginally improved ($t(3) = 1.582$, $p = 0.212$) but were now not different from controls ($t(10) = -2.136$, $p = 0.058$). Patients swayed more, both on ($t(10) = -4.034$, $p = 0.002$) and off ($t(10) = -3.620$, $p = 0.005$) PPN stimulation. PPN stimulation did not reduce sway ($t(3) = -0.624$ $p = 0.577$). The Romberg coefficient (RC = EO/EC) was >1 for all participants. Patients off stimulation RCs were not different to controls ($t(10) = -2.096$, $p = 0.063$). Patients stimulation RCs were greater than controls ($t(10) = -3.309$, $p = 0.008$).

Conclusions: Our results suggest that when on stimulation, patients have improved sensory integration. This is consistent with a view that the vestibular system has a critical function in postural control when visual and proprioceptive information is unreliable.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 5

EP3201

The unilateral high-grade internal carotid artery changes: brain focal impairment and hemodynamic parameters in relation to the type of collateral supply

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Introduction: To study the relationship between collateral flow via different pathways and cerebral hemodynamic parameters in patients with unilateral high-grade internal carotid artery (ICA) changes.

Methods: 71 patients (41 with severe stenosis and 30 with occlusion of ICA) underwent brain MRT (1.5 ,3 T), 3D TOF-MR-angiography, Color Dopller of extra-intracranial vessels to investigate collateral flow via the circle of Willis (AComA, PComA) and via the ophthalmic artery (OphA). The cerebral perfusion parameters maps were calculated.

Results: In 50 (70 %) cases "symptomatic" cerebral ischemia was marked. In symptomatic patients prevealed cortical MCA infarctions (13(26 %)), and border-zone infarctions (10(20 %)). In ICA occlusion cases compensatory dilatation of contralateral ICA and enhancement of flow volume by 60 %, enhancement of flow in the vertebral arteries was marked. Whether patients without collateral flow via the circle of Willis or flow via the PComA only have a high incidence of brain infarction (13(85 %)) and impaired hemodynamic parameters in the MCA (V mean-38sm/s, PI-0.69), than patients with collateral flow via the AComA. Patients with reversed OphA could prove an additional risk for infarction. Patients with collateral flow via both anterior and posterior communicating arteries had less increased rCBV than those without.

Conclusions: Patients with collateral flow via the PComA and reversed OphA flow have more impaired hemodynamic parameters and a higher risk of brain infarctions, than patients with collateral flow via the AComA. Complex use of TCCD, 3D TOF-MR-angiography and PWI gives all necessary information about type and hemodynamic parameters of collateral supply in high-grade carotid artery changes.

Disclosure: Complex use of TCCD, 3D TOF-MR-angiography and PWI gives all neccessary information about type and hemodynamic parameters of collateral supply in high-grade ICA changes.

EP3202

Rapidly progressive dementia, gait disorder and myoclonic jerks, mimicking CJD

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Introduction: Rapidly progressive dementia and myoclonia may point to the diagnosis of sporadic Creutzfeldt Jacob's disease (sCJD). We present a similar case with a different, yet treatable diagnosis.

Methods: *Case report*: A female patient aged 77 was admitted with left-sided and generalized myoclonic jerks and seizures. During the last weeks she had developed severe ataxia, rapidly progressive dementia and irregular myoclonia. Neurologically, she showed mild spastic tetraparesis and akinetic mutism. Eye movements were normal. Series of irregular myoclonic jerks could easily be triggered by sensory stimulation or by the initiation of movements.

Results: EEG showed moderate slowing with periods of rhythmic generaliized sharp waves, and triphasic waves, most pronounced over the left fronto-precentral region. CSF was normal, protein 14-3-3 was negative. MRI showed multifocal confluent T2 hyperintensities of cerebral white matter, associated with multiple small spots of signal extinction in SWI. Stereotactic brain biopsy yielded multiple amyloid plaques and deposits of beta amyloid in the walls of small arteries, where also cytotoxic T lymphocytes and macrophages were found, thus confirming the diagnosis of "amyloid beta-related angiitis" (ABRA). Treatment with steroids lead to partial improvement.

Conclusions: ABRA is the inflammatory/vasculitic variant of cerebral amyloid angiopathy (CAA). As vasogenic edema of the subcortical white matter often develops within a few weeks, its clinical appearance may include rapidly progressive dementia, thus being an important differential diagnosis of CJD. The typical MRI pattern and a relatively good response to steroids lead to the correct diagnosis, which may be confirmed by brain biopsy.

Disclosure: Nothing to disclose.

EP3203
Cerebral vein and dural sinus thrombosis: an evaluation of 54 cases

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Introduction: Cerebral vein and dural sinus thrombosis (CVT) generally manifest in various non-specific clinical forms. The aim of our study was to identify CVT causes and risk factors, to describe the demographic, clinical, laboratory, and neuroimaging data, and to evaluate the treatment and outcome.

Methods: We analysed 54 CVT consecutive patients, which were examined at admission and after 3 months, using the mRS scores.

Results: Mean age was 37.3 years (SD 7.6), sex ratio: male/female was 1/2. 83.3 % of women were fertile. The most frequent neurological syndrome was intracranial hypertension. CT showed direct signs of dural sinuses thrombosis in 8 pts, and venous cerebral infarcts in 20 cases. MRI identified thrombosis of SSS in 38 pts, transverse sinus in 20 cases, cavernous sinus in 4 pts. 12 out of 54 MRI had a normal prior CT. DSA revealed isolated cortical veins occlusion, without sinus occlusion in 4 cases. Risk factors were identified in 40 pts (74.1 %); congenital thrombophilia being the most common (18 cases). All pts received anticoagulant therapy. After 90 days from admission, functional outcome was good, with a mRS score ≤ 2 in 32 pts, moderate/severe disability in 15 cases, the death rate being 12.9 % (7 pts). Severity of CVST was found to be associated with presence of rapidly worsening symptoms ($p = 0.001$), and occlusion of 4 or more sinuses ($p = 0.005$).

Conclusions: CVT was common in women of fertile age. The outcome was favorable if the pts were promptly diagnosed and adequately treated.

Disclosure: Nothing to disclose.

EP3204
Selective serotonin reuptake inhibitors for the prevention of post stroke depression: a meta analysis

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Introduction: Depression following stroke has often been overlooked and is associated with decreased functional recovery and increased mortality. Data regarding its prevention is conflicting.

Objective: The objective of the study is to determine if selective serotonin reuptake inhibitors (SSRIs) are effective and safe in preventing post-stroke depression (PSD).

Methods: We searched for articles evaluating the efficacy of any SSRI for prevention of PSD. The pooled relative risk (RR) and 95 % confidence intervals were calculated. Frequency of side effects was also calculated.

Results: A total of 4 articles and 405 patients were included in this study. Our meta-analysis has demonstrated that SSRIs reduced the incidence of PSD (RR = 0.36, 95 % CI 0.22–0.60) without significant heterogeneity. Also, the occurrence of adverse effects was not significantly different from that of the control group.

Conclusions: SSRIs are beneficial for the prevention of PSD and in doing so, it may increase functional recovery and decrease mortality.

Disclosure: Nothing to disclose.

EP3205
Endovascular treatment of stroke patients with large pretreatment DWI lesions

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Introduction: Initial diffusion-weighted imaging (DWI) lesion volume on MRI before acute stroke therapy has been identified as predictor of outcome and patients with large volumes are usually excluded from therapy in clinical practice and treatment studies. The aim of this study was to analyze the impact of large lesion volumes on outcome in a larger cohort of endovascular treated patients.

Methods: 372 patients with middle cerebral artery or internal carotid artery occlusions, who had baseline MRI and were treated since 2004 were included. Baseline data and 3 months follow up were recorded prospectively. DWI lesion volumes were obtained semi-automatically.

Results: DWI lesion volumes were an independent predictor of favourable outcome (mRS 0-2), survival and symptomatic intracerebral bleedings (sICH)($p < 0.001$ each). Of 66 patients with lesions >70 ml, 11/31 (35.5 %) reached favourable outcome after TICI 2b-3 reperfusion in contrast to 3/35 (8.6 %) after TICI 0-2a reperfusion ($p = 0.014$). Similar outcome rates were obtained in 39 patients with lesions >100 ml (33.3 % good outcome after TICI 2b-3 and 8.3 % after TICI 0-2a reperfusion). Reperfusion success, the patient's age and DWI lesion volume were independent predictors of favourable outcome in patients with DWI lesions >70 ml.

Conclusions: Despite raising risk for poor outcome and sICH with increasing initial DWI lesion volumes, favourable outcome was achieved anyhow in every third patient with DWI lesions >70 ml after successful endovascular reperfusion, whereas only every twelfth reached favourable outcome after poor or failed reperfusion.

Endovascular therapy may be considered especially in young patients with large initial DWI lesions.

Disclosure: Nothing to disclose.

EP3206

Human angular path integration, timing and the temporoparietal junction

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Introduction: Path integration is the process of updating one's travelled distance from motion cues. For linear path integration, haptic and vestibular cues contribute whereas vestibular cues predominate for angular path integration. Theoretically, path integration could involve a temporal integration of motion cues, requiring a timing mechanism.

Methods: We tested whether unconscious updating of internal estimates of self-position can update internal estimates of motion duration perception in 16 healthy volunteers. In a second series of experiments, we assessed perceived self-location, perceived self-motion duration, and perceived self-motion angular velocity in a vestibular-guided task in the dark in 18 right hemisphere stroke patients and 14 age-matched controls.

Results: In healthy subjects, when vestibular-derived angular position was updated by masked imperceptible visual landmarks, motion duration estimates were congruently updated. Furthermore, angular path integration was severely disrupted by right temporoparietal junction (TPJ) lesions for leftward (not rightward) whole-body turns. The navigational deficit was unrelated to neglect of self-motion velocity perception however TPJ patients displayed a timing bias, perceiving leftward rotations as briefer than rightward.

Conclusions: These data suggest that human angular path integration is mediated by the TPJ and involves an internal representation of temporal self-motion duration.

Disclosure: Nothing to disclose.

EP3207

Relevance of glycemia, blood pressure levels and temperature in acute stroke

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Introduction: The effect of blood pressure (BP) variations, hyperglycemia and hyperthermia is actually well documented, however the results of studies are controversial.

Methods: We studied 446 patients with acute ischemic admitted at the stroke unit between July 2009 to July 2010. xe recorded admission blood pressure and blood pressure values from continuous 72 h monitoring, admission glycemia and serial mean temperature from admission until 7 days after stroke. Clinical data including NIHSS (National institute of health stroke score)(admission and discharge), infarct volume and mortality (30 days and long term) were included into the analysis. Data were analysed using SPSS 19.0

Results: Admission NIHSS, lesion volume and early mortality did not correlate with hypertensive episodes within the first 72 h or admission hyperglycemia. However there were a significative relation between low admission systolic BP < 140 mmHg, admission hyperglycemia and increased risk of death 1 year after stroke. Mortality was higher in patients with hyperthermia >37.5°c 48 h after stroke: $P = 0.009$ $OR = 2.783$ (IC 95 %;1.257–6.162), also sever stroke (NIHSS > 6) was more frequent in these patients: $P = 0.030$ $OR = 20{,}66$ (IC95 %; 1.31–320.580).

On the other hand 84 % of patients with admission NIHSS > 6 had a mean temperature > 37.548 h after stroke.

Conclusions: The role of blood pressure and hyperglycemia is not well established because of used thresholds considered by studies and methodological differencies.

Disclosure: Nothing to disclose.

EP3208

Clinical and neuroimaging particularities of posterior reversible encephalopathy syndrome in pregnancy

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Introduction: Posterior reversible encephalopathy syndrome (PRES) may be associated with pregnancy and sometimes its diagnostics is very difficult.

Methods: We observed seven cases of PRES in patients with preeclampsia and eclampsia during 2010–2013 in Republican clinical hospital, Kazan.

Results: All patients had headache and impairment of consciousness (up to coma). Six patients had visual signs and four of them also had motor deficits and mild or moderate meningeal signs. There were seizures (tonico-clonic and myoclonic ones) in the onset of the disease in six cases. In one case we saw only headache, rapid impairment of consciousness up to soper associated with distinctive MR signs. The symptoms always developed against the background of raised blood pressure. Authentic diagnosis of vasogenic edema of brain, represented in PRES is based on MR DWI and ADC map images. The regions of vasogenic edema are characterized by hypo- or isointensed signals on DWI and increased signals on ADC maps. Initial MR imaging demonstrated areas of vasogenic edema of occipital and parietal lobes in every case, in three cases frontal lobes were involved and one patient had lesions of cerebral peduncles, pons and basal ganglia. There were associated acute ischemic lesions in two cases and hemorrhagic imbibition in the other one. If treatment was proper neuroimaging and clinical signs regressed in 1–4 weeks.

Conclusions: Prompt definition of this condition allows to choose correct tactics of treatment and consequently leads to laudable outcome for a patient.

Disclosure: Nothing to disclose.

EP3209

Abstract withdrawn

EP3210

Knowledge about symptoms and risk factors of stroke among students of medical and non-medical University in Poland

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Introduction: Stroke is one of the leading causes of death and disability worldwide. Knowledge about risk factors is an essential element of

primary prevention, and awareness of the stroke symptoms may accelerate hospitalization and the therapy. The aim of the study was to assess knowledge about stroke among young people—university students.

Materials and methods: The study included 341 students of the Silesian University of Medicine and Higher School of Labour Protection in Katowice, divided into three groups: MS—sixth-year students of medicine (n = 102), ES—third-year students of medical emergency (n = 32), NMS - students of non-medical faculties (n = 207). In the study the authored questionnaire was used.

Results: Average numbers of correctly listed risk factors were: 2.9 ± 1.2 (MS), 2.5 ± 1.3 (ES) and 0.5 ± 0.8 (NMS). Smoking and hypertension were the most frequently reported by all the groups. Average numbers of listed symptoms were: 3.8 ± 1.2 (MS), 2.9 ± 0.9 (ES) and 1.3 ± 1.2 (NMS). The most frequently reported were: paresis, speech and visual disorders (MS); loss of consciousness, paresis (ES); paresis, headache (NMS). The majority of respondents would call an ambulance when stroke was suspected (MS-94 %, ES-97 %, NMS-79 %). MS knew significantly more stroke symptoms than ES ($p < 0.001$) and NMS ($p < 0.001$), while ES significantly more than NMS ($p < 0.001$). In addition, both ES and MS knew more stroke risk factors than NMS ($p < 0.001$).

Conclusions: Knowledge of the risk factors and symptoms of stroke among young people—non-medical students—is insufficient and should be complemented with an extensive educational program.

Disclosure: Nothing to disclose.

EP3211

Microembolic signals detected with transcranial Doppler sonography differ between symptomatic and asymptomatic middle cerebral artery stenoses in northeast China

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Introduction: The clinical significance of microembolic signals (MES) in asymptomatic middle cerebral artery (MCA) stenosis remains unclear at present. We aim to investigate the frequency of MES and the value of MES in predicting ischemic stroke secondary to asymptomatic MCA stenosis.

Methods: From June 2011 to December 2012, microembolus monitoring was performed in 83 asymptomatic and 126 symptomatic subjects with MCA stenosis in The First Hospital of Jilin University.

Results: By comparing the demographics and risk factors between the symptomatic and asymptomatic subjects, we found the ratio of male sexuality and smoking history differed (101/126 vs 43/83, and 88/126 vs 38/83, respectively, $p < 0.01$). The frequency of MES was significantly higher in the symptomatic group than in the asymptomatic group (49/126 vs 2/108, $p < 0.01$). Specifically, the frequency of MES in the symptomatic and asymptomatic groups with mild stenosis, moderate stenosis, severe stenosis and occlusion groups were 4/18 (22.22 %) vs 0/30 (0), 13/31 (41.94 %) vs 1/28 (3.57 %), 30/62 (48.39 %) vs 1/39 (2.56 %), 2/15 (13.33 %) vs 0/11 (0), respectively. Except for the occlusive group, the frequency of MES is correlated with stenosis degree and symptom. Two patients in the asymptomatic group were found positive for MES, and the MES number was 1 for both. During the one-year follow-up, neither of them developed ischemic stroke.

Conclusions: MES detected with TCD differ between symptomatic and asymptomatic MCA stenoses. Due to the low frequency, the value of MES as a predictor of subsequent ischemic stroke in patients with asymptomatic MCA stenosis might be limited.

Disclosure: Nothing to disclose.

EP3212

Blocking of TRPM2 channels protects from ischemic neurodegeneration in mice by reducing oxidative stress, blood-brain-barrier damage and inflammation

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Introduction: TRPM2 is a highly Ca^{2+}-permeable member of the transient receptor potential melastatin-related (TRPM) family of cation channels activated under conditions of oxidative and nitrosative stress. TRPM2 is functionally expressed on the surface membrane of blood-borne and CNS-resident cells of the innate immune system and CNS neurons and has thus been implicated in innate immunity and neurodegeneration within the CNS. Thus, we study the role of TRPM2 channels in innate inflammation and neurodegeneration following focal cerebral ischemia in wild-type and trpm2-deficient mice.

Methods: RT-PCR, western blot, immunocytochemistry, immunohistochemistry, hippocampal neuronal cell culture, brain slice preparations, whole cell patch clamp recording, transient MCA occlusion (tMCAO), flow cytometry.

Results: TRPM2 channels contribute neuronal cell death as well as microglia activation, production of reactive oxygen species and recruitment of neutrophil granulocytes following transient focal cerebral ischemia. Consistently, genetic deficiency and pharmacological inhibition of TRPM2 channels reduce infarct size, cerebral edema and neurological impairment following tMCAO.

Conclusions: We here identify TRPM2 as a key player in stroke pathophysiology. Blocking of TRPM2 could become a novel strategy to achieve neuroprotection in the ischemic brain.

Disclosure: Nothing to disclose.

EP3213

Relative risk of ischemic stroke in patients with increased carotid intima media thickness

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Introduction: Ischemic stroke is a heterogeneous disease, with various etiopathogenic aspects in which atherosclerosis play a crucial role. Common carotid artery intima-media thickness (IMT) is a marker of atherosclerosis. The purpose of our study was the estimation of relative risk of stroke in patients with increased, above normal, carotid IMT.

Methods: In a prospective study 430 patients with ischemic stroke and 177 patients without ischemic stroke hospitalized in Neurology Department of Academic Emergency Hospital Sibiu, Romania was evaluated by cervical ultrasound. We measured carotid IMT bilaterally by B mode ultrasound.

Results: Increased carotid IMT was associated with patient age ($p < 0.0001$), patient gender ($p < 0.0001$), hypertension ($p = 0.005$) and smoking ($p = 0.02$), independent of the presence or absence of

stroke, confirming carotid IMT status of independent marker of vascular damage.

Each 0.1 mm increase of carotid IMT above the normal produces a proportional increase in the relative risk of stroke between 1.9× and 2.8× (OR = 1.92 for the range 0.9–1 mm, OR = 1.99 for the range 1–1.1 mm, OR = 2.36 for the range 1.1–1.2 mm, OR = 2.67 for the range 1.2–1.3 mm, OR = 2.79 for the range 1.3–1.4 mm). Carotid IMT increment above the normal value produces an increase of the risk of ischemic stroke by about 3× (OR = 3.0617, 95 % CI: 1.635–5.733).

Conclusions: Carotid IMT increment above the normal values has positive predictive value of 27.8 % for subsequent occurrence of stroke, with a sensitivity of 95.3 % and only 13 % specificity.

Keywords: Atherosclerosis, Ischemic stroke, Intima media thickness, Ischemic stroke risk

Disclosure: Nothing to disclose.

EP3214

Relative frequencies of TOAST subgroups are age dependent

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Background: Atherosclerosis, cardiac embolism and small vessel disease are the most common causes of cerebral infarction.

Objective: We hypothesized that the relative frequencies of these causes are age dependent.

Patients and methods: We included all consecutive patients with acute cerebral infarction admitted to the Stroke Unit, Department of Neurology, Haukeland University Hospital between 2006 and 2012. Cause was defined by the Trial of Org 10172 in Acute Stroke Treatment classification (TOAST) criteria comprising large-artery atherosclerosis, cardio-embolism, small vessel disease, other, and unknown. Relative frequencies of TOAST subgroups are displayed by mean of the lowess function. Correlation analyses were performed post hoc based on the lowess analyses.

Results: In total, 2217 patients with acute cerebral infarction were included. Mean age 70.8 years (SD 14.9), 1274 females (57.5 %) 943 males (42.5 %). 205 patients under 50 years old.

Conclusion: We found that the relative frequencies of TOAST subgroups are age dependent. Cardiac embolism is frequent among the very young and the elderly patients.

Atherosclerosis declines among the very elderly. Small vessel disease is most frequent among middle aged patients. This probably reflects different age dependent pathophysiological mechanisms in TOAST subgroups.

Disclosure: Nothing to disclose.

EP3215

Prolonged atrial electromechanical interval in patients with cryptogenic stroke

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Introduction: Undetected paroxysmal atrial fibrillation (AF) may be the cause of stroke in cryptogenic stroke. Prolonged atrial electromechanical interval has been known as a predictor of paroxysmal AF. We sought to investigate whether the prevalence of prolonged atrial electromechanical interval suggesting the presence of atrial substrates for paroxysmal AF is higher in patients with cryptogenic stroke.

Methods: Patients with cryptogenic stroke and non-stroke controls matched for age, sex, and risk factors were compared. Atrial electromechanical interval (PA interval) was defined as the time from the initiation of P wave on surface electrocardiogram to the initiation of trans-mitral inflow on pulse wave Doppler echocardiography. The clinical variables, electrocardiographic and echocardiographic findings were compared between the groups.

Results: A total of 260 persons (130 in each group) were analyzed. The PR interval (178 ± 27 vs. 165 ± 27 ms, $p < 0.001$) and PA interval (74 ± 15 vs. 61 ± 13 ms, $p < 0.001$) were longer in cryptogenic stroke group. The body mass index (23 ± 3 vs. 24 ± 3, $p = 0.043$) was lower and mitral E/E' ratio (8.8 ± 3.0 vs. 8.0 ± 2.6 ms, $p < 0.001$) was higher in cryptogenic stroke group. In multiple logistic regression analysis, prolonged PA interval (Odd ratio [OR], 1.060; 95 % confidence interval [CI], 1.035–1.086; $p < 0.001$) and PR interval (OR, 1.019; 95 % CI, 1.004–1.034; $p = 0.011$) were independent factors related with cryptogenic stroke.

Conclusions: The atrial electromechanical interval was prolonged in patients with cryptogenic stroke. Our findings suggest that paroxysmal AF may be the underlying cause of stroke in a substantial proportion of cryptogenic stroke.

Disclosure: Nothing to disclose.

Critical care & neurotraumatology

EP3216

Potential risk factors and value of bedside examination in critical illness polyneuropathy and myopathy

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Introduction: Neuromuscular complications are quite common in the intensive care unit. It is a common cause of failure of weaning from ventilation, and substantially contributes to mortality and rehabilitation problems. However pathomechanism and the actual etiological factors are poorly understood. In this retrospective study, we analysed the utility of bedside clinical examination, blood tests and etiology of critical illness myopathy and polyneuropathy.

Methods: Medical records of 142 patients diagnosed with critical illness myopathy and neuropathy between 2000 and 2013 were reviewed. Multiple linear regression tests were generated between blood test parameters, time on respirator, age and gender, etiology, muscle strength, pneumonia, sepsis, antibiotics, muscle relaxants as well as clinical outcome variables. Furthermore we compared laboratory and clinical parameters between the subgroup of patients admitted with respiratory failure and were treated only 7–10 days on respirator versus patients with multiple organ failure long time respirator treatment and sepsis.

Results: Clinical outcome was significantly correlated with age at admittance ($p < 0.001$), positively correlated with muscle strength at time of the neurophysiology examination ($p < 0.001$). From the laboratory parameters creatine phosphokinase was the only significant predictor of outcome ($p = 0.045$) There were no significant differences in laboratory parameters and outcome at follow-up between the subgroup of patients with isolated respiratory failure and multiple organ failure. Duration of mechanical ventilation had no effect on long term outcome of the patients.

Conclusions: Careful clinical and laboratory examinations could help the early diagnosis and may prevent serious neuromuscular complications in the intensive care unit.

Disclosure: Nothing to disclose.

EP3217

Does therapeutic hypothermia affect the prognostic accuracy of a clinical neurological examination and SSEP?

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Introduction: Therapeutic hypothermia is recommended in guidelines as neuroprotective treatment after cardiac arrest (CA). However, it has become increasingly clear that the reliability of several prognostic variables has changed since its introduction. The specific aim of this study is to determine whether hypothermia affects the prognostic accuracy of clinical findings and somatosensory evoked potential (SSEP).

Methods: The data were drawn from the Target Temperature Management trial (TTM) which is an international, multicenter, randomized, assessor-blinded clinical trial of temperature management in CA-survivors. A total of 950 patients were randomized to treatment at 33 or 36 °C after return of spontaneous circulation (ROSC) between Nov 2010 and Jan 2013. Neurological prognostication including results of a clinical neurological examination (motor response to pain, pupillary and corneal reflexes) and neurophysiological investigations (electroencephalogram, EEG and SSEP), were protocolized and systematically recorded. In this study we compared the predictive value (sensitivity, false-positive rate) of clinical findings and SSEP between the two intervention groups at the time of prognostication (72 h after the end of the intervention period). Sensitivity, specificity, and false positive rates for each predictor were calculated.

Results: The results of the data analysis are currently being complied.

Conclusions: The TTM trial is the largest randomized controlled trial on comatose CA-patients and the database contains a collection of systematically assessed prognostic parameters from two temperature intervention groups. Our results are highly relevant and will be presented at the meeting.

Disclosure: Nothing to disclose.

EP3218

Outcomes for different levels of hospitals in major trauma patients with head injury: a nationwide population-based study of Taiwan

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Introduction: Since Trunkey described the concept of the "golden hour," outcomes for trauma patients in different levels of hospitals become of particular interest.

Methods: All the major trauma patients with head injury were identified by ICD-9- CM system from one million beneficiaries data of NHI claim data (2006–2008). ICD-MAP was used to calculate the injury severity score (ISS). The major trauma patients were defined as having an ISS more than 15. The Charlson Comorbidity Index (CCI) was used for controlling comorbidity. All these factors were adjusted in a logistic regression model for analysis.

Results: There were 2,034 major head injury patients during these years. There were 772 patients treated in the trauma centers, 1,262 patients treated in non-trauma centers. The total mortality rate was 14.45 %. After controlling all these variables, compared with the risk of mortality in trauma centers, the risk of mortality was 1.31 times higher in the non-trauma centers ($P = 0.09$). However, the odds ratio of mortality was 1.25 in the youngest patients ($P = 0.50$), 1.11 in the older patients ($P = 0.75$), and 1.61 in the oldest patients ($P = 0.03$). There was insignificant difference between two levels of hospitals. But, only in the oldest group (>60 y/o), the survival rate was significant better in trauma centers.

Conclusion: Based on the insignificant difference in mortality rates between trauma centers and non-trauma centers, major trauma patients with head injury could also be transferred to non-trauma centers. But, the patients older than 60 should still be transferred to the trauma centers.

Disclosure: Nothing to disclose.

EP3219

Outcomes analysis for direct versus indirect transport to trauma centers in major trauma patients with head injury: a nation-wide population based research in Taiwan

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Introduction: Since Trunkey described the concept of the "golden hour," outcomes for trauma patients with direct or indirect transfer to the trauma centers become of particular interest.

Methods: All the major trauma patients with head injury were identified by ICD-9- CM system from one million beneficiaries data of NHI claim data (2006–2008). ICD-MAP was used to calculate the injury severity score (ISS). The major trauma patients were defined as having an ISS more than 15. The Charlson Comorbidity Index (CCI) was used for controlling comorbidity. All these factors and the condition of transfer were adjusted in a logistic regression model.

Results: We excluded the patients direct and indirect-transferred to the local hospitals, and the patients who died in emergency departments. There were 1398 major trauma patients with head injury in these years. There were 448 patients direct-transferred to trauma centers, 759 patients direct-transferred to regional hospitals, and 191 patients indirect-transferred to trauma centers from the other hospitals. The total mortality rate was 19.9 %. After controlling all the variables, compared with the patients who were indirect-transferred to trauma centers, the risk of mortality was insignificant higher in the patients direct-transferred to the trauma centers ($OR = 1.26$, $P = 0.39$). But the risk of mortality was significant higher in the regional hospitals ($OR = 1.65$, $P = 0.04$).

Conclusions: Based on the non-significant difference in the risk of mortality between direct-transferred and indirect-transferred patients, major trauma patients with head injury should be transferred (directly or indirectly) to the trauma centers.

Disclosure: Nothing to disclose.

EP3220

Long-term cognitive and functional outcome after cardiac arrest and therapeutic hypothermia: a prospective study

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Introduction: The vast majority of studies investigating cardiac arrest (CA) patients categorize outcome as "good" (Cerebral Performance Categories: CPC 1–2) versus "poor" (death or severe functional impairment: CPC 3–5). We characterized long-term cognitive and functional outcome of CA survivors using a comprehensive neuropsychological assessment. These refined outcome measures may help establishing which early variable could provide functional prognostic information.

Methods: Consecutive survivors after CA treated with therapeutic hypothermia (TH) between September 2012 and May 2013 were followed prospectively. Detailed neuropsychological assessments (testing 10 cognitive domains) at 6 months categorized cognitive impairment as absent (no or minimal impairment in <2 domains) versus moderate/severe (≥ 3 domains significantly impaired). Early prognostic variables (demographics; clinical, biochemical and neurophysiological evaluations) were correlated with long-term outcome.

Results: 20/33 patients (61 %) survived CA, and 15 (75 % of survivors; 11 men; age 55.3 ± 14.2 years) were included. At 6 months, all patients lived independently and had CPC 1–2; out of these 15 patients,

7 (47 %) had moderate/severe cognitive impairment (mainly reduced processing speed and attention deficits) and 5 had serious cognitive complaints (33 %); 33 % of those previously working did not return to work; quality of life was subjectively impaired in 2 patient (13 %). Early predictors failed to predict outcome in this preliminary cohort.

Conclusions: All CA survivors had CPC 1–2 and were living independently; however, a refined evaluation identified cognitive difficulties in a substantial proportion, so far without correlation with early prognostic variables. This cohort is ongoing; updated results will be presented at the meeting.

Disclosure: Nothing to disclose.

EP3221

Investigation the effects of memantin and melatonin treatment after traumatic brain injury in mice

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Introduction: Brain injury following head trauma occurs after complex pathophysiological processes including activation of *N*-methyl-D-aspartate receptor, disruption of intracellular calcium (Ca+2) homeostasis and oxidative stress. Extrasynaptic NMDA receptor inhibitor, memantin, and free radical scavenger, melatonin, have fewer side effects and are used in humans in treatment of neurodegenerative disorders.

Methods: In this study, the effects of memantine and melatonin on traumatic brain injury was investigated in male Balb/C mice. Brain trauma was generated by cold injury; liquid nitrogen fulled tube was exposed to animals brain to following areas; 2.5 mm lateral, 2.5 mm posterior from bregma on the skull, under rompun and ketasol anesthesia. Immediately after trauma memantine, melatonin and memantine/melatonin combination were administrated. At the end of behavioral examination, injury volume 24 h later than trauma and apoptotic cell death were determined.

Results: In these studies, both agents reduced traumatic brain injury and DNA-fragmentation but it was not at the significant level. However, melatonin/memantine combination reduced brain injury and DNA-fragmentation significantly further as compared with melatonin and memantine treated animals which was associated with reduced stress kinases JNK-1/2 and p38 activations. Behavioral tests revealed that the animal- activity, anxiety and depression were improved in all treated animals.

Conclusions: Here, we provide evidence that both clinical safe agents reduce traumatic brain injury especially when combined.

Disclosure: Nothing to disclose.

EP3222

Prognosis of severe Guillain–Barre syndrome clinical course

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Introduction: Guillain–Barre syndrome (GBS) is one of severe neurological diseases in which the correct therapy allows to get a complete recovery. The early prognosis of clinical course might be helpful for the timely diagnosis of the life threatening disturbances. We investigated the prognostic role of the neurofilament heavy chains (NfH) in the clinical course of GBS.

Methods: The NfH level in serum and cerebrospinal fluid (CSF) of 61 patients who fulfilled GBS diagnostic criteria were analysed at the admission. We also measured the NfH concentration in serum of 15 healthy persons to estimate the normal level of NfH. All patients were divided into groups depending on presence of respiratory failure and dysphagia and their serum and CSF concentrations of NfH were compared.

Results: We estimated normal concentration of NfH in serum ($Me = 0.020$ [$LQ = 0.015$, $UQ = 0.025$]). We determined the good correlation between NfH level in serum and CSF and severity of GBS by R.Hughes-score in admission ($R = 0.424$ ($p = 0.014$) and $R = 0.467$ ($p = 0.005$) respectively). The concentration of NfH was significantly higher in CSF ($p = 0.028$) and in serum ($p = 0.020$) in patients who developed respiratory failure. We also determined the significantly higher NfH level in CSF ($p = 0.014$) and in serum ($p = 0.007$) among patients with dysphagia. The serum level of the NfH > 0.144 ng/mL could predict the respiratory failure (AUC 0.804, $p < 0.0001$) and the serum level NfH > 0.094 ng/mL indicating the development of dysphagia (AUC 0.773, $p = 0.001$).

Conclusions: Serum level of NfH can be the prognostic marker in the clinical course of GBS.

Disclosure: Nothing to disclose.

EP3223

Early robot-assisted therapy in patients with stroke in Intensive Care Unit

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Introduction: Pulmonary embolism (PE) increases risk of unfavorable outcome and mortality in stroke.

Methods: This case–control study included 66 patients (49 males, 17 females, median age 59.3) within 7 days from onset of ischemic and hemorrhagic stroke, admitted to the Intensive Care Unit from November 2010 to November 2012. We used National Institutes of Health Stroke Scale (NIHSS) and Glasgow Coma Scale (GCS) scores and assessed the rate of deep vein thrombosis (DVT) revealed with ultrasound scanning, the rate of PE and mortality from admission to Day 21.

Results: Patients were equally divided into two homogenous groups-Intervention and Control to receive standard stroke therapy plus daily robot-assisted arm and leg therapy (MOTOmed letto 2) in Intervention group. Groups had similar stroke severity on admission (GCS: Me = 13 [LQ-10, UQ-15] vs. Me = 14 [LQ-10, UQ-15], p = 0.11; NIHSS: Me = 20 [LQ-16, UQ-29] vs. Me = 18 [LQ-15, UQ-27]), p = 0.5 in Intervention and Control group, respectively). There was no significant difference in neurological outcome on Day 21 (GCS: Me = 15 [LQ-14, UQ-15] vs. Me = 15 [LQ-15, UQ-15], p = 0.12; NIHSS: Me = 11 [LQ-8, UQ-25] vs. Me = 15 [LQ-10, UQ-19], p = 0.4 in Intervention and Control group, respectively), in the rate of DVT on Day 21 (58 vs. 45 %, p = 0.147; respectively). Rate of PE and mortality on Day 21 were higher in the Control vs. Intervention group (39 vs. 12 %, p = 0.014 and 39 vs. 12 %, p = 0.014; respectively).

Conclusions: Early robot-assisted therapy in severe stroke patients was associated with significant reduction of PE rate and mortality on Day 21, but did not influence neurological outcome and DVT rate.

Disclosure: Nothing to disclose.

EP3224

Light-controlled niche-astrocytes promote neuronal differentiation of human mesenchymal stem cells and improve the neurological deficit in stroke rats

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Introduction: Astrocytes have been identified as key components of the stem cell niche. However, it is not clear whether astrocyte-derived ATP plays a vital role in modulating the function of mesenchymal stem cells (MSCs).

Methods: We co-cultured MSCs with light-stimulated-channelrhodopisn-2 (ChR2)-astrocytes, and the real-time PCR was used to examine the expression of neuronal markers by MSCs. The light-controlled astrocytes were also co-transplanted with MSCs to the ischemic area of stroke rats for examining the influence of depolarized astrocytes on the MSCs-based therapeutic effects in the stroke rats.

Results: We observed those MSCs expressed more neuronal markers, Tuj1 and NeuN. Furthermore, the ChR2-astrocyte-conditioned medium markedly up-regulated mRNA expression of Tuj1 and Pax6 indicating some component(s) from the photostimulated ChR2-astrocytes contributed to the differentiation-enhancing effects. Optical stimulation of ChR2-astrocytes significantly increased ATP accumulation in their bathing medium without impairing the cell membrane. We further demonstrated either FZD8 or b-catenin mRNA level was significantly increased by ATP, and this effect could be reversed by application of the selective P2X receptor antagonist, TNP-ATP. Finally but importantly, our study also demonstrated that light-controlled astrocytes stimulated endogenous ATP release into the ischemic area to influence the transplanted MSC-niche, resulting in steering the MSCs towards neuronal differentiation and improvements of neurological deficit in the stroke rats.

Conclusions: Together these data provide convergent evidence that ATP from photostimulated- astrocytes, through binding to the P2X receptors expressed by MSCs, activates the wnt/b-catenin signalling, and as a consequence, upregulates neuronal differentiation of MSC within a special niche.

Disclosure: Nothing to disclose.

EP3225

Initial management of mild traumatic brain injury: variability of clinical presentation and accuracy of diagnosis

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Introduction: Reliability of mild traumatic brain injury (MTBI) diagnosis seems to be quite a common problem, because the majority of MTBI symptoms are mainly of a subjective and rapidly reversible character. That is why time of assessment and some other interfering factors significantly influence the patients' triage and the accuracy of MTBI diagnosis. To improve the standard diagnostic protocols and clarify the significance of some diagnostic criteria we analyzed the structure of the main clinical signs, natural course of recovery and some other features in initial management of MTBI patients.

Methods: This study embraces 184 MTBI patients (aged 16–39) consecutively admitted to the regional hospital. In 61 patients the accident took place on the background of mild and moderate alcohol intoxication. The quantitative analysis (duration/intensity) of MTBI symptoms was carried out.

Results: Several factors and critical points in regard to clinical presentation and initial MTBI diagnosis were identified: age of patients, mechanism of trauma, history of the accident, traumatic signs of head soft tissues, disorders of consciousness and amnesia at the moment of accident, patterns of posttraumatic headache and some other symptoms, concomitant alcohol intoxication, and time of admission to hospital. Special MTBI diagnostic algorithm based on time scale and constellation of different symptoms allows us to classify the diagnosis of MTBI in three categories of reliability: significant (62 %), probable (25 %) and possible or doubtful (13 %).

Conclusions: Optimal time for the assessment and confidential diagnosis of MTBI seems to be the first 3 days after the trauma.

Disclosure: Nothing to disclose.

EP3226

Significance of unusual movements in the diagnosis of brain death

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Introduction: Reflex movements can observe in brain death and these unusual movements might cause arguments in diagnosis. This

prospective study investigates the significance of spinal reflexes in patients who fulfilled the criteria for brain death.

Methods: We evaluated 176 patients with brain death (32 % female, 58 % male, the mean age 57.2 years. Brain death was caused most commonly by intracranial hemorrhage (39 %) and this was followed by subarachnoid hemorrhage (24 %), ischemic stroke (16 %), tumor (10 %), anoxic encephalopathy (6 %), traumatic brain injury (3 %) and meningoencephalitis (2 %).

Results: Thirty-seven (21 %) of 176 patients presented unexpected movements spontaneously or during examinations. These movements included undulating toe (10, 31 %), increased deep tendon reflexes (6, 19 %), plantar flexor or extensor responses (5, 15 %), Lazarus sign (4, 12 %), flexion-withdrawal reflex (3, 9 %),facial myokymia (1, 3 %), neck-arm flexion (1, 3 %), finger jerks (1, 3 %) long-lasting fasciculations in the muscles of the extremities, chest, and abdomen (1, 3%).

Conclusions: In comparison, there were no significant differences in age, sex, etiology of brain death and hemodynamic laboratory findings in patients with and without reflex motor movement. Regardless of artificial respiratory and cardiac support, brain death is medically and legally a "whole and certain death". Although brain death implied total unresponsiveness, reflex and spontaneous movements have been previously described in patients with brain death, and these unusual movements might raise a suspicion in diagnosis. Spinal reflexes should be well recognized by the physicians and it should be born in mind that the brain death can be determined in the presence of spinal reflexes.

Disclosure: Nothing to disclose.

EP3227

Brain mapping utilizing quantitative EEG (Q-EEG) with Loretta 3-dimensional source analysis in traumatic brain injury (TBI)

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Objective: Quantitative electroencephalograms (Q-EEGs) were performed on selected patients (n = 3) with traumatic brain injury (TBI) to correlate functional brain activity with the results of MRI and neuropsychological tests.

Methods: Three patients with TBI are described: one with seizure; one with diffuse brain injury; and one with focal brain damage. Q-EEG provides a mathematical transformation of raw EEG data which associates specific EEG frequency bands with specific brain states. This, combined with the built-in Loretta MRI template, allows the patient and experimenter to see detailed feedback of brain activity in real time. All analyses were completed using Deymed Hardware and Neuroguide Database. Nineteen cortical sites were monitored in linked ear montage with two ground reference points. Impedance measures were all at acceptable levels and below 25Ω suggesting valid results. Average split half and test–retest correlation coefficients were at .96 or higher.

Results: Brain MRI scans revealed focal right frontal atrophy; right hemispheric gliosis (seizure patient) and one was normal. Neurological exams were minimally abnormal. However, neuropsychological testing revealed significant cognitive abnormalities that were confirmed by Q-EEG including focal seizure activity and disrupted cortical activity (e.g., excessive Delta waves). Q-EEG brain mapping correlated with abnormal neuropsychological testing more than minimally abnormal brain MRI and neurological exams.

Conclusions: Q-EEG demonstrated superiority over brain MRI and neurological exams in diagnosing brain injury in TBI. The findings provided by Q-EEG provided crucial information for cognitive therapy.

Disclosure: Nothing to disclose.

Headache and pain 2

EP3228

Contact heat-evoked potentials (CHEPs) in healthy subjects and patients with episodic or chronic migraine

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Introduction: Habituation and 1st block amplitude of sensory evoked potentials are commonly reduced in episodic migraine between attacks, whereas in chronic migraine 1st block amplitude is increased and habituation tends to normalize like during an attack. The aim of our study was to compare Contact Heat-Evoked Potentials (CHEPs) in healthy subjects (HS), episodic migraine without aura (EM) and chronic migraine (CM).

Methods: Ninety subjects participated in the study: 53 HS, 31 EM and 6 CM. CHEPs were obtained using 53 °C stimuli on the forehead and the wrist. Twenty responses were averaged and partitioned in five blocks of four responses. We measured P1, N2 and P2 latencies and P1–N2 and N2–P2 amplitudes. The linear regression slope over the five successive blocks defined habituation. Pain was rated using a visual analog scale (VAS).

Results: There was no significant difference in CHEPs latency, amplitude or habituation between HS and EM either in the forehead or at the wrist. By contrast, in CM patients P1–N2 amplitude after forehead stimulation was increased ($p = 0.04$) and habituation more pronounced ($p = 0.04$). Both at forehead and wrist VAS pain ratings were significantly higher in CM than in HS ($p = 0.02$) or EM ($p = 0.01$).

Conclusion: We found no difference between HS and interictal EM for thermonociceptive evoked potentials. Contrasting with these findings, CM patients display increased CHEPs amplitude, CHEPs habituation and pain perception. Such a pattern is similar to that found in these patients with visual evoked responses and may be due to central sensitisation and increased thalamo-cortical drive.

Disclosure: Nothing to disclose.

EP3229

Chronic headache (CH) and obstructive sleep apnoea (OSA): preliminary findings

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Introduction: CH is frequently associated to sleep disorders, mainly habitual snore, OSA, insomnia and restless legs syndrome (RLS).

Methods: Prospective study, from May 1st and December 20th 2013, 419 patients were submitted to Polysomnography (PSG) in our Sleep Laboratory, including all OSA patients(AHI $\geq$ 5/h).

Results: OSA was present in 318 individuals (75.9 %) and it was mild in 24.5 % (AHI = 5–15/h), moderate in 28.9 % (AHI = 15–30/h), and severe in 45.6 % (AIH $\geq$ 30/h).79.2 % had headache in the

last 12 months and 12.9 % had CH (≥15 attacks/month). Morning headache predominates in the CH group (61 vs. 31 %; $p = 0.004$). No difference was found in other pain characteristics. There was no relationship between severity of OSA and prevalence of headache or CH. Fibromyalgia (14.6 vs. 3.2; $p = 0.007$) and previous stroke (7.3 vs. 1.1; $p = 0.030$) were more frequent among CH individuals and there was a trend to higher prevalence of COPD in CC group (9.8 vs. 3.2 %; $p = 0.072$). Beck Anxiety (16.3 ± 11.8 vs. 10.5 ± 8.9; $p = 0.005$) and Depression (13.6 ± 7vs.10.4 ± 7.3; $p = 0.007$) scores were higher in CH group. Insomnia was more frequent in CH patients (65 vs. 31.3 %; $p < 0.0001$), but only difficulty initiating sleep (35 vs. 13.5 %; $p < 0.0001$), and early-morning awakening (30 vs. 12.7 %; $p = 0.020$). There was a tendency for higher prevalence of RLS in CH individuals (31.7 vs. 17.7 %; $p = 0.055$). There was no difference in PSG findings (AHI index, arousal index, Os saturation levels), except tendency to lower REM sleep latency (128.8 ± 55.5 vs. 146.9 ± 85 min; $p = 0.087$), and lower sleep efficiency (79.5 ± 13. vs. 84.3 ± 24.8 %; $p = 0.073$) in CH group.

Conclusions: CH in OSA patients was not related to OSA severity, was more frequent in the morning, and was more prevalent in fibromyalgia, previous stroke, insomnia.

Disclosure: Nothing to disclose.

EP3230

Efficacy and safety of venlafaxine for the treatment of chronic migraine: a randomized, double-blind, controlled trial

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Introduction: The purpose of this randomized controlled trial was to evaluate and compare the effects of extended-release venlafaxine with topiramate in patients with chronic migraine and medication overuse headache to investigate whether venlafaxine could be at least as effective as topiramate.

Methods: A prospective, 4-week run-in phase was followed by a 12-week treatment phase which consistent of a 4-week titration and 8-week maintenance period. The evaluation of efficacy was based on headache diary information. The change in number of headache days from baseline to the last 28-day of the double-blind period, considered as the primary end-point and mean intensity of attacks (Visual Analog Scale) considered as secondary variable.

Results: The total of 88 intent-to-treat population consisted of 50 patients receiving venlafaxine and 38 patients receiving topiramate. There was no significant difference in terms of primary or secondary efficacy measures between topiramate- and venlafaxine-groups. Topiramate significantly reduced the mean number of headache days as the primary efficacy end-point in the patients from 23.5 ± 6.4 days/month at baseline by 16.9 ± 5.6 days/month after 12-week double-blind phase ($p < 0.001$) whilst, venlafaxine reduced the mean number of headache days per month (4 weeks) from 23.29 ± 6.5 by 18.30 ± 5.83 ($p < 0.001$).

Conclusions: In this study extended-release venlafaxine 150 mg/day found to be effective in chronic migraine. Our study showed a clear effect that was in subgroup of subjects with medication overuse. In addition, in this study, the low number of adverse events showed venlafaxine to be well tolerated.

Disclosure: Nothing to disclose.

EP3231

New kynurenic acid derivative decreases pain-related behaviour and neuronal activation induced by orofacial formalin in caudal part of spinal trigeminal nucleus of the rat

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Introduction: Activation of the trigeminal system is essential in the pathomechanism of headaches, involving glutamate and alpha7-nicotinic acetylcholine receptors. It has been also shown that the inhibition of these receptors results in a reduction of nociception. Kynurenic acid, an endogenous antagonist of above mentioned receptors has poor ability to cross the blood–brain barrier limiting its potential, its new derivative (SZR81) with a side-chain substitution to facilitate brain penetration was therefore used in the present study to investigate its modulatory effect on the biphasic rubbing activity during the orofacial formalin-test and on number of c-Fos immunoreactive neurones in caudal part of spinal trigeminal nucleus (TNC).

Methods: One hour after intraperitoneal vehicle or SZR81 injection, rats received 50 µl physiological saline or 1.5 % formalin solution subcutaneously into their whisker pad. For a period of 45 min after the subcutaneous injection, the rubbing activity directed to the injected whisker pad was measured. Four hours after formalin injection, TNC was removed and subjected to c-Fos immunohistochemistry as a marker of neuronal activation induced by nociception.

Results: SZR81 was able to significantly decrease the time spent rubbing in second phase of the formalin test. The number of c-Fos immunoreactive neurones was also reduced significantly in TNC as well 4 h after s.c. formalin.

Conclusion: Efficacy of SZR81 in this animal model suggests that inhibition of glutamate and alpha7-nicotinic acetylcholine receptors may modulate trigeminal nociception therefore it might be a potential candidate for the treatment of trigeminal pain.

Disclosure: Nothing to disclose.

EP3232

The impact of cognitive symptoms on migraine attack related disability

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Background: The socio-economic impact of Migraine is related to work loss either by absenteeism or decreased work performance. Migraine associated cognitive dysfunction during an attack may be the cause of this difficulties.

Objective: To analyze the presence and relevance of cognitive symptoms during migraine attacks, relating their intensity and symptom related disability with other migraine defining symptoms.

Methods: Consecutive migraine patients of headache clinic fulfilled diaries scoring each migraine symptom (including cognitive symptoms) intensity and symptom related disability.

Results: One hundred consecutive patients were included in this study (eight males, age average 31.2 ± 7.5 years), 34 (all females, age average 31.8 ± 8.8 years) returned information on 229 attacks, on average 6.7 per participant. This population had a moderate to severe impact of migraine (HIT-6 63.4 ± 4.4). Intensity of each symptom is always rated slightly higher than disability. Pain is the symptom scored with the highest intensity and disability, followed by cognitive symptoms (difficulty in thinking and worsening with mental effort) and photo and phonophobia.

Conclusions: Cognitive symptoms are frequent during migraine attacks, their intensity and perceived symptom-related disability is second only to pain, during the attack. New acute migraine drugs trial should include cognitive evaluation as a secondary end-point, in order to be able to diminish decreased work performance and Migraine burden.

Disclosure: Nothing to disclose.

EP3233

Clinical parameters for the relationship between migraine and persistent foramen ovale (PFO)-closure

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Introduction: The epidemiologic association between a persistent foramen ovale (PFO) and patients with migraine aura was postulated in literature. The focus of this prospective pilot study was the relationship between migraine and a PFO-closure to avoid, in a best case scenario, a lifelong migraine medication.

Methods: In this prospective study (FOMI study) migraine patients ($n = 41$) with a right left shunt within a persistent foramen ovale were included and selected in 4 groups. The primary goal was a significant 50 % reduction of pain intensity in patients with aura and ischemic lesion patterns in the MRI. This PFO-closure group was compared with patients who were treated conservatively over the observation period of 6 and 12 months after study inclusion.

Results: The PFO-closure group (group 1) showed 6 months after the intervention a significant reduction for pain intensity ($p < 0.05$) as well as pain medication ($p < 0.05$). However, this effect could not be statistically confirmed after 12 months so that an association with the co-founding platelet inhibitors, especially acetylsalicylic acid (ASS), necessary after PFO-closure, could be postulated.

Conclusions: The interventional PFO-closure alone could not show a long term statistical effect on migraine symptoms. The initial 6 month pain reduction and pain medication reduction is most likely associated with the necessary co-medication of acetylsalicylic acid after PFO-closure, that has an anti-inflammatory, analgesic and migraine-prophylactic effect. Out of the clinical study parameters it is not possible to identify certain criteria to justify an interventional PFO-closure in migraine patients.

Disclosure: Nothing to disclose.

EP3234

Idiopathic intracranial hypertension

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Introduction: Idiopathic Intracranial hypertension (IIH) is a headache syndrome defined as a raised cerebrospinal fluid (CSF) pressure in the absence of intracranial mass lesion or ventricular dilatation. The purpose is to study clinical presentation, imaging finding and to analyze prognosis of BIH.

Methods: A retrospective review of 30 Tunisian patients diagnosed as IIH in Sahloul university Hospital from 2005 to 2010 was carried out. Patients fulfilled the modified Dandy criteria for IIH. Data collected included age and sex, body mass index (BMI), comorbid conditions, and medication use. Findings of ophthalmic examination, neuroimaging, CSF analysis and neurological assessment were recorded.

Results: We analyzed 30 patients (1 male and 29 female) with a mean age of 35 years. Obesity was the main risk factor (60 %), followed by drug therapy (16.7 %) and thyroid dysfunction (10 %). Clinical presentation included headache (93.7 %), visual disturbances (86.7 %), dizziness (36.7 %), tinnitus (33.3 %) and impaired visual acuity (30 %). Neurological examination noted a six nerve palsy in 5/30 cases. Grade II or III papilledema was noted in 56.7 % of patients. MRI was normal in 14 patients, 5 patients showed narrow ventricles and 9 showed empty sella. Hydrops of the optic nerve was noted in 1 case. Patients were treated by acetazolamide. Lumbar puncture was used for 28 of them. Outcomes noted recovery in 43.3 %, chronic headache in 20 % and persistent impaired visual acuity in 6.7 %.

Conclusions: IIH is characterized by elevated CSF pressure of unknown cause. It predominantly occurs in obese women during the childbearing years. The only major morbidity with IIH is visual loss.

Disclosure: Nothing to disclose.

EP3235

Abstract withdrawn

EP3236

Tolosa-Hunt syndrome: is it really necessary to show granuloma?

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Introduction: Tolosa-Hunt syndrome (THS) is a rare entity, described in The International Classification of Headache Disorders (ICHD), as unilateral orbital pain associated with paresis of one or more of the III, IV and/or VI cranial nerves caused by a granulomatous inflammation in the cavernous sinus, superior orbital fissure or orbit. The low prevalence of THS with broad spectrum of other disorders that could cause painful ophthalmoplegia resulted in stricter diagnostic criteria of THS in ICHD-III.

Current criteria require demonstration of granuloma by magnetic resonance imaging (MRI) or biopsy. In clinical practice, THS is highly variable in its presentation, thus, reducing the number of patients that, based on clinical presentation could be THS, but not fulfill all diagnostic criteria complicates establishing of correct diagnosis on time to start treatment.

Methods: Hereby we present six patients diagnosed and treated as THS. Inspite the exclusion of other causes of painful ophthalmoplegia, granuloma could not been demonstrated in half of patients.

Results: Clinical presentation of THS in patients with and without shown granuloma, did not significantly differ concerning headache characteristics (localization, intensity, quality, duration preceding cranial nerve palsy, response to steroids), cranial nerve palsy (affected nerve, response to steroids, number of episodes, relapsing after steroids withdrawal) and types of diagnostic procedures that were performed in ruling out other diseases from extensive differential diagnosis of painful ophthalmoplegia.

Conclusions: Of this observation raised the question is it really necessary is to demonstrate granuloma in order to establish diagnosis of THS.

Disclosure: Nothing to disclose.

EP3237

Cluster headache: epidemiological, clinical and therapeutic study in a Tunisian population

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Background: Cluster headache (CH) is a primary headache form within the trigeminal autonomic cephalgias spectrum. Iís characterized by its double periodicity and the severity of pain, also called suicidal headache.

Methods: A retrospective study was conducted from January 2008 to December 2012 in the headache consultation of the department of neurology. Patientś demographic, clinical and therapeutic data were analyzed.

Results: Twenty patients were diagnosed with CH (2.5 % of total 770 headache patients). There was an evident masculine predominance (prevalence in male: 5.2 %, prevalence in female: 0.2 %; $p < 10^{-3}$). Mean age of onset was 39 years (12–64 years). All patients presented chronic headache satisfying the International Headache Socity for CH. Episodic CH was found in 90 % of patients. Accompanying autonomic signs were eye redness (80 %), tearing (70 %), nasal obstruction (30 %) and facial edema (10 %). One patient presented a narcolepsy-catalepsy associated to CH. Acute and preventive treatment association and efficacy were analysed. Twenty five percent of patients were refractory.

Discussion: CH is a primary headache syndrome with complex and incompletely understood pathogenesis. The double circadian and circannual periodicity suggest an implication of the hypothalamus. Our series shows a male prevailing though this predominance tends to decrease in the literature. Treatment of CH still a challenge to praticians since 20 % of patient in the literature and 25 % in our serie are refractive despite a well conducted therapy.

Conclusion: While the diagnosis of CH seems to be simple, our study emphasizes the complexity of its management.

Disclosure: Nothing to disclose.

EP3238

Auriculotemporal neuralgia: a clinical study of eight cases

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Introduction: Auriculotemporal neuralgia (AN) is a strictly unilateral pain perceived in temporal region, temporomandibular joint, parotid, auricular and retro-orbital region. There is tenderness over the nerve, and pain is abolished by local anaesthetic blockade. Only small series or isolated cases of AN have been published. We aimed to analyze clinical characteristics and therapeutic results in a consecutive series of eight cases.

Methods: Patients with AN attended in headache units of two tertiary hospitals. In every patient we gathered age at onset, sex, and clinical characteristics of pain. We also considered therapeutic results.

Results: 8 patients (7 females, 1 male). Six of them in the headache registry of one of the hospitals out of 2,700 cases (0.2 %). Mean age at onset 52.8 ± 14.3 years (26–69). Pain was strictly unilateral, in five left and in three right sided. Pain was always triggered or made worse by pressing preauricular area. In three cases background pain mostly dull and rated 5.3 ± 1.1 (4–6) on verbal analogical scale (VAS). In six patients burning exacerbations, lasting from 2 s to 30 min, intensity of 6.7 ± 1.5 (5–8) on VAS. In three cases an anaesthetic blockade was required with complete relief lasting from 2 weeks to 7 months; one patient did not required therapy, three achieved complete response with gabapentin and one with topiramate prescribed due to a comorbid migraine.

Conclusion: Auriculotemporal neuralgia is a quite uncommon disorder in our headache units. According to our experience, gabapentin is a good therapeutic option and anaesthetic blockade is not always required.

Disclosure: Nothing to disclose.

EP3239

Targeted autologous epidural blood patch with computerized tomography-myelography is an effective treatment modality in patients with spontaneous intracranial hypotension

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Introduction: Spontaneous intracranial hypotension (SIH) is a rare cause of the new onset daily persistent headaches. Although the epidural blood patch (EBP) emerged as the important treatment for SIH, the success rate with each EBP is variable. We aim to assess the efficacy of the strategic autologous epidural blood patch based on CT myelography.

Methods: Between January 2004 and July 2012, we retrospectively reviewed prospectively collected clinical and radiographic data of 43 patients who were diagnosed with SIH according to the criteria of the ICHD-2. The efficacies of EBP were evaluated based on degree and duration of symptom relief and on the need for repeated EBP.

Results: Forty-three patients (14 men and 29 women; mean age 43.6 years; age range 22–74 years) were included in this study. Orthostatic headache (100 %) was the most frequent symptom. Dural enhancement of brain MRI was the most common imaging finding (83.7 %). In eight patients, spine MRI demonstrated significant spinal epidural venous enlargement. Most common leakage site in patients with SIH was in the T-spine level (46.5 %). CT myelography was performed in 33 patients and appeared to be an effective diagnostic tool for the detection of CSF leakage site. (Sensitivity: 93.8 %, specificity: 100 %, positive predictive value: 85.9 %, negative predictive value: 1.8 %). In the 26 patients who received a targeted EBP, 21 patients (80.7 %) had clinical improvement after first administration. Compared with the efficacy of blind EBP, targeted autologous EBP was an effective treatment in patients with SIH. (OR: 4.2, 95 % CI 0.52–18.80, P = 0.207).

Disclosure: CT myelography is an effective diagnostic tool to identify the CSF leakage site and guides effective EBP near the leakage sites. Targeted autologous EBP is an effective treatment modality to relieve the headache in patients with SIH.

EP3240

Morning headache (MH) among Southern Brazilian habitual snorers

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Introduction: MH is common complaint among snorers and sleep apnoea patients, but also frequently associated to other sleep conditions, bruxism, mood disorders.

Methods: In a prospective study including all adult patients, between July 1st and December 20th 2013, we evaluate 311 habitual snorers, all submitted to full night polysomnography.

Results: 49.2 % were female, mean age 50.6 ± 14.7 years. Obesity was frequent (48.9 %). 81.3 % had headache in the last year and MH was present in 28.6 %. Headache (81.9 % women and 73.4 % men) and MH (62.7 vs. 37.1 %; p = 0.03) were more common among female patients. No difference related to age, but MH had later beginning of symptoms (37.6 ± 16.0 vs. 30.7 ± 16.2 years; p = 0.002). MH patients described more frequent attacks and chronic headache was more prevalent in this group (37 vs. 11.2 %; p < 0.0001). Analgesic use was less frequent among MH sufferers: 67.4 vs. 80.5 %; p = 0.004. Sleeping as coping strategy was less successful among MH individuals: 29.9 vs. 38.1 %; p = 0.006. Headache on awakening on the next morning of PSG was more common on the morning headache group (24.7 vs. 14.9 %; p = 0.048). MH patients had a tendency to higher sleep latency (24.8 ± 38 vs. 17.5 ± 17.1 min; p = 0.085) and less N1 stage (4.8 ± 2.6 vs. 5.7 ± 4.9; p = 0.032) than the others. There was no difference in other polysomnographic data nor in O_2 saturation. OSA was equally prevalent (77.5 vs. 78.4 %) and had no show difference in severity.

Conclusions: MH had a prevalence of 28.6 % among snorers and predominates in females. MH sufferers had more frequent attacks and chronic headache but their analgesic use is less frequent. MH in snorers is not related to OSA, O_2 saturation nor sleep fragmentation.

Disclosure: Nothing to disclose.

EP3241

Characteristics of the diagnostic criteria for migraine in international classification of headache disorder III-beta (ICHD III beta)

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Introduction: What kind of characteristics does the diagnostic criteria for migraine in international classification of headache disorder III-beta (ICHD III beta) possess? C part in diagnostic criteria for migraine without aura has four features; unilateral location (UL), pulsating quality (PQ), moderate or sever pain intensity (MSPI) and aggravation by or causing avoidance of routine physical activity (ARPA). Do the four features have any relationships each other in whole kinds of headaches?

Methods: We studied four features of C part in criteria for migraine without aura, using questionnaires given to 265 headache outpatients (99 males, 164 females, with an average age of 47.3 years) from January 2008 to July 2008. We calculated odds ratios between each two of four features (UL, PQ, MSPI and ARPA).

Results: Of 265 patient cases, 107 had migraine, 60 had tension type headaches, 5 had cluster headache, 37 had occipital neuralgia and 3 had trigeminal neuralgia. The odds ratio between UL and PQ was 1.23, the odds ratio between UL and ARPA was 0.97, the odds ratio between UL and MSPI was 1.25, the odds ratio between PQ and ARPA was 4.62, the odds ratio between PQ and MSPI was 8.45 and the odds ratio between ARPA and MSPI was 7.59.

Conclusions: PQ, MSPI and ARPA have strong relationships each other. If any headache has one of three features, there is a very high chance that the headache also has other two features simultaneously.

Disclosure: Nothing to disclose.

EP3242

Prevalence, risk factors and treatment of headache disorders in medical students

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Introduction: The aim of our study was to estimate the prevalence of headache disorders using the newly published third edition

International Classification of headache Disorders-3beta, evaluate their risk factors and treatment in students of the Urals State Medical University.

Methods: The study population consisted of 1042 students (719 females, 323 males, mean age 20.6, range 17-40). All were interviewed using a semi-structured validated interview conducted by a neurologist or by trained senior medical students.

Results: 1-year prevalence of headache in students was 93 % (females 95 %, males 88 %), prevalence of headache during the last month—63 % (66 % among females, 54 % among males), during the last week—43 % (48 % among females, 32 % males) and point prevalence -17 % (17 % among females, 17 % among males). 1-year prevalence of tension type headache was 75 %, among females — 69 %, among males—90 %. 1-year prevalence of migraine was 33 %, among females—39 %, among males—21 %. 1-year prevalence of chronic tension type headache—1 %, chronic migraine—1 % and medication overuse headache—3 %. Risk factors for headache were female sex ($p < 0.0001$), family history of headache ($p < 0.0001$),not enough sleep ($p < 0.0001$), frequent tiredness ($p < 0.0001$), history of head trauma ($p < 0.0001$), low alcohol beverage consumption ($p = 0.0003$), anxiety ($p = 0.002$), oral contraceptives ($p = 0.005$), depressed mood ($p = 0.02$), overwork ($p = 0.04$). Only few (24 %) had consulted because of headache. Most students (75 %) used analgesics or NSAIDs for the acute treatment of headache, only 3 % used triptans. Only 0.2 % of students received prophylactic treatment.

Conclusions: Prophylactic and treatment strategies must be developed to manage the high prevalence of headache disorders in students.

Disclosure: Nothing to disclose.

EP3243

Monitoring the use of symptomatic drugs in headache: a population study

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Background: Headache is an extremely common neurological problem. Italy is the first European country for OTC consumption with related problems of self-medication, inappropriate use and, risk of MOH.

Aim: To collect information about symptomatic assumption behavior, to monitor the consumption of symptomatic drugs for headache and to prevent drugs abuse/dependence.

Materials and methods: 274 patients consuming symptomatic drug for headache were recruited in 32 pharmacies in the Pavia Health District. A telephonic interview to collect clinical general information on headache was carried out in 199 patients; 179 were followed-up at baseline (T0) and 129 at three month (T3). The study design includes T6 and one year follow up in the headache out-clinic.

Results: 22.9 % were Males and 77.1 % Females. The mean age was 45.3 ± 11.5 years. Forty-five patients had chronic migraine and MOH at telephone interview; 39 at T0 and 15 at T3. Days with headache decreased comparing T3 vs T0 (4.69 ± 5.22 vs 9.66 ± 8.12, $p = 0.0001$). The same for the decrease on headache intensity at T3 vs T0 and the doses of analgesics per month ($T0 = 15.67 \pm 21.77$ at $T3 = 11.32 \pm 17.89$). MIDAS scores at T0 vs T3: 25.13 ± 31.31 vs 16.91 ± 29.82 ($p = 0.005$) and HURT score: T0 vs T3: 9.86 ± 5.3 vs 6.74 ± 5.12; $p = 0.0001$).

Conclusions: These results highlight that the change from self medication to medical care may reduce the numbers of symptomatic treatment, the number of headache attack per month and ameliorate the quality of life in patients with headache. A longer follow-up may be necessary to prevent drug abuse headache.

Disclosure: Nothing to disclose.

Neuroimaging

EP3244

Cortical thickness in mild cognitive impairment patients showing different biomarker profiles

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Introduction: Mild cognitive impairment (MCI) patients with different biomarker profiles might be characterized by different patterns of cortical thinning.

Methods: 53 MCI (mean age 71, female 49 %) were enrolled from 2 Italian Memory Clinics. Abeta42 and Tau CSF levels, temporo parietal hypometabolism and hippocampal volumes were measured. According to their biomarker profiles, patients were divided in two groups: (i) suspected non-amyloid pathology (SNAP, $N = 21$) and (ii) patients with amyloid plus neurodegeneration ($A + N$, $N = 32$). Cortical thickness was quantified using the free surfer pipeline. Comparisons were made at group level with 15 subjective memory complainers (SMC), considered as the control group.

Results: SMC were cognitively intact, younger than SNAP and $A + N$ patients ($p < .006$). Relative to SMC group, $A + N$ showed cortical thinning in the left/right parietal inferior and superior regions ($p < .028$), temporal middle and superior temporo-lateral gyri ($p = .05$), left inferior frontal gyrus ($p = .009$), right lateral fusiform gyrus ($p < .002$), insula and precentral sulcus ($p = .01$). SNAP patients compared to SMC exhibited cortical thinning in the left central sulcus ($p = .025$), right superior and inferior temporo-lateral ($p < .002$) and parietal ($p = .04$) gyri, precentral sulcus ($p = .011$). The direct comparison between $A + N$ and SNAP showed significant cortical thinning only in the $A + N$ group in the right and left lateral fusiform gyrus ($p < .039$), left occipital middle and lingual gyri ($p = .020$ and $p = .007$), parietal regions ($p < .049$) and orbito-lateral sulcus ($p = .041$).

Conclusions: Our results support the hypothesis that SNAP patients are characterized by a different cortical thickness involvement relative to $A + N$ due to different underlying pathologic changes.

Disclosure: Nothing to disclose.

EP3245

Optimized objective SPM analysis improves accuracy of [^{18}F]FDG-PET imaging in dementia diagnosis

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Introduction: [^{18}F]FDG-PET imaging has been proven to be a sensitive biomarker for dementia diagnosis. Diagnostic accuracy, however, crucially depends on the operating procedure. In this study, we evaluated the advantage of objective voxel-based evaluation of [^{18}F]FDG-PET scan (SPM-t Map) over: a) visual inspection of FDG-uptake distribution (Rainbow Map) and b) clinical details.

Methods: Nine neuroimaging experts made a forced-choice diagnosis for 89 patients (i.e., Mild Cognitive Impairment-MCI, Alzheimer's Disease-AD, Frontotemporal Lobar Degeneration-FTLD, Dementia with Lewy bodies-DLB) by the independent evaluation of three types of information: clinical details, Rainbow and SPM-t Maps. Long-term clinical follow-up was used as gold standard for the diagnostic classification. A new optimized procedure was applied to provide SPM-t Maps. In addition, in AD and FTLD patients, we quantified the specific contribution to correct classification of Rainbow vs. SPM-t Map when added to clinical details.

Results: SPM-t maps showed higher sensitivity and specificity, and better diagnostic positive and negative likelihood ratio compared to Rainbow Map and clinical details. Moreover, SPM-t Map added an extra value to clinical information, increasing accuracy and confidence for correct diagnosis compared to Rainbow Map. In the MCI subgroups which progressed to dementia or reverted to normal at follow-up, SPM-t Maps showed higher predictive prognostic value by identifying, respectively, hypometabolic patterns or normal metabolism.

Conclusion: An optimized tool for objective voxel-based evaluation of [^{18}F]FDG-PET scan is helpful for dementia diagnosis. Thanks to the detection of specific topographic patterns of metabolic abnormalities, it improves diagnostic confidence even in the case of neuroimaging experts.

Disclosure: Nothing to disclose.

EP3246

Mapping microstructural changes in nigrostriatal and extranigral pathways in Parkinson's disease

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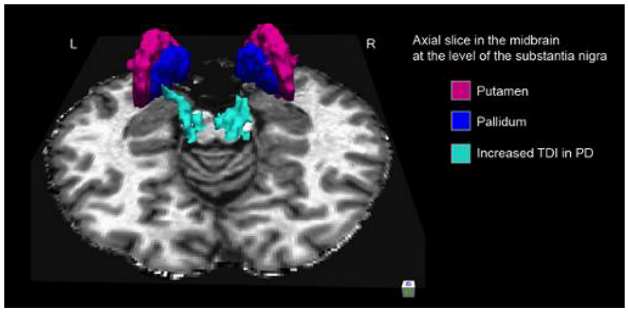
Introduction: In order to identify the pattern of microstructural brain disturbances in a cohort of Parkinson's disease (PD) patients without dementia, we used track density imaging (TDI), a diffusion-weighted imaging (DWI) method that quantifies the number of streamlines per voxel defined on a finer grid as compared with the native magnetic resonance imaging (MRI) data.

Methods: DWI data (120 diffusion directions; b value = 2,500 s/mm^2) were acquired at 3 Tesla in 27 non-demented PD patients and 26 controls matched for age, sex, and education level. We performed a voxel-wise analysis of whole-brain high-resolution (1 mm^3) spatially normalized maps of fractional anisotropy (FA), mean diffusivity (MD), tensor mode (TM) streamline counts (SC). Results were thresholded at $p < 0.05$, corrected at the cluster-level using the family-wise error rate.

Results: The only group difference was an increase in SC in the patients. The most widespread cluster encompassed the pons and extended upward to the substantia nigra and ventral tegmental area, up to the medial aspect of the posterior putamen, bilaterally. We also observed less widespread group differences at the level of posterior subcortical cerebral hemispheres in the parietal, occipital, and temporal lobes, bilaterally.



[see http://www.youtube.com/watch?v=kjJbIx9GBxY]

Conclusions: These preliminary results identified in this advanced MRI study show for the first time a large overlap with the known distribution of neuropathological changes in non-demented PD patients. Increased SC in the patients may be related to a bias in the model used to resolve fibre orientation distributions in regions with complex microstructural organisation.

Disclosure: Nothing to disclose.

EP3247

Diagnostic effectiveness of ioflupane I^{123} injection (DaTSCAN^{TM}) for prediction of clinical diagnosis in clinically uncertain Parkinsonian syndrome (CUPS)

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Introduction: [^{123}I]Ioflupane injection (DaTSCAN^{TM}) is approved for SPECT imaging visualizing dopamine transporter binding in the brain. This study assessed the test characteristics of DaTSCAN imaging for 102 patients with clinically uncertain parkinsonian syndrome (CUPS).

Methods: One-year clinical diagnosis and DaTSCAN imaging results were reference standards used for calculating the sensitivity, specificity, positive and negative predictive value (PPV and NPV), and diagnostic accuracy of the DaTSCAN imaging vs clinical diagnoses at other visits. DaTSCAN results were interpreted using blinded

image evaluation, without consideration of the subject's symptoms or clinical signs and categorized as Normal or Abnormal.

Results: At baseline, 75 % of the subjects were in the early stages of CUPS (Hoehn and Yahr stages 0 to 2). Using 1-year clinical diagnosis as reference standard, specificity, PPV, and NPV were better for the DaTSCAN imaging vs baseline clinical diagnosis: 0.9535 vs 0.5238 ($P = 0.0005$), 0.9583 vs 0.6970 ($P < 0.0001$), and to 0.9762 vs 0.8462 ($P = 0.0335$). Using DaTSCAN imaging as the exploratory reference standard, specificity, PPV, and NPV of the 4-week clinical diagnosis (imaging results known by clinician) were better than baseline clinical diagnosis (0.9184 vs 0.4773 [$P = 0.0001$], 0.9259 vs 0.6462 [$P = 0.000001$], and 0.9783 vs 0.7241 [$P = 0.009$]), sustained for 12-week and 1-year clinical diagnoses.

Conclusions: This study demonstrated high sensitivity and specificity, PPV, NPV, and diagnostic accuracy of DaTSCAN imaging in prediction of clinical diagnosis in CUPS. One-year clinical diagnosis and DaTSCAN results without clinical information were similar. Study results suggest that DaTSCAN imaging is a useful adjunct in the diagnosis of CUPS.

Disclosure: ID Grachev is employee of GE Healthcare, Princeton, NJ, USA.

EP3248

Sonographic alterations of brain structures in patients with Huntington disease

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Introduction: Transcranial sonography (TCS) is a method for the visualization of changes in echogenicity of the substantia nigra and basal ganglia in movement disorders. Changes in echotexture of raphe nuclei in patients with depression with neurodegenerative disorders (Parkinson's disease, Wilson's disease, Huntington's disease) were reported. The aim of this study was to test the usefulness of TCS in detection of changes of basal ganglia in patients with genetically confirmed HD.

Methods: TCS was performed on 84 patients with HD confirmed genetically. Patients were allocated to the two groups: presymptomatic gene carriers (15 persons), and with motor symptoms (>5 pts in UHDRS TMS score) (69 persons). All patients underwent complete neurological and psychiatric examination. Psychiatric symptoms were assessed using the battery of tests: the Hamilton Rating Scale for Depression, the Beck Depression Inventory. Transcranial sonography was performed with the Aloca Ultrasound System. Echogenicity of substantia nigra, basal ganglia and raphe nuclei was assessed and correlated with neurological and psychiatric status.

Results: Hyperechogenic substantia nigra was found in 32/84 (38 %) patients. Hypoechogenicity of raphe nuclei we found in 40 % of presymptomatic patients (6/15), in 84 % of patients with depression (31/37) and in 18 % of patients without present or past history of psychiatric disturbances (6/32). Hyperechogenicity of nucleus leniformis was visualized in 29 % (25/84), and hyperechogenicity of heads of caudate nuclei in 21 % (18/84) patients with motor symptoms.

Conclusions: Both presymptomatic and symptomatic HD patients characterize frequent presence of changes in basal ganglia echogenicity.

Disclosure: Nothing to disclose.

EP3249

Contribution of global and regional damage of the gray and white matter to fatigue in MS

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Introduction: We combined atrophy and diffusion tensor (DT) MRI measures to investigate the role of damage to lesions, normal-appearing white matter (NAWM) and gray matter (GM) to the pathogenesis of fatigue in multiple sclerosis (MS).

Methods: Brain dual-echo, double inversion recovery (DIR), high-resolution T1-weighted and DT MRI scans were acquired from 63 MS patients and 35 healthy controls. Patients were classified in fatigued (F-MS) and non-fatigued (nF-MS) based on Fatigue Severity Scale (FSS) scores. Between-group differences of GM and WM regional volumes were assessed using voxel-based morphometry ($p < 0.05$ FWE corrected). Diffusivity values of cortical lesions (CLs), skeletonized cortex, WM lesions and NAWM were assessed. Tract-based spatial statistics was used to define the regional distribution of DT MRI abnormalities in the T2-lesions.

Results: Thirty-one patients were classified as F-MS. Diffusivity values of CLs, skeletonized cortex, WM lesions and NAWM and regional WM atrophy did not differ significantly between F-MS and nF-MS patients. Compared to nF-MS, F-MS patients showed atrophy of the right accumbens and inferior temporal gyrus (ITG). ITG atrophy was correlated with FSS ($r = -0.42$) and EDSS ($r = -0.48$). Compared to nF-MS, F-MS patients had lower fractional anisotropy of the forceps major, left inferior fronto-occipital fasciculus and right anterior thalamic radiation (ATR), and a higher frequency of T2 lesions at the level of the right ATR ($p < 0.01$).

Conclusions: Regional analysis of measures derived from different MR modalities, specific towards different substrates of MS pathology, might improve our understanding of the pathophysiology of fatigue.

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EP3250

Functional correlates of impaired working memory in MS patients: a multicentre study

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Introduction: To assess the fMRI correlates of frontal lobe dysfunction in multiple sclerosis (MS) patients with and without cognitive impairment.

Methods: This study was conducted at six European sites using 3.0 Tesla scanners. FMRI scans during a N-back task were acquired from 42 right-handed MS patients and 52 matched right-handed healthy controls (HC). MS patients underwent the Rao battery and the Wisconsin Card Sorting test. Patients with at least two abnormal tests were considered as cognitively impaired (CI). fMRI data were analysed modelling regions showing a load-dependent activation/deactivation with increasing task difficulty.

Results: Twenty-two MS patients were cognitively preserved (CP) and 20 (47 %) were CI. Task-related activations/deactivations were found in similar regions for HC and MS. Compared to HC, MS showed a reduction of fMRI activity with increasing task difficulty in the bilateral parietal, left inferior frontal and left middle frontal regions. While CP showed fMRI patterns similar to those detected in HC, CI patients had a distributed reduced fMRI activity (in bilateral parietal and frontal regions, and in the bilateral insula) and fMRI deactivations (in the bilateral precuneus, posterior cingulate cortex and parahippocampal gyrus) compared to HC and CP patients. A failure of activation of frontal regions was correlated with a longer disease duration, higher T2/T1-lesion volumes, lower Z-score of global cognitive, attention-executive and visual functions.

Conclusion: This multicenter study support the theory that preserved fMRI activity of the frontal lobe is associated with a better cognitive profile in MS.

Disclosure: Nothing to disclose.

EP3251

Prevalence of DLB features in possible dementia with Lewy bodies and its relationship to changes in dementia diagnostic category after dopamine transporter imaging using DaTSCAN™

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Introduction: The clinical diagnosis of dementia with Lewy bodies (DLB) is based on core and suggestive features. We set out to investigate whether dopamine transporter imaging using DaTSCAN™ would help in diagnosing DLB (by changing the diagnosis to probable DLB or non-DLB) and to identify which core and suggestive features would most be associated with probable DLB.

Methods: 187 patients with possible DLB were recruited from 21 centres in 6 European countries. Patients were randomized to have a DaTSCAN™ ($n = 127$) or to have no imaging ($n = 60$). The proportion of patients with changes in clinical diagnosis was assessed in terms of DLB features at baseline and after obtaining DaTSCAN™ results. The evolution of features and diagnosis was compared at 8 and 24-weeks of follow-up.

Results: Among 170 subjects considered for the primary endpoint assessment parkinsonism was the most frequent DLB feature (28.8 %), followed by fluctuations (28.2 %), hallucinations (23.5 %) and RBD (16.5 %). No patients reported neuroleptic sensitivity. More patients in the DaTSCAN™ group had a change in diagnostic category after 8-weeks (61 vs 4 %; $P < .0001$) while at 24-weeks there continued to be a major difference between the two groups. The only feature that increased in frequency over the 24-weeks was parkinsonism which was observed more often in patients with final diagnosis of probable DLB and abnormal DaTSCAN™ imaging results.

Conclusions: Changes in diagnostic category were more frequent in the DaTSCAN™ group particularly in those with abnormal images. Parkinsonism, but not other clinical features increased during the 24-weeks of follow-up.

Disclosure: This study was supported by GE Healthcare Ltd. (Chalfont St. Giles, UK). DaTSCAN is not approved for DLB indication in US; Z. Walker received consultancy and speaker fees and research support from GE Healthcare, consultancy fees from Bayer Healthcare and Novartis and research support from Lundbeck; A. Thomas received research support from GE Healthcare; N. Tabet received speaker fees from Eli Lilly and Pfizer and consultancy fees from GE Healthcare; E. Moreno and I. Grachev are full-time employees of GE Healthcare.

EP3252

A comparative value of ^{123}I-Ioflupane single photon emission computed tomography (DaTscan) and transcranial sonography (TCS) for Parkinson's disease diagnostics: a 8-year retrospective study

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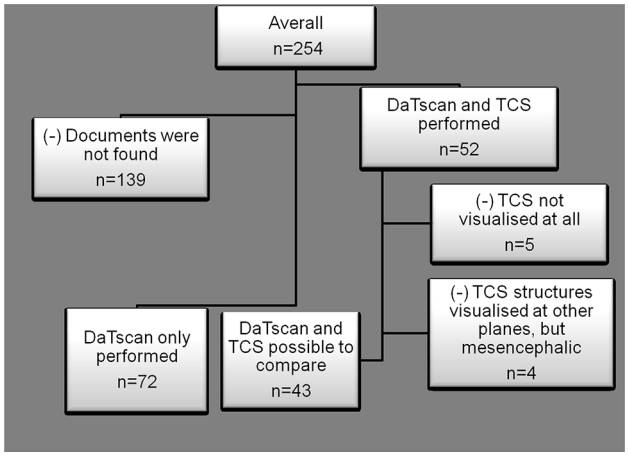
Introduction: The aim of the study was to:

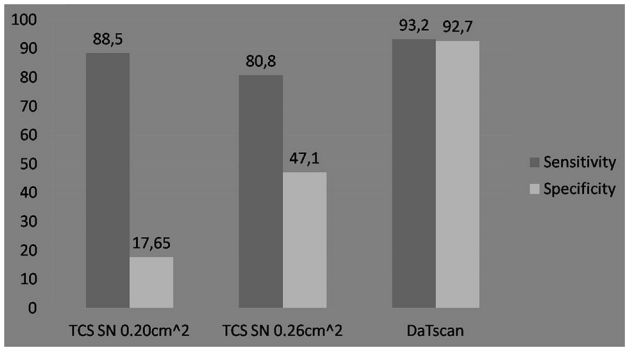
1. evaluate diagnostic accuracy of DaTscan and TCS for the patients with idiopathic Parkinson's disease (IPD);
2. estimate the relationship between two imaging methods.

Methods: A retrospective study of 115 out of 254 patients in total was performed, who were investigated at Kaunas Clinics from 2006 until 2013 (Fig. 1). An experience of DaTscan imaging at Kaunas Clinics is since 2006 (^{123}I-Ioflupane, GE, the UK), and of TCS—since 2010 (Voluson 730 Expert, GE, Austria). The threshold values of

substantia nigra hyperechogenicity (TCS-SN+): moderate $\geq$0.20 cm^2, high $\geq$0.26 cm^2.

Results: The majority of the referred for imaging patients were female 70 (60.9 %), the mean (±SD) age was 63.6 ± 13 years (min.22–max.85 years), median symptom duration 2 years (min.0.05–max.40 years). For those patients to whom IPD was diagnosed n = 59 (51.3 %), median stage according to Hoehn-Yahr was 2 (min.1– max.4), 34 (57.6 %) were tremor predominant. The main DaTscan and TCS accuracy findings are presented in Fig. 2. For 53 (46.1 %) patients diagnoses changed after imaging: 26 (49.1 %) were reclassified to essential tremor, 17 (32.1 %) to IPD (p = 0.003). For 86.1 % patients, DaTscan was abnormal, who were TCS-SN+. TCS missed 3 cases (7 %) when SN < 0.20 cm^2 with abnormal DaTscan, and 6 (14 %)—at <0.26 cm^2.





Conclusions: A high percentage of diagnostic reclassification (46.1 %) after imaging represents high diagnostic impact of two methods. For the majority (86.1 %), when TCS was abnormal, DaTscan reduced binding was detected, however no significant correlation between the tests was found.

Disclosure: Nothing to disclose.

EP3253

Language dominance assessment in a bilingual population: validity of fMRI in the second language

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Introduction: Assessment of language dominance using fMRI is a standard tool to estimate the risk of language function decline after epilepsy surgery. Little is known about the effect of performing language fMRI in a second language in bilingual subjects, and how this may affect the lateralization of language assessed by fMRI in the patients. In this study we investigate language representation in a population of non-native English speakers to assess differences in fMRI language lateralization between first (native) and second language (English).

Methods: Sixteen non-native English speaking patients with focal drug resistant epilepsy underwent language fMRI in their first (native) language (L1) and in English (L2). Differences between language maps using L1 and L2 paradigms were examined at the single subject level by comparing within subject lateralisation-indexes obtain for each language. Differences at the group level were examined for each of the tasks and languages.

Results: Group maps for second language (English) showed greater areas of activation, and more bilateral distribution than for the 1st language. However, at the individual level, lateralisation indexes were concordant between the two languages, except for one patient with atypical dominance.

Conclusions: Language lateralisation can be reliable derived from fMRI tasks in a second language provided that the subject can follow the task. Subjects with greater likelihood of atypical language representation should be more carefully evaluated, using more than one language paradigm.

Disclosure: Nothing to disclose.

EP3254

Diffusion tensor imaging evidence of corticospinal pathway involvement in frontotemporal lobar degeneration

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Introduction: Clinical and neurophysiological evidence of the possible occurrence of Motor Neuron dysfunction in Frontotemporal Lobar

Degeneration (FTLD) have been recently reported providing support to the FTD-MND continuum hypothesis. The alteration of the motor system functioning in FTLD may result from the pathological involvement of the primary motor cortex. However, the white-matter changes possibly affecting the motor pathway in FTLD are not still investigated. The present study aims to explore potential changes affecting the corticospinal tract (CST) microstructure in a large cohort of FTLD patients.

Methods: 34 FTLD subjects (patients with behavioral variant of frontotemporal dementia, primary progressive aphasia and corticobasal syndrome) and 20 healthy controls participated in a Diffusion Tensor Imaging study to assess the microstructural integrity of the CST. Patients also underwent a first clinical evaluation, including a complete neurological examination and an electromyographic investigation. At the baseline, none of them fulfilled the diagnostic criteria for Motor Neuron Disease (MND). Additionally, all patients undertook a clinical follow-up in order to evaluate the possible development of MND.

Results: About 50 % of patients presented evidence of upper and/or lower motor neuron suffering, but none of them developed MND. Group comparison of CST diffusion properties highlighted significant changes in patients compared to controls, which correlated with clinical variables (e.g., disease duration).

Conclusions: Our results suggest that white-matter alterations affecting the motor pathway in FTLD may represent an anatomical substrate of the motor neuron suffering observed in patients. However, the presence of motor system degeneration in FTLD cannot be directly associated to the development of MND.

Disclosure: Nothing to disclose.

EP3255

Dopaminergic modulation of the resting-state sensorimotor network in drug-naive patients with Parkinson's disease

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Introduction: RS-fMRI allows to investigate the spatio-temporal distribution of the spontaneous coherent fluctuations of blood oxygen level-dependent (BOLD) signals within and between functionally related cortical regions, representing the so-called resting-state networks (RSN). In patients with Parkinson's Disease (PD), functional cortical changes, as assessed by fMRI, are thought to be secondary to a functional deafferentation caused by dopamine neurons degeneration of nigrostriatal system which results in a disruption of basal ganglia-thalamocortical loops.

Methods: 20 DNPD patients were scanned twice, immediately before and 60 min after either levodopa or placebo administration; RS-fMRI data were also acquired in 18 healthy, age-matched control subjects (HCs). RS-fMRI data were collected with a 3Tesla MRI scanner. Independent component analysis (ICA), using Brain Voyager, was performed on all scans to extract SMN maps. A statistical threshold of $p < 0.05$ corrected for multiple comparisons was used for both within and between groups analyses.

Results: Acute levodopa administration increases the connectivity at rest in the supplementary motor area (SMA) of DNPD patients, a region where the same signals were found suppressed in all untreated DNPD patients, compared to HCs; within the SMA, the levodopa effect is maximally selective in the "pre-SMA". No other cortical motor regions showed statistically significant differences between experimental groups.

Conclusions: Our findings are consistent with previous fMRI activation studies demonstrating an hypoactivation of SMA in PD patients. The functional deafferentation at rest of the SMA is partially restored by levodopa administration. No other cortical motor regions revealed a functional disrupted connectivity in DNPD.

Disclosure: Nothing to disclose.

EP3256

Reduced activity of resting state networks in multiple sclerosis

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Background: Multiple sclerosis is an inflammatory disease in the central nervous system. The pathology affects mainly the white matter in the forms of lesions and also in the normal appearing white matter. Such alterations cause disconnection of the brain networks that might be behind some of the disability in multiple sclerosis. Our aim was to investigate the functional networks in MS using resting-state MRI.

Methods: Thirty-eight patients with multiple sclerosis and thirty-eight healthy individuals were included in this study. Resting fMRI was acquired with a 1.5 T scanner. Independent component analysis (MELODIC) was used to identify resting state networks. The groups compared with FSL's dual regression analysis. The time course of the resting-state components of the individual subjects were decomposed to five frequency bands with discrete wavelet decomposition. Mean amplitude of the envelope of these decomposed time courses was compared with independent sample T-test.

Results: MELODIC and dual regression analysis revealed six networks, which showed significant differences between the two groups, four resting state networks being significantly larger in MS patients, and two in healthy controls. Moreover, in the slowest frequency bands three components showed higher amplitude activity in the control group compare to patients.

Conclusions: Former studies showed enlarged resting-state networks in MS and hypothetised that this could be part of a compensatory mechanism. In our analysis we verified this hypothesis, showing that the resting state networks show a lower amplitude activity in patients. We hypothetise that the result of a disorganized network caused by the white matter structural disconnection.

Disclosure: Nothing to disclose.

EP3257

Executive resting-state network connectivity in migraine with and without aura

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Introduction: Converging neuropsychological evidence suggests that in migraine executive functions (EF) may be affected during interictal periods. Recent imaging studies have shown a significant functional connectivity decrease within the fronto-parietal networks (FPN), known to be associated with EF, in patients with migraine without aura (MwoA) in absence of significant executive dysfunction.

Objective: To further explore FPN functional connectivity in patients with migraine with aura (MwA) and patients with MwoA, in the interictal period.

Methods: Using RS-fMRI, we compared functional connectivity within the FPN in 14 patients with MwA, versus 14 sex- and age-matched HC. To examine the specificity of any observed differences in FPN functional connectivity between patients and HC, we further studied 14 age- and gender-matched patients with MwoA. Finally, we used voxel-based morphometry to assess whether between-group differences in functional connectivity were dependent on structural differences.

Results: Neuropsychological data revealed no significant executive dysfunction in both migraine groups compared to HC. RS-fMRI showed that both patients with MwA and MwoA, compared to HC, have a significant functional connectivity decrease within the right FPN and specifically in the middle frontal gyrus and the dorsal anterior cingulate cortex. There were no structural differences between the three groups.

Conclusions: Our data demonstrate that, even in the absence of clinically evident EF deficits, MwA and MwoA are associated with reduced FPN functional connectivity. We suggest that observed FPN connectivity changes may represent a migraine biomarker, probably related to well-known maladaptive stress response in migraine patients.

Disclosure: Nothing to disclose.

EP3258

Basal ganglia structural changes in primary focal dystonia

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Introduction: To investigate basal ganglia (BG) volumetric and microstructural abnormalities in primary focal dystonia.

Methods: Seventy-five patients with focal dystonia (20 blepharospasm [BL], 21 spasmodic torticollis [ST], 19 writer's cramp [WC], 15 spasmodic dysphonia (SD)] and 83 controls underwent 3D T1-weighted and DT MRI. Caudate nucleus, putamen, globus pallidus and thalamus were automatically segmented. Volumes, and mean fractional anisotropy (FA), mean diffusivity, axial diffusivity, and radial diffusivity were measured for each grey matter nucleus.

Results: Compared with controls, focal dystonia patients did not show significant differences in the BG volumes. DT MRI metrics were altered in BL in caudate nucleus ($0.827 \leq$ C index ≤ 0.874), globus pallidus ($0.817 \leq$ C index ≤ 0.875), putamen ($0.815 \leq$ C index ≤ 0.856) and thalamus bilaterally ($0.858 \leq$ C index ≤ 0.872). ST showed diffusivities and FA alterations in caudate nucleus ($0.696 \leq$ C index ≤ 0.737) bilaterally, right globus pallidus ($0.755 \leq$ C index ≤ 0.757)), thalamus (C index $= 0.717$) and putamen ($0.691 \leq$ C index ≤ 0.723). In WC, caudate nucleus ($0.651 \leq$ C index ≤ 0.754), globus pallidus ($0.715 \leq$ C index ≤ 0.782) and putamen ($0.700 \leq$ C index ≤ 0.733) showed DT MRI abnormalities only on the right side. SD showed significant changes in right caudate nucleus ($0.744 \leq$ C index ≤ 0.766), globus pallidus ($0.684 \leq$ C index ≤ 0.764) and putamen ($0.733 \leq$ C index ≤ 0.747). In all patients, damage to the caudate nucleus and globus pallidus correlated with disease severity.

Conclusions: BG microstructural abnormalities, but not volume changes, occur in patients with primary focal dystonia, which may contribute to the defective sensorimotor integration of these patients. DT MRI has the potential to add a valuable piece of information to the understanding of the pathophysiology of these complex disorders.

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EP3259

Microstructural alterations detected by combined resting-state fMRI and diffusion tensor imaging in patients with mild traumatic brain injury

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Introduction: To evaluate brain activity in resting state and white matter structural alterations in mild traumatic brain injury patients by combined resting-state fMRI (RS-fMRI) and diffusion tensor imaging (DTI).

Methods: Seventeen patients with MTBI (median initial Glasgow Coma Scale (GCS) score, 13-15) and seventeen healthy people underwent conventional MRI, RS-fMRI and DTI. RS-fMRI data were used to identify abnormal areas comprising the regions of interest (ROIs). For DTI, fractional anisotropy (FA) and apparent diffusion coefficient (ADC) values were measured in the ROIs. At 6 months after functional MR imaging, the Chinese version of the Mini-Mental State Examination (MMSE)was used for neurocognitive evaluation to assess general cognitive functions of all participants.

Result: Compared to healthy individuals, MTBI patients had more bilateral frontal lobe and cerebellar posterior lobe activation in the resting state, as revealed by RS-fMRI BOLD signals, but less activation in the right thalamus, right hippocampus, brainstem, bilateral occipital lobe, left post-central gyrus, and right corona radiata. In the ROIs identified by RS-fMRI in MTBI patients, we observed FA value decreased in the bilateral frontal lobe, brainstem, and left occipital

gyrus, and by ADC in the left thalamus, bilateral hippocampus and right cerebellar posterior lobe. MTBI gave significantly lower MMSE scores than the control group. Changed ALFF was correlated with diminished neurocognitive functions in patients with MTBI.

Conclusion: Combined RS-fMRI and DTI provides greater detection of abnormal microstructural alterations, enabling detection of the underlying causes of the pathophysiological mechanisms of complicated sequelae after MTBI.

Disclosure: This study was supported by the Natural Science Foundation of Guangdong Province, China (grant No. S2012010008974).

EP3260

Using ^{1}H-MR spectroscopy and resting-state fMRI to study the metabolic and functional alternations of brain caused by opioid codeine

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Introduction: We aim to evaluate the alternations of brain function using resting-state fMRI and detect the metabolic alternations in the both sides frontal lobe by 1H-MRS for the healthy volunteers after taking opioid codeine.

Methods: Twenty right-handed healthy participants were included. The healthy participants were begun to collect the data before and 1 h after taking opioid codeine. A GE 1.5T MR scanner was used for resting-state fMRI and MRS data acquisition. The resting-state fMRI data was processed by REST, DPARSF and SPM8. The results of amplitude of ALFF and ReHo values were calculated. MRS data were collected by PRESS sequence. The voxels were separately put in the symmetrical frontal lobe. The data of MRS was disposed by LCModel software. The concentrations of metabolites were ultimately measured. All the data were analyzed by SPSS 17.0.

Results: After taking the opioid codeine, the ALFF and ReHo altered in different brain areas. These brain areas are mainly involving: sensorimotor system, limbic system, connected system of hemispheres, reward system. The metabolites' concentrations were changed in the both frontal lobe after taking the opioid codeine. Compared the choline compound of the right frontal lobe, it was increased; compared the metabolites concentrations of the left frontal lobe, the Ins was decreased, but the choline compound was increased. The other metabolites had no statistical significance after taking the opioid codeine.

Conclusions: After taking the opioid codeine, the ALFF and ReHo altered in different brain areas. The metabolites' concentrations were changed in the both frontal lobe.

Disclosure: We infer that Glu is a potential metabolite for estimating the drug-dependent.

EP3261

Regional metabolic change in occipital cortex in patients with mild traumatic brain injury: study by magnetic resonance spectroscopy (MRS)

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Introduction: To investigate the changes of cerebral metabolites in occipital cortex in Patients with Mild Traumatic Brain Injury by magnetic resonance spectroscopy (MRS).

Methods: Fifty individuals (18–35 years old) with Mild Traumatic Brain Injury patients (median initial Glasgow Coma Scale score, 13–15) and 15 healthy controls (aged-matched) underwent conventional MR and 1H-MRS (single voxel in the occipital gray matter) by 1.5T MR Scaner. *N* acetyl aspartate (NAA), *N* acetyl aspartate(NAA)/creatine(Cr), choline(Cho), choline(Cho)/creatine(Cr) in occipital cortex were calculated by MRS and analysed by LCmodel in all subjects.

Results: Conventional MRI showed no abnormal in all subjects. Compared with normal control group, MRS showed regional metabolic of the concentration of NAA,NAA/Cr in occipital cortex in mild traumatic brain injury patients decreased, the difference was significant ($P < 0.05$). Cho concentration and Cho/Cr increased slightly, there was no significant difference between patients and normal control group.

Conclusions: 1H-MRS can detect the changes of cerebral metabolites in patients with MTBI, which is beneficial to provide additional information for MTBI diagnosis.

Disclosure: This study was supported by the Natural Science Foundation of Guangdong Province, China (grant No. S2012010008974).

Sleep disorders

EP3262

Post-H1N1 narcolepsy-cataplexy in Germany: case series of 9 children and adolescents

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Introduction: Increasing evidence supports the hypothesis of narcolepsy being an immune-mediated disorder. An association between H1N1 vaccine and the onset of narcolepsy-cataplexy (NC) is reported.

Methods: We retrospectively and prospectively followed the cohort of nine post-H1N1 NC affected children and adolescents. Assessment included socio-demographic characteristics, sleep questionnaires, vaccination data, clinical features, laboratory data including hypocretin, sleep laboratory results and therapy. Patients are now followed for 2 years (mean).

Results: Onset of NC was usually rapid and severe in both excessive daytime sleepiness (EDS) and cataplexy. Fragmentation of sleep (7/9 patients) and nightmares (5/9) occurred within 6 months after onset of NC. In 3 patients, REM sleep behaviour disorder was confirmed. Another striking feature was the low to extremely low vitamin D level in all nine patients. In one patient, hypocretin was 106 pg/ml 4 weeks and 56 pg/ml 7 weeks after vaccination. The clinical course of the patients was very variable: some patients showed a spontaneous improvement, some patients deteriorated, in particular in nighttime sleep and excessive daytime sleepiness. Treatment included modafinil, methylphenidate and sodium oxybate.

Conclusions: Our study adds new information on clinical and laboratory findings in post-H1N1 NC. The underlying immunological mechanism warrants further research.

Disclosure: Nothing to disclose.

EP3263

Sleep promotion with baclofen improves functional recovery and promotes neuroplasticity after stroke in rats

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Introduction: Sleep disruption in the acute phase after stroke has detrimental effects in both humans and animals. Conversely, the

effect of sleep promotion is unknown. Baclofen (Bac) is a known NREM sleep promoting drug in both humans and animals. The aim of this study was to investigate the effect of Bac in a rat model of focal cerebral ischemia (isch).

Methods: 24 h after initiation of focal cerebral ischemia (MCAo) rats were treated with Bac (10 mg/kg) or saline and then twice daily during 10 consecutive days. Three groups of rats were designed: Bac/isch, saline/isch and Bac/sham. Sleep was assessed by EEG recordings and sensorimotor function by single pellet reaching test (SPR). Axonal sprouting was analysed by biotinylated dextran amine (BDA) tracing as a measure of neuroplasticity. Brain damage was assessed by Nissl staining.

Results: Repeated Bac treatment after MCAo affected sleep, neuroplasticity and motor function but not the size of brain damage. NREM sleep amount was increased significantly during the dark phase in Bac/isch compared to the saline/isch group ($p < 0.05$, unpaired t-test). SPR performance dropped to 0 immediately after MCAo in both ischemic groups and recovered slowly thereafter. Bac-treated ischemic rats performed significantly better than saline-treated rats ($p = 0.01$, Tukey–Kramer). The BDA stained areas of the ipsilesional motor cortex and striatum were larger in the ischemic group treated with Bac ($p < 0.0001$, Tukey–Kramer).

Conclusion: Delayed repeated Bac treatment after stroke promotes neuroplasticity and functional recovery. These data give further support to a role of sleep in post-stroke recovery.

Disclosure: Nothing to disclose.

EP3264

Narcolepsy marks DNMT1-associated disorders

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Introduction: DNMT1 gene mutations cause two syndromes: hereditary sensory and autonomic neuropathy with dementia and hearing loss type IE (HSAN IE) and autosomal dominant cerebellar ataxia, deafness and narcolepsy (ADCA-DN). We report five Italian patients carrying *DNMT1* mutations.

Methods: A global assessment was performed in three ADCA-DN and three HSAN IE patients.

Results: The three ADCA-DN patients suffered from narcolepsy, cataplexy, deafness and cerebellar ataxia from the fourth/fifth decade, sensorineural deafness, optic neuropathy, and axonal sensory polyneuropathy. The elder one (57 years) also developed mild extrapyramidal, pyramidal and autonomic dysfunction signs. CSF hypocretin-1 was low-intermediated, Tau protein was increased and brain MRI showed cerebral and cerebellar atrophy. The three HSAN IE patients developed deafness and polyneuropathy signs in the third/fourth decade. The two younger patients, siblings, showed mild ataxic gait and isolated deficiencies in verbal, attention or logical task, and reported mild daytime drowsiness. The third patient, now 59 years, presented spontaneous feet bones fractures, arthropathy, foot ulcers, ataxia and cognitive impairment. He also complained excessive daytime sleepiness, dream enactments and atypical cataplexy. All showed sensorineural deafness, severe axonal sensory polyneuropathy, optic neuropathy, and increased CSF Tau protein. Neuroimaging studies disclosed brain atrophy, and sleep recordings were diagnostic for narcolepsy in all HSAN IE patients.

Conclusion: We report for the first time that narcolepsy, as well as optic nerve involvement, can characterize HSAN IE. Cataplexy and low CSF hypocretin-1 levels are typical of ADCA-DN. The two methylopathies can represent two manifestations of a single neurodegenerative *DNMT1*-related spectrum.

Disclosure: Nothing to disclose.

EP3265

Iron deficiency in pregnant women with Restless Legs Syndrome

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Introduction: Restless Legs Syndrome (RLS) is a frequent neurological disorder affecting 7–9 % of population. It presents with urge to move one's legs in order to relieve unpleasant sensory symptoms. These feelings occur at rest and usually at night what leads to sleep disturbances and reduced quality of life (QoL). Aim of this study is to disclose changes in iron metabolism in pregnant women with RLS.

Methods: We examined 300 consecutive women in the third trimester of pregnancy. After signing informed consent, they filled in the questionnaire based on official diagnostic criteria. Demographic data and RLS characteristics were obtained. All responders underwent routine blood examination.

Results: From 300 responders, 31.33 % met all criteria and were considered positive for RLS (RLS+). Comparing RLS+ and RLS negative (RLS−) group, we found significantly lower levels of haemoglobin (Hb), haematocrit (Ht) and red blood cells (RBC) in RLS+ ($p > 0.001$). Mean corpuscular hemoglobin (MCH) and its concentration (MCHC) were also lower in RLS+ ($p = 0.005$ and 0.001) what is typical of iron deficiency. Iron supplementation was significantly lower in RLS−; positively correlated with serum ferritin level and with birth weight (not observed in RLS+). Serum iron levels correlated with Ht and MCH only in RLS−, also birth weight with pregnancy duration.

Conclusions: We disclosed significantly lower parameters of iron metabolism in RLS+ compared to RLS− in pregnant women. We emphasized the importance of iron deficiency detection in pregnancy with adequate supplementation if necessary. That prevents the pregnant from decreased QoL and possible pregnancy and/or delivery complications.

Disclosure: Nothing to disclose.

EP3266

Sleep related violence and sexual behaviour in sleep: a systematic review of medical-legal case reports

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Objective: To systematically review medical-legal cases of sleep related violence (SRV) and sexual behaviour in sleep (SBS).

Search methods: We searched Pubmed and PsychINFO (from 1980 to 2012) with pre-specified terms. We also searched reference lists of relevant articles.

Selection criteria: Case reports in which a sleep disorder was purported as the defence during a criminal trial and in which information about the forensic evaluation of the defendant was provided.

Data extraction and analysis: Information about legal issues, defendant and victim characteristics, circumstantial factors, and forensic evaluation was extracted from each case. A qualitative-comparative assessment of cases was performed.

Results: Eighteen cases (9 SRV and 9 SBS) were included. The charge was murder or attempted murder in all SRV cases, while in SBS cases the charge ranges from sexual touching to rape. The defence was based on sleepwalking in 11/18 cases. The trial outcome was in favour of the defendant in 15/18 cases. Defendants were male relatively young in all cases. Victims were usually adult defendant's relatives in SRV cases, and unrelated teenager or young girls in SBS cases. In most cases the criminal events occurred 1–2 h after the defendant sleep onset and both proximity and potential triggering factors were reported. The forensic evaluation carried out widely differed from case to case.

Conclusion: SRV and SBS medical-legal cases did not show apparent difference, except for the charge severity and the victim characteristics. An international multidisciplinary consensus for the forensic evaluation of SRV and SBS should be urgently developed.

Disclosure: Nothing to disclose.

EP3267

Patients with increased blood pressure in sleep have higher numbers of periodic limb movements

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Introduction: A relation between periodic limb movements (PLMs) and blood pressure (BP) had been frequently described. The aim of this study was to verify hypothesis whether patients with increased nocturnal BP have higher numbers of PLMs.

Methods: We have analyzed polysomnographic (PSG) recordings of 104 consecutive patients undergoing PSG due to complaints of disordered sleep. We have excluded subjects with sleep disordered breathing. We have compared PLMs Index (PLMS-I) and PLMs with arousals Index (PLMSA-I) of patients with mean nocturnal systolic BP higher than 120 mmHg (Group 1; $n = 38$) and lower than 120 mmHg (Group 2; $n = 66$), and recordings of patients with mean nocturnal diastolic BP in sleep higher than 75 mmHg (Group 3; $n = 46$) and lower than 75 mmHg (Group 4; $n = 58$).

Results:

Patients in Group 1 were older than in Group 2 (51.6 years vs. 39.8) and had higher BMI (27.7 vs. 24.6).

Patients in Group 1 compared with patients in Group 2 had significantly higher PLMS-I and PLMSA-I (22.47 vs 10.18, $p = 0.0069$; and 3.88 vs. 1.78; $p = 0.01$).

Patients in Group 3 were older and had higher BMI than patients from group 4 (47.9 vs. 41.16 years and 26.7 vs 24.96). PLMS-I and PLMSA-I were significantly higher in Group 3 than in Group 4 (20.57 vs. 9.99, $p = 0.0087$; and 3,40 vs. 1.87, $p = 0.036$).

Conclusions: Patients with high nocturnal blood pressure have higher PLMS-I and PLMSA-I. This may mean that PLMs increase blood pressure or that they are a symptom of increase sympathetic tone parallel to increased blood pressure.

Disclosure: Nothing to disclose.

EP3268

Characteristics of sleep-disordered breathing in etiologic subtypes of acute ischemic stroke

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Introduction: Sleep-disordered breathing (SDB) is frequent in stroke patients. A strong association has been suggested between SDB and atrial fibrilation (AFib). In the recent study we evaluated characteristics of SDB in etiologic subtypes of acute ischemic stroke. We also investigated the relationship between SDB and AFib in acute ischemic stroke.

Methods: We prospectively enrolled patients with acute ischemic stroke. Clinical and laboratory characteristics of population were recorded on admission. SDB was assessed using standard polysomnography within 7 days after stroke onset.

Results: In 72 patients 10 strokes (13.9 %) were caused by large artery atherosclerosis, 21 strokes (29.2 %) by small vessel occlusion, 33 strokes (45.8 %) by cardioembolism. Other or unknown etiology was present in eight patients (11.1 %). Desaturation index (DI) in cardioembolic strokes and in large artery atherosclerosis strokes was significantly higher than in small vessel occlusion strokes ($p = 0.008$, $p = 0.035$). Arousal index (AI) in large artery atherosclerosis strokes was significantly higher than in small vessel occlusion strokes ($p = 0.013$), cardioembolic strokes ($p = 0.007$) and strokes of other or unknown etiology (0.027). Age (OR = 1.083, 95 % CI: 1.022–1.148, $p = 0.007$) and DI (OR = 1.037, 95 % CI: 1.004-1.071, $p = 0.026$) were the only significant variables to predict AFib in a multiple regression model.

Conclusions: We observed higher DI and AI in large artery atherosclerosis strokes what may relate to more severe neurological deficit in this subgroup. Age and DI were the only significant predictors of AFib in acute ischemic stroke. Higher DI in cardioembolic strokes may thus mirror more frequent premorbid presence of SDB in patients with AFib.

Disclosure: Nothing to disclose.

EP3269

Fatal familial insomnia: a case report of a non-reported Spanish family

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Introduction: Fatal Familial Insomnia (FFI) is an autosomal dominant disease, with incomplete penetration, linked to a missense mutation at codon 178 of the prion-protein gene and polymorphism Met-Val at codon 129. Clinical onset is in adulthood age, outcome vary between 7 and 72 months and invariably leads to death. Change in sleep pattern can be an important clinical clue for identifying FFI, accompanied shortly after by motor signs, disrupted circadian rhythms, autonomic hyperactivation as well as attention and behavior deficits.

We report a case of FFI in a patient, of a not previously reported Spanish family, with her mother and two brothers so far affected and died.

Case report: A woman 45 years old, with a known family history of FFI and genetic diagnosis was referred to our hospital with symptoms of dizziness, weight loss, mild abnormal behavior and insomnia. She was being medicated with lorazepam and omeprazole.

She had mild attention deficit, hyperreflexia, bilateral Hoffman sign, aquileus clonus, some spontaneous myoclonus, postural and intentional tremor. She also had tachycardia, hypertension and Body Mass Index of 16,3 kg/m^2. Cranial magnetic resonance showed hyperintensity in both thalami in FLAIR sequences; EEG was normal; perfusion brain SPECT revealed cortical, subcortical and both thalami hypoperfusion. Polysomnography showed severe disrupted sleep structure and absence of clear defined sleep stages.

Conclusions: This patient develops a typical course, with a depressive syndrome as initial symptom. The treatment with melatonin was unsuccessful as expected. Symptomatic treatment, genetic counseling and psychosocial support are the only measures available.

Disclosure: Nothing to disclose.

EP3270

EEG functional connectivity modifications of cyclic alternating pattern in nocturnal frontal lobe epilepsy

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Introduction: Cyclic Alternating Pattern (CAP) is the marker of sleep instability and is known to modulate some types of sleep epileptiform activity. In this study we employed a non-linear measurement of EEG functional connectivity, the Synchronization Likelihood (SL), in order to test the hypothesis that modifications of EEG synchronization occur in the A1 subtypes of CAP in patients affected by Nocturnal Frontal Lobe Epilepsy (NFLE), compared to controls.

Methods: 19-channels sleep EEG recordings of 5 non-lesional NFLE patients and 7 good sleepers were acquired. A total amount of nine hundred and twenty-three 4 s epochs, containing artifact-free and manually scored A1-CAP subtypes, were extracted from light and slow-wave NREM sleep stages. For each epoch, SL was computed between all pairs of channels in the standard frequency domains (delta 0.5–4 Hz, theta 4–8 Hz, alpha 8–13 Hz, sigma 12–15 Hz, beta 13–30 Hz, gamma 30–48 Hz). The corresponding connectivity matrix for each epoch, sleep stage and subject was averaged over channels in order to achieve a global estimation. Two-way ANOVA, using group as between subjects factor and sleep stage as within subjects factor, was used to test significant SL modifications.

Results and conclusions: The mean global SL, computed on the A1-containing epochs, was significantly higher for the gamma band in NFLE patients compared to controls ($P = 0.002$), without sleep stage effects. No significant differences were observed for the other bands. This finding indicates gamma hyper-synchronization as a key phenomenon of interictal epileptiform EEG activity, interwoven in the dynamic framework of sleep instability underlying CAP.

Disclosure: Nothing to disclose.

EP3271

Sensitivity and specificity of the "REM sleep behavior disorder-single-question screen" (RBD-1Q) in Parkinson's disease

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Introduction: REM Sleep Behavior Disorder Single-Question Screen (RBD-1Q)is a recently proposed tool for screening RBD, but its psychometrics properties have been evaluated only in sleep clinic-based patients with idiopathic RBD. We aimed to evaluate the sensitivity and specificity of the RBD-1Q in patients with Parkinson's Disease (PD) routinely seen in movement disorder clinics, and to compare it with the RBD-Screening Questionnaire (RBD-SQ).

Methods: Thirty-three non-demented PD patients ($M = 16$, age 62.6 ± 8.9 years; &Y 1.7 ± 0.8; mean PD duration: 6.1 ± 3.6 years; n. with bed partner = 19/33), consecutively seen at two movement disorders centers for their routine evaluation, filled out both the RBD1Q and the RBD-SQ. They subsequently underwent to a full nocturnal video-polysomnography and a diagnosis of RBD was made according to gold-standard criteria.

Results: Of the 17 PD patients who were diagnosed with RBD, $n = 10$ screened positively at the RBD1Q, leading to a sensitivity of 58.8 % (95 % IC: 33.0,81.5). On the other hand, $n = 15$ out of 16 patients without RBD screened negatively at the RBD-1Q, translating to a specificity of 93.7 % (95 % IC: 69.7,99.0). In the same population, RBD-SQ showed a sensitivity of 52.9 (95 % IC: 27.9,77.0) and a specificity of 93.7 % (95 % IC: 69.7, 8.9).

Conclusions: In non-demented PD patients routinely seen at a movement disorder center, RBD1Q shows a poor sensitivity and a high specificity. However, in these patients, RBD1Q might better discriminate RBD than the RBD-SQ. In contrast to idiopathic RBD, patients with PD are frequently unaware of their RBD, limiting the utility of the screening tools in this population.

Disclosure: Nothing to disclose.

EP3272

Autonomic activity during sleep in patients with nocturnal frontal lobe epilepsy: the role of cyclic alternating pattern

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Introduction: Pulse wave amplitude (PWA) drops are result of autonomic vasoconstriction and can be considered reliable markers of cortical activity shifts during sleep. We aim to clarify the correlation between PWA oscillations and sleep microstructure expressed by means of cyclic alternating pattern (CAP) in patients with nocturnal frontal lobe epilepsy (NFLE).

Methods: Video-polysomnographic recordings of 20 NFLE patients (25 ± 7 years, 12 males) were analyzed. Sleep stages and CAP measures were scored according to international rules. Only PWA drops $\geq$30 % were included. PWA drops were considered associated with a CAP A-phase only when the latter occurred 10 s before or 15 s after the onset of the PWA decrease.

Results: In NFLE patients CAP rate (76 %) was significantly higher (p/0.0001) compared to normative age-balanced values (32 %). A total of 5.870 PWA drops and 11.234 CAP A-phases were scored in non-REM sleep. 78 % of PWA drops were associated with CAP A-phases. The amount of A-phases occurring 10 s before the PWA drops (3.004) was significantly higher (p/0.0001) compared to the A-phases (359) identified 15 s after the PWA fall. Subtypes A3 occurring 10 s before PWA drops were significantly more numerous (p/0.0001) compared to A1 and A2.

Conclusions: The high values of CAP rate and the powerful modulation of CAP on PWA variations suggest an altered autonomic balance in NFLE patients. The association between PWA drops and CAP confirm that PWA recording can be used as a marker of cortical-subcortical activation. These premises may be exploited in cardio-respiratory monitoring of sleep disordered breathing.

Disclosure: Nothing to disclose.

EP3273

Diagnostic potential of nocturnal sleep stage transitions to identify narcolepsy with cataplexy

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Introduction: The diagnosis of narcolepsy with cataplexy (NC) is based on the presence of cataplexy, on MSLT findings and on cerebrospinal hypocretin-1 measurement. Hypocretin-1 is a key neurotransmitter to promote wakefulness and to stabilize wake and sleep states. We aimed at evaluating the diagnostic significance of nocturnal sleep stage transitions and of sleep onset REM periods (SOREMPs) in the context of hypersomnias of central origin.

Methods: We evaluated the occurrence of SOREMP and of sleep stage transitions between sleep and wakefulness, and non-REM - REM sleep and wakefulness, and non-REM sleep stage 1–non-REM and wakefulness (W-N1-NR-R) in the nocturnal sleep of 96 consecutive patients with NC ($n = 41$), narcolepsy without cataplexy (NwoC, $n = 7$), idiopathic hypersomnia (IH, $n = 19$), and "subjective" excessive daytime sleepiness (sEDS, $n = 29$).

Results: NC and NwoC had more frequently SOREMP than IH and sEDS. NC patients had more transitions between different combinations of sleep stages and wakefulness, most notably the W-N1-NR-R transition index. ROC curve analysis confirmed that both SOREMP (area under the curve of 0.741 ± 0.054, $p < 0.0005$) and the W-N1-NR-REM transition index (area under the curve of 0.732 ± 0.052, $p < 0.0005$) had a comparable sensitivity and specificity profile to identify NC.

Conclusions: The nocturnal occurrence of SOREMP and of high sleep stage transitions identify NC in the differential diagnosis of the hypersomnias of central origin. In their absence, the MSLT and cerebrospinal hypocretin-1 measurement are mandatory for a correct diagnosis.

Disclosure: Nothing to disclose.

EP3274

Impact of acute administration of sodium oxybate on nocturnal sleep polysomnography and on multiple sleep latency test in narcolepsy with cataplexy

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Introduction: Treatment of narcolepsy with cataplexy (NC) with sodium oxybate (SO), impacts on nighttime sleep quality, excessive daytime sleepiness (EDS) and cataplexy. We studied on the acute effects of SO on polysomnographic nighttime (PSG) and multiple sleep latency test (MSLT) of patients with NC.

Methods: Sixteen NC adult patients were recruited, together with 16 normal controls. Two consecutive PSG followed by two MSLT sessions were carried out, before and during the first night of SO assumption respectively.

Results: The administration of SO was followed by a significant decrease in number of stage shifts and awakenings, wakefulness after sleep onset, percentage of sleep stage 1. Sleep efficiency and slow-wave sleep percentage increased. Cyclic alternating pattern (CAP) rate remained unchanged but the percentage of CAP A3 subtypes decreased. The number of CAP A3 subtypes per hour of NREM sleep decreased significantly while that of A1 remained unchanged. The duration of A1 and A3 subtypes was slightly increased. Periodic and isolated leg movements (LMs) decreased their rate during NREM sleep, and their Periodicity index, which became similar to that of controls. MSLT sleep latency also significantly improved after SO intake.

Conclusions: The administration of SO in NC patients is followed by immediate important and complex effects on PSG parameters and MSLT, including an evident (over)increase in slow-wave sleep which, however, does not display a physiological microstructure, a moderate decrease in periodic and isolated LMs, possibly mediated by a dis-inhibited dopaminergic neuronal activity, and an improvement on daytime mean sleep latency at the MSLT.

Disclosure: Prof. Plazzi has consulted for UCB Pharma and Jazz pharmaceuticals. Dr. Ferri has consulted for Merck & Co., Sapio-Life and EB Neuro and has spoken for UCB Pharma. Prof. Dauvilliers has consulted for Bioprojet, UCB Pharma and Jazz pharmaceuticals. Prof. Bruni has consulted for Sapio Life. Drs. Aricò, Pizza, and Vandi have no potential conflicts of interest.

Ageing and dementia 2

EP4101

Abstract withdrawn

EP4102

A 16-year network organization of memory clinics in the North of France: new patients characteristics over time

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Introduction: Memory clinics were created to improve diagnosis and management of Alzheimer's disease. However, no data are available on the progression or their recruitment over time. We aimed at identifying changes in new patients characteristics in Northern France, where a reference memory centre runs a network of memory clinics since 1996.

Methods: We studied consecutive new consultants in all memory clinics, from 01-1997 to 12-2012, in the 4-million inhabitants Nord-Pas-de-Calais region. We collected patients' demographic characteristics, and MMSE at entry, and who referred them. We calculated the age-, gender-, and level-of-education standardized rates of new consultants reported to the region population over time.

Results: The number of memory clinics increased from 14 in 1997 to 28 in 2012, with more geriatric settings. We observed a consistent increase of new patients (from 1,565 to 6,604, total = 71,885) independently from the population age, sex, and level of education changes in the region, with an important increase of the oldest patients, an increased number of non-educated patients, a higher proportion of patients referred by specialists, and a shorter delay since first symptoms. The mean MMSE score remained stable around 22 except the oldest patients who consulted at a less severe stage with time. Most patients came to a close memory clinic and this proportion kept increasing except in the reference centre, where the proportion of young patients increased.

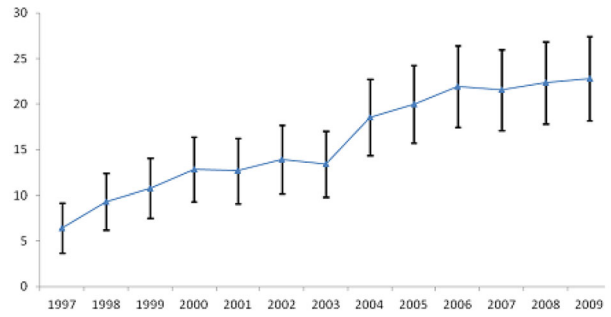

Figure 1: age-, gender-, and level-of-education standardized rates of new consultants reported to the region population over time (from 1997 to 2009, not calculated from 2010 to 2012 because of the absence of updated information on the level of education in the region since 2009)

	1997-2000	2001-2003	2004-2007	2008-2012	p
Age in all centres	70.1+/-13.1	71.5+/-13.0	73.1+/-12.5	73.7+/-13.0	<0.0001
Age in MRCC	65.7+/-14.5	65.7+/-14.4	64.9+/-15.1	63.6+/-15.6	<0.0001
MMSE in all centres	21.72+/-6.99	22.15+/-6.34	22.22+/-6.24	21.99+/-6.40	<0.0001
Missing data	12.9%	11.9%	13.1%	20.2%	
MMSE in MRCC	22.89+/-6.79	23.92+/-6.02	24.13+/-5.79	23.46+/-6.11	<0.0001
Missing data	9.25%	10.14%	9.71%	12.97%	

Table 1. Age and MMSE score (Mini Mental State Examination) at first visit, in all memory centres of the Northern of France, and in the MRCC (Memory Resource and Research Centre, reference centre for young patients). Data provided are means with standard deviations. No missing date for age.

Conclusions: Our study showed that a network organization of memory clinics in a region improves access to diagnosis and care for older and less educated people.

Disclosure: Nothing to disclose.

EP4103

Role of vitamin D deficiency and its receptor gene polymorphism in cognitive impairment in elderly

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Introduction: Evidences reveal that vitamin D deficiency and vitamin D receptor gene polymorphism can influence the cognitive abilities of the normal aged subjects.

Methods: The study was conducted on 50 non demented subjects $\geq$ 60 years old, Global assessment of cognitive function by: Modified Mini-Mental State examination test (3MS; Addenbrooke's Cognitive Examination Revised. Assessment of specific cognitive function: For attention: Paced Auditory Serial Addition Test and Trail B test. Memory: Story A from logical memory subtest of the Wechsler Memory Scale-Revised, Paired Associate learning test and Benton Visual Retention test. Language: Token test. Visuospatial abilities: Block Design test. Measurement of 25 hydroxy vitamin D in serum and genotyping using PCR to detect the polymorphisms of VDRApaI and VDR-*Taq*I.

Results: Vitamin D deficiency was found to be associated with poor performance in tests assessing memory and attention, but no relation was with performance in executive functions, language or visuospatial abilities. VDR-ApaI polymorphism was found to affect memory and psychomotor speed but no effect on the performance in tests assessing attention, executive functions, language or visuospatial abilities. No effect for VDR-TaqI polymorphism on the performance in different tests.

Conclusions: Vitamin D deficiency and vitamin D receptor gene polymorphism play an important role in exacerbating cognitive impairment of normal aging.

Disclosure: Nothing to disclose.

EP4104

TREM2 genetic variability in patients with Alzheimer's disease and frontotemporal lobar degeneration

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Introduction: Mutations in triggering receptor expressed on myeloid cells gene (*TREM2*) have previously been associated with Nasu–Hakola disease. Recent evidence highlighted an association between rare functional variants in *TREM2* and Alzheimer's disease (AD) or Frontotemporal Lobar Degeneration (FTLD). The aim of this study has been to test *TREM2* variants as susceptibility factors for FTLD and AD.

Methods: Direct sequencing has been performed in an overall Italian population consisting of 75 patients clinically diagnosed with FTLD, 607 AD patients and 612 healthy age-matched controls.

Results: Four FTLD patients (5.3 %) and 12 AD patients (2 %) were carriers, in heterozygosis, of different variants. In particular, one FTLD patient was a carrier of the T66 M mutation, that in homozygosis state leads to Nasu–Hakola disease. One FTLD patient and five AD patients were carriers of the rare variant R47H, previously associatedwith the development of AD. Lastly, two FTLD and two AD patients were carriers of the variant R62H, previously reported as a benign variant. Three more AD patients were carriers of Q33X mutation, that in homozygosis state leads to Nasu–Hakola disease, whereas another one was carrier of the rare variant D87 N. Lastly, a novel non pathological variant was found in one AD patient.

Conclusions: *TREM2* could likely act as risk factor for FTLD and AD. Further studies involving a larger size population are however required to drawn definitive conclusions. Patients carrying these TREM2 variants could have a peculiar different pathogenic disease mechanism as compared with non-carriers, possibly overlapping with the Nasu–Hakola disease.

Disclosure: Nothing to disclose.

EP4105

Anticardiolipin antibodies are associated with cognitive dysfunction in stroke: free individuals

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Introduction: The presence of anticardiolipin antibodies (aCLs) has been associated with vascular occlusive events. The role of aCLs as a risk factor for stroke has been a matter of debate, and scarce information exists on the relationship between aCLs and other cerebral disorders. Reports exist for seizures, chorea and subtle cognitive dysfunction. The association between aCLs and cognition was further explored and the relationship between aCL titres and brain magnetic resonance imaging (MRI) findings was evaluated in a large cohort of community-dwelling individuals.

Methods: The study cohort was drawn from the Austrian Stroke Prevention Study. A total of 1895 subjects had a complete risk factor assessment and measurement of aCL titres in serum. Participants were classified as aCL positive if either the immunoglobulin G (IgG) or IgM aCL titres were elevated (IgG > 21 U/ml, IgM > 12 U/ml). All subjects were also categorized based on the quartile distribution of IgG and IgM isotype titres. All underwent cognitive testing by the Mini Mental State Examination (MMSE) and a random sample of 947 participants also underwent brain MRI.

Results: aCL positive participants performed worse on the MMSE. IgG but not IgM isotype titres related to worse performance on the MMSE. No significant association existed with vascular brain abnormalities including lacunes, cortical infarcts and white matter lesions.

Conclusions: These data support the view that in normal elderly persons increasing IgG aCL titres relate to global cognitive dysfunction. It is unlikely that structural brain lesions are responsible for this finding.

Disclosure: Nothing to disclose.

EP4106

Comparison of various assessment measures on shunt effectiveness in idiopathic normal pressure hydrocephalus

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Introduction: There are various measures on assessing severity of idiopathic normal pressure hydrocephalus (iNPH). The assessment may not be the same by different examiners. In the present study, we investigate the most reliable measure on shunt effectiveness between neurosurgeons and physiotherapists.

Methods: Forty-five probable iNPH patients were treated with ventriculoperitoneal (VP) or lumboperitoneal shunts (LP). They were assessed separately by a neurosurgeon and physiotherapists. They were included modified Rankin scale (mRS), idiopathic normal pressure hydrocephalus grading scale (iNPHGS), functional independence measure (FIM).

Results: Mean age was 77 years. A VP and PL ratio was 2 to 1 and their shunt effectiveness at discharge was not different. The mRS and iNPHGS by a neurosurgeon was 51 % and 78 %, while those by physiotherapists were 40 % and 47 %. One point or more improvement on FIM by physiotherapists showed 80 %. Mean value on a change of FIM total score was 8 points; 7 points on motor and 0 point on cognition. There were no statistical differences between iNPHGS by a neurosurgeon and FIM by physiotherapists on their total scores, motor scores and cognition scores.

Conclusions: The assessment must be based on reliable measures by neurosurgeon and non-neurosurgeons. The mRS and iNPHGS by a surgeon and physiotherapists were not well corresponded. The FIM by physiotherapists and the iNPHGS by a neurosurgeon showed high improvement rate. Their changes on total, motor and cognition domains were well corresponded.

Thus, the FIM is suitable for assessment of shunt effectiveness in iNPH by non-neurosurgeons.

Disclosure: Nothing to disclose.

EP4107

Comparative evaluation of functional MRI in patients with post-traumatic and amnestic mild cognitive impairment

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One of the main causes of cognitive impairment is Alzheimeŕs disease. In addition, cognitive impairment may experience quite often as a consequence of craniocerebral trauma. At the same time, craniocerebral trauma is considered as a risk factor for neurodegenerative

process. Consequently, it may be necessary to the differential diagnosis of cognitive impairment specified etiology, especially in the early stages of the disease.

To identify specific areas of activation we conducted a comparative evaluation of the results of functional MRI (fMRI) in patients with mild cognitive impairment (MCI).

Two groups were examined: 19 patients with post-traumatic MCI (with severe craniocerebral trauma in anamnesis), and 21 patients with amnestic MCI. Data processing was performed using SPM8 software. In the study we have used a specially developed specific cognitive paradigm.

Analysis of the results showed that patients with post-traumatic MCI was characterized by the presence of activations in the right superior frontal gyrus and supramarginal, 21 and 13 fields by Brodmann, the left middle temporal gyrus, 31 and 32 fields by Brodmann, as well as in the inferior frontal gyrus and thalamus from both sides. In patients with amnestic MCI were identified activation in the right superior and inferior temporal gyrus and gyrus parahippocampalis, left 21 field by Brodmann, as well as bilateral activation in the middle cingulate cortex.

Obtained results provide additional differential criteria of amnestic and post-traumatic MCI, and allow to clarify the pathogenesis of some symptoms observed in the structure of their neuropsychological profile.

Disclosure: Nothing to disclose.

EP4108

Differences in routine clinical practice in early and late onset Alzheimer's disease: data from the Swedish Dementia Registry (SveDem)

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Introduction: Due to age of onset, Alzheimer's disease (AD) is divided into early onset (EOAD) or late onset (LOAD), but emerging data suggests that also the underlying pathology may be different. Whether differences in clinical care exist is less well investigated. We aimed to evaluate whether there are differences in demographics, diagnostic work-up and pharmacological treatment between EOAD and LOAD.

Methods: Data on patients with newly diagnosed EOAD (n = 453) and LOAD (n = 4599) was obtained from the Swedish dementia registry (SveDem). Logistic regression models were used to adjust for confounders including gender, cognitive decline and co-morbidity.

Results: The majority of patients with EOAD went through an extended diagnostic work-up including more technical investigations as well as assessments by neuropsychologists and speech therapists than patients with LOAD. The majority of EOAD and LOAD were in the mild stage of the disease when diagnosed. EOAD patients were treated with overall fewer medications but obtained treatment with cholinesterase inhibitors to a higher extent than those with LOAD, while there was no difference between the groups in antidepressant and antipsychotics use.

Conclusions: There are differences between EOAD and LOAD in diagnostic work-up and pharmacological treatment. An extensive diagnostic work-up should be recommended when EOAD is suspected.

Disclosure: Nothing to disclose.

EP4109

Prevalence and safety aspects concerning the use of dietary supplements and herbal products among demented patients attending an out-patient Clinic in North-Norway

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Introduction: Medical treatment options for dementia are scarce. Dietary supplements and herbal products (DSHEA), however, are often claimed useful for memory and mental health. Potential interactions with prescription drugs and other safety aspects concerning the use of such products in dementia are largely unknown.

Methods: The use of DSHEA among demented patients attending an out-patient memory clinic were registered by interview of the patient and a relative. Demographic data, the daily life situation and prescription drugs were also registered.

Results: 151 patients were included consecutively in 2011-2013. Mean age was 73 years and 61 % were female. Mean MSSE-Nr score was 20. Sixty-two patients (46 %) reported use of at least one DSHEA, with fish oils as the most frequently DSHEA used. The mean number of of prescribed medicines was four (range 0-17). Seven possible interactions between DSHEA and prescribed drugs were detected, of which three involved warfarin. Most patients reported help with administration of their prescribed drugs. However 61 % of the patients using DSHEA reported no help with these products regarding administration. Ten % received help from home care, while the remaining received help from relatives. Seven patients who used DSHEA lived alone and had no home care.

Conclusions: Nearly half the patients used DSHEA. Clinical relevant interactions with prescription drugs can not be ruled out. Although most patients received help with the administration of prescribed drugs, few patients received help with DSHEA.

Disclosure: Nothing to disclose.

EP4110

Evaluation of routinely used cerebrospinal fluid biomarkers in neuropathologically confirmed cases of human prion disease and other neurodegenerations: the Czech perspective

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Introduction: Cerebrospinal fluid (CSF) biomarkers are being widely used as an important diagnostic modality in differential diagnosis of dementia. Most widely used biomarkers are total tau (t-tau), phospho-tau (p-tau), amyloid-beta and protein 14-3-3 in the CSF. Their evaluation is important in differential diagnosis of Alzheimer's disease and also in the differential diagnostic workup for rapidly progressive dementia including prion diseases. The aim of our study was to evaluate and compare the biomarker levels in the cohort of patients with neuropathologically confirmed prion disease or other neurodegenerative disorder.

Methods: Of a total of 45 CSF samples with neuropathologically confirmed diagnosis, 27 had prion disease and 18 other

neurodegenerative disease. Neuropathologic evaluation was performed according to standardized protocols and the values of t-tau, p-tau and amyloid-beta were measured using commercial ELISA kits, protein 14-3-3 detection was performed by western blot.

Results: Very high h-tau levels (>1,200 pg/ml) and 14-3-3 positivity are characteristic of prion diseases when compared to other neurodegenerations. We found no significant difference in the biomarker levels among different neurodegenerations.

Conclusion: Our observation of higher T-tau levels and protein 14-3-3 presence in the CSF in prion disease patients is in agreement with previous studies. The strength of our study is in the neuropathologically-based approach when only those patients with definite diagnosis of prion disease or other neurodegeneration with excluded concomitant neuropathology were included.

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Disclosure: Nothing to disclose.

EP4111

Montreal Cognitive Assessment (MoCA) in mild cognitive impairment: correlation with cerebral perfusion in SPECT

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Introduction: The Montreal Cognitive Assessment e (MoCA) is a brief cognitive screening instrument developed for detection of milder forms of cognitive impairment. Several cohort studies confirm its high sensitivity in the identification of MCI and mild AD patients. Our main objective was the evaluation of the relationship between the performance on the MoCA and regional cerebral blood flow (rCBF) measured by single photon emission computed tomography (SPECT), in Mild Cognitive Impairment (MCI).

Methods: We included 88 patients with MCI (amnestic single or multiple domains) according to Petersen criteria, extensively studied with comprehensive neuropsychological assessment, biomarkers and longitudinal evaluation (37 % converted to dementia in 2 years). rCBF at inclusion was measured using Tc-99 m hexamethylpropyleneamine oxime (HMPAO) and quantitative analysis normalized to cerebellum were measured in 20 zones and 90 areas (Broadmann areas) using NeuroGam-software. Elementary statistical analysis, t-Student test, and VisRed software, where used to analyze rCBF data.

Results: MCI group presented a significant hypo-perfusion (more than 1.5SD) comparatively to an internal-software control group, in posterior cingulate cortex (A23 e A24), left entorhinal cortex (A28) and temporoporal area (A38). We found significant negative correlations between MoCA total scores (mean value:18,97 $\pm$ 4,637) and hypoperfusion in right caudate nucleus and angular gyrus. Orientation and Memory were the MoCA cognitive domains with strong correlations with hypoperfusion in Broadmann areas, namely the fusiform gyrus, angular gyrus and associative visual cortex.

Conclusions: Performance of MCI patients on the MoCA correlates with functional imaging, confirming sensitivity of the test to evaluate eloquent areas typically affected in AD.

Disclosure: Nothing to disclose.

EP4112

Regional difference of the Alzheimer's disease and the Parkinson's disease associated with dementia using cerebral perfusion SPECT

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Introduction: Since patterns of cognitive dysfunction in mild Parkinson's disease associated with dementia (PDD) are similar to those in mild Alzheimer's disease (AD), it is difficult to accurately differentiate between these two types of dementia in their early phases using neuropsychological tests. The purpose of the current study was to investigate differences in cerebral perfusion patterns of patients with AD and PDD at the earliest stages using single photon emission computed tomography (SPECT).

Methods: We consecutively recruited 31 patients with mild PDD, 32 patients with mild probable AD and 33 age-matched healthy subjects. All subjects underwent 99 m Tc-hexamethylpropyleneamineoxime perfusion SPECT and completed general neuropsychological tests.

Results: We found that both mild PDD and AD patients showed distinct hypoperfusion in frontal, parietal and temporal regions, compared with healthy subjects. More importantly, hypoperfusion in occipital and cerebellar regions was observed only in mild PDD.

Conclusions: The observation of a significant decrease in cerebral perfusion in occipital and cerebellar regions in patients with mild PDD is likely useful to differentiate between PDD and AD at the earliest stages.

Disclosure: Nothing to disclose.

Motor neurone diseases

EP4113

The diagnostic value of diffusion tensor MRI metrics in relation to the MND phenotype heterogeneity

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Introduction: To investigate diffusion tensor (DT) MRI metrics as predictors of motor neuron diseases (MND).

Methods: Corticospinal tract (CST), corpus callosum (CC) and extra-motor tract DT MRI measures were obtained from 123 MND patients and 35 controls. C-indices were estimated using logistic regression analyses. Support vector machine (SVM) classification algorithm assessed MRI metric accuracy as predictors of MND diagnosis at individual patient level.

Results: MND patients showed CST and motor callosal damage (C-index range: 0.65-0.74). The most severe and widespread damage was found in pure upper motor neuron (UMN)/pyramidal ALS (C-index up to 0.81 for CST and 0.91 for CC). Classical, respiratory and bulbar ALS showed CST and callosal motor damage (C-index $\approx$ 0.70). In bulbar patients, uncinate and cingulum damage was found. No damage was found in pure lower motor neuron (LMN)-variants. In classical, respiratory and bulbar ALS, patterns of damage were confirmed in cases with disease duration <12 months. Severity and extent of white matter damage increased in the following order: pure UMN/pyramidal ALS > bulbar > classical/respiratory > pure LMN. The highest C-index (up to 0.94) was found for CC measures distinguishing pure UMN/pyramidal from pure LMN patients. SVM showed the highest diagnostic accuracy (0.93) in the comparison pure UMN/pyramidal vs. pure LMN. Disease severity and UMN involvement correlated with CST, eCC and motor callosal damage.

Conclusions: DT MRI provides sensitive objective measures of UMN and extra-motor burden at the individual level in MND patients. This study provides a roadmap for translation of MRI predictors of MND into daily practice.

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Disclosure: Nothing to disclose.

EP4114

Quick and non invasive sweat function assessment to evaluate small fiber neuropathy in Fabry disease

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Introduction: In patients with Fabry disease, small fiber dysfunction is more prominent than large fiber dysfunction and A-delta fiber function is more often impaired than C-fiber function. Sudoscan is a patented device designed to perform a quantitative evaluation of sweat gland function based on an electrochemical reaction between sweat chlorides and stainless steel electrodes in contact with the palms and soles. Several studies have demonstrated the high reproducibility and sensitivity of this objective, non-invasive and quick method. This study aimed to evaluate Sudoscan in Fabry disease.

Methods: 18 patients with Fabry disease and 18 age and sex matched controls were involved in the study. Patients were required to place their hands and feet on two large electrodes and then stand still for 2 min. Results were expressed immediately as Electrochemical Skin Conductance (ESC, μS), the ratio between the current generated and the constant DC stimulus (lower than 4 V) applied on the electrodes.

Results: Good correlation was observed between hands and feet conductances both in controls and in Fabry disease ($r = 0.87$, $p < 0.001$). Hands and feet conductances were significantly lower in patients with Fabry disease compared to controls. This decrease was especially observed in patients with reported hypohidrosis (42 ± 22 vs 74 ± 11 μS, $p = 0.0014$ and 48 ± 27 vs 76 ± 10 μS, $p = 0.0056$ respectively). No correlation was observed with renal dysfunction. No significant difference was found in sensory peroneal nerve amplitude between patients and controls.

Conclusions: Sudoscan could be used for the screening and the follow-up of patients with Fabry disease.

Disclosure: JH Calvet is Medical Director of Impeto Medical.

EP4115

Evaluation of one year treatment with tafamidis in Portuguese patients with transthyretin familial amyloid polyneuropathy

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Introduction: Transthyretin (TTR) related Familial Amyloid Polyneuropathy presents as a severe sensory, motor and autonomic neuropathy. Tafamidis, an oral drug that stabilizes TTR and prevents amyloid deposition, was recently introduced in Europe to delay progression of neuropathy in ambulatory patients.

Objectives: To present Tafamidis efficacy and safety data after one-year treatment in the two Portuguese reference centers, in Porto and Lisbon.

Methods: Patients were evaluated at baseline, 6 months (M) and 12 M. Adverse events and body mass index were registered. Renal, thyroid and liver functions were screened. Neuropathy Impairment Score (NIS) and the Norfolk Quality of Life (QoL)—Diabetic Neuropathy Total Score (Norfolk) were assessed, this last only at baseline and 12 M. Patients were classified as responders if NIS change across 12 M < 2, according to Dyck's classification.

Paired Student's t test and ANOVA with repeated measures were used.

Results: 122 patients (67 males) completed a full 12 M evaluation.

Body mass index and liver, renal and thyroid functions remained stable for 12 M.

Mean NIS changed from baseline to 6 M (2.45 vs. 2,51, $p < 0.01$) and stabilized between 6 M and 12 M (2.51 vs. 2.54, $p < 0,1$), showing a delay in the stabilization effect. Norfolk score improved (3.21 *vs.* 2.89, $p < 0.001$) along 1 year.

Patients that were classified as responders ($n = 75$, 61 %) showed a significant NIS score decrease (improvement) between 6 M and 12 M (2.41 vs. 2.33, $p < 0.001$).

Conclusion: Tafamidis prevented neurological deterioration and BMI and QoL decline in 61 % of patients treated for 1 year. Stabilization effect was delayed 6 M.

Disclosure: Isabel Conceição, Teresa Coelho, Ana M Silva, Cristina Alves, Cecília Monteiro and Márcio Cardoso served at the speakers bureau of Pfizer and received support from Pfizer to attend scientific meetings.

EP4116
Immunohistochemical studies of TDP-43 in skin of patients with sporadic amyotrophic lateral sclerosis

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Introduction: Several studies of skin in patients with sporadic amyotrophic lateral sclerosis (SALS) have shown unique morphological and biochemical alterations. The lack of bedsore formation even in the terminal stages in ALS patients is considered characteristic. Recently, a nuclear protein, 43-kDa TAR DNA-binding protein (TDP-43), was identified as a component of the ubiquitinated inclusions in SALS. Subsequently, TDP-43 immunohistochemistry demonstrated that SALS is a multisystem proteinopathy of TDP-43. It is unknown, however, whether TDP-43 positive structures are present in skin of SALS.

Methods: We have performed a quantitative immunoreactive study of TDP-43 in biopsied skins from the left upper arm of 18 patients with SALS and from 15 controls with other neurodegenerative diseases. Routine formalin-fixed paraffin-embedded 6 micrometer sections were immunostained according to standard techniques. A densitometric analysis was performed using an image analysis system.

Results: The proportion of TDP-43-positive cells in the epidermis in SALS patients is significantly higher ($p < 0.001$) than in controls. There was a significant positive relationship ($r = 0.62$, $p < 0.02$) between the proportion and duration of illness in SALS patients. The optical density of TDP-43-positive cells in the epidermis in SALS patients is markedly stronger ($p < 0.001$) than in controls. There was a significant positive relation ($r = 0.72$, $p < 0.01$) between the immunoreactivity and duration of illness in SALS patients.

Conclusions: These findings suggest that changes of TDP-43 in SALS skin are related to the disease process and that metabolic alterations of TDP-43 may take place in the skin of patients with SALS.

Disclosure: Nothing to disclose.

EP4117:
iPSC-derived neural stem cells improve the phenotype of spinal muscular atrophy with respiratory distress type 1 (SMARD1)

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Introduction: Spinal Muscular Atrophy with Respiratory Distress Type 1 (SMARD1) is an infantile autosomal-recessive motor neuron disease characterized by diaphragmatic palsy and distal muscular atrophy; sensory and autonomic dysfunctions sometimes accompany the motor weakness. The disease results by mutations in the IGHMBP2 gene. We previously reported that primary neural stem cells (NSCs) can ameliorate the SMARD1 phenotype in mice even if several restrictions limit the the clinical translation of primary NSCs. The reprogramming of adult somatic cells into induced pluripotent stem cells (iPSCs) can provide an unlimited source of NSCs for therapeutic use.

Methods: We obtained iPS cell lines from human skin fibroblasts with a non-viral non integrating method based on the expression of reprogramming factors with episomal vectors. We used a protocol to differentiate iPSCs into neuronal stem cells. Hence the phenotype of these cells was analyzed by morphological, gene expression, and protein studies. Finally, iPSC-purified NSCs were transplanted by intraspinal cord injection into nmd mice, an animal model of SMARD1.

Results: NSCs from iPSCs are self-renewing and multipotent. They can differentiate in vitro into motor neurons and engraft into the spinal cord of SMARD1 animals, ameliorating their neuromuscular phenotype and significant extending transplanted nmd mice survival. iPSC-derived NSCs integrate appropriately into the anterior spinal cord, differentiate into the three neuroectodermal lineages, and exert a neuroprotective effect on endogenous motor neurons.

Conclusions: Our data support the therapeutic potential of iPSC for the treatment of motor neuron disorders and other neurodegenerative diseases.

Disclosure: Nothing to disclose.

EP4118
C9orf72 hexanucleotide repeat expansion in Turkish ALS patients

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Introduction: The expansion of the GGGGCC hexanucleotide repeat in the non-coding region of the *C9orf72* gene has been accepted as the leading cause of amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Also several studies reported expansions in the *C9orf72* gene as the cause of some neuropsychiatric disorders. Here, we aim to understand the wide clinical spectrum behind *C9orf72* pathogenicity by focusing on clinical features of Turkish patients.

Methods: In this study, we screened Turkish ALS patients for the expansion in the *C9orf72* gene using repeat-primed PCR (RP-PCR), fragment analysis and Southern blotting. Our cohort consisted of 406 ALS patients, 95 of whom displayed the familial and the remaining 311 the sporadic form of the disease.

Results: Among 95 fALS cases 13 patients, and among 311 sALS cases ten were found to be carriers of the repeat expansion. Nine patients with ambiguous results were subjected to Southern blotting to confirm the results obtained by RP-PCR.

Conclusions: Although slightly lower than other populations screened so far, the frequencies of *C9orf72* expansions in Turkish fALS and sALS cohorts are also high, being 13.7 and 3.2 %, respectively. The ages of onset of the expansion carriers were variable ranging from 32 to 80 years; progression was fast in some cases. Furthermore, intrafamilial phenotypic heterogeneity was also observed in a sib pair carrying the expansion, in whome ALS with dementia vs. pure dementia was present. Altogether, our findings recapitulate the frequent occurrence and the heterogeneous clinical background of *C9orf72* cases in the Turkish cohort.

Disclosure: Nothing to disclose.

EP4119
RNA-based strategies leading to either an increase of SMN or modulation of disease pathways ameliorated spinal muscular atrophy phenotype

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Introduction: Spinal muscular atrophy (SMA) is an autosomal recessive motor neuron disease caused by mutations of the survival motor neuron gene (SMN1) leading to infant paralysis and death. Currently, there is no effective treatment. The genetic correction of SMA induced pluripotent stem cells (iPSC) through antisense therapy is a promising strategy.

Methods: IPSCs were generated from human skin fibroblasts using non-viral non integrating episomal vectors. IPSCs were differentiated into motor neurons and their phenotype was analyzed by morphological, functional, gene expression, and protein analysis. RNA strategy based on antisense morpholino, shRNA and siRNA aiming at increasing SMN level or inhibiting Fas activation were tested.

Results: Motor neurons differentiated from SMA iPSCs displayed the disease-specific features characterized by fewer and smaller cells at late time periods in culture compared to wild-type iPSCs. After treatment with antisense morpholino or U1 shRNA leading to an increase of SMN expression, the SMA-iPSC phenotype was ameliorated. During motor neuron differentiation in SMA lines an increased Fas ligand-mediated apoptosis and caspase-8 activation were demonstrated.

Conclusions: SMA-iPSCs were confirmed to be a reliable in vitro disease model. In addition, strategies based on RNA modulation leading to either an increased expression of SMN or modifying disease pathways were demonstrated to be a promising therapeutic tool, which would be tested in in vivo models.

Disclosure: Nothing to disclose.

EP4120

ELP3-positive inclusions in motor neuron diseases

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Introduction: Recent studies have suggested that the allelic variants of elongator protein 3 (ELP3) are associated with amyotrophic lateral sclerosis (ALS). ELP3 is the catalytic histone acetyltransferase subunit of the elongator complex, which is a part of the RNA polymerase II complex and is involved in RNA processing. Our study was based on our hypothesis that ELP3 is involved in ALS pathogenesis.

Methods: We performed neuropathological studies with anti-ELP3 antibody in ALS patients. For this, we examined spinal cord sections from 10 common sporadic ALS (SALS) patients and 2 ALS patients with fused in sarcoma (FUS)-positive inclusions (FUS-ALS). These sections were immunostained with anti-ELP3, anti-TDP-43, and anti-FUS antibodies. Double-label immunofluorescence analysis was then performed on some sections by using anti-ELP3 and anti-TDP43 antibodies.

Results: In control cases, ELP3 immunoreactivities were primarily cytoplasmic in the anterior horn cells. ELP3-positive round and skein-like inclusions were noted in the cytoplasm of the anterior horn cells of SALS and FUS-ALS sections. ELP3-positive neuronal cytoplasmic inclusions (NCIs) were co-localized with TDP-43-positive and FUS-positive NCIs in SALS and FUS-ALS sections, respectively. However, cytoplasmic TDP-43-positive fine granules were not immunostained with ELP3 antibody. Furthermore, TDP-43-positive and FUS-positive glial inclusions (GCIs) were not immunostained with ELP3 antibody.

Conclusions: Our results suggest that ELP3 is a novel protein in ALS pathogenesis and that the component proteins of NCIs may be different from those of GCI in SALS and FUS-ALS.

Disclosure: Nothing to disclose.

EP4121

Respiratory failure treated by NIV is not associated with a worst outcome during PEG insertion in ALS patients

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Introduction: Enteral nutrition administered by percutaneous endoscopic gastrostomy (PEG) is probably effective in stabilizing body mass index in amyotrophic lateral sclerosis (ALS). Complications associated with PEG placement are increased when forced vital capacity (FVC) declines below 50 % of predicted value. Non-invasive ventilation (NIV) can be administered during PEG insertion in patients with a FVC below 50 %. This report aims at describing outcome after PEG insertions and comparing outcome in patients with or without NIV.

Methods: 20 ALS patients were offered a PEG between 2010 and 2013. Disease background, lung physiology, bulbar dysfunction, use of NIV, immediate complications and survival were analysed.

Results: Median age at time of PEG insertion was 68 years; 12 patients (60 %) had a predominantly bulbar form. Patients ($n = 12$, 60 %) on NIV had a median FVC of 53 % (IQR: 32–64 %) of predicted value compared to FVC of 65 % (IQR: 56-90 %) for patients not on NIV ($n = 8$) ($p = 0.04$). Propofol sedation was used in all cases. Median length of stay in hospital after PEG was similar for both groups. No death was recorded in relation to PEG. Complication rate was similar in patients with and without NIV (Table 1). Median survival post procedure was 362 days.

Conclusions: PEG can be inserted without additional peri-procedural complications in high risk ALS patients treated with NIV. Our complication rates are within the range of current published literature. Median survival after PEG was about 1 year and was independent of NIV use or presence of bulbar dysfunction at time of PEG insertion.

Disclosure: Nothing to disclose.

EP4122

Accumulation of TDP-43 outside the central nervous system in individuals with or without amyotrophic lateral sclerosis

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Introduction: Transactive response DNA-binding protein of 43 kDa (TDP-43) has been identified as a major component of the pathological inclusions in most forms of frontotemporal lobar degeneration (FTLD) and in amyotrophic lateral sclerosis (ALS). Although TDP-43 is expressed ubiquitously in the nuclei of all cells, accumulation of TDP-43 outside the central nervous system (CNS) has not been reported, with the exception of the muscles of patients with protein-aggregate myopathies.

Methods: We examined general organs of nine patients with non-ALS, and four with sporadic ALS and one with FTLD-TDP. Paraffin sections were immunostained with antibodies against phosphorylated TDP-43 (pTDP-43), TDP-43 and ubiquitin. For enhancement,

samples were autoclaved for 5 min before reaction with the antibodies, with the exception of the anti-ubiquitin antibody.

Results: Diffuse and granular accumulations of pTDP-43 and TDP-43 were observed frequently in the cytoplasm of renal tubular cells and less frequently in the cells of secretory glands, pancreas, adrenal gland, Leydig cells of testis, et al. Many TDP-43-positive cells were observed in the adrenal medulla, but these were negative for pTDP-43. However, majorities of pTDP-43-positive structures of the general organs also showed weakly positive immunoreactivities without primary antibodies after autoclave pretreatment. Immunoblotting of human kidney cytoplasmic lysate led to the detection of several bands, including a band at about 45 kDa.

Conclusions: This is the report to demonstrate the intracellular accumulations of pTDP-43 and TDP-43 outside the CNS in routine autopsied cases, however we must carefully distinguish the results from non-specific biotin reaction by other methods.

Disclosure: Nothing to disclose.

EP4123

Abstract withdrawn

EP4124

Magnetic resonance imaging brachial plexus alterations in ALS patients

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Introduction: To investigate brachial plexus MRI abnormalities in amyotrophic lateral sclerosis (ALS).

Methods: Brachial plexus MRI scans were obtained from 18 ALS patients and 9 controls. Nerve roots and limb girdle muscles were evaluated for the presence of signal alterations (T2, T1 and STIR) and volume changes. Regions of interest (ROIs) of C5, C6 and C7 roots were delineated on axial, T2-weighted volumetric images. ROIs mean volume and T2 signal intensity were measured. Linear measures of adipose tissue thickness between trapezius and supraspinatus muscles were obtained from coronal T1-weighted images.

Results: At visual inspection, increased C5, C6 and C7 nerve root T2-signals and volumes were evident in ALS patients bilaterally. Suprascapulis, supra- and infraspinatus muscles T2 and STIR signal alterations and bilateral fat infiltration associated with muscle atrophy were found. ROI analysis showed that T2-signal intensity was higher in left C6 ($p = 0.05$) and C7 ($p = 0.02$) in patients compared with controls. Right C5 and bilateral C6 and C7 root volumes were higher in patients (right C5: $p = 0.04$; right C6: $p = 0.006$; left C6: $p = 0.01$; right C7: $p = 0.003$; left C7: $p = 0.001$). Adipose tissue thickness between trapezius and supraspinatus muscles was higher in patients on the right side ($p = 0.024$). A similar trend was observed on the left side ($p = 0.08$).

Conclusions: T2-hyperintensity and increased volume of brachial plexus roots support a contribution of neuroinflammation to lower motor neuron and axonal degeneration in ALS. Denervation may explain muscle signal alterations. Increased adipose tissue between trapezius and supraspinatus muscles may represent an indirect marker of muscle atrophy.

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EP4125

What is the difference between brachial amyotrophic diplegia and upper limb onset ALS? Clinical and neurophysiological manifestations

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Introduction: When we encounter a patient who remains largely restricted to the upper limbs overt time, we should be concerned that the possible diagnosis is brachial amyotrophic diplegia (BAD) or upper limb onset ALS (U-ALS).

Methods: We reviewed the records of 385 patients who had a diagnosis as "motor neuron disease" or "amyotrophic lateral sclerosis" between 2006 and 2010. Seventy-two patients had bilateral upper extremity weakness without involvement of lower-limbs, respiratory, and bulbar weakness at the first examination. All patients were classified according to the revised El Escorial research diagnostic criteria and were categorized according to operational definitions as BAD and U-ALS. Analysis of variance F tests for continuous variables and X^2 tests for categorical variables analyzed differences in baseline data among the diagnostic categories.

Results: At first examination, the site of onset, the lowest score of the weakest muscle, and fasciculation discriminated between eventual diagnostic group; patients with BAD were proximal muscle at onset and weaker more likely to have U-ALS. Fasciculation was 0 % for BAD group, 70 % for U-ALS (26/37). The ratio of men to women was 5:1 in the BAD group compared to 2:1 in U-ALS. Two or more upper motor neuron signs was 17 % of BAD group and 35 % U-ALS group. Wide spread denervation in EMG study was 75 % for BAD group and 86 % for U-ALS group.

Conclusions: Our findings underline the several clinical and electrophysiolgocial features (sex, involved site at initial onset, MRC grade, Fasciculations) that differentiate between BAD and U-ALS.

Disclosure: Nothing to disclose.

Movement disorders 3

EP4126

Normal 0 21 Clinical evaluation of neurodegeneration with brain iron accumulation (NBIA) due to MPAN in Hungary

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Introduction: Neurodegeneration with brain iron accumulation is a progressive neurodegenerative disease causing progressing movement disorder. Symptoms may vary greatly. To date, nine genes are associated with different types of NBIA. The factors that influence disease severity and rate of progression are unknown. PANK2 and PLA2G6 gene mutations were most commonly investigated in NBIA patients. Recently the investigation of the C19orf12 gene is also recommended in NBIA patients.

Methods: Eight NBIA patients without PANK2 and PLAG6 gene mutation have been screened for the mutation of the C19orf12 gene encoding the mitochondrial membrane protein associated neurodegeneration (MPAN) by Sanger sequencing.

Results: In a young man a homozygous c.204_21del11 p.Gly69Argfs*10 mutation in the C19orf12 gene have been detected. His symptoms started in his childhood with severe visual impairment which was followed by moderate cerebellar, pyramidal signs and attention deficit. In two patients the c.335 G>A, p.W112X mutation resulted in later onset (at their 30 s). One had focal dystonia, while the other had severe and rapidly progressing symptoms such as bulbar signs, spastic palsy, total incontinance, and cognitive decline. He died at the age of 39 years.

Conclusions: In MPAN patients a wide variety of clinical signs can be seen regarding onset, symptoms and case severity even with the same underlying mutation.

Disclosure: Nothing to disclose.

EP4127

Huntington's disease: health policy differences between Italy and France

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Introduction: Huntington's disease (HD) is a severe condition that burdens patients and family. The study's objective was to identify differences in the management of HD between Italy and France.

Methods: Euro-HDB is a comprehensive, observational study conducted in several countries in Europe (including Italy and France) to assess the burden of illness of HD. Data were collected on healthcare resource utilization (including home vs. institutional care). Comparisons were made between direct costs and the amount of time caregivers provided care to HD patients.

Results: Patients and caregivers in Italy (124) and in France (176) participated in the study. About half of patients were male (47 % in Italy, 51 % in France); average age was 54 years (Italy) and 57 years (France). Despite similar patient disability profiles, clear differences were identified. A direct cost ratio of 1:5 (Italy:France), was consistent across most measures. Total direct costs (SD) were evaluated at €6,461 (14,524) in Italy and €30,572 (34,212) in France. Reflecting indirect costs, families in Italy care for patients for an average of 22 h per day whereas in France they reported 9 h.

Conclusions: Families in Italy provide more home patient management than in France, where institutionalization is more common. More research is needed to identify how much social and health policy differences contribute to sizeable gaps in direct cost of medical management and indirect costs for patients and families.

Disclosure: ElizaBeth Grubb is an employee of Teva Pharmaceuticals.

EP4128

Initial Parkinson's disease treatment choices and costly health outcomes: a retrospective analysis

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Introduction: Increase understanding of pharmaceutical treatments in newly identified Parkinson's disease (PD) patients and associated major and costly outcomes.

Methods: Newly diagnosed US PD patients is from Truven's MarketScan databases, 1 January 2006–31 December 2011. The initial PD prescription (index date) was matched 1–1 with newly diagnosed PD patients not receiving PD pharmacotherapy. Patients had continuous insurance coverage from 12 months prior through 12 months after index date. Logistic regressions examined associations between index PD treatments and subsequent falls and fractures, ER visits, and hospitalizations.

Results: 15,900 patients (3,950 aged $\leq$ 64 years, 11,950 aged 65 +) met inclusion criteria. Carbidopa/Levodopa (C/L) was most commonly prescribed medication (37 % age $\leq$ 64; 72 % for those 65 +). Dopamine agonists (DA) were more common for the younger than older (32 vs. 12 %) cohort, as were MAOB inhibitors (13 vs. 4 %). For the 65+ group, compared to patients receiving MAOB treatment, Adjusted Odds Ratios (OR) and 95 % confidence intervals revealed associations between index PD medication and falls and fractures, C/L, the OR = 1.954 (1.163–3.284) and for DA, the OR = 2.091 (1.203–3.635). For ER visits: C/L OR = 1.510 (1.142–1.997) and DA OR = 1.599 (1.173–2.180). For hospitalizations: C/L OR = 1.314 (0.970–1.780) and DA OR = 1.311 (0.938–1.832.)

Conclusions: Patients age 65+ tended to be prescribed C/L as initial PD treatment. Those aged $\leq$64 were more likely to receive DA or MAOB. Among older patients odds of a fall, fracture or other outcome requiring a costly intervention was greater for those prescribed C/L or DA compared to those receiving an MAOB.

Disclosure: ElizaBeth Grubb is an employee of Teva Pharmaceuticals.

EP4129

Regional change in glucose metabolism of essential tremor: FDG-PET study using SPM analysis

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Introduction: There is growing evidence that essential tremor (ET) is a multiple-system disorder. Previous PET studies in ET typically measure the brain oxygen consumption and the cerebral blood flow. We compared ET patients with control subjects to investigate any regional change in cerebral glucose metabolism through SPM analysis of FDG-PET.

Method: We studied 17 patients with ET (17 male, mead age 67.3 $\pm$ 4.8 years) and age-sex matched normal subjects. We attempted to measure the severity of tremor symptoms with the score of the Fahn-Tolosa-Marin rating scale (FTM). The evaluation procedure consisted of taking detailed medical history, neurological examinations, laboratory tests, MRI and FDG-PET of brain.

Result: The mean age of tremor onset was 57.6 $\pm$ 12.9 years and the mean score of FTM is 15.1 $\pm$ 4.9 (Part A: 4.5 $\pm$ 1.5, Part B: 7.4 $\pm$ 2.6, Part C: 3.2 $\pm$ 1.1). A brain FDG-PET analysis demonstrated hypometabolism in the medial frontal lobe, medial temporal lobe and precuneus of parietal lobe.

Discussion: Current research provides converging evidence for the role of the cerebellum in ET, although some inconsistencies exist. These discrepancies may depend on the high clinical heterogeneity of ET and on differences among the experimental methods. In our study, there was

no significant difference of glucose metabolism in cerebellum. More interesting results were the decreased glucose metabolism in other brain regions that do not mainly participate in motor function. We assumed that abnormal glucose metabolism in these area might be the early marker of non-motor manifestations such as cognitive impairment. However, this assumption requires further studies.

Disclosure: Nothing to disclose.

EP4130

Case report: concurrent occurrence of Fragile X syndrome and Fragile X associated tremor ataxia syndrome due to CGG repeat and methylation mosaicism

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Introduction: Fragile X syndrome (FXS) is a genetic disorder resulting from CGG trinucleotide repeat lengths greater than 200 and subsequent methylation of the *FMR1* gene on the X chromosome. Fragile X associated tremor/ataxia syndrome (FXTAS) is a recently described syndrome of tremor and ataxia in a relative of a FXS patient with clinical signs not seen in typical FXS patients. This syndrome is typically seen in patients over the age of 50 and is thought to be a result of neuronal toxicity from excess mRNA production due to CGG repeat lengths of 55–200.

Results: We present a 34-year-old gentleman with a previous diagnosis of FXS presenting with phenotypic features of FXTAS including cerebellar ataxia. Genetic testing with methylation assay revealed that he is a FXS and FXTAS mosaic with methylated CGG repeat lengths of 110 and 540 contributing to FXS and unmethylated CGG repeat lengths of 90 and 600 contributing to cerebellar ataxia and diagnosis of FXTAS.

Conclusions: Despite the close genotypic relationship between FXS an FXTAS there are distinct phenotypic differences attributable to different methylation state. This is the first case to be reported of FXS/FXTAS mosaicism and adds to the increasing understanding of the role played by methylation in determining phenotypic expression of genetic disorders, in particular the importance of methylation mosaicism. We suggest that in a FXS patient presenting with cerebellar ataxia or tremor without an apparent cause, further genetic testing with methylation analysis should be considered in the diagnostic process.

Disclosure: Nothing to disclose.

EP4131

Apraxia of eyelid opening: a differential diagnosis of myasthenia

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Background: Apraxia of eyelid opening (AEO) is a non paralytic motor abnormality characterized by difficulty initiating the act of eyelid elevation. We report the case of a woman with AEO who was diagnosed initially as a myasthenia.

Case report: A 50-year-old woman presented fluctuating dropping of the upper eyelid. The diagnosis of myasthenia was initially suspected. There was no history of diplopia, swallowing or respiratory disorders. Ptosis was noted during hospitalization, especially in the late afternoon. The response to Neostigmine (Prostigmine®) was negative. EMG was normal. Anti-acetylcholine receptor and anti-muscle-specific receptor tyrosine kinase (MuSK) antibodies were not detected. Repeated neurological examination revealed difficulty in reopening the eyes after closure of the eyelid, without blepharospasm. The diagnosis of isolated AEO was made. Brain MRI was normal. The patient was treated by botulinum toxin injections with significantly improvement.

Discussion: AEO occurs in the absence of ocular motor nerve dysfunction and ocular myopathy. Initiation of eyelid elevation requires activation of the elevator palpebrae superioris (LPS) and the concurrent inhibition of orbicularis oculi activity. AEO is thought to occur with prolonged inhibition of the LPS with or without concurrent clinical or subclinical contraction of the pretarsal portion of the orbicularis oculi. In consequence, a fluctuant ptosis can appear, mainly in idiopathic forms of AEO. Confusion with myasthenia can occurs, as seen in our case.

Conclusion: AEO is an important and often undetected cause of non-paralytic disorder of eyelid motility. It is important to distinguish between these two entities due to therapeutic and prognostic implications.

Disclosure: Nothing to disclose.

EP4132

Structural MRI of the cervical spine in patients with cervical dystonia

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Introduction: We used MRI to investigate, if structural changes of the cervical spine are more frequent in patients with cervical dystonia (CD) compared to healthy controls and which clinical parameters correlate with these abnormalities. Finally, we investigated whether there are clinical parameters which strengthen the indication for an MRI of the cervical spine in those patients.

Methods: We recruited 30 consecutive patients with CD. Three months apart, two identical examinations were performed including a neurological examination and the evaluation of the CD by established rating scales. An MRI of the cervical spine was analyzed by three experienced neuroradiologists with different MRI rating scales. For comparison, 21 age-matched healthy participants were recruited, who underwent the same examinations.

Results: Inter-rater reliability of each MRI rating scale revealed good results. We found no significant differences between both groups regarding structural changes of the cervical spine. Structural changes in patients with CD were associated with several clinical parameters predominantly in segments C3/C4 and C4/C5.

Conclusions: Based on our results, there is no indication for routine MRI of the cervical spine in patients with CD, since degenerative changes are comparable in both groups. An MRI should therefore only be ordered if clinical signs or symptoms of a cervical radiculopathy, excessive pain or spinal cord abnormality are present. If patients with CD are more prone to develop degenerative changes in segments C3/4 and C4/5—in contrast to non-dystonia patients in whom structural changes are usually found in lower segments—needs to be further investigated.

Disclosure: Nothing to disclose.

EP4133

The "striatal thumb" sign for Parkinson's disease

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Introduction: Hand deformities named striatal hands (SH) in patients with Parkinson's disease (PD) were originally described by Charcot in 1864. Although SH had been reported in 10 % of patients with advanced PD, prevalence of SH has not been systemically studied. We focused on the IP joint of the thumbs and studied the prevalence of striatal thumb deformities in young adult volunteers (YAV), age-matched volunteers (AMV) and patients with PD and dementia with Lewy bodies (PD/DLB).

Methods: Hands of YAV, AMV and PD/DLB were photographed by digital camera. The patients and the volunteers were asked to sit on a chair and put their hands on their thigh, and relax. The IP joint angle of the thumb was measured using a photograph of the lateral view.

Results: In the YAV ($n = 42$, mean age was 31.7 year old) and the AMV group ($n = 40$, mean age 73.9 years) mean IP joint angle was 150.3 ± 7.9 and 155.6 ± 8.2 degree, respectively. Meanwhile, mean IP joint angle in patients with PD/DLB was 170.8 ± 13.80 degree, and was significantly greater than YAV ($P < 0.001$) or AMV ($P < 0.001$) by one way ANOVA. The area under the receiver operating curve for thumb IP angle was 0.807. To maximize the Youden index, the cut off value for the IP joint angle should be 165 degree. The sensitivity of striatal thumb was 65.9 % and the specificity was 92.8 %. Likelihood ratio of striatal thumb for diagnosing PD/DLB was 8.78.

Conclusions: The "striatal thumb" is a very specific sign for detection of PD/DLB.

Disclosure: Nothing to disclose.

EP4134

Gait assessment in neurorehabilitation

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Introduction: Gait is often affected in people suffering from neurological disorders. To examine gait impairments or to evaluate interventions aimed at improving gait disorders, effective and efficient measurements are necessary. Therefore, we developed a new device-independent gait assessment (previously evaluated for healthy subjects, $n = 37$) to quantify typical spatiotemporal gait parameters for daily clinical setting.

Methods: Groups of 14 Multiple Sclerosis (MS) and 20 Morbus Parkinson (MP) patients were compared with a healthy ($n = 17$) control group (CG) (Table 1). Gait parameters were measured with participant's self-paced velocity over a predefined distance (Table 2 and 3). Statistical analyses were conducted by multiple t-tests.

Results: The MS Group showed significant differences in gait velocity (GV) and stride length (SL) compared to CG. There were no significant differences in MP compared with CG.

Table 1: Sample characteristics

Group	Numbers [n]	Age [years]	Rating scale [Score]
Morbus Parkinson (MP)	20	60.1±10.3	UPDRS motor score: 22.4±9.2
Multiple Sclerosis (MS)	14	53.9±9.1	EDSS: 3.2±1.3
Control Group (CG)	17	20.8±1.4	...

Table 2: Descriptive data of MP compared to CG

Group	Distance [m]	Gait velocity (GV) [m/s]	Stride length (SL) [m]	Stride time (ST) [s]
Morbus Parkinson (MP)	40.38	1.41±0.04	0.73±0.01	0.53±0.01
Control Group (CG)	40.38	1.48±0.03	0.75±0.01	0.51±0.01

Table 3: Descriptive data of MS compared to CG (**p<0.03)

Group	Distance [m]	Gait velocity (GV) [m/s]	Stride length (SL) [m]	Stride time (ST) [s]
Multiple Sclerosis (MS)	18	1.34±0.05 **	0.69±0.02 **	0.52±0.01
Control Group (CG)	23.17	1.51±0.03	0.77±0.01	0.51±0.01

Conclusions: Analyzing biomechanical outcomes in MS patients, the lower GV is traced back to the shortened SL despite a physiological ST. A possible explanation is a strength deficit in lower extremities which leads to gait instability. Even though, this could not be identified in MP patients. In contrast to typical clinical tests, this new gait assessment enables more differential consideration in patients' biomechanical system. As a consequence, this allows more detailed and subtle decisions in neurorehabilitation. Additionally, the test is both, reasonably practicable and well-tolerated by patients with neurological diseases. We suggest integrating this new method in already existing assessments. However, more research is required on analyzing greater sample sizes, different neurological disorders and disease severities.

Disclosure: Nothing to disclose.

EP4135

Evaluation of a new device-independent gait assessment in neurorehabilitation

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Introduction: Obtaining feasible parameters from gait assessments is a central issue in clinical reasoning. Beside many-faceted reasons, erroneous therapeutic decisions in neurorehabilitation might be also

based on typical clinical tests which only provide few sensitive and objective gait parameters due to practicability. On the other hand, providing objective biomechanical outcomes are associated with high technical, temporal, and financial effort. Therefore, we developed an innovative device-independent gait assessment which allows the quantification of spatiotemporal parameters from overground walking.

Methods: A group of healthy subjects (n = 20, age: 22 ± 2.7) were asked to walk at their individual self-paced velocity along a corridor (5 trials, distance: 40.38 m). A second group of healthy subjects (n = 17, age: 20.8 ± 1.4) performed the test with varying distances (40.38 m; 23.17 m; 9.41 m). Detailed description is shown in Fig. 1. Test–retest-reliability and the influence of distance effects were examined. Visual marking and time measurement were validated using video analysis and a pressure plate, respectively (sample rates = 100 Hz).

Results: Test–retest-reliability showed very high Intraclass Correlation Coefficients ($ICC_{3,1}$) for distances of 40.38 and 23.17 m (Table 1). Concerning validity, the error in time measurement was very low (0.082 ± 0.047 s), as well as the error in visual marking (0.67 ± 0.54 cm).

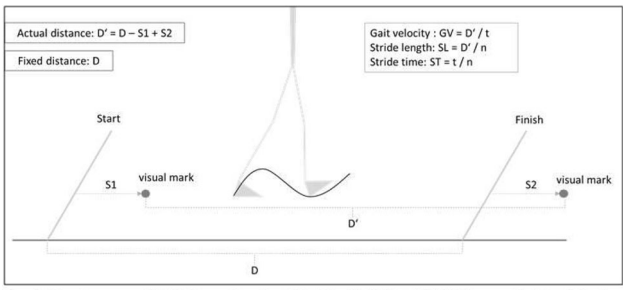

Figure 1: Two raters are needed. The trespassing of predefined lines (start: S1 and finish: S2) was marked visually (heel strike) by the first rater (Fig.1). The number of steps was counted by rater one and the time from first to last heel-strike was taken by rater two. The following parameters were calculated: gait velocity (GV), stride length (SL), strides time (ST). Gait initiation and termination were excluded from the measurement.

Table 1: Intraclass Correlation Coefficients

Modality	Gait Velocity (GV)	Stride Length (SL)	Stride Time (ST)
Group A (40.38m)	.961	.941	.922
Group B (40.38m)	.897	.916	.841
Group B (23.17m)	.918	.884	.855
Group B (9.41m)	.686	.921	.744

Conclusions: It is shown that the gait assessment is a valid and reliable method to easily obtain feasible biomechanical spatiotemporal parameters. Hence, it is a useful tool in neurological diagnostics which might have the potential to provide an advanced basis in order to come to better therapeutic decisions (first results are shown in a second abstract).

Disclosure: Nothing to disclose.

EP4136
White matter changes predict cognitive dysfunction in patients with essential tremor

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Introduction: As previous research has not examined changes in white matter related to vascular risk factors and has not sufficiently explained why cognitive deficits occur in patients with essential tremor (ET), the objective of the present study was to evaluate relationships among vascular risk factors, MRI measures of white matter lesions (WMLs), and the rate of decline in the global cognitive functioning of elderly patients with ET.

Methods: We used the Mini-Mental State Examination (MMSE) to assess cognitive decline in patients with ET. The MMSE results of 106 patients were compared with those of 67 age- and sex-matched healthy controls without any vascular risk factors. All participants underwent cranial MRI examinations to exclude other possible causes of cerebellar or extrapyramidal disorders. WMLs were identified via T2-weighted MR scans and then evaluated. We examined correlations of MMSE scores with vascular risk factors, cranial MRI findings, and factors of age, educational level, and sex.

Results: Lower MMSE scores were related to WMLs and age in the patient group ($p < 0.05$), and WMLs independently predicted mental status in this group (Beta value = -0.233, $p = 0.016$).

Conclusions: We found no correlation between MMSE scores and commonly seen vascular risk factors. Cognitive assessments should be part of clinical dialogues with elderly patients with ET, and prospective neuro-imagining studies should be performed when cognitive impairment related to ET is suspected.

Disclosure: Nothing to disclose.

EP4137
Frequency of buccopalpebral reflex in Parkinson disease

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Introduction: To investigate frequency of BPR according to the stage of Parkinson Disease and to compare findings age-sex matched control group.

Methods: 115 patients with Parkinson disease and 107 control subjects were investigated prospectively. Demographic data and information about Parkinson disease were collected for each patient. Unified Parkinson's Disease Rating Scale (UPDRS) was used for staging of Parkinson' s disease and BPR was evaluated.

Results: The mean age in patients with Parkinson's disease was 69,8 ± 8,6. It was 66,8 ± 8,4 in control subjects. BPR frequency of the control group was 3.7 %, while those of were in 13.9 %, respectively. This difference was statistically significant ($p < 0.05$). In the analysis of UPDRS sub-groups, activities of daily living sore was 13.3 ± 7.1 in reflex positive group and 9.6 ± 7.7 in reflex negative group. According to the motor score evaluation of BPR positive and negative patients, it was the Motor score was 26.2 ± 13.8 and 19.2 ± 13.0, respectively. These differences were statistically significant ($p < 0.05$).

Conclusions: BPR that mainly was observed in neurodegenerative disease such as Parkinson Disease may be as result of the removal of cortical inhibition; therefore it should be primitive reflex. Since UPDRS scores were higher in BPR positive groups, BPR frequently seen in more severely affected patients.

Disclosure: Nothing to disclose.

EP4138
Do dyskinesias and motor symptoms begin in the same body region in Parkinson's disease?

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Introduction: In a retrospective work in Parkinson's disease (PD) we found only a partial relationship between the body site of motor

symptoms onset and the body site of levodopa induced dyskinesias (LID) onset (Fabbrini et al. 2009).

Methods: In this study we now investigated this relationship using objective assessment of LID onset. We included 70 PD patients (37 men, mean age 72.1 ± 7.7 years, mean symptoms duration 9.2 ± 5.5 years) who did not have LID and in whom LID onset was objectively observed by the neurologist during a routine follow-up visit.

Results: Motor symptoms (determined retrospectively) started unilaterally in the limbs in 91.4 % of the patients and bilaterally in the limbs in 8.6 % of the patients. LID (assessed objectively) started unilaterally in the limbs in 25.8 % of the patients, bilaterally in the limbs in 7.1 % of the patients, in the craniocervical/axial region in 40 % of the patients, and in both the craniocervical/axial region and limbs in 27.1 % of the patients. Statistical analysis disclosed a borderline significant association between the site of onset of motor symptoms onset and the site of LID onset ($p = 0.05$). The association was highly significant when considering only when considering the subgroup of patients with unilateral onset of motor symptoms and LID ($P = 0.001$).

Conclusions: The association between body site of motor symptom onset and body site of LID onset is clear only in those patients with unilateral onset of both motor symptoms and LID.

Disclosure: Nothing to disclose.

EP4139

Pathological changes in the brain assessed by diffusion tensor MRI and TCS can differentiate Parkinson's disease patients with dementia

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Introduction: Magnetic resonance diffusion tensor imaging (DTI) and transcranial sonography (TCS) are promising new non-invasive methods for developing neuroimaging biomarkers in Parkinson's disease (PD).

Aim: To measure the changes in PD patients with dementia (PD-D) using the DTI and TCS methods.

Methods: Fifty-three subjects (33 with PD; 9 demented, 24 non-demented individuals, and 20 age- and gender-matched controls) were studied using a DTI protocol at 1,5T Philips Intera scanner and TCS using Toshiba Aplio XG system. Neuropsychological assessment included Mini-Mental State Examination (MMSE), Frontal Assessment Battery (FAB), Parkinson's Disease-Cognitive Rating Scale (PD-CRS).

Results: DTI identified significantly decreased fractional anisotropy and increased apparent diffusion coefficient (ADC) in corpus callosum ($p = 0.009$ and $p = 0.0005$ respectively) in PD-D patients. Additionally, widespread white matter degeneration with increased total ADC in the anterior regions of the brain ($p = 0.009$), particularly posterior regions ($p = 0.003$), was detected in PD-D. Bilateral mean substantia nigra (SN) area measured with TCS was higher in PD-D versus non-demented patients (0.36 ± 0.05 cm^2 vs. 0.32 ± 0.07 cm^2, $p = 0.042$), while in healthy controls mean SN area was 0.16 ± 0.04 cm^2. Diameter of the third ventricle was wider in PD-D versus non-demented PD patients (9.97 ± 2.10 mm vs 7.38 ± 1.71 mm, $p = 0.003$), healthy controls—6.81 ± 1.73 mm. PD patients with dilation of III ventricle over 7 mm in 90 % of cases had cognitive decline.

Conclusions: These findings suggest that DTI and TCS may be sensitive to cognitive changes in PD and provide additional information in the diagnostics of PD-D patients.

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Disclosure: Nothing to disclose.

Multiple sclerosis and related disorders 3

EP4140

QualiCOP: an open-label, prospective, observational study of glatiramer acetate in patients with relapsing-remitting multiple sclerosis

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Introduction: Multiple sclerosis (MS) has a profound impact on patients' quality of life (QoL), and improvement of cognitive function, depressive symptoms and levels of fatigue remains a goal of disease-modifying therapy. Such improvements would in turn potentially support adherence to therapy, consequently further enhancing treatment outcomes.

Methods: QualiCOP was a prospective, observational, non-interventional, open-label study similar to the Coptimize trial and conducted at 170 sites in Germany. Patients ($N = 754$), primarily (95.6 %) with relapsing-remitting MS, with or without previous treatment, were observed for 24 months following conversion to treatment with once-daily glatiramer acetate 20 mg/1 mL s.c. (GA). A series of 11 examinations was conducted, including assessment of relapse rate, disease progression, overall functioning, QoL, cognition, fatigue, and depression.

Results: Treatment with GA over 24 months was associated with a reduction of annual relapse rate from 0.87 to 0.49 ($P < .0001$), while the proportion of relapse-free patients rose from 11.3 to 69.5 %. Total remission was achieved in 56.4 % of patients. MSFC scores showed slight improvement in overall functioning ($P < .0001$), while PASAT and MUSIC showed robust improvement in cognition (both $P < .0001$). The CES-D also showed significant improvement of depressive symptoms ($P = .0006$). Scores on the EDSS, MUSIC-Fatigue and FAMS (all NS) showed that disease severity, fatigue, and QoL were stable over the observation period.

Conclusions: These findings suggest that patients experiencing inadequate symptom control will benefit from conversion to GA therapy, with improvements going beyond the standard measures of relapse and disease severity.

Disclosure: Dr. Ziemssen has received speaker honoraria from Almirall, Bayer Schering Pharma, Biogen Idec, Genzyme, GSK, Sanofi-Aventis, Merck Serono, MSD, Novartis, and Teva; he serves as a consultant for Bayer Schering Pharma, Biogen Idec, Novartis, and Teva.

EP4141

Active T1 hypointense lesions over 12 months in RRMS subjects from the GALA study: methodological evaluation

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Background: There are no clinical trial guidelines whether to assess all active T1 hypointense lesions (T1H) on pre-contrast MRI scans (T1H-total) or just those T1H on pre-contrast MRI scans that are simultaneously non-enhancing on post-contrast scans (T1H-non-enhancing).

Objective: To examine new/enlarging T1H-total and T1H-non-enhancing between 0-6 and 6-12 months in the Glatiramer Acetate Low-frequency Administration (GALA) study.

Methods: GALA was a phase III trial that randomized 1,404 relapsing-remitting MS subjects to receive GA 40 mg/1 mL tiw or placebo for 12 months. MRI was obtained at baseline and months 6 and 12. Cumulative numbers of T1H-total and of T1H-non-enhancing were calculated and analyzed using an adjusted negative binomial regression model of the 1,325 subjects who provided T1H-total data at all timepoints, 2 had missing T1H non-enhancing data.

Results: Analyses of T1H-total revealed that 884 GA-treated patients developed a mean of 1.8 vs. 2.6 lesions in the 441 placebo arm patients [Risk Ratio (RR) = 0.67; 95 % confidence interval 0.55–0.81, $p < .0001$]. Analysis of T1H-non-enhancing revealed that GA-treated patients developed a mean of 1.3 vs. 1.9 lesions in the placebo arm patients (RR = 0.71 [0.57–0.87], $p = .0009$).

Conclusions: Results using the two methodologies are similar. However, T1H non-enhancing lesions may represent a distinct stage of lesion evolution, potentially showing a more advanced pathological substrate of tissue damage compared with T1H-total. On the other hand, T1H-total may capture additional aspects of lesion evolution, such as remyelination, thus obscuring mechanistic interpretation. This study is relevant to future clinical trials aiming to clarify mechanisms of treatment effect.

Disclosure: Dr. Zivadinov received personal compensation from Teva Pharmaceuticals, Biogen Idec, EMD Serono, Novartis, Claret and Sanofi-Genzyme for speaking and consultant fees. Research support from Biogen Idec, Teva Pharmaceuticals, Sanofi-Genzyme, Novartis and EMD Serono.

EP4142

Norwegian multiple sclerosis prevalence study: no effect of latitude and no critical age of migration

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Introduction: Multiple Sclerosis (MS) prevalence is unevenly distributed worldwide, and the risk increases after migration from low to high prevalence regions. We performed the first Norwegian nationwide MS prevalence study in order to investigate variation with latitude, to identify differences in prevalence between the immigrant groups and a possible critical age of migration.

Methods: Patients were identified from the Oslo MS registry, the Norwegian MS registry and Biobank and the Norwegian Patient Registry. Information about county of residence for all patients on 1 January 2012, and country of birth and age of migration for the immigrants, was obtained from Statistics Norway. We calculated a standardized prevalence ratio (SPR) for the largest immigrant groups in order to adjust for differences in age and gender distribution.

Results: The crude MS prevalence in Norway 1 January 2012 was 203/100,000 inhabitants (95 % CI 199–207/100,000). There was no significant difference in prevalence between the northern and southern regions. We identified major differences in the prevalence between the immigrant groups, spanning from SPR 1.14 (95 % CI 0.89–1.44) in patients born in Denmark to 0.12 (95 % CI 0.04–0.30) in patients from Somalia. The median age of migration was 28 years for European patients, and 24 years for immigrants from non-European countries.

Conclusions: The MS prevalence in Norway was among the highest ever reported, and there was no evidence of a latitude gradient. The prevalence varied between the different immigrant groups, and we found no indication of a critical age of migration to Norway.

Disclosure: Nothing to disclose.

EP4143

Restoration of aberrant circulating miRNAs levels after fingolimod treatment in patients with relapsing remitting multiple sclerosis

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Introduction: MicroRNAs (miRNAs) have recently found to be dysregulated in serum from Multiple Sclerosis (MS) patients. We investigated the effect of Fingolimod treatment on the expression of selected cell free circulating miRNAs (miR-15b, miR-23a, miR-223), previously described to be differentially expressed in MS.

Methods: Circulating miR-15b, -23a and 223 levels were analysed by Real Time PCR in a cohort consisting of 30 serum samples from Relapsing Remitting MS patients considered in the pre-treatment condition, 3 and 6 months after the beginning of therapy with Fingolimod. miRNA levels were also compared to levels obtained from a control population consisting of 15 healthy subjects.

Results: We found a generalized down-regulation of miRNA levels in patients in the pre-treatment condition with respect to controls (miR-15b: 0.6- vs 1.9-fold change, miR-23a: 0.3- vs 1.3-fold change and miR-223: 0.2- vs 0.7-fold change, $P < 0.001$). miRNA levels slightly increased after three months of treatment when compared to the pre-treatment condition (miR-15b: 0.7- vs 0.6-fold change, miR-23a: 0.4- vs 0.3-fold change and miR-223: 0.2 vs 0.1, $P > 0.05$). The trend of increase in miRNA levels was even stronger and reached a statistical significance after 6 months of treatment (miR-15b: 1.2- vs 0.6-fold change, miR-23a:0.6 vs 0.3 and miR-223: 0.3- vs 0.2-fold change, respectively, $P < 0.05$).

Conclusions: Preliminary results of this study suggest that aberrant levels of circulating miRNAs are restored in Fingolimod treated MS patients. Circulating miRNAs profiling could thus represent an easy detectable biomarker of disease and response to treatment.

Disclosure: Nothing to disclose.

EP4144

Disability progression in NARCOMS participants who switched treatment after 2 years of natalizumab

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Introduction: NARCOMS provides a registry of 37,000+ persons with MS. Disability, measured by Patient Determined Disease Steps (PDDS), was retrospectively compared between NARCOMS participants who remained on natalizumab and those who switched to fingolimod or injectable treatments (INJ) (interferon-beta and glatiramer acetate) after 2 years of natalizumab treatment.

Methods: Participants with PDDS reported at the start of and ≥6 months after 2 years of natalizumab treatment were included (N = 527). Groups were defined by treatments reported after 2 years of natalizumab (Table 1). The proportion of participants with PDDS increase from the start of natalizumab treatment to final assessment was compared with Likelihood Ratio Test. Mean PDDS changes were compared by covariate-adjusted ANOVA.

Results: There were no group differences in age, sex, insurance status or starting PDDS; median follow-up time differed significantly (Table 1). There were no group differences in PDDS following 2 years of natalizumab treatment ($p = 0.11$); the proportion of participants with PDDS increases at the end of follow-up differed significantly (natalizumab = 30.8 %; fingolimod = 46.0 %; INJ = 42.3 %; $p = 0.0296$). PDDS changes were independent of follow-up time ($p = 0.6930$), but older age ($p = 0.0014$), male gender ($p = 0.0235$), and lower initial PDDS ($p < 0.0001$) predicted increased PDDS worsening. Mean PDDS increase was lower ($p = 0.0065$) for natalizumab (0.31) than INJ (0.71); but not different between fingolimod (0.58) and either natalizumab or INJ.

Conclusions: Participants treated only with natalizumab were less likely to report disability increases than those who switched to fingolimod or INJ. Participants who switched to INJ reported higher increases in disability than those who remained on natalizumab.

Characteristic	Natalizumab only (n=406)	Fingolimod (n=50)	Injectable treatments (n=71)	*p*-values
Age at MS diagnosis, years, mean (SD)	36.4 (9.4)	36.6 (9.0)	36.5 (9.0)	0.9614
Age at start of nat treatment, years, mean (SD)	49.4 (9.3)	49.1 (8.4)	50.0 (8.8)	0.8858
Sex, % female	79.5	70.0	81.7	0.2489
Health insurance, % with	97.8	98.0	98.6	>0.9999
Follow-up from start of nat treatment, months, median (range)	48 (12-72)	54 (18-72)	60 (24-72)	<0.0001
Follow-up after treatment switch, months, median (range)	NA	12 (0-42)	18 (0-54)	0.0123

Abbreviations: nat = natalizumab; NA = not applicable; SD = standard deviation

[Table 1]

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EP4145

Neurosteroidogenesis: relevance of neurosteroid levels in cerebrospinal fluid of Relapsing-Remitting Multiple Sclerosis patients with acute relapse or stable disease

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Introduction: Many studies showed an involvement of central nervous system steroids, defined neurosteroids, in Multiple Sclerosis (MS) course as neuroprotective and antiinflammatory agents. Our aim is to assess neurosteroid levels in MS patients compared to a control group to help clarify their possible role in MS pathogenesis and promote the development of future therapeutic approaches.

Methods: We evaluated the profile of Pregnenolone (PREG), Dehydroepiandrosterone (DHEA), Cortisol and Allopregnenolone (ALLO) by liquid chromatography-mass spectrometry in the cerebrospinal fluid (CSF) of 32 treatment-naive Relapsing-Remitting MS (RR-MS) consecutive patients, during acute relapse or stable disease and in 30 control subjects with other inflammatory neurological diseases (OIND). All patients and controls underwent lumbar puncture and brain and spinal cord magnetic resonance imaging (MRI).

Results: Compared to controls, PREG, DHEA and Cortisol levels were higher and ALLO levels were lower in CSF of MS patients, in particular during clinical relapses than in stable phase. A significant difference was found in Cortisol level, which was higher in female MS patients. We did not observe any difference in DHEA and ALLO levels in MS patients with (Gd+) or without (Gd−) gadolinium enhancing lesions at brain MRI. On the contrary, PREG and Cortisol levels were higher in Gd+ compared to Gd− patients.

Conclusions: Our results confirm a dysregulation of neurosteroid metabolism during different phases of RR-MS, suggesting their presumptive involvement in the pathogenesis of MS as neuroprotective and antiinflammatory agents. The complex interplay between the neuroimmune and neurosteroidogenesis responses in MS course opens new interesting therapeutic possibilities.

Disclosure: Nothing to disclose.

EP4146

Lymphocyte count reductions in relapsing-remitting multiple sclerosis (RRMS) patients treated with delayed-release dimethyl fumarate: integrated analysis of the placebo-controlled studies

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Introduction: Here we describe the clinical relevance of lymphocyte count reductions with delayed-release dimethyl fumarate (DMF),

based on integrated analyses of the placebo-controlled Phase 2b, DEFINE, and CONFIRM studies.

Methods: Analyses comprised 2,428 RRMS patients who received placebo (n = 836) or delayed-release DMF 240 mg twice (BID; n = 769) or three times daily (TID; n = 823) for up to 96 weeks. CONFIRM included a glatiramer acetate reference comparator arm (n = 351; results not shown).

Results: In delayed-release DMF-treated patients, mean white blood cell and lymphocyte counts decreased by approximately 11 and 30 %, respectively, through week 48, then plateaued, but remained within normal limits throughout the observation period. Percentages of patients with worst post-baseline Common Terminology Criteria (CTC) Grades 1, 2, or 3, respectively, were higher in the BID (10, 22, 6 %) and TID (8, 18, 3 %) groups than with placebo (2, 2, <1 %). Percentages of patients with >1 Grade 3 or 4 lymphocyte count were 0 % (placebo), 3 % (BID), and 1 % (TID), and with consecutive Grade 3 or 4 lymphocyte counts were 0 % (placebo), 2 % (BID), and 1 % (TID). The incidence of Grade 3 or 4 lymphopenia increased through week 48, then stabilized. There was no clear pattern of increased incidence of infections or serious infections with increasing post-baseline lymphocyte CTC grade. No patients discontinued study drug due to lymphopenia. Four weeks after stopping delayed-release DMF, mean lymphocyte counts increased but did not return to baseline.

Conclusions: Treatment with delayed-release DMF was associated with decreased lymphocyte counts but no overall increased risk of infection.

Disclosure: Study supported by: Biogen Idec, Inc.

EP4147

Clinical and demographical features of early onset multiple sclerosis: report of 221 cases from Isfahan, Iran

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Introduction: The aim of this study was to present the update of the clinical and demographic features of early-onset multiple sclerosis in Isfahan, Iran.

Methods: This retrospective study concerned MS patients who were referred to the only clinic of MS in Isfahan from October 1997 through February 2013. All EOMS patients underwent magnetic resonance imaging(MRI). MRI findings were analyzed according to the Barkhof's criteria.

Results: Among 4,536 MS patients, 221 EOMS patients were identified. The female to male ratio was 5.7:1. The mean age of onset was 14.7 ± 1.8 (range: 6–16) years. In 152 (69.4 %) patients, the onset was monosymptomatic. In this group, the most common initial presentation was optic nerve involvement (36.1 %) followed by cerebellar sign and symptoms (14.6 %), sensory problems (11 %), and motor deficit (7.8 %). In the mean follow-up period of 6.2 years, 196 (89 %) patients were classified as relapsing-remitting MS (RRMS), 20(9 %) as secondary progressive MS (SPMS) and 5(2 %) as primary progressive MS (PPMS). The mean ± SD EDSS was 1.5 ± 1.1 at the last evaluation. EDSS ≥ 6 was found in only 2 patients with EOMS The characteristic MRI findings for MS according to Barkhof's criteria, were found in 212 (97 %) patients.

Conclusions: In our study, a high rate of childhood MS was observed that may be because of geographical or ethnic differences. Our study also showed that Barkhof's criteria, which is mostly used in adult patients, could be also applied to EOMS cases.

Disclosure: Nothing to disclose.

EP4148

Laquinimod reduces the proportion of patients with disease worsening

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Introduction: Multiple sclerosis (MS) is a chronic disease in which disability and brain tissue loss worsen over time. We assessed the effects of laquinimod on disease worsening with a post hoc analysis of data from the ALLEGRO study using a composite measure of disability progression and brain volume change.

Methods: 1,106 patients were randomly assigned 1:1 to receive once-daily oral laquinimod 0.6 mg ($n = 550$) or placebo ($n = 556$) for 24 months. Exploratory analyses were conducted on the proportion of patients who were free of disease worsening, as defined by disability progression (a 1-point increase in Kurtzke Expanded Disability Status Scale [EDSS], or 0.5-points if baseline EDSS was equal to 5.5, confirmed 3 months later) or brain tissue loss (defined as a decrease in percent brain volume >1 % from baseline to 24 months). The proportions of patients with no disease worsening were compared between treatment groups using a logistic regression model adjusted to baseline covariates.

Results: A greater proportion of patients were free from disease worsening in the laquinimod group vs placebo: 51.4 % vs 34.6 % (OR = 2.000, $P < .0001$). There were also significant positive effects for laquinimod in both individual components of the disease-worsening composite measure (no brain tissue loss greater than 1 %: 58.6 % vs 42.5 %, OR = 1.917, $P < .0001$; disability-free: 90.2 % vs 86.0 %, OR = 1.499, $P = .0314$).

Conclusions: The results of this exploratory analysis indicate that, relative to placebo, laquinimod significantly increases the proportion of patients free of disease worsening measured by disability and brain atrophy.

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EP4149

4-year follow-up of delayed-release dimethyl fumarate treatment in relapsing-remitting multiple sclerosis (RRMS): integrated clinical efficacy data from DEFINE, CONFIRM, and the ENDORSE extension study

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Introduction: ENDORSE is an ongoing, 5-year, dose-blind extension of the Phase 3 DEFINE and CONFIRM studies evaluating the efficacy and safety of delayed-release dimethyl fumarate (DMF) in RRMS. Here we present a 2-year interim analysis of clinical efficacy data from ENDORSE.

Methods: Patients randomized to delayed-release DMF 240 mg twice (BID) or three times daily (TID) in DEFINE/CONFIRM continued the same dosing regimen in ENDORSE. Placebo (PBO; DEFINE/CONFIRM) and glatiramer acetate (GA; CONFIRM) patients were randomized 1:1 to delayed-release DMF BID or TID. Efficacy was analyzed (June 12, 2013 cutoff) according to treatment arm in parent/extension study: BID/BID, TID/TID, PBO/BID, PBO/TID, GA/BID, GA/TID.

Results: Of 2,079 patients completing DEFINE/CONFIRM, 1,736 were dosed in ENDORSE (n = 501 [BID/BID], 502 [TID/TID], 249 [PBO/BID], 248 [PBO/TID], 118 [GA/BID], and 118 [GA/TID]). Adjusted annualized relapse rate (ARR) (95 % confidence interval [CI]) during year 1 and year 2 (DEFINE/CONFIRM) and year 3 and year 4 (ENDORSE) were: 0.202 (0.162–0.252), 0.163 (0.128–0.208), 0.138 (0.104–0.183), and 0.142 (0.108–0.187) for BID/BID, and 0.239 (0.195–0.294), 0.123 (0.094–0.162), 0.167 (0.128–0.217), and 0.198 (0.155–0.252) for TID/TID. ARR (95 % CI) in year 4 (second year of delayed-release DMF treatment) was 0.126 (0.083–0.194) for PBO/BID, 0.138 (0.092–0.209) for PBO/TID, 0.128 (0.070, 0.233) for GA/BID, and 0.184 (0.105, 0.325) for GA/TID. Disability progression remained low among patients continuing delayed-release DMF treatment.

Conclusions: Delayed-release DMF was associated with low relapse rates and disability progression in continuously treated patients and patients who switched from PBO or GA.

Disclosure: Study supported by Biogen Idec, Inc.

EP4150

Multiple sclerosis brain lesion measurements in clinical practice

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Accurate detection of brain lesions in multiple sclerosis (MS) patients is important for diagnosis and measuring therapeutic response. In clinical practice, lesion load is often visually inspected or quantified by manual or semi-automated segmentation of Magnetic Resonance Images (MRI), which is time-consuming, costly, and associated with large inter- and intra-observer variability.

We propose an automated lesion segmentation method, with high reliability and accuracy. In this approach, 2D or 3D T1-weighted and FLAIR MR images are used to classify the brain into GM, WM and CSF. In addition, by using a healthy brain atlas, MS lesions are detected as an outlier to the normal brain.

The method is evaluated on the brainWeb's MS simulated dataset. For evaluation, three types of MS patients are considered, namely, mild, moderate and severe. In case of mild patient, the average overlapping of the lesion segmentation with the ground truth is 55.48, 85.07 % in moderate and 83.67 % in severe. The average lesion volume difference between the segmentation and the ground truth in the mild case is 3.41, 0.68 % in the moderate and 2.19 % in the severe.

As a result, the number and volume of brain lesions is measured and can be followed-up in clinical practice. In addition, the number and volume of the brain lesions is quantified for different brain regions, such as the frontal lobe, midbrain, parietal lobe, etc. Clinicians can then relate lesion volume changes as well as the number of new lesions in different brain regions with changes in the clinical situation.

Disclosure: Nothing to disclose.

EP4151

How to increase the detection rate of chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS)

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Objectives: Chronic Lymphocytic Inflammation with Pontine Perivascular Enhancement Responsive to Steroids (CLIPPERS) is an inflammatory CNS disorder characterized by (1) sub-acute onset of cerebellar and brainstem symptoms, (2) mainly peripontine contrast-enhancing perivascular lesions with a "salt-and-pepper" appearance on MRI, and (3) angiocentric, predominantly T-lymphocytic infiltration as revealed by brain biopsy. Neuroinfectious diseases, CNS lymphoma and, of note, neurosarcoidosis must be excluded. As CLIPPERS has been described as recently as 2010, many patients may have been misdiagnosed in the past.

Methods: We searched the medical records from the Department of Neurology at Rigshospitalet, Copenhagen University Hospital, for patients discharged between 1999 and 2013 with a diagnosis of "sarcoidosis with other localization" (D86), "other acute disseminating demyelination" (G36), "other demyelinating disease in the CNS" (G37) or "encephalitis, myelitis or encephalomyelitis" (G04.9).

Results: Of 206 identified patients, 24 had been examined by brain biopsy and were included for further evaluation. Following clinical, neuroradiological and neuropathological review, 3 patients (12.5 %) were reclassified as having CLIPPERS. To the authors' knowledge these are the first reported Scandinavian cases of CLIPPERS; median long-term follow-up was 75 months.

Conclusions: The present results suggest that clinical review of patients previously diagnosed as neurosarcoidosis or unspecified inflammatory demyelinating CNS disease might increase the detection rate of CLIPPERS.

Disclosure: Nothing to disclose.

EP4152

Immunogenicity with peginterferon beta-1a in patients with relapsing-remitting multiple sclerosis: 2-year data from the randomised phase 3, multicentre ADVANCE study in relapsing-remitting multiple sclerosis

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Objectives: We assess the immunogenicity of subcutaneous peginterferon beta-1a (PEG-IFN) in patients with relapsing-remitting multiple sclerosis during year 2 and over 2 years of the ADVANCE study.

Methods: At the end of the placebo-controlled first year of ADVANCE, patients on placebo were re-randomised to PEG-IFN every 2 (Q2W) or 4 weeks (Q4W); during year 2 all patients received dose-frequency-blinded PEG-IFN. Serum samples were collected predose on weeks 60, 72 and 96, and tiered testing was used to measure interferon beta-1a binding antibodies (BAbs; using a validated enzyme-linked immunosorbent assay [ELISA]), interferon beta-1a neutralising antibodies (NAbs; using a validated cell-based assay), and antibodies to polyethyleneglycol (PEG, which is attached to the interferon beta-1a molecule; using a validated ELISA). We present results for patients with 2 years of data at cut-off.

Results: The incidence of persistent treatment-emergent antibodies during year 2 was low in those switched to PEG-IFN from placebo and in patients on PEG-IFN Q2 W and Q4 W over 2 years: BAbs incidence, 1 % across groups; NAbs incidence, <1 % across groups; anti-PEG antibodies incidence, 3, <1 and 2 %, respectively; NAbs and anti-PEG titres were low. Incidences over the 2-year period for Q2W and Q4W were reported as: BAb 4 and 2 %; NAb: <1 and <1 %; anti-PEG: 2 and 6 %, respectively. No discernible impact on clinical efficacy or safety was observed in this study.

Conclusions: The overall incidence and titre levels of treatment-emergent antibodies were low for PEG-IFN Q2W and Q4W over 2 years of treatment, with no overall discernible clinical impact.

Disclosure: Study sponsored by Biogen Idec Inc. (Cambridge, MA, USA). BCK: honoraria from Bayer Schering, Biogen Idec Inc., Merck Serono, Novartis, Roche, Sanofi Aventis, and Teva Neurosciences, and financial support for research from Bayer Schering, Biogen Idec Inc., Merck Serono, and Teva; SDN: consulting fees from Biogen Idec Inc., and Genzyme; JTW, YZ, YC, AS, SH, AD, MS: employees of Biogen Idec Inc.

EP4153

A study of total Tau protein in the cerebrospinal fluid of patients with multiple sclerosis and clinically isolated syndrome

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Multiple sclerosis (MS) is the most common chronic demyelinating disorder of the central nervous system (CNS). In the patients with probable MS the initial event is indicated as clinically isolated syndrome (CIS) that doesn't necessarily convert to MS. Studies in patients with CIS provide important information about immunological mechanisms. Data suggest that tau concentration in the cerebrospinal fluid (CSF) may be a marker of progressive forms of the disorder.

Total tau (tTau) was determined and analyzed, using SPSS statistical package 17.0, in 68 CSF samples, from 55 MS patients (43 ± 12) and 13 controls (40 ± 12) who didn't suffer from any inflammatory or degenerative disease of CNS. MS patients were 44 females and 11 males, and controls were 4 females and 9 males. 18 (33 %) of the patients suffered from CIS, 23 (42 %) from relapsing/remitting MS (RRMS), 4 (7.3 %) from primary progressive MS, 5 (9.1 %) from secondary progressive MS, 3 (5.4 %) from relapsing progressive type of MS. We used the Elisa technique and the commercial available kits (Innogenetics, Belgium).

Females were found to have higher levels of tTAU-Ag comparing with the males ($U = 336$, $z = -1.9$ $p = 0.049$) and decreased levels where found in older healthy individuals ($rho = -0.687$, $p = 0.01$).

Patients with RR type and patients with CIS had higher concentrations of tTAU in comparison with controls, as shown using non-parametric tests (Mann–Whitney) $U = 172{,}5$, $z = -2{,}1$, $p = 0{,}035$ and $U = 69.5$, $z = -1.9$, $p = 0.05$, respectively.

Our findings indicate the correlation between the increased CSF tTau levels and MS at the early stages, as well as CIS in comparison with controls.

Disclosure: Nothing to disclose.

Neuroimmunology

EP4154

Comparative case series of GABA(B) and AMPA receptor antibodies associated with limbic encephalitis

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Background: We present clinical and paraclinical features of antibodies (abs) to GABA(B) and AMPA receptors associated with limbic encephalitis (LE).

Methods: Serum and CSF samples of 12 patients who were suspected to have LE were tested for a broad panel of antineural abs and found to be positive for GABA(B) and AMPA receptor abs. Clinical data were retrospectively compiled.

Results: In nine patients we detected abs to GABAB receptor (GABA(B)R). Median age was 65.1. All female and 3/6 male patients were diagnosed with small cell lung cancer. GABA(B)Rabs were found in serum samples of all patients but only in 6 CSF samples. Intrathecal GABA(B)R ab synthesis was found in 2/4 patients with sufficient data available (median ab-index: 71.2). On MRI we found bilateral mediotemporal and in one case cortical abnormalities, EEG revealed encephalopathy. 3 patients died, 1 patient showed slight improvement and in 5 patients bodily and cognitive functions declined gradually.

AMPA receptor (AMPAR) abs were detected in three patients with mnestic disturbances (1 female). Median age was 60.7. The only female patient was diagnosed with ovarian cancer. AMPAR abs were present in all serum samples but only in 1 CSF sample without intrathecal AMPARab synthesis. MRI findings showed mediotemporal abnormalities, EEG was normal in all patients.

Discussion: Our data reveal that GABABR abs more likely lead to full clinical picture of LE with a poor outcome. Patients with AMPAR abs were less impaired with less pronounced abnormalities on MRI and EEG pointing to a more confined cerebral process.

Disclosure: Dr. Bien served on scientific advisory boards of UCB, Eisai (both Germany), undertook industry-funded travel with support of UCB, Eisai, Desitin, Grifols (all Germany), received honoria for speaking engagements from UCB, Eisai, Desitin, Glaxo-Smith-Kline, diamed and Fresenius. Dr. Dogan undertook industry-funded travel with support of Fresenius and UCB(both Germany).

EP4155

CD138$^+$ plasma cells predominate in the cerebrospinal fluid of patients with anti-N-methyl-D-aspartate receptor encephalitis

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Introduction: Anti-N-methyl-D-aspartate receptor (NMDA-R) encephalitis is a recently described autoimmune panencephalitis with characteristic clinical features that include neuropsychiatric symptoms, seizures, abnormal movements and autonomic instability. Antibodies cause a reversible selective cross-linking and internalization of surface NMDA-Rs and subsequent disturbance of synaptic transmission and plasticity. Here, we studied the composition of the cellular infiltrates in the cerebrospinal fluid in patients with NMDA-R encephalitis before and during the course of the disease using flow cytometry.

Methods: A total of 8 patients with NMDA-R encephalitis underwent detailed analysis of the cellular composition of blood and cerebrospinal fluid samples before and during the course of the disease using flow cytometry and were compared to a cohort of 35 patients with psychogenic neurological symptoms.

Results: We found exceedingly increased numbers of activated B cells, i.e. CD138$^+$ plasma cells in the cerebrospinal fluid of patients with NMDA-R encephalitis compared to controls, whereas numbers of activated HLADR$^+$ CD4$^+$ and CD8$^+$ T cells were only slightly increased. The fraction of CD138$^+$ plasma cells in the cerebrospinal fluid decreased under immunotherapy in parallel to clinical improvement during the disease course.

Conclusions: CD138$^+$ plasma cells represent the major fraction of activated lymphocytes in the cerebrospinal fluid of patients with NMDA-R encephalitis may serve as a marker of response to immunotherapy.

Disclosure: Nothing to disclose.

EP4156

Cytotoxic CD8$^+$ T cells predominate in the cerebrospinal fluid of patients with limbic encephalitis associated with antibodies to the voltage-gated potassium channel complex

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Introduction: Limbic encephalitis (LE) associated with antibodies to voltage-gated potassium channel (VGKC) complex usually presents with rapidly progressive short-term memory deficits, neuropsychiatric symptoms, and temporal lobe seizures. Antibodies disrupt the presynaptic and para-/juxtanodal VGKC complex consisting of the VGKC and associated proteins leucine-rich glioma-inactivated 1 (LGI1) and contactin-associated protein-like 2 (CASPR2) and thus cause altered synaptic transmission and neuronal excitability. Here, we studied the composition of the cellular infiltrates in the cerebrospinal fluid in patients with anti-VGKC complex LE before and during the course of the disease using flow cytometry.

Methods: A total of 6 patients with anti-VGKC complex LE underwent detailed analysis of the cellular composition of blood and cerebrospinal fluid samples before and during the course of the disease using flow cytometry and were compared to a cohort of 35 patients with psychogenic neurological symptoms.

Results: We found predominantly increased numbers of activated HLADR$^+$ CD8$^+$ T cells in the cerebrospinal fluid of patients with anti-VGKC complex LE compared to controls, whereas numbers of activated B cells i.e. CD138$^+$ plasma cells were only slightly increased.

Conclusions: Predominantly increased numbers of activated HLADR$^+$ CD8$^+$ T cells may in the cerebrospinal fluid of patients with anti-VGKC complex LE may point towards a pathogenic role of these cells.

Disclosure: Nothing to disclose.

EP4157

Three case with Familial Mediterranean fever and multiple sclerosis

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Introduction: FMF is an autosomal recessive inflammatory disease and characterized by recurrent episodes of fever and serositis or synovitis. Few cases having both MS and FMF have been reported.

Methods: *Case 1*: 27 years old woman diagnosed with Familial Mediterranean fever (FMF) 10 years ago and treated with colchicine presented with headache and urinary incontinentia. She had two siblings who had FMF. The magnetic resonance imaging (MRI) of

brain showed a hyperintense enhancing lesion at the bilateral cerebral white matter and mesencephalon. *Case 2*: 45 years old man diagnosed with FMF 15 years ago and treated with colchicine. He admitted to our clinic for left arm weakness and numbness. The cervical MRI showed hyperintense lesion alt the left side at the level of C3-4 and C6-7. *Case 3*: 34 years olds male admitted to our clinic fever, arthralgia and vertigo. He diagnosed with FMF 17 years ago. Complete visual loss observed on his left eye and partial visual loss observed on the right eye. He had diagnosed as an optic neuritis. MRI of brain showed a hyperintense, demyelinating lesion at the bilateral cerebral periventricular white matter. Pattern VEP response distal latency was delayed at the right side. Tibial and median sensory evoked potential responses were not obtained.

Results: All of their oligoclonal bands were positive.

Conclusions: Here we assess three cases with both FMF and MS, in order to clarify any relationship between FMF and MS, and to evaluate disease characteristics.

Disclosure: Nothing to disclose.

EP4158

Expression of apoptosis-related genes in relapsing-remitting multiple sclerosis and clinically isolated syndrome

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Introduction: The pathogenesis of multiple sclerosis (MS) involves failure of lymphocyte apoptosis leading to persistence of neuroinflammation. Identifying mediators that govern apoptotic pathways is critical for better understanding of MS as well as for the discovery of new therapies and biomarkers. Our aim was to identify a new prognostic biomarker that would predict conversion from clinically isolated syndrome (CIS) to MS.

Methods: The study included 46 subjects (11 RRMS, 20 CIS, 16 controls) that were studied neurologically and the blood samples were collected. The expression of apoptotic genes in mononuclear cells was analysed with Taqman array in two separate cohorts. First, 96 transcripts were measured in patients with RRMS and controls. Thereafter, such transcripts that appeared to be upregulated in RRMS were studied in patients with CIS annually over the four years.

Results: We detected 11/93 upregulated transcripts in RRMS. They belong to the Bcl-2 family (BBC3, BAD, *BCL2L14, BIK, BOK*), death receptor pathway (*TNFRSF25, FADD*) and NF-KB family (*IKBKE, NFKBID*). In CIS, half of the patients fulfilled the diagnostic criteria for MS, but none of the studied genes was associated with conversion to MS. Longitudinal analysis of subjects with CIS showed marked intra- and interindividual variability in the levels of gene expression.

Conclusions: Proapoptotic gene changes are detectable in patients with clinically silent early MS. Most likely such changes are consistent with peripheral immune activation and proapoptotic gene changes may also be responsible for worsening of MS. However, in CIS, the upregulated transcripts did not predict conversion to MS.

Disclosure: Nothing to disclose.

EP4159

New mouse model mimicking IFN-alpha-related depression in hepatitis C virus infected patients

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Introduction: We have previously identified 15 genes (DRIIs) that are associated with the development of severe depressive episodes during the standard therapy with interferon alpha (IFN-α) and ribavirin in the peripheral blood of hepatitis C virus (HCV) infected patients. Hereby, through direct intracerebroventricular application of IFN-α and poly(I:C) in mice, we mimic the depression conditions affecting HCV patients and the genetic response of DRIIs and cytokines.

Methods: Miniosmotic pumps were implanted into the lateral ventricle of 10- to 12-weeks-old C57Bl6/j mice for administration of saline, recombinant mouse IFN-α (mIFNα) and/or poly(I:C) during 14 days. After the treatment animals underwent behavioral tests: open field test (OFT) for 20 min, tail suspension test (TST) for 6 min and forced swim test (FST) during 6 min/session. Hippocampus and prefrontal cortex were dissected to assess the expression of nine of the DRIIs, Ccl5, Cxcl1 and Timp-1 by RT-PCR.

Results: The TST and FST showed that concomitant administration of mIFNα and poly(I:C) promoted a depression-like behavior which was not detectable with the single treatments. Additionally, the OFT revealed a strong tendency to anxious-like behavior. Except *Mef2A*, the rest of the DRIIs and cytokines showed a significant or strong upregulation, especially with costimulation treatment and in hippocampus.

Conclusions: Intracerebroventricular administration of mIFNαA and poly(I:C) in mice may partially mimic the neural environment present in depressed-HCV patients undergoing IFN therapy. As suggested by our previous ex vivo studies, the upregulation of selective DRIIs and production of inflammatory cytokines may be involved in the pathophysiological mechanisms underlying IFN-α-associated depression.

Disclosure: Nothing to disclose.

EP4160

Refractory IgG4-related intracranial hypertrophic pachymeningitis

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Introduction: IgG4-related-disease is usually described in gastrointestinal/respiratory systems. Involvement of the central nervous system is uncommon, with principal neurological manifestations including hypophysitis and HP. Leptomeningeal disease has also been reported. Generally, it does not affect the brain parenchyma. In some cases, previously known idiopathic-HP may represent IgG4-related-HP, affecting the intracranial and/or intraspinal dura. Most cases resolve with surgery and/or steroid therapy; other reports describe efficacy of radiation therapy and anti-tumor necrosis factor

antibodies. Only three cases of recurrent IgG4-related-HP have been described, one case treated with rituximab with excellent clinical response, and two cases treated with mycophenolate mofetil (MMF) producing stable clinico-radiological findings after 12 and 18 months respectively.

Methods: We report a rare case of IgG4-related intracranial-HP, initially presenting with seizures, complicated subsequently with multiple cranial neuropathies. This disease has been refractory to steroids, azathioprine, methotrexate and did not improve with MMF. We have been closely following this patient at the UTMB since 2003.

Results: After initial presentation with seizures, the patient developed cranial neuropathies. Most recent brain MRI demonstrated progressive dural enhancement along the falx, bilateral frontotemporal convexities and around the right cavernous sinus. Serum IgG fractionation showed elevation of systemic IgG4 levels. Biopsy of the affected dura revealed many inflammatory B-cells, though no evidence of lymphoma, there was over 25 % of immunostain-positive IgG4-mast cells. Despite treatment with steroids, azathioprine, methotrexate and MMF, lesions continued to grow into the right cavernous sinus and maxillary sinus.

Conclusions: This case highlights a refractory IgG4-related intracranial-HP. Rituximab has been initiated.

Disclosure: Nothing to disclose.

EP4161

Non-stiff anti-amphiphysin syndrome: clinical manifestations and their favorable outcome after immunotherapy

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Introduction: Classically, anti-amphiphysin antibody causes paraneoplastic stiff-person syndrome. However, the antibody is responsible for various neurological manifestations, and here we investigated the clinical spectrum of non-stiff anti-amphiphysin syndrome (NSAS) and their responses to immunotherapies.

Methods: From October 2012 to September 2013, patients with encephalomyelitis, limbic encephalitis, brainstem encephalitis, subacute ataxia, dysautonomia, or polyneuropathy of unknown etiology were screened for classical paraneoplastic or autoimmune synaptic encephalitis antibodies. Patients who are positive for anti-amphiphysin antibody were included and the clinical features, laboratory findings and radiological tests were analyzed.

Results: Total 21 patients had anti-amphiphysin antibody. The most common neurological manifestation was limbic encephalitis, followed by dysautonomia, cerebellar dysfunction, brainstem encephalitis, peripheral neuropathy, and myelitis. Cancer was detected in 7 patients but not in the majority of the patients (mean follow-up period: 2.8 years). Immunotherapy was performed in 13 patients, and most of the patients demonstrated favorable response to the treatment. Intravenous immunoglobulin or steroid treatment was effective in majority of the patients. Three patients improved only after rituximab treatment.

Conclusions: Anti-amphiphysin antibody can be detected in non-stiff encephalomyelitis, and is partially associated with cancer. Active immunotherapy improved the symptoms, and novel immune modulating therapies including rituximab might be beneficial to treat the disease.

Disclosure: Nothing to disclose.

EP4162

CLIPPERS: a case report with atypical MRI-findings

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Introduction: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is an inflammatory central nervous system (CNS) disorder which is increasingly diagnosed in the last years. The aetiology is up to now unknown. Pathological marks are infiltrations of T-lymphocytes predominantly in the perivascular spaces of the brainstem. Characteristics are a number of typical clinical features with a favorable responsiveness to immunotherapy and gadolinium enhancing punctiform lesions in the brainstem in the magnetic resonance images.

Case report: We report the clinical, magnetic resonance imaging (MRI) and brain biopsy findings of a 68 year old Italian man who presented with dysphagia, numbness and paresthesia in his right face and a progressive gait ataxia. Brain and spine MRI showed a lesion in pons at the junction of the medulla oblongata with a second lesion in the cervical spinal cord. Several analyses could not give evidence for a neoplastic, infectious or different inflammatory process. Histopathology showed a blood vessel associated inflammation indicative for CLIPPERS.

Conclusion: Previous reports in the literature show cases of CLIPPERS with a spread of lesions in MR imaging and discuss the nosological position of CLIPPERS. The current case demonstrated an atypical MRI feature suggesting that CLIPPERS can present with heterogeneous morphological properties.

Disclosure: Nothing to disclose.

EP4163

Development of Guillain-Barré syndrome in patients receiving ganglioside treatment

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Introduction: The acute motor axonal neuropathy (AMAN) model has been successfully established by sensitizing Japanese white rabbits with a bovine brain ganglioside mixture including GM1 and and the pathological findings in the peripheral nerves of the immunized rabbits were similar to pathological changes in patients with AMAN. However, observational studies on the relationship between the incidence of Guillain-Barré syndrome (GBS) and the intravenous use of ganglioside failed to reveal a positive correlation. Thus far, the relationship between ganglioside and occurrence of GBS remains controversial.

Methods: We presented five cases who developed GBS following ganglioside treatment. Additionally, we reviewed the literatures on the relationship between GBS and ganglioside therapy.

Results: All the five patients developed GBS after receiving ganglioside treatment range from five to fourteen days, without antecedent infectious. Three of them were prescribed ganglioside because of trauma or surgery. They all presented with acute or progressively flaccid paralysis. And the cervical MRI scan was normal which ruled out acute paralysis of the limbs caused by acute cervical myelopathy. The cerebrospinal fluid (CSF) examination showed an increase in protein level with cell count within the normal range. The diagnosis of GBS was further confirmed by electrophysiological examinations.

Conclusions: Ganglioside treatment, which is widely prescribed in China with few reports on the side effects, is suspected to be related to the development of GBS in our opinion. The history of trauma or surgery might made a patient prone to develop GBS after receiving exogenous ganglioside through influencing the hunman immunity.

Disclosure: Nothing to disclose.

EP4164

Demographic description of Guillain-Barré syndrome: a retrospective analysis of 516 patients in northeast China

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Introduction: Guillain-Barré syndrome (GBS) is generally considered as an immune-mediated disorder in the peripheral nervous system. Although the prognosis is generally favorable, mortality is up to 10 % and approximately 20 % of patients are left with severe disability.

Methods: We retrospectively analyzed the characteristics of 516 inpatients diagnosed as GBS in the First Hospital of Jilin University between 2003 and 2012.

Results: The median age of the subjects was 39.1 years old, and 60.47 % of them were male. About 57.56 % had an antecedent infection and 36.43 % developed GBS between April and June. Hyporeflexia or areflexia was present in 91.47 % of all patients. Additionally, cranial nerves were involved in 40.31 % of patients, among whom the glossopharyngeal nerves and the facial nerves were frequently involved, accounting for 70.19 and 53.37 %. Sensory and autonomic deficits were present in 42.83 and 44.38 % of all patients, while disturbances of consciousness and paralysis of respiratory muscles occurred in 3.3 and 24.61 %. The cerebrospinal fluid (CSF) examinations were performed 2-4 weeks after disease onset. The albumin-cytologic dissociation was noted in 73 % of patients. The electrophysiological revealed that impairment of axonal, demyelinating and both involved accounted for 23, 52 and 25 %, respectively. The Hughes Functional Grading Scale (HFGS) score was used to access the severity of GBS. HFGS scores from 1 to 6 corresponded to 10, 10, 21, 46, 12 and 1 % of all patients.

Conclusions: GBS is commonly triggered by antecedent infection, occurs with seasonal predilection and mainly affects males. The most common subtype is demyelinating form. Glossopharyngeal nerves are frequently involved.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 6

EP4201

Factors associated with early hospital arrival in acute ischemic stroke patients

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Introduction: Early diagnosis and treatment in acute ischemic stroke are crucial in terms of survival and disability. Many stroke patients remain disabled because of the treatment delay. The purpose of this study was to investigate the factors associated with the early hospital arrival in acute ischemic stroke patients.

Methods: 113 patients diagnosed with acute ischemic stroke were included in this prospective study performed at the Karadeniz Technical University Medical Faculty Hospital. Patients' characteristics and patients' and relatives' emotional and behavioral reactions were compared between early (within 3 h) and late (after 3 h) arrival groups.

Results: 72.6 % of patients arrived at hospital within 3 h from symptoms onset. Univariate analysis revealed that history of atrial fibrillation ($p = 0.04$) and coronary heart disease ($p = 0.02$), sudden onset of symptoms ($p = 0.001$), loss of consciousness ($p = 0.03$), recognizing symptoms as stroke ($p = 0.01$), seeking immediate medical attention ($p < 0.001$), feelings of fear and panic ($p = 0.001$), arriving at hospital by ambulance having called the emergency medical services ($p = 0.04$) and National Institute of Health Stroke Scale (NIHSS) score ($p = 0.001$) were associated with hospital arrival within 3 h. A multivariate regression model demonstrated that NIHSS score (OR, 1.1; 95 % CI: 1.01–1.2) and recognizing symptoms as stroke (OR, 3.5; 95 % CI: 1.2–10) were independent factors associated with early arrival.

Conclusions: The role in early arrival at hospital of recognizing symptoms as stroke and seeking immediate medical attention with transportation by ambulance emphasize the importance of public awareness concerning recognizing the symptoms of stroke and accessing emergency medical assistance.

Disclosure: Nothing to disclose.

EP4202

Differences of lesion patterns and clinical outcomes in patients with cryptogenic ischemic stroke between with aortic atheroma and without aortic atheroma

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Introduction: Complex aortic atheroma (CAA) has been considered as a possible cause of aortogenic embolism in patients with cryptogenic ischemic stroke. We aim to investigate the differences of imaging and clinical outcomes in patients with cryptogenic ischemic stroke between with CAA and without CAA.

Methods: Between April 2010 and March 2013, consecutive ischemic stroke patients who had CAA and were admitted within 7 days after symptoms onset were included. We retrospectively reviewed the imaging and clinical data. CAA was evaluated by the transesophageal echocardiography (TEE) and/or multidetector CT (MDCT). Lesion patterns on diffusion-weighted imaging (DWI) and clinical outcomes on modified Rankin scale (mRS) score at 3 months after stroke onset were compared.

Results: A total of 141 cryptogenic ischemic stroke patients (mean age, 64.4 years old; 90 men versus 51 women) were included in this analysis. Cryptogenic ischemic stroke with CAA were 18 patients (12.8 %) and cryptogenic ischemic stroke without CAA were 123 (87.2 %). Multivariate analysis showed that old age (Odds ratio 1.149; 95 % CI 1.065–1.236, $p = 0.001$), male sex (Odds ratio 3.864; 95 % CI 1.026–14.556, $p = 0.046$), bilateral lesions (Odds ratio 3.65; 95 % CI 1.134–11.748, $p = 0.03$) were independently associated with cryptogenic ischemic stroke with CAA. There was no significant difference of mRS at 3 month between cryptogenic with CAA and without CAA ($p = 0.241$).

Conclusions: It may help determine to perform TEE or MDCT in cryptogenic ischemic stroke patients and provide more information about pathomechanism of cryptogenic ischemic stroke with CAA.

Disclosure: Nothing to disclose.

EP4203

Abstract withdrawn

EP4204

Correlation of visual and motor recovery in stroke patients during early rehabilitation period

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Introduction: Two dysfunctions that may coexist within a stroke are motor paresis (or palsy) and visual disorders. The purpose is to explore the recovery of the motor and visual disorders of stroke patients during early rehabilitation and define any correlations between these changes.

Methods: This is a prospective study of 19 consecutive stroke patients involving both motor and visual deficits in a single rehabilitation center from 2011 till 2012. The 1st evaluation was made on the acute phase (within the first week of stroke's appearance) and the 2nd at least 8 weeks poststroke. Evaluation included medical assessment (neurological and ophthalmological including acuity and perimetry) and speech & language therapist examination by the hemispheric stroke scale. During inpatient rehabilitation patient received similar intensity and frequency of therapies. Statistical analysis included paired *t* test to explore significant differences of variable means and Spearman correlation coefficient of changes of variables between 2 evaluations.

Results: At the last follow-up (94.5 ± 45.2 days), there was statistical significant improvement ($p < 0.001$) both in motor and visual function of the hemispheric stroke scale. There was moderate correlation ($ro = 0.47$, $p < 0.05$) between the total hemispheric score change and the change of visual acuity but no correlation between the improvement of visual fields and improvement of motor function.

Conclusions: In the early rehabilitation period of stroke patients with both motor and visual deficits, there was independent improvement of motor and visual functions, however the visual acuity improved symmetrically as the total neurologic function of these patients recovered.

Disclosure: Nothing to disclose.

EP4205

Abstract withdrawn

EP4206

Effectiveness of three anti-smoking interventions of different intensities in patients after ischemic stroke: a pilot data from randomized controlled trial

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Introduction: Continued smoking after stroke increases the risk of death and stroke recurrence within a few years. Smoking cessation is recommended for secondary stroke prevention, but cessation rates in stroke survivors are not satisfactory and range from 30 to 40 %. The primary objective of the present study is to compare the effectiveness of three anti-smoking interventions of different intensities.

Methods: Randomized, controlled trial in patients hospitalized because of their first in a lifetime ischemic stroke. Three antismoking interventions based on the "5A's" method differing in follow-up intensity

Group 1—20 min counseling by physician, no early follow up and two follow-up visits 3 and 12 months after stroke; Group 2—as above, additional visit 7 days after stroke, Group 3—as above, and four follow-up visits within 6 weeks after discharge from the hospital. Smoking status at 3 months was determined by self-report and verified by measurement of exhaled carbon monoxide; smoking status at 12 months were determined by self-report.

Results: 120 smokers with ischemic stroke were randomized to one of the intervention groups. The 3-months smoking cessation rates were 35.4, 45, and 38 % for Group1, Group2 and Group 3, respectively. There was no difference between routine and more intensive programs (Group 1 vs. Group 2, Chi square = 0.8365, P = 0.36; Group 1 vs. Group 3, Chi square = 0.0361, P = 0.85.

Conclusions: Our preliminary results are similar to observations of Fransden et al. (2011). Searching for other conditions that may influence on smoking status after stroke is needed.

Disclosure: The study is supported by National Science Center (grant NCN nr 2011/01/B/NZ7/05402).

EP4207

Abstract withdrawn

EP4208

Risk factors of infection, poor outcome and mortality in stroke patients

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Introduction: Stroke is the third leading cause of death in developed countries. Post-stroke infections are suggested to have an additive effect on stroke mortality and poor functional outcome. In this study, we evaluated the incidence, types and risk factors of infection. Furthermore, risk factors of mortality and poor outcome were studied in stroke patients.

Methods: The data of 388 stroke patients between 2005 and 2012 were extracted through chart reviews retrospectively; age, gender, types of stroke, feeding characteristics, respiratory status, information on defecation, swallowing ability, vomiting, details of neurological examination, the consultation details conducted by Infectious Diseases specialist, use of medications, the cause and time of death, scores of Glasgow coma scale, modified Rankin severity scale (mRS), Barthel index of daily living on admission, stroke risk factors. Multivariant analysis was used in the evaluation of risk factors.

Results: Infection was found in 29.9 % patients with stroke. Pneumonia was the most common type of infection, being *E. coli* and *Acinetobacter* spp the most common responsible pathogens. Hypoxia was the common risk factor for infection, poor outcome and mortality. Dysphagia was the risk factor for infection and mortality. Presence of infection was found to be the poor outcome risk factor.

Furthermore infection was being higher, mortality was being lower in the presence of constipation.

Conclusions: It could be suggested that preventive measures and careful treatment of risk factors, such as hypoxia, dysphagia could reduce mortality by preventing infection and a good care of constipation could lessen infection.

Disclosure: Nothing to disclose.

EP4209

Is prestroke statin treatment associated with a better short term functional outcome in patients with atherothrombotic stroke?

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Introduction: Experimental and clinical data suggest that beside lipid lowering effect, statins also have pleiotropic actions and possibly neuroprotective effects after acute cerebral ischemia.

Methods: We performed a cross-sectional study with prospectively collected data about 587 patients consecutively hospitalized for acute ischemic stroke. The aim of the study was to assess the relationship between statin therapy before stroke onset (prestroke statin use) and short term functional outcome in patients with ischemic stroke attributable to large artery atherosclerosis. For every patient data were collected about clinical and laboratory characteristics at admission and during hospitalization, concomitant diseases and prior treatment. Stroke subtype was defined according to TOAST criteria. Good functional outcome was defined as a modified Rankin score (mRS) 0-2 at one week after stroke onset. No patient was treated with recombinant tissue plasminogen activator.

Results: 136 patients (23.1 %) were classified as having ischemic strokes due to large artery atherosclerosis. On bivariate analysis there was no association between age ($p = 0.06$), arterial hypertension ($p = 0.08$), diabetes mellitus ($p = 0.21$), high LDL-cholesterol levels ($p = 0.16$), high triglycerides levels ($p = 0.28$) and short term functional outcome. Prestroke statin use was associated with good short term functional outcome ($p = 0.02$). In logistic regression analysis with adjustment for confounding variables, prestroke statin use increased by 3.3 the patient's chance to have an mRS score between 0 and 2 at 1 week after stroke onset (OR = 3.3; 95 %CI 1.16–10.7; $p = 0.04$).

Conclusions: Prestroke statin use is associated with good short term functional outcome in patients with ischemic stroke attributable to large artery atherosclerosis.

Disclosure: Nothing to disclose.

EP4210

Epidemiology of intracerebral hemorrhage in Grodno, Belarus

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Introduction: No population-based studies of incidence of intracerebral hemorrhage (ICH) have been performed yet in Belarus.

Methods: All suspected ICH occurred among 342 444 residents of Grodno-city during a 12-month period of 2011 were identified and assessed for all age groups. Multiple overlapping sources of notification were used to ascertain cases, and standard criteria for ICH and case-fatality were used. Patients with cerebral hemorrhages related to cerebral aneurism, tumour, trauma, or haematological malignancy were excluded.

Results: During the study period 107 cases of ICH were registered, with 96 being first-ever-in-a-lifetime strokes. The diagnosis of ICH were confirmed by CT/MRI/autopsy in 96 %, patient age ranged from 20 to 86 years (mean ± SD age, 60 ± 13.6 years). The crude incidence rate for ICH was 28.0 per 100,000 [95 % confidence intervals (95 % CI): 22.8–34.1]; for men 32.6 (95 % CI: 24.2–43.0) and for woman 24.2 (95 % CI: 17.6–32.3). ICH incidence adjusted to the World Health Organization world standard population was 23.0 per 100 000 (95 % CI: 22.8–32.9). 62 from 96 patients (64.6 %) died within 28 days of ICH onset. The 28-day case-fatality rate was 60.8 % for men and 68.9 % for women.

Conclusions: ICH incidence and case-fatality rates in Grodno were found to be of highest among other studies.

Disclosure: Nothing to disclose.

EP4211

Intravenous thrombolysis for acute ischaemic stroke: the experience of a Greek tertiary care hospital

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Introduction: To compare the safety and efficacy of intravenous thrombolysis with alteplase for acute ischaemic stroke at Papageorgiou General Hospital of Thessaloniki Stroke Unit patients to that of the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST).

Methods: Between July 2004 and May 2013, 92 patients received thrombolysis within 3 h from the onset of the symptoms of acute ischaemic stroke.

Results: In comparison with SITS-MOST, the Greek patients were younger (median, 60.5y vs 68y, $p < 0.001$), without differences in gender distribution (male/female: 63/37 % vs 60.2/39.8 %, $p = 0.326$) and symptom severity (National Institute of Health Stroke Scale score median: 11 vs 12, $p = 0.381$). The proportion of patients with symptomatic intracerebral haemorrhage (per SITS-MOST protocol) (1.1 vs 1.7 %, $p = 0.5$) and the mortality rate at 3 months (13.5 vs 11.3 %, $p = 0.314$) were comparable between the two groups. At 3 months, the proportion of functionally independent patients (Modified Rankin Scale = 0-2) was higher in our sample (68.2 vs 54.8 %, $p = 0.008$).

Comparison of the time from symptom onset to treatment initiation showed no difference in the Onset-To-Needle time between the two groups (median, 140 min, $p = 0.913$). However, the Door-To-Needle time was higher in our group (median, 79 min vs 68 min, $p < 0.001$).

Conclusions: Intravenous thrombolysis with alteplase for the treatment of acute ischaemic stroke is considered safe and efficacious in the Stroke Unit of the Neurological Department of Papageorgiou General Hospital of Thessaloniki. In general, our results are comparable to those from the SITS-MOST study. Our present efforts concentrate on the shortening of the door-to-needle time.

Disclosure: Nothing to disclose.

EP4212

NMDA antagonist memantine induces functional neurological recovery in the post-acute ischemic brain

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The balance of synaptic and extrasynaptic NMDA receptor signaling controls brain plasticity in the post-acute ischemic brain. The NMDA receptor antagonist memantine, which is widely used for treatment of Alzheimer's disease, preferentially blocks extrasynaptic NMDA receptors. In view of these properties, memantine appeared particularly promising for modulating brain plasticity in the ischemic brain. To elucidate such actions, we now exposed adult male C57Bl6 mice (8–10 weeks) to focal cerebral ischemia induced by 40 min intraluminal middle cerebral artery (MCA) occlusion and subsequently delivered normal saline or memantine (4 or 20 mg/kg) subcutaneously via mini-osmotic pumps starting at 72 h post-stroke over as long as 28 days, investigating effects on motor recovery and cognitive performance by means of Tight rope, Rotarod and Barnes maze tests ($n = 12$ animals per group). Importantly, memantine significantly enhanced motor recovery and cognitive performance. Unlike other neurorestorative treatments evaluated in our lab in the past, this effect was detectable immediately after the initiation of treatment, persisting beyond treatment discontinuation up to 42 days post-stroke, when animals were sacrificed. A strong advantage of memantine in stroke treatment is that the NMDA antagonist may systemically be administered. Structural correlates of the enhanced neurological recovery are currently assessed.

Disclosure: Nothing to disclose.

EP4213

Distribution of intracranial and extracranial artery stenosis and the relevant risk factors

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Introduction: Extracranial carotid stenosis is the main cause of ischemic stroke in Western countries, while for Asians, Blacks and Hispanics intracranial artery stenosis is more common in patients of ischemic cerebral stroke. This study aims to explore intracranial and extracranial artery stenosis distribution characteristics of Chinese people with combined utilization of TCD and carotid artery colour ultrasound.

Methods: We enrolled the 14,793 subjects who performed both TCD and carotid artery color ultrasound to analyze the artery stenosis distribution.

Results: The intracranial and extracranial artery stenosis incidence differed significantly (4,255 vs 2,809, $P < 0.05$), while the former was more common. And mere intracranial and extracranial artery stenosis had significant difference (2,632 vs 1,186, $P < 0.05$). Further, by comparing the incidence of both intracranial and extracranial artery stenosis in each age group, we found that intracranial artery stenosis was more common. Additionally, the stenosis incidence of both the intracranial and extracranial artery were correlated with increasing age ($P < 0.05$), and both were more common in male ($P < 0.05$).

Conclusions: Intracranial artery stenosis is more common compared to the extracranial artery regardless of age or sexuality. The rate of intracranial and extracranial artery stenosis which is correlated with increasing age is significantly higher in male for both.

Disclosure: Nothing to disclose.

EP4214

Ischemic cerebrovascular disease in young adults and post-stroke depression

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Introduction: Etiological factors are more heterogenous in young ischemic stroke. In this study, demographic characteristics, risk factors, stroke subtypes, etiologic studies, mortality rates and post-stroke depression state in young ischemic stroke were evaluated.

Materials and methods: Between 1st January 2010 and 1st March 2013, 124 ischemic stroke patients (age: 18–50 years) were hospitalized. They diagnosed by cranial CT/diffusion MR. Infarct localizations were classified by Oxfordshire Community Stroke Project classification. Age, sex, hypertension (HT), diabetes mellitus (DM), hyperlipidemia, previous ischemic stroke, cardiac disease, smoking and alcohol were risk factors. Hamilton Depression Rating Scale (HDRS) was performed to evaluate post-stroke depression.

Results: The mean age of 124 patients (43.5 % female, 56.5 % male) was 41.5 ± 6.9 years (18–50 years). Twentytwo percent of the patients were aged between 18 and 35 years (Group 1) and 78.2 % were between the ages of 36–50 years (Group 2). The most frequent infarct localization was PACI followed by POCI. The frequent risk factors were smoking, HT and alcohol abuse in males and HT, DM and HL in females. According to the TOAST classification, in females the undetermined group was the highest subtype followed by cardioemboli and other reasons, but in males cardioemboli was the first, followed by large artery disease. HDRS showed 51.2 % mild or moderate post-stroke depression.

Conclusion: Ischemic stroke in youngs differ from elderly by etiological factors, incidence and prevalence. It is important to identify the modifiable risk factors, treatable underlying causes and post-stroke depression for quality of life and psychosocial effects in these patients who has long life-expectancy.

Disclosure: Nothing to disclose.

EP4215

The correlation between location of intracerebral hemorrhage and mortality

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Introduction: Intracerebral hemorrhage (ICH) accounts for 10–15 % of all strokes and carries a high risk of mortality (22–50 %) and severe disability. The aim of this paper was to determine the correlation between location of hemorrhagic areas and mortality.

Methods: We included 276 patients (mean age 66.15 ± 11.71; 165 men and 111 women) hospitalized in the Department of Neurology, Wroclaw Medical University, with the diagnosis of spontaneous ICH confirmed on neuroimaging (CT of the head or brain MRI). The location of ICH was divided into four subgroups: ICH located in the basal ganglia and thalamus, in the brainstem, lobar and subtentorial ICH. We analyzed 73/276 patients (23 women and 50 men) who died within the first 30 days of symptom onset. The population was divided into two subgroups: those aged below and above 75 years.

Results: The location of ICH ($n = 276$ patients) was: ICH in the basal ganglia and thalamus in 136 (49.3 %), in the brainstem in 14 (5.1 %), lobar in 104 (37.7 %) and subtentorial ICH in 22 (7.9 %). In the group of 73 non-survivors: 35 (47.9 %) were below 75 years (range: 43-75), 38 (52.1 %) were over 75 years of age (range: 76-86 years). The location of ICH in the non-survivors group was: ICH in the basal ganglia and thalamus in 31 (42.5 %), in the brainstem in 7 (9.6 %), lobar in 29 (39.7 %) and subtentorial ICH in 6 (8.2 %).

Conclusions: The worst prognosis was associated with lobar location, intraventricular hemorrhage and the presence of multiple simultaneous intracerebral hemorrhages.

Disclosure: Nothing to disclose.

Movement disorders 4

EP4216

Switching L-dopa therapy from "pulsatile" to "pulse" reduces wearing-off and dyskinesia in complicated Parkinson's disease: A waking day monitoring study

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Introduction: Conventional modality of L-dopa administration consisting in intermittent multiple daily small doses (the so called "pulsatile" treatment modality) may determine an intermittent stimulation of dopamine receptors leading to motor fluctuations. A therapeutic regimen consisting in standard oral doses at specific interdoses intervals exploiting the long-duration response to the drug and designated as oral "pulse" L-dopa therapy could instead result in a more physiological and tonic stimulation of dopamine receptors, reducing motor fluctuations and dyskinesia.

Methods: Thirty-four Parkinson's disease (PD) patients with motor complications (N = 21 fluctuating; N = 13 dyskinetic) underwent two consecutive standardized waking day motor status evaluations using UPDRS-ME and the Abnormal Involuntary Movement Scale (AIMS) after switching L-dopa administration from "pulsatile" to "pulse" modality. To quantify predictable motor fluctuations, a Wearing-Off Index (WOI) was computed based on changes in L-dopa response magnitude between the two assessments.

Results: We found a significant reduction in number of daily doses while an increase in average single dose between the two assessments, with no differences in cumulative daily dosage of L-dopa. Maximal AIMS score detected during the motor status monitoring was significantly lower at the second assessment. In fluctuating patients, there was a significant reduction in UPDRS-ME average score as well as in WOI. In dyskinetic patients, there was a significant reduction in average and maximal AIMS scores with no changes in average and maximal UPDRS-ME scores.

Conclusions: Switching L-dopa therapy from "pulsatile" to "pulse" reduces wearing-off and dyskinesia in complicated PD.

Disclosure: Nothing to disclose.

EP4217

Chorea in neurometabolic diseases

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Introduction: Neurometabolic diseases (NMD) are a heterogeneous group of genetic disorders which could involve the basal ganglia. Chorea is reported as a sign of a complex clinical picture in NMD. We report on 13 children with chorea due to NMD and describe clinical features, imaging, aetiologies and treatment.

Methods: We conducted a retrospective study over a 4-year period (from 2009 to 2013) including all children diagnosed with chorea due to NMD. Clinical features, videos of patients, imaging, and treatment were analyzed.

Results: Thirteen children over 70 patients with chorea were included (9 boys and 4 girls, mean age: 8.6 years, mean age of onset: 3.8 years). Consanguinity rate was 69.2 %. Family history showed 38.5 % of similar cases. Associated movement disorders to chorea were noted: dystonia (53.8 %), myoclonus (46.2 %) tremor and stereotypies (23.1 %). Brain MRI was performed in all patients and showed basal ganglia abnormalities in 33 %. Main NMD observed were mitochondriopathies and glutaric aciduria type 1. 46.2 % of our patients were treated with neuroleptics, with good improvement.

Conclusions: The high rate of consanguinity and the presence of familial chorea in our study suggest a genetic origin. The frequency of chorea in NMD could be explained by the vulnerability of basal ganglia to metabolic disturbance. NMD should be evoked in every child with chorea belonging to a consanguineous family.

Disclosure: Nothing to disclose.

EP4218

An autopsy case of the homozygous dentatorubral-pallidoluysian atrophy

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Dentatorubral–pallidoluysian atrophy (DRPLA) is a hereditary neurodegenerative disease caused by an expansion of the CAG repeat in the DRPLA gene. The size of expanded CAG repeats is inversely correlated with the onset age and also associated with clinical phenotype. It was reported that expanded polyglutamate stretches are more widely and densely distributed in the central nervous system in the juvenile-onset than adult-onset cases. Here we report a juvenile-onset case of the homozygous DRPLA. This Japanese male initially developed ataxic gait and choreoathetosis at the age of 17 years. These symptoms were gradually worsened, and epilepsy and related psychotic features, personality change, and dementia subsequently occurred. His parents were first cousins. His four siblings developed intellectual deterioration and epileptic seizures, and all of them died at age 12–13. Genetic analysis disclosed a homozygous state of small expansions (57 repeats) of his CAG repeats in the DRPLA gene, although his onset age was young. He died of pneumonia at age 45. Pathologically, many nuclei diffusely labeled by an anti-atrophin-1 antibody, as well as those labeled by 1C2, were observed in the basal ganglia, cerebellum, and spinal cord, including the dentatorubral and pallidoluysian system. In addition, these labeled nuclei were frequently found in the neocortex, hippocampus, and subiculum, which distribution was similar to that observed in young-onset heterozygous cases having long expansion of CAG repeats. Given these findings, homozygous state of expanded CAG repeats may be associated with the earlier age at onset and more severe involvement of extra-dentatorubral and pallidoluysian system.

Disclosure: Nothing to disclose.

EP4219

Longitudinal outcomes from the international disease registry for Niemann-Pick disease type C (NP-C)

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Introduction: NP-C is a progressive neurological disease where progression varies depending on age at onset. We report progression of disability in patients continuously treated with miglustat for ≥1 year.

Methods: The NPC Registry is a prospective observational cohort of NP-C patients. Enrolled patients who received ≥1 year of continuous miglustat therapy (for ≥90 % of the observation period, with no single treatment interruption >28 days) were included in this analysis. Disability was measured using a scale rating the four domains, ambulation, manipulation, language and swallowing from 0 (normal) to 1 (worst). Patients were categorised as 'improved/stable' if ≥3/4 domain scores were lower/unchanged, and as 'progressed' if <3 scores were lower/unchanged between enrolment and last follow-up visit.

Results: In total, 283 patients were enrolled between September 2009 and October 2013; 92 received continuous miglustat therapy. The mean (range) miglustat exposure from enrolment to last follow-up was 2.0 (1.0–3.7) years. Among 84 evaluable patients, 9 (11 %) had early-infantile (<2 years), 27 (32 %) had late-infantile (2 to <6 years), 30 (36 %) had juvenile (6 to <15 years) and 18 (21 %) had adolescent/adult (≥15 years) onset of neurological manifestations. The overall mean (95 %CI) composite disability score was 0.37 (0.32,0.42) at enrolment and 0.44 (0.38, 0.50) at last follow-up. In total 55/81 (68 %) miglustat-treated patients were 'improved/stable': 33 % of early-infantile, 50 % of late-infantile, 79 % of juvenile, and 94 % of adolescent/adult-onset patients.

Conclusions: Disability status was improved/stable in the majority of patients who received continuous miglustat therapy for an average period of 2 years.

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EP4220

Apomorphine responsivity in Hemiparkinson hemiatrophy syndrome: a case report

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Introduction: The Hemiparkinsonism-Hemiatrophy-Syndrome (HPHA) is hallmarked by hemiatrophy and ipsilateral parkinsonian symptoms (rigidity, tremor and bradykinesia) and often combined with dystonia.

Methods: We report the case of a 54-year-old man of Bosnian ancestry, who suffered from head injury at the age of 7, followed by atrophy of his right upper and lower limb. The hemiatrophy began at the first dorsal interosseous muscle at the age of 21. Twenty-seven years later, at the age of 48, tremor occurred at the right upper extremity, accompanied by dystonia of digit V and cramps in the right foot. His mother suffered from tremor, but there was no evidence of Parkinson's Disease. Apart from his mother, there were no neurological disorders in his family.

Results: The neurological examination showed right-sided limb atrophy associated with moderately severe bradykinesia and rigidity (MDS UPDRS III: 42; H&Y: 3). The finger–nose test was dysmetric and there was rest and kinetic tremor in addition to dystonic posturing of the right upper limb. Power of the right upper and lower extremity was decreased. MRI demonstrated an increased apparent diffusion coefficient as well as an enhanced iron content in the substantia nigra. His response to oral L-Dopa treatment was poor, therefore, he received an Apomorphine-pump and pen, which improved tremor and bradykinesia (MDS UPDRS III: 30; H&Y: 2).

Conclusions: History, clinical findings and MRI results are consistent with HPHA. Our case report demonstrates that dopaminergic responsiveness may be achieved by invasive continuous dopaminergic stimulation.

Disclosure: Nothing to disclose.

EP4221

Opicapone pharmacokinetics and pharmacodynamics comparison between healthy Japanese and matched Caucasian subjects

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Introduction: Opicapone (OPC) is a novel third generation COMT inhibitor endowed with an exceptionally high binding affinity, which translates into a slow complex dissociation rate constant and a long duration of action.

Objectives: Compare the pharmacokinetics and pharmacodynamics (COMT-activity) of OPC between healthy Japanese and matched (age ±5 years, gender and body-mass-index ±4 kg/m^2) Caucasian subjects.

Methods: Single-centre, randomized, double-blind, parallel, placebo-controlled, multiple-ascending-dose study. Three sequential groups of up to 38 (19-Japanese plus 19-Caucasian) subjects each were randomized to receive once-daily, for 10-days, 5, 25 and 50-mg OPC or Placebo (14:5 ratio per group). Geometric mean ratios (GMR) and corresponding 95 % confidence intervals (95 % CI) for main parameters were calculated and compared to (80–125 %) interval.

Results: No statistical differences were found for OPC pharmacokinetics (t_{max}, C_{max} and AUC) and pharmacodynamics (t_{Emax}, E_{max} and AUEC) when different doses of OPC were compared between populations. Point-estimates (PEs) of pharmacokinetics GMR (95 % CI) following last-dose regimen were as follows: C_{max} 123 (78–195), 134 (95–189) and 120 (91–160); $AUC_{0\text{-}t}$ 136 (94–197), 118 (89–157) and 119 (88–161) for 5, 25 and 50-mg OPC, respectively. PEs of pharmacodynamics GMR (95 % CI) following last-dose regimen were as follows: E_{max} 96 (80–116), 96 (90–102) and 98 (94–101); AUEC: 110 (65–175) and 112 (88–153) and 95 (64–140) for 5, 25 and 50-mg OPC, respectively.

Conclusion: Only minimal differences were noted that were deemed not to be statistically significant between the Japanese and Caucasian population. Thus, ethnicity had no significant impact on the pharmacokinetics and pharmacodynamics of OPC in the conditions of the study.

Disclosure: Nothing to disclose.

EP4222

Positive effects of Erythropoietin on a rat model of Parkinson's disease

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Introduction: Erythropoietin (EPO) is a peptide hormone synthesized from kidneys. This hormone also produces in brain, liver, testis, lung, and spleen. Aim of this study represented is to investigate effects of EPO, whose neuroprotective effects were previously reported, in the rat model of Parkinson's Disease (PD).

Methods: Eighteen Sprague–Dawley adult male rats were included in the study and were divided 3 groups ($n = 6$). Rotenone + Dimethyl sulfoxide (DMSO) was sterotactically injected to left substantia nigra compacta and ventral tegmental area of the group 1 and group 2. Only DMSO was applied to the same localization of the third group as a sham group. Rotation test was applied to rats awaited for 10 days by administering intraperitoneally apomorphine. Rats having continuous rotation in the same direction 7 times per minute in apomorphine-induced rotation test (AIRT) were considered as PD. 2,500 IU/kg EPO was applied to Group 1, and isotonic saline was applied to Group 2 for 28 days. Then apomorphine-induced rotation numbers for 10 min were recorded, malondialdehyde levels in plasma and thyrosine hydroxylase (THA) (dopamine degradation product) levels in brain of the rats were examined.

Results: AIRT values and plasma malondialdehyde levels of the group 1 were statistically significantly decreased in comparison with the group 2. THA levels were higher in the group 1 compared to group 2 ($p < 0.005$).

Conclusions: In this study, EPO was detected to have positive effects on rat model of PD. This result may provide an insight to new treatment alternatives for PD treatment.

Disclosure: Nothing to disclose.

EP4223

Apathy in early Parkinson's disease

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Introduction: Apathy is a common behavioural problem in Parkinson's disease (PD), with severe impact on quality of life. Apathy in early PD have been linked to ventral striatum and mesolimbic dopaminergic denervation, but involvement of norepinephrinergic and serotoninergic metabolism has also been suspected.

Objective: We examined the frequency and clinical characteristics of apathy in 113 nondemented patients with newly diagnosed PD Hoehn and Yahr (HY) stage 1 and 137 control subjects matched for age, sex and education level.

Methods: All participants underwent psychiatric investigation with the Starkstein's Apathy Scale (AS), and the 17-item Hamilton Depression Rating Scale (HDRS-17), Neuropsychiatric Inventory assessment (NPI), motor scoring with HY staging, and the Unified Parkinson's Disease Rating Scale (UPDRS); and cognitive screening with the The Addenbrooke's Cognitive Examination Revised (ACE-R) on the same day. Apathy was diagnosed based on proposed consensus criteria.

Results: Apathy was found in 41.2 % of the PD patients, of whom 31.2 % had significant depressive symptoms. Apathy was significantly associated with male gender, more severe motor symptoms and higher depression scores, but was not associated with ACE-R scores. When excluding patients with significant depressive symptoms, apathy remained significantly associated with motor severity.

Conclusion: Apathy remains main psychiatric symptom even in early PD. Association between apathy and motor severity suggests a common underlying pathophysiological mechanism.

Disclosure: Nothing to disclose.

EP4224

[^{123}I]FP-CIT SPECT (DaTSCAN) in unclear parkinsonism: a useful tool to differentiate between Parkinson's disease and vascular or drug-induced parkinsonism

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Introduction: We systematically reviewed the utility of dopamine system imaging [^{123}I]FP-CIT SPECT (DaTSCAN) in unclear parkinsonism, namely in the differential diagnosis between idiopathic Parkinson's disease (PD) and vascular (VP) or drug-induced (DIP) parkinsonism.

Methods: We searched MEDLINE and CENTRAL to identify studies reporting enough data to determine accuracy measure (sensitivity, specificity, diagnostic Odds Ratio—DOR, positive and negative likelihood ratios—pLR, nLR) of [^{123}I]FP-CIT SPECT in differentiating between PD and VP/DIP in unclear parkinsonism. The methodological quality of studies was evaluated with QUADAS.

Results: Five studies were included. Pooled accuracy measures in the differential diagnosis between PD and VP were: sensitivity: 86.2 % (95 % CI 81.3–90.1 %); specificity 82.9 % (95 % CI 67.9–92.8 %); pLR 4,813 (95 % CI 1,523–15,211); nLR 0.190 (95 % CI 0.139–0.259); DORs 28,528 (95 % CI 8,450–96,309). Pooled accuracy measures in the differential diagnosis between PD and DIP were: sensitivity 86.2 % (95 % CI 81.3–90.1 %); specificity 93.8 % (95 % CI 69.8–99.8 %); pLR 5,366 (95 % CI 1,913–15,050); nLR 0.178 (95 % 0.125–0.253); DORs 39,638 (10,380–15,136).

Conclusions: [^{123}I]FP-CIT SPECT might accurately differentiate between early PD and VP/DIP in patients with unclear parkinsonism. However, all the studies conducted show methodological limits, which prevent to draw conclusions on the real accuracy of [^{123}I]FP-CIT SPECT. Further studies with higher methodological quality and homogeneous diagnostic criteria of VP and DIP are needed to definitely evaluate the diagnostic utility of [^{123}I]FP-CIT SPECT in differentiating between PD and VP or DIP.

Disclosure: Nothing to disclose.

EP4225

Parkinsonism associated with liver cirrhosis: a case report

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Introduction: We present a case report of a patient with cirrhosis and secondary parkinsonism. The patient is a 58-year-old male who is complaining of clumsiness of the movements of his right arm, general

slowness of his body movements, mild changes in his gait. The symptoms have relatively rapid progression over months. The patient have had chronic C hepatitis and liver cirrhosis with portal hypertension for several years.

Methods: We have used detailed neurological examination, EMG, MRI, general blood tests plus ammonia, manganese, copper and ceruloplasmin levels in blood.

Results: We found hypomimia, bradykinesia, mild rigidity in his right arm, slowed walk with decreased symkinesias of the right arm on clinical examination, MRI data pointing towards acquired hepatocerebral degeneration, increased levels of ammonia and manganese and normal levels of copper and ceruloplasmin in blood.

Conclusions: We concluded that the extrapyramidal symptoms in our patient were secondary to liver impairment. This clinical case shows the importance of considering acquired hepatocerebral degeneration in the differential diagnosis when managing patients with parkinsonism.

Disclosure: Nothing to disclose.

EP4226

Dopa-responsive dystonia presenting with spastic dysphonia

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Introduction: Dopa-Responsive Dystonia (DRD) is a broad term used to describe forms of dystonia that respond to levodopa.

Methods: A 50-year-old female visited the Outpatient Clinic of Neurogenetics of General Hospital Papageorgiou with a long history of gait disorders with childhood onset and progressive deterioration. She had started to walk at the age of 20 months but never actually managed to run properly. By the age of 4 she had been presenting with a dystonic right leg and during childhood she recalled tiptoe walking. Progressively during puberty and adulthood she established writer's cramp and right torticollis. The most prominent feature, however, was spasmodic dysphonia present the last few months. Family history was free with the exception of cervical muscle cramps of the mother.

Results: On the clinical suspicion of DRD levodopa was initiated. Genetic test revealed a GCH1 mutation. Sequencing analysis of the GCH1 gene revealed an Arg88Trp variation that was reported as pathogenic in GCH1 variation viewer. Due to the spectacular response of dysphonia to levodopa, it was titrated up to 200mg $\times$ 3. 2 months later, dysphonia was dramatically improved however the rest of the symptoms were fairly ameliorated.

Conclusions: Clinical manifestations of DRD cover a broad spectrum of signs and symptoms from generalized, severe dystonia to subtle signs only seen upon induction. This patient presented with a rather typical onset and progression of the disease apart from spasmodic dysphonia which is relatively rare in DRD. The elective response of one symptom only to dopaminergic therapy is rather unusual.

Disclosure: Nothing to disclose.

EP4227

Lewy body dementia: a 3 years clinical follow up study

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Few studies systematically investigated the relationships between the symptoms and the clinical course of DLB with a long term follow up. Aim of this study is to analyze a broad pattern of clinical aspects of the disease in patients affected by DLB, with a 3 years follow up.

We selected 77 patients with DLB probable. We retrospectively analyzed the age of onset, the prevalent type of onset, motor disease severity, the acute and chronic response to levodopa (LD) and the LEDD. MMSE, cognitive fluctuations (CFs), visual hallucinations (VHs), therapies with cholinesterase inhibitors or memantine and neuroleptic treatments were also investigated. 47 patients had a 3 years follow up. The most common onset type was a mixed phenotype, followed by the motor and cognitive phenotype. The postural instability and gait disorders phenotype (PIGD) was predominant. A positive LD response was present in 40.3 %. In the 3 years follow up, all tremor dominant patients converted to PIGD. An earlier onset was associated to a prevalent PIGD. PIGD was associated to a higher occurrence of VHs, higher worsening of rigid/akinetic subscores at UPDRS part III and worsening of MMSE during 3 years. VHs occurred at baseline in 30.4 % and were associated to a more prevalent PIGD and younger disease onset and with a faster MMSE and rigid akinetic UPDRS subscores decline. The presence of VHs was associated to CFs.

We found significant associations between symptoms and if confirmed by larger studies, some of them could represent possible predictors of follow up outcome.

Disclosure: Nothing to disclose.

EP4228

Postural control changes in visual height intolerance: body sway and anti-gravity muscle activity

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Introduction: Visual height intolerance (vHI) occurs when a visual stimulus causes the apprehension of loosing balance and falling. Although vHI affects almost one-third of the general population and has relevant consequences on the quality of life, a quantitative assessment of physiological alterations that may trigger postural imbalance in vHI is missing.

Methods: VHI-related changes in postural control were assessed by center-of-pressure displacements and electromyographic recordings of selected leg, arm, and neck muscles in 16 subjects with vHI while standing at heights on an emergency balcony vs. standing in the laboratory at ground level. Characteristics of open- and closed-loop postural control were analyzed. Body sway and muscle activity parameters were correlated with the subjective estimates of fear at heights.

Results: During height exposure, (1) open-loop control was disturbed by a higher diffusion activity ($p < 0.001$) and (2) the sensory feedback threshold for closed-loop control was lowered ($p < 0.010$). Altered postural control was predominantly associated with increased co-contraction of leg muscles. Body sway and leg and neck muscle co-contraction correlated with the severity of subjective anxiety ($p < 0.050$). Alterations in postural control diminished if there were nearby stationary contrasts in the visual surrounding or if subjects stood with eyes closed. The performance of a cognitive dual task also improved impaired balance.

Conclusions: Visual heights have two behavioral effects in susceptibles: a change occurs in (1) open- and closed-loop postural control strategy and (2) co-contraction of anti-gravity leg and neck muscles, both of which depend on the severity of evoked fear at heights.

Disclosure: Nothing to disclose.

EP4229

Quality of life in patients receiving combination therapy with Pramipexole

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Introduction: Non-motor disorders such as depression, anxiety, cognitive impairment, pain, sleep disorders, etc. have a great role in disability in patients with Parkinson's disease (PD). They lead to the restriction in all spheres of patient's life consistently reducing its quality. Rational therapy is able to delay the offensive some of these symptoms and ensure the best quality of life.

Methods: 38 patients with PD (22 women and 16 men) aged 37–76 years (mean age was 64.7 ± 9.0), average duration of disease was 7.18 ± 4.2 years. The disease stage at Hyun and Yar scale was: II—29 % of patients, III—68.4 %, IV—2,6 %. There were such forms of the disease like tremor-in 7.9 %, akinetic-rigid-44.7 %, mixed-47.4 %. All patients receiving the combination therapy were divided into groups: I—8 people who did not receive therapy with Pramipexole, II—13 people who received pramipexole 1.5 mg/day and less, III—17 people who received Pramipexole at a dose of more than 1.5 mg/day. Quality of life was determined by questionnaire MOS Shot-form 36-Item (MOS SF-36).

Results: Patients in II group had the best performance in Role-Physical Functioning, Bodily pain, Vitality, Social Functioning, Mental Health, Physical health according to the SF-36. The greatest difference between the groups was in Role-Emotional, due to the emotional state: I—1.0 ± 35.4; II—64.1 ± 46.1; III—22.3 ± 28.2 points ($p < 0.01$). There was no statistically significant difference between groups I and II in the life quality assessing by the overall health ($p > 0.05$).

Conclusions: Using the dopamine receptor agonist pramipexole in the average therapeutic dose greatly improves the quality of life of PD patients.

Disclosure: Nothing to disclose.

Multiple sclerosis and related disorders 4

EP4230

Computer assisted cognitive rehabilitation in patients with multiple sclerosis and parenchymal neuro-Behçet's disease

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Introduction: Cognitive dysfunction is frequent in patients with multiple sclerosis (MS) and parenchymal neuro-Behçet's disease (pNBD). Cognitive rehabilitation has been proven successful in ameliorating this dysfunction, although its efficacy varies considerably. In this study, we aimed to test home-based computer assisted rehabilitation (HB-CACR) for cognitive rehabilitation in MS and pNBD.

Methods: We recruited 59 MS and 33 pNBD patients. Both groups were randomized to two subgroups. Twenty-nine of MS patients and 16 of pNBD patients were instructed to exercise HB-CACR (MSsoft v.1.0.1) for 2 days per week for 8 weeks. Neuropsychological test scores of symbol digit modalities, Addenbrook's cognitive examination, digit span, verbal fluency, Burdon attention, 10/36 spatial recall test, selective reminding, and Beck depression inventory at the end of the study period were compared with the scores at baseline.

Results: MS patients who underwent HB-CACR performed better in terms of verbal fluency ($p < 0.001$), and symbol digit modalities tests ($p = 0.035$) at the end of the study, whereas pNBD patients did not benefit from HB-CACR in any of the cognitive domains. Digit span test scores of MS patients were higher than the scores of pNBD patients at baseline ($p = 0.02$). Despite the absence of a change in cognitive domains in pNBD patients, patients who received rehabilitation showed less depression scores at the end of the study period.

Conclusions: HB-CACR seems to be effective in patients with MS. Although our software trained different domains of attention, we could detect some improvements exclusively on tasks of verbal fluency, attention, concentration and inhibition.

Disclosure: This study is partially sponsored by TEVA.

EP4231

Cognitive impairment in relapsing-remitting multiple sclerosis (RRMS): psychometric properties of the Brief Repeatable Battery of Neuropsychological tests (BRB-N)

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Introduction: Cognitive impairment in Multiple Sclerosis (MS) patients is difficult to detect in a routine neurological examination. A comprehensive neuropsychological evaluation is necessary to assess patient's cognitive status and to describe possible cognitive, emotional and behavioral disorders. The aim of the present study was to find out reference values for the Spanish version A of the Brief Repeatable Battery of Neuropsychological Tests (BRB-N) for Relapsing-Remitting Multiple Sclerosis (RRMS) patients according to their degree of disability.

Methods: Observational, cross-sectional and multicenter study. The study group consisted of 293 RRMS patients from 23 Neurology Departments in Spain. The mild disability group (EDSS scale score 0-3) included 148 patients and the moderate disability group (EDSS scale score 3.5-5.5) included 132 patients. A subgroup of 63 patients were evaluated a second time within a week interval (retest visit). Enrollment period finished in October 2013 and final results report will be ready by February 2014.

Results: Psychometric properties of the battery will be analyzed: (a) Reliability through the study of the stability of the scores between the first and the second application; (b) Convergent validity by studying the relationship between BRB-N and EQ-5D questionnaire scores; (c) Construct validity through the association between BRB-N and Beck Depression Inventory (BDI) scores; d) Predictive validity and reference values as well as cut-off points will be estimated from scores obtained in the mild and moderate disability groups.

Conclusions: Results will provide reference values of the BRB-N for RRMS patients in the Spanish population according to the degree of disability.

Disclosure: The study is funded by Novartis Farmacéutica S.A.

EP4232

Relapsing syndrome of an inappropriate antidiuretic hormone secretion in an anti-aquaporin-4 positive pediatric patient with neuromyelitis optica spectrum disorders

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Introduction: Pediatric neuromyelitis optica spectrum disorders (NMOSD) is a rare disease. Although reported in patients with NMOSD, to our best knowledge, syndrome of an inappropriate antidiuretic hormone secretion (SIADH), has not been described repeatedly in single patient.

Case report: A previously healthy girl experienced the first episode of encephalopathy preceeded by intractable vomiting at the age of 14 years. Physical examination revealed no edema, while serum biochemical analyses showed hyponatremia and criteria for SIADH diagnosis were fulfilled. Routine CSF findings were normal. Brain magnetic resonance imaging (MRI) showed nonenhancing T2-weighted hyperintensities in hypothalamus, basal ganglia and right thalamus. High-dose methylprednisolone (HDMP) for 5 days was administrated, intravenously, followed by oral prednisone tapering, and recovered completely. Eight months later, vomiting, hiccup and respiratory failure occurred. CSF analysis revealed normal findings apart from elevated protein level (2.23 g/L). Criteria for the diagnosis of SIADH were again fulfilled. She was euthyroid with elevated anti-thyreoglobulin and antithyroid microsomal antibodies, and normal/negative other serological tests for autoimmunity. New MRI lesions were detected. The patient was treated with HDMP for 5 days, with no improvement. Intravenous immunoglobulins (IVIG) were then administered (100 g/day, 2 days); patient recovered completely. Afterwards, she was treated, with IVIG, 0.4 g/kg/day, monthly, during 5 months. The patient was relapse-free for 17 months. Afterwards, she experienced cerebellar manifestations. Patient was tested for anti-aquaporin 4 antibodies in serum which were positive. Rituximab was introduced with good response.

Conclusion: Patient with pediatric NMODS may present with SIADH, even repeatedly and as one of the initial manifestations.

Disclosure: Nothing to disclose.

EP4233

NMO and NMOSD: clinical presentation, imaging, CSF, laboratory abnormalities and outcome in 50 patients

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Introduction: A little information has been published about the clinical, imaging and laboratory characteristics of NMO specially in the middle east region. We reviewed on the characteristics of a cohort of 50 Neuromyelitis optica (NMO) patients in our center In Tehran, Iran.

Methods: 50 fulfiled the 2006 criteria, analyzed for the presenting symptoms, number of recurrences, associated disorders, CSF abnormalities, anti NMO and anti MOG antibody, imaging and outcome.

Results: 13 % were male, 87 % female. Mean age was 36.76 years. Mean disease duration was 71.08 months and the mean follow up time 27.60. 34.8 % had Optic Neuritis as the presenting symptom. 43.5 % were not affected by Myelitis. 50 % had cervical myelitis and 6.5 % both cervical and thoracic myelitis. 23.9 % had atypical brain symptoms. 80.4 % had experienced recurrence from which 62.16 % had one time. 24.32 % 2 or 3 and 4.3 % more than 3. 50.1 % had EDSS between 0–2 at presentation. 26.1 % 2–4. 23.9, 4–7 at presentation. 17.4 % indicated positive NMO Abs. 30 patients did Anti MOG antibody, positive appeared in 86 %. 24.5 % had CSF from which 23.9 % were OCB positive and 23.9 % had elevated IgG index. 54.3 % had normal brain in imaging. 37 % atypical brain abnormalities in MRI.37.9 % LEMS. We found pain in 69.6, 28.3 % were misdiagnosed as MS.

Conclusions: Despite the relatively high recurrence rate Outcome revealed no significant disability. Inspite of low positivity of NMO antibody, antiMOG antibody was remarkably positive in our patients, however, further studies seem essential to prove the exact sensitivity of these laboratory tests.

Disclosure: Nothing to disclose.

EP4234

Safety and tolerability of teriflunomide in MS patients in clinical practice

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Introduction: Teriflunomide is a novel, once-daily, oral immunomodulator approved by the EMA in August 2013 for use in patients with relapsing multiple sclerosis as a first line therapy. The aim of this study is to assess the short-term safety and tolerability of teriflunomide in clinical practice.

Methods: Observational study in patients with relapsing remitting MS starting treatment with teriflunomide 14 mg in compasive use. Blood samples were obtained every month and neurological evaluation was performed at baseline and every 3 months.

Results: Data of the first 20 patients included in our center were analyzed. Mean age was 41 years (28–64), 60 % women. Mean time since onset of symptoms of 96 months (12–232) 65 % of patients had a previous first-line treatment and 20 % of them had two first-line treatments. 45 % of the patients were followed more than 6 months. The main reason for the switch was adverse events (55 %), followed by intolerance to previous treatment. The naive patients have needle phobia. Adverse events were recorded in 35 % of patients with the most frequent being very mild lymphopenia (20 %), hair thinning (20 %), mild liver enzyme elevation (<2ULN), and diarrhea (5 %). There was no case of infection. One patient discontinued the treatment due to withdrawal of consent. Only two patients forgot to take some pills.

Conclusions: The results obtained in this preliminary analysis support that teriflunomide in clinical practice was well tolerated, the adherence of the patients was very good and the short-term safety of teriflunomide was favourable.

Disclosure: Celia Oreja-Guevara received honoraria as consultant on scientific advisory boards or as speaker from Biogen-Idec, Genzyme, Almirall, Merck-Serono, Teva and Novartis.

EP4235

Abstract withdrawn

EP4236

The default mode network: the resting-state network most sensitive for cerebral functional changes over short-term in multiple sclerosis

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Introduction: Applying resting state functional MRI (RS-fMRI) in patient cohorts bears great potential to explore functional cerebral reorganization, obviating performance bias associated with task-related fMRI. Given the dynamics of the disease, multiple sclerosis (MS) represents an attractive candidate to test the feasibility of longitudinal RS fMRI to explore such changes over short-term.

Methods: For this purpose, we selected two patient groups, 9 MS patients on conventional disease-modifying treatment (DMT; glatirameracetate or β-interferons) and 11 MS patients with active disease in whom Natalizumab treatment had been initiated recently (NAT). Participants underwent structural, functional MRI, neurological and neuropsychological examinations at baseline (BL) and at 3 months of follow-up (FU).

Results: At BL, we succeeded in identifying nine networks in both groups, without any differences between groups. At FU, significant changes had occurred in only one out the nine networks, i.e., the default mode network (DMN). Functional increases were greater in the DMT group than in the NAT group, comprising the anterior and posterior cingulate, the middle frontal gyrus, the supramarginal gyrus, the occipital pole, and the cerebellum.

Conclusions: This study demonstrates that changes in RS activation in MS may already be captured over short-term. The stability (and thus reproducibility) of all but one RS networks attests to the validity of the analytical approach used. Consistent with the notion of the DMN as a critical functional hub sensitive to changes in brain integrity, the only changes observed affected the DMN changes, suggesting its potential relevance for sensitive monitoring of disease evolution in MS.

Disclosure: Nothing to disclose.

EP4237

Long-term safety of fingolimod: interim evaluation of data from the LONGTERMS trial

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Introduction: Multiple sclerosis patients participating in the fingolimod phase 2/3 core and extension studies were eligible to transfer to LONGTERMS, an open-label, multicentre, single-arm, long-term safety and tolerability study. We compared the long-term fingolimod (0.5 mg dose) safety data in the LONGTERMS study (up to data cut-off), with shorter-term (1–2 years) safety data pooled from the randomised controlled trials.

Design and methods: In this study, patients from two cohorts (Core Cohort, CC; LONGTERMS cohort, LC) were compared. Patients in CC [n = 1212; median (range) exposure: 1.6 (0.01–2.4) years] were pooled from the fingolimod 0.5 mg arms of the core phase 2/3 trials. Patients in LC [n = 1655; median (range) exposure: 3.7 (0.01–7.4)] included CC and phase 2/3 core comparator patients transitioned to fingolimod 0.5 mg in their extensions. Incidence rates (number of patients experiencing ≥1 event/100 patient–years) were determined for adverse events (AEs) of special interest.

Results: The Incidence rates for AEs of special interest were similar or lower in LC compared with CC, for: infections (LC, 68.3; CC, 91.0), skin cancer and other malignant neoplasms (LC, 0.7 and 0.4; CC, 1.3 and 0.4), thromboembolic events (LC, 0.9; CC, 1.0), hypertension (LC, 3.6; CC, 5.5), respiratory conditions (LC, 1.2; CC, 1.5) and reactivation of viral infections (LC, 5.3; CC, 5.9).

Conclusions: With long-term use of fingolimod (median: 3.7 years), incidence rates for AEs of special interest were comparable with those in controlled studies. There were no new safety signals detected with the long-term use of fingolimod.

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EP4238

Cognitive and neural correlates of TNFRSF1A gene polymorphism (rs1800693) in multiple sclerosis

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Introduction: TNFRSF1A encodes a major receptor for the tumor necrosis factor-alpha. Its functional genome-wide supported multiple sclerosis (MS) risk variant (rs1800693) has recently been the focus of intense research. However, these studies have not demonstrated any associations between clinical disability and global radiological indices with the rs1800693 genotype in MS. Here we investigated the impact of this polymorphism on regional neuroanatomical measures and cognitive performance in MS patients.

Methods: Eighty-nine individuals with relapse-onset MS underwent structural brain MRI, clinical examination and cognitive assessment with SDMT, PASAT and CVLT. Association between test scores and genotypes were assessed using general linear models, with age and gender as covariates. Vertex-wise analysis of cortical thickness and surface area were carried out using the CIVET pipeline (Lerch and Evans 2005).

Results: Results from the MANOVA with three cognitive measures as the dependent variables revealed a significant main effect for rs1800693 genotype status [Wilks' λ $F_{3,72} = 3.485$, $P = 0.02$]. G-allele carriers performed significantly worse in SDMT [$F_{1,85} = 7.2$, $p = 0.009$] and PASAT [$F_{1,78} = 4.2$, $p = 0.044$], whereas no significant gene effect was observed for CVLT scores. Vertex-wise analysis—while covarying for EDSS, age and gender—demonstrated bilateral decreased surface area in medial temporal area (parahippocampal gyrus) and the left occipital pole, with increasing G-allele dosage. Only left-sided surface area changes remained significant after correction for multiple comparisons (at false discovery rate <10 %).

Conclusions: Our findings demonstrate how a genome-wide supported MS-risk variant could regionally impact brain structure and result in specific pattern of cognitive deterioration in the course of the disease.

Disclosure: Nothing to disclose.

EP4239

Acute disseminated encephalomyelitis in a natalizumab treated patient

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Introduction: Natalizumab is a highly effective treatment for relapsing-remitting multiple sclerosis (RRMS) patients. It implies close follow-up, mainly regarding PML-risk.

Clinical case: A 26-year-old male with RRMS treated with Natalizumab for 28 months and JC virus seronegative (at 12th month of treatment) started rapid progressive headache, vomiting, fever and consciousness impairment. Cerebral CT angiogram was normal and CSF was hemorrhagic with pleocytosis and increased proteinorrachia. Empiric antibiotics were initiated. His alertness was fluctuating, he had frontal and left pyramidal syndromes. EEG suggested encephalopathy. Brain MRI showed generalized white matter T2-hyperintense lesions, including corpus callosum, not suggesting PML. Microbiological and serological studies were negative but showed JC virus seroconversion; blood, urine and CSF samples were JC-negative, even with high sensitivity techniques. On day 24, patient became comatose and MRI showed aggravation, including thalamic lesions and extensive spinal cord involvement. Aquaporin-4 antibodies were negative. Intravenous high dose corticosteroids were ineffective. Brain biopsy showed active demyelinating process without infection (including JC virus) or neoplasm. He was submitted to plasmapheresis, with progressive clinical/imaging improvement and CSF normalization. After 9 months without disease modifying treatment, he suffered another relapse (motor), starting Copaxone®. Five months later, another motor relapse, with new active lesions on MRI, starting Fingolimod. Actually, after 17 months, his EDSS is 5 and he has recovered autonomy.

Conclusion: As far as we know, this is the only reported case of ADEM in a Natalizumab treated patient. It was a severe life-threatening condition which etiology remained unknown after extensive investigation, but plasmapheresis was effective.

Disclosure: Nothing to disclose.

EP4240

Language performance in patients with multiple sclerosis: a linguistic approach

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Introduction: Language is frequently impaired in Multiple Sclerosis (MS). No comprehensive study has yet been done investigating MS abilities in all the major language domains. The aim of this research was to investigate whether different levels of language production were altered in patients with MS, and to compare those results with a control group.

Methods: 50 MS patients and 50 healthy control subjects matched by age and education were studied. First of all participants were instructed to talk about their life for 15–20 min and then one receptive and one expressive test was used for each of syntax, semantics, phonology, and written language to assess patterns in MS language skills. The patients were then divided according to MS subtype.

Results: The results of the group analysis indicate that MS patients are significantly impaired in receptive syntax, word-finding, spelling and non-word repetition. Syntax was impaired in exactly half of each subset, and double dissociations were seen between syntax and semantics. An individual analysis showed that subsets of individuals are significantly impaired all the major language domains in patients with MS.

Conclusions: MS patients should be investigated for language difficulties clinically, as they may well benefit from speech and language therapy. Furthermore, evidence of language impairment following from subcortical damage is of interest to the field of linguistics and neurology, and might prove fruitful for investigators interested in the neural substrates of language. Language impairment could be an early warning sign of MS, and this possibility is worthy of further investigation.

Disclosure: Nothing to disclose.

EP4241

Effects of different natalizumab treatment modalities on pharmacokinetics and -dynamics

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Introduction: Natalizumab inhibits leukocytes migration into CNS blocking VLA-4. In long-term treatment natalizumab exerts significant effects on central immunosurveillance leading to substantial risk for PML. Little is known about effects of long-term treatment compared to infusion intervals or treatment holidays on immune cell VLA-4-expression, cell-bound and free natalizumab.

Methods: Measures of free and cell-bound natalizumab concentrations in addition to VLA-4-expression was done by FACS-based-assay. Blood samples from 10 natalizumab treated MS-patients were drawn including baseline, month 1, 2, 3, 6, 9, 12, 24 and 36. Infusion intervals of 4, 5 and 8 weeks and treatment holidays versus restart were analyzed.

Results: After initiating natalizumab, VLA-4-expression significantly decreased whereas cell-bound natalizumab and saturation increased. During long-term treatment stable values of cell-bound natalizumab and saturation where presented while VLA-4-expression demonstrated constant decrease. A high inter-individual variability was detected. Free natalizumab concentration remained stable during 3 years follow up. Extension of treatment intervals caused significant lower concentrations of free and cell-bound natalizumab in periphery and CSF. After natalizumab cessation, free and cell-bound natalizumab and saturation constantly reduced, VLA-4-expression ran opposed. Three up to 5 months after last infusion, 4/5 patients developed severe relapses. At relapse, only low amounts of free natalizumab could be detected in serum and CSF. After restart, parameters proceeded as seen in long-term treatment.

Conclusions: We present different pharmacokinetics and -dynamics of cell-bound and free natalizumab and VLA-4-expression during several natalizumab treatment-modalities. Evaluation of these parameters could be potential monitoring and dosing tool for effectiveness and safety in natalizumab therapy.

Disclosure: K. Thomas received personal compensation for oral presentation from Novartis. T. Ziemssen received personal compensation from Biogen Idec, Bayer, Novartis, Sanofi, Teva, Synthon for consulting services. He received financial support for research activities from Bayer, Biogen Idec, Novartis, Teva, Sanofi Aventis. U. Hainke and T. Sehr have nothing to disclose.

EP4242

Effect of aspirin pretreatment or slow dose titration on number and duration of flushing and gastrointestinal (GI) events associated with delayed-release dimethyl fumarate

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Introduction: A study in healthy volunteers evaluated the effect of aspirin (ASA) pretreatment and slow dose titration (SDT) on the incidence and severity of flushing and GI events with delayed-release dimethyl fumarate (DMF). Here we report number and duration of these events.

Methods: Subjects were randomized to four groups: PBO/PBO received placebo ASA 30 min before placebo delayed-release DMF (weeks 1–8). PBO/DMF received placebo ASA 30 min before delayed-release DMF (weeks 1–4), then delayed-release DMF alone (weeks 5–8). ASA/DMF received ASA 30 min before delayed-release DMF (weeks 1–4), then delayed-release DMF alone (weeks 5–8). In both groups, delayed-release DMF was dosed at 120 mg BID (week 1) and 240 mg BID (weeks 2–8). PBO/SDT received placebo ASA 30 min before delayed-release DMF (weeks 1–4), then delayed-release DMF alone (weeks 5–8); delayed-release DMF was administered with SDT (120 mg QD [week 1], 120 mg BID [week 2], 240 mg morning/120 mg night [week 3], 240 mg BID [weeks 4–8]). Flushing and GI events were rated in an eDiary.

Results: In PBO/PBO, PBO/DMF, ASA/DMF, and PBO/SDT, respectively, mean (median) number of overall flushing events in weeks 1–4 was 5.1 (0), 25.8 (23.0), 11.7 (2.0), and 24.5 (18.0), and in weeks 5–8 was 3.7 (0), 28.0 (22.0), 15.9 (6.5), and 21.6 (15.0); median duration (minutes) of flushing in weeks 1–4 was 57.3, 61.8, 53.8, and 62.5, and in weeks 5–8 was 60.0, 54.6, 68.7, and 53.7. GI results will be presented.

Conclusions: ASA reduced number but not duration of flushing events. SDT had no effect on the flushing event profile.

Disclosure: Study supported by: Biogen Idec, Inc.

EP4243

Safety and tolerability of delayed-release dimethyl fumarate administered as add-on therapy to beta interferons or glatiramer acetate in relapsing-remitting multiple sclerosis (RRMS) patients

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Introduction: Here we describe the safety and tolerability of delayed-release dimethyl fumarate (DMF) as add-on therapy to beta-interferons (IFNβ) or glatiramer acetate (GA) in the Phase 2, open-label EXPLORE study.

Methods: Eligibility criteria included age 18–55 years, RRMS diagnosis (McDonald criteria), EDSS score 0–5.0, established therapy with the same dose of IFNβ or GA for ≥12 months, and ≥1 relapse within 12 months or gadolinium-enhancing lesion(s) on MRI within 6 weeks prior to enrolment. Patients continued on their prescribed MS therapy for 2 months (monotherapy period), then received delayed-release DMF 240 mg three times daily (TID) in addition to their prescribed MS therapy for 6 months (add-on therapy period).

Results: During the add-on therapy period, in the delayed-release DMF/IFNβ (n = 57) and delayed-release DMF/GA (n = 47) groups, the overall incidence of adverse events (AEs) was 95 and 100 %; the most common AEs were flushing (42 and 53 %), diarrhea (32 and 15 %), and abdominal pain (21 and 6 %). Most AEs were reported as mild or moderate in severity. There was no overall increased risk of infection. No malignancies were reported. At week 24, mean percentage decrease of lymphocyte counts from baseline was 22 % (delayed-release DMF/IFNβ) and 7 % (delayed-release DMF/GA). There was a transient increase in liver transaminases; no case fulfilled Hy's law. There were no deaths.

Conclusions: The safety profile of delayed-release DMF in combination with IFNβ or GA was similar to the known safety profile of delayed-release DMF monotherapy.

Disclosure: Study supported by: Biogen Idec, Inc.

Neurogenetics 2

EP4244

Cerebral metabolism of glucose in mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes

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Mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes—(MELAS) is one of the family of mitochondrial cytopathies. A feature of these diseases is that they are caused by defects in the mitochondrial genome which is inherited purely from mothers. Our aim was to study investigate cerebral metabolism by 2-[18F]fluorodeoxy-D-glucose uptake using PET and cerebrovascular reverse capacity by transcranial Doppler sonography in MELAS. Previous studies on some mitochondriopathie's patients revealed

abnormal accumulations of mitochondria in endothelium, smooth muscle cells, in blood vessels, different parts of CNS (thalamus, cerebellum) and skeletal muscle. Some investigators suggested a pathogenic role of vascular involvement in the MELAS syndrome and other encephalopathies. The patients were divided into three groups: interictal MELAS (6); progressive external ophthalmoplegia (8); and pure mitochondrial myopathy and neuropathy (10). The results were compared with normal control subjects. The diagnoses were based on clinical phenotype and histopathologic and molecular analysis. Cerebral glucose uptake was impaired in 6 patients, with and without CNS symptoms, particularly in the occipital and parietal lobes. The vasoreactivity of the small arterioles to acetazolamide did not differ significantly between patients and healthy control subjects or between the different groups of mitochondrial disorders. MELAS does not appear to be a functional disturbance of arterioles leading to ischemic vascular event. The clinical symptoms in MELAS are not the result of a mitochondrial angiopathy but are the consequences of a mitochondrial cytopathy affecting neurons or glia. There is no correlation between the decreased glucose metabolism and the duration of the disease.

Disclosure: Nothing to disclose.

EP4245

Cerebellar ataxia with CoQ10 deficiency due to a novel mutation in ADCK3

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Background: Inherited ataxias are a group of heterogeneous neurodegenerative disorders transmitted by either an autosomal dominant or a recessive trait. It has been reported that cerebellar ataxia and coenzyme Q10 (CoQ10) deficiency were associated, and, in some cases, carried ADCK3 gene mutations.

Objective: To report a case of adult onset cerebellar ataxia with a severe muscle CoQ10 deficiency due to a novel homozygous mutation of ADCK3 gene.

Case report: We report a 48-year-old man that, since he was 20 years old, complained of a mild gait imbalance. Neurological examination revealed ataxic gait, dysarthria, mild bilateral ptosis, dysmetria and dysdiadochokinesia. Brain MRI showed mild cerebellar atrophy. EMG showed slight neurogenic changes. Serum lactate was increased. Muscle biochemistry revealed a severe reduction of complex II + III activities. Fibroblasts evidenced spared capacity and coupling efficiency in the lower range of controls and normal mitochondrial respiratory chain enzymes activities. CoQ10 was severely decreased in skeletal muscle and normal in fibroblasts. Molecular studies revealed a novel homozygous two base deletion (p.504del_CT) in ADCK3 gene causing a premature stop codon in the kinase domain of the protein. The patient started supplementation with 600 mg/day of CoQ10. After a year of treatment, a follow up revealed no clinical improvements.

Conclusions: Molecular diagnosis of cerebellar ataxic syndromes represents a challenge for neurologists. When the most common causes of recessive ataxias have been excluded, CoQ10 level need to be measured in skeletal muscle because its deficiency is potentially treatable.

Disclosure: Nothing to disclose.

EP4246

ARCA3 due to *ANO10* mutations: delineation and genotype/phenotype correlation study

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Introduction: *ANO10* mutations have been reported to cause a novel form of autosomal recessive cerebellar ataxia (ARCA). Our objective was to report 9 ataxic patients carrying 8 novel *ANO10* mutations to improve the delineation of this form of ARCA and provide genotype/phenotype correlation.

Methods: Between 2010 and 2013, 186 unrelated index patients were consecutively recruited in 4 tertiary centers for inherited neurodegenerative disorders. Genetic analysis of *ANO10* was performed in 44 patients by conventional Sanger sequencing. 142 patients were directly analyzed by a targeted exon-capture strategy coupled with multiplexing and high-throughput sequencing of 57 genes causing ataxia when mutated, including *ANO10*. Detailed phenotype of patients with *ANO10* mutations was investigated and compared to the 12 previously reported cases.

Results: Mean age at onset was 33 (17–43) and disease progression was slow. Cortico-spinal tract signs were frequent including extensor plantar reflexes and/or diffuse tendon reflexes and/or spasticity. No patient of our series had peripheral neuropathy. Brain MRI showed marked cerebellar atrophy. The most frequent mutation, a mononucleotide expansion from a polyA repeat tract (c.132dupA) and causing protein truncation, was never observed in homozygosity. Only two truncating mutations were reported in homozygosity, one of which (c.1150-1151del) was associated with juvenile/adolescent onset and mental retardation while we show that the presence of at least one missense or also in-frame mutation is associated with adult onset and slow progression.

Conclusions: ANO10 defect is responsible for ARCA mainly characterized by cerebellar atrophy and lack of peripheral neuropathy. We therefore suggest naming this entity ARCA3.

Disclosure: Nothing to disclose.

EP4247

No excess of loss-of-function variants in *COQ2* in pathologically confirmed multiple system atrophy

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Introduction: The etiology of MSA is obscure. The only reported association is with variants in the *SNCA* gene, and recently, Mitsui et al. reported an association with *COQ2* variants in familial and sporadic clinically-diagnosed Japanese patients. The *COQ2* paper was based on linkage analysis in MSA families and genome-sequencing which detected homozygous and compound heterozygous *COQ2* variants in two families. A yeast complementation assay found decreased growth rates in *COQ2* mutants, consistent with the view that the association with disease was caused by loss-of-function.

Methods: In a multicentre collaboration, we collected ~ 300 neuropathologically proven MSA cases. We sequenced the coding region in the longest transcript of *COQ2* in definite Caucasian cases and 262 British controls.

Results and conclusions: We identified a *COQ2* nonsense mutation that was present at higher frequency in controls than in MSA (R22Stop, 24 vs 9 alleles, $P < 0.0024$) and two other variants which were also found at higher frequency in controls (rs6818847 and rs6535454). No association between the synonymous *COQ2* SNPs rs183012002 and rs1129617 was observed. Four heterozygous rare coding-variants were detected: the p.S57T mutation reported by Mitsui et al. was present in one case and one control, the p.P68S variant was present in one MSA case as was rs121918231, and the rare SNP rs183012002 was identified in 2 MSA cases and 6 controls. These data suggests that loss-of-function of *COQ2* variants are not associated with MSA in Caucasians and suggest that the reported association in the Japanese population should be re-evaluated in further populations.

Disclosure: Nothing to disclose.

EP4248

Bladder and bowel dysfunction in female carriers of X-linked adrenomyeloneuropathy

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Introduction: Adrenomyeloneuropathy (AMN) is, an X-linked disorder caused by mutations of the ABCD1 gene, and characterized by involvement of the spinal cord and peripheral nerves. The aim of this study was to evaluate bladder and bowel symptoms in men with AMN and female carriers.

Methods: In this cross-sectional study, AMN patients attending a tertiary care service completed standardized questionnaires for bladder and bowel, i.e., the Urinary Symptom Profile (USP), Qualiveen Short Form (SF-Qualiveen), International Prostate Symptom Score (IPSS) and the neurogenic bowel dysfunction (NBD) questionnaires.

Results: Forty-eight patients participated, 19 males [mean EDSS score ($n = 16$) 3.9 (0–8.0)] and 29 females [mean EDSS score ($n = 25$) 3.2 (0–8.0)]. Overactive bladder (OAB) symptoms were common in both males (100 %, $n = 19$) and females (86.2 %, $n = 25$). There was no significant gender difference in severity of OAB symptoms ($P = 0.35$) and impact on quality of life ($P = 0.13$). Furthermore, there was no significant difference in OAB severity when symptoms were compared between female carriers and a cohort of women ($n = 17$) with spinal cord damage due to multiple sclerosis ($P = 0.27$). Twenty-one percent ($n = 4$) of males and 10 % ($n = 3$) of females had moderate to severe bowel dysfunction.

Conclusions: Bladder and bowel complaints are common in AMN and have a significant impact on quality of life, yet are under-recognized and under-treated. Female carriers in this X-linked disorder can experience bladder symptoms as severe as in males, and comparable to bladder symptoms following spinal cord damage from other causes.

Disclosure: Dr Tudor is a recepient of EFNS Department—Department Co-operation Programme.

EP4249

The dystrophin gene and cognition in the cognitively healthy population

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Introduction: Mutations in dystrophin gene (*DMD*) have been recognized as a cause of the most common form of muscular dystrophy during childhood, Duchenne muscular dystrophy (DMD). The DMD patients have increased risk for intellectual disability and neurocognitive function impairment and a higher incidence of different neuropsychiatric disorders, such as autism spectrum, attention deficit hyperactivity disorder and obsessive–compulsive disorders. The aim: To investigate whether single nucleotide *DMD* variants associate with variability in cognitive functions in healthy populations.

Methods: The study included 2,704 participants from the Erasmus Rucphen family (ERF) and Rotterdam Study (RS) whose exomes were sequenced and who were assessed for various cognitive traits. The association between *DMD* variants and cognitive ability was determined using linear (mixed) modeling with adjustment for age, sex and education.

Results: We found evidence of association of rs147546024 ($\beta = 1.786$, p-value $= 2.56 \times 10^{-4}$) with block design test in ERF and rs1800273 with block design test in ERF ($\beta = -0.424$, p-value $= 0.066$) and Mini-mental state examination test in the RS ($\beta = -0.465$, p-value $= 0.002$). Both variants are highly conserved, although rs147546024 is an intronic variant with unknown effect on the protein, whereas, rs1800273 is a missense variant in the *DMD* which has a predicted damaging effect on the protein.

Conclusions: The analysis of sequence variants in the exon of *DMD* suggests the existence of variants in the *DMD* which may effect cognitive functioning in the general populations. Larger studies are required for confirmation.

Disclosure: Nothing to disclose.

EP4250

Relapsing remitting multiple sclerosis in X-linked Charcot-Marie-Tooth disease with central nervous system involvement

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Introduction: X-linked Charcot-Marie-Tooth disease (CMTX) is a hereditary sensorimotor neuropathy caused by mutations in the *GJB1* gene coding for connexin-32 (Cx32). Cx32 is a gap junction protein expressed in peripheral Schwann cells, but also found in oligodendrocytes within the central nervous system (CNS). Subclinical CNS involvement, documented on brain MRI or electrophysiological tests and, less commonly, clinical involvement ranging from extensor plantars to acute transient encephalopathy, can be observed in patients with CMTX. To date, there have been two case reports of patients with CMTX that developed CNS demyelinating disease compatible with the diagnosis of multiple sclerosis (MS).

Case report: We report a patient who developed clinically typical relapsing remitting MS with characteristic MRI findings and also had CMTX, carrying a novel *GJB1* mutation affecting Cx32 (c.191G>A, p. Cys64Tyr). This report is unique compared to previous similar cases in that other family members carrying the same mutation were documented as having mild clinical or subclinical CNS involvement, with diffuse white matter hyperintensity on brain MRI.

Conclusions: Although the co-occurrence of MS and CMTX may be a chance association, the increasing number of cases reported, especially with GJB1 mutations appearing to affect the CNS, may imply some causative effect and provide insights into MS pathogenesis.

Disclosure: Nothing to disclose.

EP4251

Monogenic ischemic stroke in young adults: A 5-year experience at the Neurological Institute of Pisa, Italy

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Introduction: Ischemic stroke is a complex disorder resulting from the interplay of genetics and environment. In some instances (especially in young adults) stroke is the direct result of a monogenic disease. Ischemic stroke in young adults is a major health problem being associated with increased morbidity and mortality and with a stroke recurrence rate of 25 % during the first decade. However, exact epidemiological data are not known. Identifying the cause of ischemic stroke in young adults might be of major importance to prevent stroke recurrence.

Methods: A total of 120 cases (55 % women) aged 18–55 years who developed a first ischemic stroke were identified in the Cerebrovascular Register of our Institut (2008–2013). After exclusion of 55 patients with identified stroke cause (e.g., cardiologic, thrombophilic and/or immunological conditions), we evaluated the etiology in the remaining 65 cases.

Results: We identified three MELAS cases, two cases of Fabry disease, six CADASIL cases, one pseudoxanthoma elasticum, one hereditary hemorrhagic telangiectasia and one case of Moya–Moya. The percentage of molecular proven genetic stroke in our juvenile population was 10.8 % (13/120).

Conclusions: Given the wide variety of potential underlying causes, the diagnostic work-up of stroke in young adults requires a different approach from that in the elderly. Once excluded medical conditions potentially causing stroke, a comprehensive genetic screening should be performed. Despite such a comprehensive work-up, about 80 % of cases will remain unexplained, leading to the diagnosis of idiopathic ischemic stroke.

Disclosure: Nothing to disclose.

EP4252

Hereditary spastic paraplegias: design of a diagnosis kit using next generation sequencing

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Introduction: Hereditary spastic paraplegias (HSP) are heterogeneous neurological disorders that can be explained by mutations in $\sim$70 genes. Phenotype-genotype correlations exist for few genetic entities but it is often impossible to predict the mutated gene on the basis of clinical grounds which complicates genetic diagnosis in clinical practice.

Methods: We designed a diagnosis kit to sequence 34 HSP genes simultaneously. All coding exons of groups of 12 patients (multiplexing) are captured in two successive assays using ROCHE/NIMBLEGEN probes and then sequenced on the Miseq sequencer (ILLUMINA). The results were analysed using Genomics Workbench (CLC Bio).

Results: Data analysis of 60 patients (including 8 with known genotypes) indicated that 95 % of the sequence reads mapped to the targeted human genomic regions, indicating high specificity of the designed probes. <3 % of the targeted regions were not captured. 96 % of target bases were covered >50×. All known variants were detected and included single nucleotide variations (SNV), insertions, deletions (up to 29pb), and exon inversion.

In patients with unknown genetic status, a mean of 25 variants were identified. Data filtering based on their nature, effects and frequency in public exomes pinpointed 1–3 variants in 50 % of the patients, including a duplication, two exon deletions and a large deletion of 3 successive exons that are under validation (Sanger sequencing, cosegregation analysis and CGH).

Conclusion: The combination of targeted exon capture and next generation sequencing is efficient to detect SNV and rearrangements in HSP patients and to reduce cost/time in clinical practice.

Disclosure: Nothing to disclose.

EP4253

Effects of polymorphisms of the CXCR5, TNFSF14 and SLC30A7 genes in multiple sclerosis patients in Csongrád County in Hungary and the North-Bácska region in Serbia

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Introduction: Multiple sclerosis (MS), an inflammatory autoimmune disease affecting the central nervous system, is potentially the most common cause of neurological disability in young adults. Genetic factors and environmental impacts have been implicated in the aetiology. The major histocompatibility complex has been reported to be the strongest genetic susceptibility factor, but there are single nucleotide polymorphism (SNP) differences, which may be protective or risk factors. In the present work, three loci have been associated with MS.

Methods: Taqman probes were applied for allele discrimination in the 477 MS (relapsing-remitting or secondary progressive) and age and sex-matched 481 control samples. For data evaluation, SPSS software version 20.0 was used.

Results: Our results indicated the association of the SNP rs630923 (located in the CXCR5 gene) genotype with MS ($p = 0.029$); the protective effect of the A allele was confirmed ($p = 0.010$). Two further genes influenced the age at onset of the disease. The A allele of the TNFSF14 gene rs1077667 polymorphism showed a protective effect ($p = 0.031$), whereas the G allele was a risk factor ($p = 0.0079$). The G allele of the SLC30A7 rs11581062 polymorphism was identified as a risk factor as concerns the age at onset of the disease ($p = 0.013$).

Conclusions: Our results verify the connection of these three newly identified MS risk loci with the disease, and demonstrate for the first time the impact of the SNPs of these two genes on the age at onset of MS.

Disclosure: Nothing to disclose.

EP4254

Gene expression profiles in neuro-Behcet's disease during active and inactive stages

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Introduction: Neuro-Behcet Disease (NBD) primarily causes lesions in the brain parenchyma but rarely it can also lead to dural sinus thrombosis (vascular). In individuals with genetic susceptibility, microorganisms as well as several environmental factors are believed to trigger the inflammation attacks.

Methods: To determine gene expression differences in parenchymal and vascular NBD subtypes and uncover genetic factors causing NBD attacks, whole-genome expression profiles were examined in the peripheral blood mononuclear cells of 1 vascular and 3 parenchymal NBD patients during active and inactive stages using gene expression microarray method by Illumina Human HT12 BeadChip. Raw data were analyzed by GenomeStudio Gene Expression Module v1.0. Quantile normalization and log transformation were performed by bioconductor and R-package. Genomic differences between active and inactive stages were calculated by rank product method.

Results: Genes with more than 2-fold expression increase during active stage (with a significance of $p \leq 0.05$) were defensin alpha 1, defensin alpha 3, olfactomedin 4 and neutrophil expressed elastase. Both vascular and parenchymal NBD patients displayed a significant increase in the expression of these four genes.

Conclusions: Defensins and elastase are involved in anti-microbial host defense, whereas olfactomedin 4 is an anti-apoptotic factor. All four differentially expressed factors are primarily produced by neutrophils and NK cells emphasizing the significance of these cell subsets in NBD pathogenesis. Vascular and parenchymal NBD patients overexpress identical genes suggesting that anatomical allocation of NBD lesions is regulated by environmental rather than genetic influences. Our studies need to be validated with larger number of patients.

Disclosure: Nothing to disclose.

EP4255

Progressive external ophthalmoplegia - a common phenotype of SPG7 in Norway

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Introduction: Spastic paraplegia 7 (SPG7) is an autosomal recessive form of Hereditary Spastic Paraplegia (HSP) caused by mutations in the SPG7 gene, which encodes paraplegin, a member of the AAA family of ATPases, located at the inner mitochondrial membrane. Respiratory chain dysfunction has been reported in muscle in SPG7 patients, but the molecular aetiology of the disease remains unknown. We have previously reported secondary mtDNA damage in SPG7 patients. We report a novel SPG7 mutation in four Norwegian families presenting with a phenotype consistent with mitochondrial disease.

Materials and methods: Patients from four Norwegian families with a phenotype of progressive external ophthalmoplegia (PEO) and spastic paraplegia were examined clinically. Of four index patients, Sanger sequencing of the SPG7 gene was done in two, and exome sequencing done in two.

Results: By Sanger sequencing of the SPG7 gene we found a novel SPG7 missense mutation in two families, c.2102A>C, which was homozygous in the first family and compound heterozygous in trans with the known pathogenic mutation c.1454_1462del in the second family. Exome sequencing in two patients from two other families showed compound heterozygous mutations with c.2102A>C and c.1529C>T.

Discussion: We report a novel SPG7 mutation causing a complex HSP phenotype with PEO, a common mitochondrial disease phenotype. Exome sequencing proved to be a good diagnostic method. Our findings confirm that PEO is not an uncommon presentation of this disorder, and we recommend SPG7 gene analyses to be included in the diagnostic workup of autosomal recessive PEO, especially when spasticity is present.

Disclosure: Nothing to disclose.

Neurological manifestation of systemic diseases

EP4256

Anti-aquaporin 4 autoantibodies in patients with systemic lupus erythematosus without CNS involvement: a long-term assessment

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Introduction: Anti- AQP4 autoantibodies are specific for the Neuromyelitis Optica-Spectrum Disorders (NMOSD). They have been previously described in patients with Systemic Lupus Erythematosus (SLE) who concurrently have neurological signs consistent within NMOSD. Whether these autoantibodies are also present in the sera of non-CNS-SLE patients, is unknown.

Methods: Sera from 89 non-CNS-SLE patients identified by clinical record review were screened for anti-AQP4 autoantibodies by an in-house cell-based-assay (CBA) using M23-AQP4-transfected cells. Seropositivity was confirmed by a commercial CBA assay. Archived samples from seropositive patients, obtained over a 10-year period were also analyzed.

Results: Two out of 89 (2.2 %) of non-CNS-SLE patients were anti-AQP4 seropositive. Archived samples (7 and 16 from each patient, dating back 8 and 10 years, respectively) were also AQP4-positive as confirmed by both assays. These AQP4-positive SLE patients are women with disease duration of 16–17 years, a mild type of renal involvement and a wide spectrum of other autoantibodies. Both patients had never exhibited any CNS-related symptoms based on neurologic examination. A current brain and spinal cord MRI did not reveal any NMOSD-compatible lesions.

Conclusions: AQP4-antibodies are present in some SLE patients and persist for many years, even without developing clinical or MRI signs of NMOSD. It is a possible that the antibodies in these patients result from the underlying polyclonal B cell activation of the immune system, typical for SLE, and may not be pathogenic. Alternatively, the possibility that the antibodies might herald the potential of developing CNS disease even after a decade, cannot be excluded.

Disclosure: Nothing to disclose.

EP4257

Abstract withdrawn

EP4258

Cerebral vasculitis: a report of 17 cases

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Introduction: Cerebral vasculitis (CV) is rare. They may be primary or related to systemic, infectious or neoplastic diseases.

Methods: Retrospective study of 17 cases of CV. All patients underwent a neurological and ophthalmological examination, cerebral imaging and immunological analysis.

Results: There were 11men and 6 women, whose mean age: 56 years (25–75 years). The history was noteworthy with arterial hypertension in 1 patient, diabetes in 2 patients, pulmonary embolism in 1patient, retinal vasculitis in 1 patient and meningioma in 1 patient. The CV was diagnosed at primarily motor impairment in 6 patients, headache in 4 patients, dementia in 2 patients, intracranial hypertension in 2 patients, coma and in 1patient and psychiatric disorders in 2 patients. Five patients had generalized tonic–clonic seizures. All patients had T2 hyperintensities in the periventricular white matter in 13cases, in the brainstem 2 cases and in the cerebellum in 2 cases. CV was secondary to Behçet's disease in 5cases, Sjogren's syndrome in 4 cases, giant cell arteritis in 3 cases, systemic lupus erythematosus in 2 cases, antiphospholipid syndrome in 2 cases and Susac syndrome in 1 case. All patients were treated with high dose corticosteroids regimen, associated with Cyclophosphamide in 2 cases, Azathioprine in 2 cases, anticoagulant drugs in 3 cases and antiplatelet drugs in 13 cases. The outcomes were quite favorable with complete or partial recovery of neurological deficit in 16 cases and disappearance of psychiatric disorders in 1 patient.

Conclusions: We present different clinical features of CV, main causes, its management and prognosis. The diagnosis is held on a basis of clinical, biological and MR findings even if the definite diagnosis is based on cerebral biopsy.

Disclosure: Nothing to disclose.

EP4259

A case series of giant cell arteritis: vascular risk factors, manifestations and diagnostic evaluation

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Introduction: The giant cell arteritis (GCA) is the most common vasculitis after the age of 50. It is more frequent in the female gender. The mainstays of GCA diagnosis are: clinical judgment, exclusion of other diagnosis and temporal artery biopsy.

Methods: We conducted a retrospective, transversal study of patients with GCA hospitalized between 2006 and 2012. The aim of this study was to characterize the hospitalized population with GCA concerning vascular risk factors, manifestations of the disease, and diagnostic evaluation.

Results: We included 30 patients with ACG. The mean age at the diagnosis was 74.8 years and the female:male ratio was 2:1. Hypertension was present in 70 %, hyperlipidemia in 40 %, diabetes in 20 % of patients and 17 % were smokers. Five (17 %) patients had a stroke as first manifestation of GCA. The classification criteria (American College of Reumatology 1990) were fulfilled in 87 % of patients. Fourteen temporal artery biopsies were performed and 79 % had compatible alterations. Forty-five percent of the 22 temporal artery Doppler ultrasound done had compatible alterations with GCA.

Conclusions: The mean age and the gender ratio are similar to other series of GCA. The higher prevalence of stroke comparing to other series may be due to the high prevalence of vascular risk factors or due to a selection bias (hospitalized patients with possible more severe disease). Temporal artery biopsy is still considered the gold standard exam to diagnose GCA, nevertheless Doppler ultrasound is an high specific, easy, accessible and non invasive exam that may help in its diagnose.

Disclosure: Nothing to disclose.

EP4260

Functional disorders in the neurology ward

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Introduction: Functional disorders are frequent in neurological practice, placing diagnostic and therapeutic uncertainty. We aim to characterize a group of patients with neurological functional disorders and determine prognostic factors.

Methods: Retrospective study in patients admitted to neurology ward with final diagnosis of functional disorder, in five years. Demographics, clinical, investigation, therapeutics and evolution were analysed.

Results: Seventy patients identified: 71.4 % female, mean age 43.2 years, admitted mainly from the Emergency Room, 35.7 % had history of psychiatric disorder and 17.1 % neurological. Most had acute presentation (51.4 % $\leq$24 h; 77.1 % $\leq$1 week) and 65.8 % with multiple symptoms, predominantly sensory deficit and paresis (42.9 %). Neuroimaging (98.6 %) and neurophysiological (41.4 %) examinations prevailed in the investigation. Only 22.9 % had psychiatric evaluation. At discharge, 37.5 % maintained symptoms and 27.1 % had complete resolution. Psychotropics were prescribed in 80 %. Inconsistencies in neurological examination (27.1 %) and findings incongruous with organic lesion (12.9 %) chiefly supported the diagnosis. At discharge, 41.4 % were referred to neurology outpatient, 27.1 % to psychiatry, 15.7 % to both. With mean follow-up of 866.4 days in 54 patients, 27.8 % maintained symptoms or had recurrences, only two were readmitted. In none the diagnosis changed to organic disorder. No association was found between prognosis and gender, previous psychiatric or neurological disorder, evolution time, clinical status at discharge, psychotropic therapy or specific outpatient referral.

Conclusions: The approach to these patients was diverse. Despite the favourable outcome in most, symptoms persisted or recurred in many and prognostic factors were not identified. The establishment of multidisciplinary follow-up and effective therapeutic strategies is warranted.

Disclosure: Nothing to disclose.

EP4261

Multifocal motor neuropathy associated with infliximab treatment

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Introduction: Multifocal motor neuropathy (MMN) is an immune-mediated disorder characterized by motor-conduction block in nerve-conduction studies. Infliximab is a TNF blocker which is used to treat inflammatory diseases. Several immune-mediated conditions have been reported as adverse events of infliximab use.

Methods: We report 2 cases of MMN associated with the use of infliximab.

Results: *Case A*: A 24-year-old male presented with a slowly progressive asymmetrical weakness of the arms, without sensory loss. He has been on treatment with infliximab for Crohn's disease for 3 years. Clinical examination revealed signs of lower-motor-neuron disease. A complete diagnostic workup was performed. Conduction studies showed motor conduction blocks in several nerves of both upper and lower limbs. *Case B*: A 82 years old female, with Crohn's disease, has a chronic mobility problem that was strongly exacerbated when she was started on treatment with infliximab 4 months before consultation. Clinical examination showed diffuse pyramidal sings in relationship with her prior condition, but also revealed flaccid and areflexic paraplegia. A complete diagnostic workup was done. Conduction studies revealed motor conduction blocks in several nerves of her legs. In both cases, infliximab was withdrawn and treatment with intravenous immunoglobulin was established.

Conclusions: The use of TNF-alfa blockers has been linked to a variety of neurological immune-mediated disorders as adverse effect. Withdrawing the offending agent and immunomodulatory therapy may be required to improve clinical outcome. MMN is a condition that has rarely been linked before to infliximab.

Disclosure: Nothing to disclose.

EP4262

Neurologic complications after bariatric surgery

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Introduction: Obesity is a major public health problem worldwide and the concern about obesity and diseases related to that is also increasing. Hence an increasing number of patients undergo various bariatric surgical procedures. However these procedures can lead to many complications and those affecting the nervous system are often particularly disabling. We describe the neurologic complications observed among 21 patients who underwent bariatric surgery.

Methods: We describe the neurologic complications following bariatric surgery in 21 patients who were seen in a tertiary referral Neurology Centre in Kuwait during a period of 3 years from 2010 to 2013.

Results: The most common neurological complication observed was painful peripheral neuropathy. Other manifestations include optic neuritis, central demyelination, polyradiculoneuropathy, myelopathy and myopathy. One patient who had been on treatment for multiple sclerosis (MS) developed rapid deterioration of disability and progression of the disease following bariatric surgery. Another patient had acute polyradiculoneuropathy and subsequently developed MS. Vitamin D deficiency was the most common nutritional deficiency detected and some had B 12 and one patient had copper deficiency. There was no definite correlation of any specific nutritional deficiency with the neurologic complications.

Conclusions: A wide spectrum of neurologic complications can occur following bariatric surgery. Proper pre-operative and post operative evaluation with intensive nutritional management and frequent follow up assessment is necessary to reduce these complications.

Disclosure: Nothing to disclose.

EP4263

Encephalopathy and neuroimaging in acute porphyria

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Introduction: The aim of the study was to characterise a spectrum of clinical manifestations and neuroimages in patients with encephalopathy and acute porphyria.

Methods: Brain MRI/CT was performed in ten well-characterised patients with acute intermittent porphyria (AIP, confirmed biochemically and genetically) in various stages of encephalopathy.

Results: Acute encephalopathy manifested as severe mental symptoms and signs of focal CNS involvement such as seizures,

Babinski signs, hemiparesis or ataxia. In all patients, acute encephalopathy was a sign of an acute attack. Other symptoms included abdominal pain (n = 8), dysautonomia (n = 10), acute motor neuropathy (n = 7) and at least 10-fold elevation of urine porphobilinogen. In two patients, focal lesions corresponded posterior reversible encephalopathy syndrome (PRES) when brain MRI/CT were performed soon after seizures. In a patient with syndrome of inappropriate antidiuretic hormone secretion (SIADH), the bright signal from the neurophypophysis was reduced. In other seven patients, brain MRI/CT was normal.

Conclusions: Seizures can predict PRES if neuroimaging was taken within a day. Focal symptoms were transient and no residual MRI lesions could be detected. The frequency of reversible brain oedema in AIP is probably under-estimated since it may be short-lasting and often indistinguishable on MRI. Mental symptoms even though severe, caused no abnormalities in brain MRI. PRES could partly explain the pathogenesis of encephalopathy in acute porphyrias. However, the primarily mechanisms disrupting blood–brain barrier, thereafter permitting access of neurotoxins (porphyrin precursors) into the CNS, are unknown. SIADH during an acute attack may result from an inappropriate release rather than an inappropriate synthesis of ADH.

Disclosure: Nothing to disclose.

EP4264

Treatment of an acute attack with severe neurological manifestations in patients with acute intermittent porphyria (AIP): haem arginate vs. glucose

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Introduction: Currently, no evidence based data of benefit for heam treatment vs. glucose to achieve neurological recovery in patients with acute intermittent porphyria (AIP) manifesting neurological deficits exists.

Methods: 14 AIP patients with a severe acute attack, complicated by peripheral neuropathy (PNP, n = 12) and/or encephalopathy (n = 3).

Acute attacks were treated with 20 % glucose-infusions (300–500 g/day, 5–12 days, n = 7) or haem arginate (Normosang®, 2.5–3 mg/kg, 4 days, Orphan Europe, n = 7) after the diagnosis of AIP was confirmed (6–52 days after the onset of an attack). The choice of treatment was based on availability of haem arginate solely.

Results: The plateau phase was detected significantly earlier in patients treated with haem than those treated with glucose (7.0 ± 2.4 vs. 10.8 ± 3.1 days, p = 0.035). Minimal improvement of muscle weakness could be recorded a week after the last infusion. In two cases, progression of neurological deficit required additional infusions of haem resulting in a second plateau phase in one case, but not in another, who died due to septicemia.

Haem arginate infused 1-4 days after the onset of recurrent attacks has prevented neurological deficits (n = 8). In contrast, the patient treated with 20 % glucose 4 days after the onset of new acute attack, experienced recurrent PNP.

Conclusion: Haem arignate is more efficient than glucose in achieving the plateau phase for progressing neurological deficits in AIP. This allows to shorten the duration of mechanical ventilation, activate patients and to prevent complications of an attack. There is no clear benefit of haem in stable or self-resolving neurological deficits.

Disclosure: Nothing to disclose.

EP4265

Acute transverse myelitis following stem cell transplantation for haematological malignancies: a series of three cases

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Matched unrelated haematopoetic stem cell transplantation (HSCT) is a high risk but potentially curative treatment increasingly used for a range of haematological malignancies. Following the procedure, a number of neurological problems can arise, including opportunistic infections, complications of bone marrow suppression, relapse of the haematological disease with neurological involvement, and a number of dysimmune phenomena such as polymyositis and inflammatory polyneuropathies.

We report a series of three cases of acute transverse myelitis (ATM) following HSCT. All were male with age ranges between 46 and 55. Two had a diagnosis of Acute Myeloid Leukaemia and one Acute Lymphoblastic Leukaemia. The first neurological symptom developed between 86 and 195 days post HSCT. In each case the presentation was of a rapidly progressive myelopathy clinically typical of ATM. All had high signal lesions within the spinal cord on MR imaging, and in two of the cases the abnormality met the radiological criteria for longitudinal extensive transverse myelitis. In each case the patients were extensively investigated to exclude an infectious or malignant aetiology for ATM. None of the patients were found to have Aquaporin 4 antibodies in the serum. A combination of treatments with steroids, plasma exchange and intravenous immunoglobulin were given, and there have been variable degrees of improvement up to full recovery.

Although there are other cases in the literature, this is the largest series of post HSCT myelopathy yet reported. Neurologists who deal with haematology units need to be aware of this syndrome and its important differential diagnosis.

Disclosure: Nothing to disclose.

EP4266

Neurological disorders in children with ichthyosis: lessons from eight patients diagnosed with Sjogren-Larsson syndrome and a patient with lamellar ichthyosis in a Rural hospital

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Introduction: Ichthyosis is a dermatological disorder with more than 28 subtypes. Some rare congenital forms like Sjogren-Larsson Syndrome (SLS) may be accompanied by neurological symptoms. SLS is a very rare (1/200,000), autosomal recessive disease and is diagnosed clinically when the classic triad including congenital ichthyosis, mental retardation and spastic paraparesia is seen in a child. In addition, other forms of ichthyosis with severe dermatological problems may rarely cause vitamin D deficiency and hypocalcemia presenting with neurological manifestations.

Method: We present clinical, laboratory and neuroradiological findings of eight patients with SLS and one patient with severe lamellar

ichthyosis who are all diagnosed in a rural hospital in Turkey and discuss neurological manifestations seen in patients with ichthyosis. Results: Four male and four female patients (aged between 2 and 19 years) with ichthyosis, mild to moderate mental retardation and severe spastic paraparesis were diagnosed clinically with SLS. All patients except one were from the same kindred. All patients had mild skeletal deformities, two patients had epilepsy and one patient had whole body tremor, additionally. Brain magnetic resonance imaging of five patients revealed symmetrical, periventricular white matter lesions which is characteristic for SLS. Ninth patient with severe lamellar ichthyosis applied to neurology clinic with moderate to severe muscle weakness and cramps. Hypocalcemia, hyperphospatemia and high alkalene phosphatase levels were detected. His symptoms recovered after replacement therapy.

Conclusion: Although skin apperance attracts most of the attention, it should be kept in mind that several neurological manifestations may also be seen in children with ichthyosis.

Disclosure: Nothing to disclose.

EP4267

Neuro-Behcet syndrome with spinal cord involvement

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Introduction: Central nervous system parenchymal involvement is named as parenchymal neuro-Behcet syndrome (NBS) or intra-axial NBS. Neurological manifestations are usually related to brainstem. In comparison to brainstem lesions, spinal cord involvement (SCI) is rarely seen in parenchymal NBS. It is reported that the prevalence of spinal NBS ranges between 2.5 and 30 %. We examined 19 NBS patients with SCI to determine clinical aspects and course of disease in this subgroup.

Methods: Nineteen patients were included in the study who attended our NBS center and were diagnosed as NBS myelitis. Clinical features and outcomes of patients were evaluated.

Results: Fourteen patients were men, five were women. Behcet Syndrome and NBS mean age at time of diagnosis were 24.2 ± 6.1 and 25.5 ± 6.6, respectively. Most patients were presented with paraparesis and/or sphincter dysfunction evolving over time and four had more than one spinal attack. Accordingly spinal cord MRIs revealed single/multiple, mostly long segment, cervical and/or dorsal lesions or spinal cord atrophy. Some patients had normal cranial imaging, others had additional cranial involvement, mainly brainstem lesions. Intravenous methylprednisolone followed by oral corticosteroids were administered for myelitis attacks. Azathioprine was the first choice of long-term treatment, in more severe or recurrent myelitis, infliximab was another option. Median follow-up was 77 months, average EDSS was 5.2.

Conclusions: Lesions in NBS myelitis are usually relatively long, located in the center of the cord with peripheral edema. Differential diagnosis is important, since NBS myelitis associated with disability is recognised in general as a poor prognostic factor.

Disclosure: Nothing to disclose.

EP4268

A subgroup of neuro-Behcet syndrome: intracranial arterial involvement

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Introduction: Parenchymal neuro-Behcet syndrome (NBS), the most common type of NBS is seen as a result of small-vessel vasculitis mainly with brainstem lesions. In non-parenchymal NBS, involvement of large vessels and dural sinus thrombosis are seen. We report 15 NBS patients with cranial arterial involvement(CAI) to determine clinical-radiological features of CAI in NBS which is extremely rare.

Methods: Fifteen patients who attended our NBS-center between 1994-2013 were diagnosed as NBS with CAI. Clinical features, risk factors(RF), prognosis were examined.

Results: All patients were men. Behcet Syndrome and NBS mean age at time of diagnosis were 31.5 ± 9.5 and 37.6 ± 13.1, respectively. One patient had hypertension, one had diabetes, one had hyperlipidemia as stroke RF. One patient had migraine, one had pulmonary-artery aneurysm, six patients were smoking, one had history of opioid use. The most frequent onset symptom was hemiparesis. Thirteen patients had middle cerebral artery infarction (AI), two had posterior cerebral AI, one had superior cerebellar AI. Echocardiography-cranial MR angiography examinations were normal except one patient had cardiac-septal hypokinesia and one had superior cerebellar artery aneurysm. After ischemia, apart from immunosupresive therapy (azathioprine and/or corticosteroid and/or colchicine), nine patients had acetylsalicylic acid (ASA), two patients had ASA-dipyridamol and one had warfarin treatment. Average follow-up was 67 months, modified-Rankin-Scale scores before and after treatment were 1.7 and 0.8, respectively.

Conclusions: Venous inflammation is the main neurological involvement in BS patients, whereas intracranial arterial involvement in NBS is rare, but it can occur during the course of disease independent of other stroke RF.

Disclosure: Nothing to disclose.

EP4269

Nocturnal seizures: a misdiagnosis of hypoglycemic episodes

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Introduction: Hypoglycemia is commonly diagnosed in Emergency departments. Nevertheless, this diagnosis may be a challenge when sympathoadrenal manifestations go unnoticed and neuroglycopenic symptoms prevail; moreover, glycemia measurement may be normal at the time of the evaluation. We report two cases who presented neuropsychiatric symptoms suggestive of nocturnal seizures, related to severe hypoglycemia.

Methods: A 40 years old type I diabetic patient, treated with insulin for five years, reported recurrent episodes of confusion,

automatisms, optical illusions and uncontrolled laugh, ocurring always during the early morning hours. They lasted from 10 to 15 min being followed by drowsiness. A 50 years old man exhibited bizarre behaviour at morning, with uninhibited and infantile conducts, always detecting normal glycemia levels at the emergency room. MRI and repeated EEG were normal in both cases.

Results: During admission, morning glycemia of 39 mg/dl was detected in the first case, and after insulin adjustment the symptomatology was solved. In the second case, a tomography performed several weeks later, showed a pancreatic insulinoma. After distal pancreatectomy symptoms did not ever recur.

Conclusions: The most frequent causes of hypoglycemia are sulphonilureas or insulin; other include alcohol, Addison's disease or insulinoma, which is the most common cause of endogen hyperinsulinemic hypoglycemia. In large series, 20 percent of patients with unknown insulinoma had been misdiagnosed of a neurologic or psychiatric disorder. Serial determinations of glycemia are mandatory in the evaluation of a patient with any behavioural disorder or confused state, as hypoglycemia can mimic many neurologic disorders, including stroke or epilepsy.

Disclosure: Nothing to disclose.

EP4269

Abstract has been withdrawn

EP4270

Neuro-Wilson disease: about seven cases and review of the literature

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Introduction: Wilson disease is an autosomal recessive disorder of copper overlap, dominated by neuropsychiatric and hepatic symptoms. The aims is to to review the genetic aspects, diagnosis and treatment of Neuro-Wilson through a series of patient followed in the neurology department sahloul, CHU Sousse.

Methods: We report seven cases collected in the department of neurology CHU Sahloul Sousse. All patients had neurological signs with or without extraneurological symptoms. The diagnosis of Wilson's disease was based on clinical, biological and radiological result.

Results: Seven patient, two boys and five girls. The mean of age was 25.5 with an extreme ranging from 14 to 48 years. The neurological signs were reviling the disease in six patients and the most common symptoms were tremor. One patient had cerebellor ataxia and another has had seizure. Three of patients had a familial form with an autosomal recessive transmission. The ring of kayser flecher was found in one patient. Cupric balance was disturbed in all patients including one associated hemochromatosis. The cerebral MRI was pathologic in two patients with lesions in basal ganglia. All patients was treated by D penicillamine with good evolution in five patients.

Conclusions: When left untreated, the evolution of Wilson's disease is always fatal. Treatment is based on the chelating copper, zinc salts and liver transplantation.The prognosis of Wilson's disease appears even better than the neurological and liver symptoms are not pronounced.

Disclosure: Nothing to disclose.

EP4271

Abstract withdrawn

EP4272

Neurological manifestations of acute intermittent porphyria (AIP)

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Introduction: Acute peripheral neuropathy (PNP) and/or encephalopathy may occasionally develop in attack of acute intermittent porphyria (AIP). Most of the studies on neurology in porphyria were published 40–60 years ago, before the DNA-diagnostics of AIP allowing the precise diagnosis and neuroimaging became available.

Methods: 18 AIP patients with severe peripheral neuropathy and/or encephalopathy studied clinically, by neuroimaging and electroneuromyography prospectively during an acute attack and in remission (1996–2013).

Results and conclusions: PNP or encephalopathy are signs of a complicated acute attack and usually iatrogenic since they mainly develop due to administration of porphyrinogenic drugs used when the diagnosis of acute porphyria was not considered. The major pattern of PNP associated with abdominal pain, dysautonomia, CNS involvement and mild hepatopathy could be demonstrated. If more strict biochemical criteria (>10-fold increase in excretion of urinary porphobilinogen) are applied, neurological manifestations of porphyria are probably more homogeneous than described previously, which suggests that some of the neurological patients described previously may have secondary porphyrinuria rather than acute porphyria. Based on nerve conduction studies, PNP is primarily axonal. However, in severe cases definite features of demyelination appear early in the course of PNP. Porphyric encephalopathy can be visualized as a posterior reversible encephalopathy syndrome (PRES) if MRI performed within a few hours from the onset manifested with seizures. Currently the prognosis of neuropathy and encephalopathy in acute porphyria is good even in severe attacks, but physicians should be aware of a potentially fatal outcome of the disease.

Disclosure: Nothing to disclose.

Paper poster sessions

Ageing and dementia 1

PP1001

The medial temporal-lobe atrophy index relates to memory impairment in early Alzheimer's disease

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Introduction: Memory impairment is not only the earliest clinical symptom but a central and prominent feature throughout the course of Alzheimer's disease. AD-related pathological alterations in the medial temporal structures may account for the memory impairments in these patients. The Medial Temporal lobe Atrophy index (MTAi) as a simple method for assessing atrophy of the medial temporal lobe using clinically available neuroimaging. Herein we report a retrospective analysis correlating the MTAi and memory function in a subgroup of patients with MCI who converted to AD.

Methods: We took the results of the neuropsychological assessment performed to a cohort of nine patients now diagnosed with AD when they were at the MCI stage and related their scores with the MTAi at the MCI stage. We assessed the executive functioning (Stroop Test; Letter Fluency), verbal memory (California Verbal Learning Test), visual memory (Benton Visual Retention Test), visuospatial cognition (Judgement of Line Orientation), and visuoconstruction (Pentagon Copy).

Results: The MTAi correlated significantly with scores on the verbal and visual memory tests, while the MTAi did not correlate with the executive, visuospatial and visuoconstruction tests. The strongest correlations were found for the left-MTAi with scores on the CVLT and for the right-MTAi with scores with scores on the BVRT.

Conclusions: MTAi relates to memory function in early AD. More specifically, MTAi on the left side correlates with verbal memory, while MTAi on the right side correlates with visual memory. Larger prospective studies are needed to verify our results.

Disclosure: Nothing to disclose.

PP1002

Fatal familial insomnia in one patient with both D178N and E200K prion protein gene mutations

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Introduction: Hereditary prion diseases are fatal autosomal dominant disorders linked with mutations in prion protein gene (PRNP). E200K mutation have been found in patients with familial Creutzfeldt-Jakob disease (fCJD) whereas D178N mutation has been associated with both fatal familial insomnia (FFI) and fCDJ phenotypes depending upon the non-pathogenic polymorphism at codon 129, respectively *cis*-methionine or *cis*-valine. However, several genotype-phenotype correlation studies have shown large intra- and inter-familial clinicopathological heterogeneity and overlap.

Case report: A 42-year-old Portuguese man started to complain of insomnia and rapidly developed global dementia, gait freezing, multifocal myoclonus and dysautonomia. The clinical situation evolved to akinetic mutism and death, five months after the onset of symptoms. The patient's mother had died aged 62 from a similar disease. Brain MRI showed hyperintensity in the left basal ganglia on T2/FLAIR and DWI, and the ^{99m}Tc-ECD SPECT detected generalized hypoperfusion. The polysomnography disclosed disorganized sleep patterns. There was hyperproteinorraquia and absence of 14-3-3 protein in cerebrospinal fluid. Genetic sequencing of PRNP identified both D178N and E200K mutations and homozygoty for methionine in codon 129. Brain pathology revealed severe neuronal loss and gliosis in thalamic and inferior olivary nuclei and no prion protein deposition by immunohistochemistry.

Discussion: This unique case of compound heterozygosity for prion disease adds further complexity to the genotype-phenotype correlation studies. Our patient evidenced predominant FFI phenotype over the few findings resembling fCJD. We hypothesize a genetically determined earlier expression of the D178N mutation or a dominant expression of the D178N mutation over the E200K mutation.

Disclosure: Nothing to disclose.

PP1003

Relationship between cardiovascular risk factors and all cause mortality in patients with Alzheimer's disease

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Aim: To evaluate the relationship between selected cardiovascular risk factors and the all cause mortality in patients with Alzheimer's Disease (AD).

Methods: We evaluated 1,083 patients with AD (390M, 693F, mean age 76.6 ± 7.0 range 50–94 years) referred to the Department of Neurology in Warsaw through years 2000–2006. The AD was diagnosed according to NINCDS-ADRDA and DSM-IV criteria for AD. Cardiovascular risk factors, antihypertensive treatment and the results of laboratory tests were also evaluated. All cause mortality was estimated on the basis of data on deaths from the Central Statistical Office.

Results: After the mean follow-up of 4.86 years (range 0–13 years) all cause mortality was 66.1 % [714 patients of mean age 77.3 years (range 50–96 years)]. The patients who have died were characterized by older age (77.3 vs 74.1 years, $p < 0.01$) and more severe cognitive impairment (median MMSE score 17 vs 20, $p < 0.01$) as compared to the patients who stayed alive during follow-up. There was no difference in the gender distribution between presented groups. Multivariate Cox model showed that male gender (Exp(B) = 0.796, ps < 0.05), smoking (Exp(B) = 1,363, ps < 0.05), older age (Exp(B) = 1,055, ps < 0.0r), and lower score in MMSE ((Exp(B) = 0.950, ps < 0.01) increased the risk of death in 1 year.

Conclusions: Our results show that in patients with AD, among analyzed cardiovascular risk factors, only age, gender and smoking, but not the presence of hypertension and dyslipidemia status was associated with higher all cause mortality.

Disclosure: Nothing to disclose.

PP1004

Semantic associative abilities in mild cognitive impairment: gender asymmetries?

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Introduction: Semantic impairment is well recognized as a cognitive deficit in patients with Alzheimer's Disease, but it is under investigated in the early stage. Aim of this study was to explore the ability to access to semantic associative relations and the loss of these relations during the time in mild cognitive impairment patients, amnestic type (aMCI).

Methods: We conducted a longitudinal study on 32 subjects, aged between 60 and 80 years old (17 male and 15 female; $M_{age} = 75.15 \pm 5.04$). The patients were subjected to a

neuropsychological evaluation and to a verbal semantic experimental battery, composed by a naming task and a semantic associative task. They were tested at baseline and were followed at 11 months to identify, in those who remained stable over time, which associative relation was deteriorated. Five associative relations were analysed: Superordinate, Contiguity, Attribute, Function and Part/All.

Results: Our results suggest a progressive impairment in the associative ability, but not in the naming task, in which there were no variance between test and retest conditions. The most interesting difference is between the performance of male and female: analysing the five associative relations separately we found in post hoc analysis a significant decrease in Function and Contiguity relations only in male ($p < 0.001$). Female performance was stable during the year.

Conclusions: Our data seem to suggest that semantic linkage in a-MCI may be early indicator of possible transition to dementia. The findings seem also to suggest gender asymmetries in the management of semantic associative relations.

Disclosure: Nothing to disclose.

PP1005

Association study of interferon-γ and interleukin 10 gene polymorphisms in Alzheimer disease

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Introduction: An inflammatory response has been hypothesised to be involved in the pathogenesis of Alzheimer's disease (AD) and, likely, also of other types of primary dementias. This study was undertaken to evaluate the possible role of interferon-γ (IFN-γ) +874T/A, and Interleukin 10 (IL-10) 1082G/A polymorphisms in AD.

Methods: The study included 93 probable patients with AD who met the diagnostic criteria of National Institute of Neurological and Communicative Disorders and Stroke-AD and Related Disorders Association, and 150 control subjects (C).

Results: No significant difference in mean age or in the distribution of genders between AD and C groups was found. Moreover, we reported a positive association between the −1082 G/A genotype and AD.

(OR = 1.76 (1.15–2.69, p = 0.0061). Similarly, a significant association was found between +874T/A genotype and AD (OR = 1.94 (1.09–3.47, p = 0.0016).

Conclusions: Our findings indicate that the IL-10 A/G and IFNG A/A genotypes are associated with AD and support the involvement of theses cytokines in AD etiology. Key Words: interferon-γ, Interleukin 10, Alzheimer disease, single nucleotide polymorphism.

Disclosure: Nothing to disclose.

PP1006

Clock drawing test in mild cognitive impairment: correlation with cerebral perfusion in SPECT

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Introduction: The Clock Drawing Test (CDT) was originally proposed as a measure of visuospatial abilities related with the parietal lobes; its most recent interpretation indicates a multi tasking processing, involving symbolic and graphomotor representation, language, hemiattention, semantic memory, conceptual abilities and executive functions. There is a recent interest in the study of the relation between the performance on CDT and several cerebral areas/regions of interest, especially in Alzheimer's disease (AD). The same research with Mild Cognitive Impairment (MCI) is sparse.

Methods: We studied 94 patients with amnestic MCI and correlated their performance on the CDT, according to three scoring systems (Rouleau et al. 1992; Cahn et al. 1996; Babins et al. 2008), and regional cerebral perfusion (rCBF) on SPECT.

Results: There was no relation between CDT total scores and rCBF in any of the scoring systems used. We found significant correlations between the several clock elements and underlying subjective errors (stimulus-bound response and conceptual deficit) and rCBF, namely in the entorhinal cortex, posterior cingulated cortex, associative visual cortex and angular gyrus.

Conclusions: Performance of MCI patients on the CDT appears to correlate with functioning of cortical and subcortical areas typically affected in AD. This study shows that, more than a quantitative score, a qualitative assessment of the clock drawing (e.g., error analysis) corresponds to dysfunction in AD key areas, supporting the utility of the CDT in the early diagnosis of AD.

Disclosure: Nothing to disclose.

PP1007

Is high-fat high-carbohydrate diet (HFCD) neuroprotective? A magnetic resonance imaging study in Wistar rats

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Introduction: Obesity was associated with accelerated aging and elevated risk of neurodegenerative diseases. In animal models, high-fat high-carbohydrate diet (HFCD) is commonly used to induce obesity. We hypothesized that HFCD will lead to poorer memory, smaller hippocampi and lower concentrations of brain metabolites in hippocampi, which are predictors of neurodegenerative diseases both in humans and in laboratory animals.

Methods: Twenty five male Wistar rats were put on HFCD (∼35 % fat, ∼35 % carbohydrates) on their 55th day of life, while 25 control male rats (CON) remained on chow. Both groups underwent memory tests in 8-arm radial maze at 3rd, 6th, and 9th month. At one year, all animals underwent MRI to evaluate hippocampal volumes and 1H magnetic resonance spectroscopy at 7T.

Results: HFCD rats consumed slightly more calories than CON, but less proteins. However, their protein intake was within recommended amounts. Levels of sugar and ketone bodies were within healthy norms in both groups; however, numerically they were higher in the HFCD group. Contrary to our hypotheses, HFCD rats had better scores of memory than CON throughout the experiment. At one year, their hippocampi were by 3 % larger than in CON (p = 0.05), whereas concentration of N-acetylo-aspartate (NAA, marker of neuronal viability) was 8 % higher.

Conclusions: The results do not support the thesis that HFCD per se leads to degeneration of the nervous system. On the contrary, they consistently suggest that HFCD enhances memory and slows aging. More research is needed to pinpoint the mediating factors.

Disclosure: Nothing to disclose.

PP1008

Abstract withdrawn

PP1009

Abstract withdrawn

PP1010

Disturbed default mode network connectivity patterns in Alzheimer's disease associated with visual processing (an fMRI study)

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Introduction: The default mode network (DMN) is characterized by decreasing activity (deactivation) during a goal-directed task. The objective of our study was to detect specific alterations in DMN connectivity when switching from baseline to task condition (here the visual task) in 15 patients with Alzheimer disease (AD) as compared to 16 healthy controls (HC) using psychophysiological interactions (PPI) analysis.

Methods: The fMRI imaging was performed using a 1.5 T Siemens Symphony scanner. The experiment comprised 2 parts: a complex visual scene-encoding task and anatomical T1 images. To determine the brain regions that showed significantly greater activation or deactivation with respect to active periods, a General Linear Model as implemented in SPM5 was used. PPI were used to assess the effect of the task on connectivity with posterior DMN node. Age, gender, education and measure of atrophy were used as covariates.

Results: HC showed decreased correlation during the the task than during the baseline with middle temporal/middle occipital gyrus (MTG/MOG) and posterior cingulate/precuneus bilaterally, and increased correlation during the task with the right inferior parietal lobule. In contrast to HC, AD showed decreased correlation during the task with the small area of the right MTG and the right superior temporal gyrus.

Conclusions: We have found specific disturbances in the DMN connectivity in AD during visual processing that probably reflect changes in network plasticity representing either malfunction or insufficient compensation.

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PP1011

A study on the association of dementia and multilingualism among patients in Jose R. Reyes Memorial Medical Center

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Introduction: Dementia is a common disabling and distressing neurological disorder that is not considered a feature of normal aging. The diagnosis of dementia based on the standardized criteria from DSM-IV required substantial cognitive decline from a previous level of performance in one or more domains. The recognition of dementia in the Philippines is still in its infacncy. This study determined the correlation of multilingualism on delaying the onset of dementia in the elderly and maintaining the cognitive reserve among diagnosed patients in Jose R. Reyes Memorial Medical Center.

Methods: A sample of 34 patients from February to June 2013 with cognitive complaints were initially selected, 11 of whom were excluded. Patients who were diagnosed with probable dementia who had scores of <21 in MoCA-P were included. The criterion for multilingualism was that patients had spent most of their lives regularly using two or more languages in the Philippines, including English.

Results: These group showed delay of symptom onset of 10.6 years as compared to the unilingual group. The multilingual also scored higher in the MoCA-P. This delay in onset translates into a reduction of prevalence rate of dementia in the Philippines.

Conclusions: This strengthens the fact that multilingualism keeps the brain in shape and reinforces mental function, rather than the earlier thought that it creates conflict and confusion. In the Philippines with 8 languages and 175 + dialects, this would aid in having a low prevalence rate of the disease.

Disclosure: Nothing to disclose.

PP1012

Functional characteristics across milder end of cognitive spectrum

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Introduction: We sought to characterize the functional aspects of no cognitive impairment (NCI), subjective cognitive impairment (SCI), non-amnestic and amnestic mild cognitive impairment (NA-MCI, A-MCI) as a cognitive continuum, and to identify the possible role of specific functional tasks as a diagnostic utility.

Methods: A total of 702 participants sampled from the residents aged 65 years or older living in Seongnam, Korea. The participants were defined as NCI, SCI, NA-MCI, and A-MCI according to original Peterson criteria with standardized interview and neurological examination by physicians and neuropsychological assessments by neuropsychologists. Functional status was measured using the K-ADL and K-IADL.

Results: There was a significant difference between discrete cognitive status groups on three items (washing, bathing, eating), and

total scores of K-ADL. In terms of K-IADL, the differences were significant for six items (outgoing for a short distance, using transportation, shopping, handling money, using telephone, taking medication, and total score. ANCOVA with Bonferroni post hoc adjusting age, gender, educational level, and geriatric depression score showed that A-MCI performed poor at bathing, shopping, handling money, and using telephone compared to others, and the sum of the items which were significantly different among groups (three items of K-ADL plus six items of K-IADL) was higher in A-MCI than others.

Conclusions: These findings demonstrate the declining feature of functional characteristics according to the progress of cognitive impairment in mild end of cognitive continuum, which is definite between A-MCI and others. In addition, specific tasks, which could be discriminative between discrete cognitive statuses, were identified.

Disclosure: Nothing to disclose.

PP1013

House-design test in vascular cognitive impairment

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PP1014

A 12-week, multi-center, open-label evaluation of caregiver preference, safety and tolerability of Exelon® Patch in patients with Alzheimer's disease

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PP1015

Verbal fluency tests as short and effective instruments to detect early cognitive deficits in mild cognitive impairment and mild Alzheimer disease

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PP1016

Memory evaluation in early Alzheimer's patients using the 7 Minute Screen: useless cueing

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PP1017

Relationship of age with the size of the interventricular foramina and aqueductus sylvii: a morphometric evaluation

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PP1018

Preliminary results of a program for Alzheimer's disease (AD) family caregivers in Limousin, France: effect on AD psychosocial burden

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PP1019

Ma2 encephalitis presenting with psychiatric manifestations in a 62-year-old female: a case report

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PP1020

Predictors of response to 13.3 mg/24 h rivastigmine patch in patients with severe Alzheimer's disease

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PP1021

Efficacy of 13.3 versus 4.6 mg/24 h rivastigmine patch on activities of daily living in severe Alzheimer's disease: a factor analysis

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PP1022

Cognitive efficacy of 13.3 versus 4.6 mg/24 h rivastigmine patch in severe Alzheimer's disease: Severe Impairment Battery factor analysis

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PP1023

Early onset Alzheimers disease in Armenia

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PP1024

Abstract withdrawn

PP1025

Post-stroke dementia: diagnosis and treatment

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PP1026

Abstract withdrawn

PP1027

Abstract withdrawn

PP1028

Human amniotic membrane- and adipose tissue-derived stem cells extend healthspan and lifespan in F344 rats

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Autonomic nervous system disorders

PP1029

Approximate entropy of heart rate variability as a predictor of survival after ischemic stroke

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Introduction: The purpose of prospective cohort study was a definition of relationship between the survival of patients after ischemic stroke (IS) with approximate entropy (ApEn)—the nonlinear parameter of heart rate variability (HRV).

Methods: The study included 302 patients with non-cardioembolic IS, admitted in 2007-2013; average age—66.4 ± 10.9 years. Short-term HRV registration (about 5 min) was performed on the 4 {3, 7} days of stroke onset. The value of ApEn was calculated by method of Pincus in 2 versions—ApEn15 (m = 2, r = 0.15SDNN) and ApEn20 (m = 1, r = 0.2SDNN). The survival analysis of patients with IS was made using Kaplan–Meier curves for 90-day follow-up after stroke.

Results: It has been performed the comparison of survival in patients with ApEn15 not more Q1 level (0.891), with survival in patients with higher entropy (Q2–Q4). ApEn15 corresponded to the lowest quartile in 12 (46.2 %) cases among the 26 died patients and it was in 61 (22.3 %) ones among 275 survivors. Low ApEn15 (Q1) level was associated with an increasing risk of death within 90 days after stroke onset: OR = 2.9, 95 % CI: 1.3–6.8, p = 0.009. ApEn20 corresponded to the lower quartile of entropy (1.109) in 14 (51.9 %) cases among died patients and it was in 60 (22.0 %) ones among the survivor persons. The first quartile of ApEn20 was associated with an increasing risk of death within 90 days of observation after stroke: OR = 3.8; 95 % CI: 1.7–8.6; p = 0.001.

Conclusions: Low ApEn values of HRV is associated with a lethal outcome within 90 days after IS.

Disclosure: Nothing to disclose.

PP1030

Gender differences in autonomic imbalance in chronic migraine patients with arterial essential hypertension

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Introduction: Autonomic cardiovascular activity is impaired in migraine and hypertension patients and gender could play a major role in its expression.

Methods: Study sample include 154 subjects divided in 4 groups: Gr. I (n = 60)—chronic migraine with hypertension (Mg +HBP), Gr. II (n = 40) chronic migraine without hypertension (Mg − HBP), Gr. III (n = 30)—high blood pressure (HBP) and Gr. IV (n = 24) healthy controls (C). All subjects underwent ambulatory blood pressure monitoring for 24 h. Data collected was analyzed using SPSS.

Results: Study sample was stratified by sex and analyzed male and female subjects separately. Males sample include 10 pts. from the Gr. I, 5 pts.—Gr. II, 13 pts.—Gr. III and 11—Gr. IV. Mean age was 46.7 ± 8.9 Gr. I vs. 40.8 ± 8.7 Gr. II vs. 39.18 ± 12.33 Gr. III vs. 43.3 ± 12.33 Gr. IV, p ≥ 0.05. Female sample consist of 44 pts.—Gr. I, 34 pts.—Gr. II, 16 pts.—Gr. III and 13—Gr. IV, mean age 47.22 ± 6.68 Gr. I vs. 41.82 ± 11.59 Gr. II vs. 50.06 ± 8.25 Gr. III vs. 39.46 ± 11.42, p ≥ 0.05. In the male sample was no statistical significant differences between groups for HRV indices. Females from the patients groups (I, II, III) presented the reduced HRV time and frequency domain parameters, especially in the Gr. I (Mg + HBP).

Conclusion: Chronic migraine patients with hypertension presented reduced HRV in the female sample but not in the male, which reflect the female susceptibility to autonomic imbalance in cardiovascular activity.

Disclosure: Nothing to disclose.

PP1031

Episodic hypopnea and hypotension in a patient with a craniocervical ependymoma - a case report and review of the literature

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Introduction: Central hypopnea can be a manifestation of lower brainstem lesions since the neuroanatomical pathways for the control of respiration likely originate in pons and medulla with connections into upper segments of the cervical spinal cord. Vasomotor instability has been described as a complication of medulla oblongata lesions. This case report illustrates the supposable mechanisms of central hypopnea and hypotension caused by interruptions of the central respiratory and vasomotor control.

Case report: A 68-year-old woman presented with subacute and profound worsening of a residual spastic hemiparesis 10 years which

after partial resection of an upper cervical cord ependymoma. She had a history of arterial hypertension and had experienced several syncopal episodes prior to evaluation.

After admission, she was found comatose with insufficient respiration, apnea episodes and systolic blood pressure of 70 mmHg. She immediately regained consciousness with stabilisation of blood pressure and ventilation but experienced several further episodes with this symptoms until continuous mechanical ventilation and sympathomimetic medication were applied. MRI revealed an increase in size of the residual tumor (as compared with former images) with affection of medulla oblongata and signs of subacute hemorrhage. After several months of hospitalisation the patient regained her previous functional state without respiratory or vasomotor failures.

Conclusions: Disruptions of medullary and upper cervical autonomic pathways can cause coma and a life-threatening breakdown of the central respiratory and vasomotor control which can be reversible if the acute crisis can be overcome. Recovery of this patient was interpreted due to resolution of intratumoral hemorrhage.

Disclosure: Nothing to disclose.

PP1032

Decreasing of parameters of heart rate variability after early stroke rehabilitation

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Introduction: The aim of this study was to reveal an influence of early stroke rehabilitation on parameters of heart rate variability (HRV).

Methods: We prospectively included 80 patients (75.0 % males; mean age 61.1 ± 8.6) with stroke (81.2 % were ischemic) within 48 h of stroke onset. All patients were treated using the standard medical and physiotherapy. 50 patients (main group) were passive tilted for first 2 weeks using tilt table under blood pressure, heart rate and SpO2 control. 30 patients enrolled in control group. The analysis of HRV using short-term recordings (5 min) was performed. Total power (TP; ms2), standard deviation (SDNN; ms) and very low frequency % (VLF %), low frequency % (LF %), high frequency % (HF %) components were investigated.

Results: The analysis of HRV revealed on admission TP in main group 857.0 (427.5;1,632.5) vs. 843.0 (376.0;1.123.0) in control LF/HF 3,8(1.2;6.8) vs. 2.8(1.2;5.7), LF% 22.0 (14.0;34.6) vs. 26.0 (15.0;34.0), HF% 7,2(2.9;16.5) vs. 10.0(5.0;21.5), SDNN 29.0 (21.0;35.0) vs. 25.0 (18.0;32.0). We haven't estimated difference between two groups. The NIH score in main group completed 10.0 (7.0;18.0) vs. 9.0 (6.0;17.0). On discharge TP and SDNN decreased in main group: 450.5 (376.0;990.3), $p = 0.012$ and 24.0(13.0;38.0), $p = 0.021$. In control presented: 390.5(210.5; 775.5), $p = 0.015$ and 18.5(12.8;28.5), $p = 0.024$, respectively. The frequency analysis did not reveal dynamics in both groups.

Conclusion: We found that such parameters as TP and SDNN decrease after stroke independently from method of rehabilitation. It may occur due to strong connections of such parameters and damage of central regulation of autonomic nervous system.

Disclosure: Nothing to disclose.

PP1033

Heart rate variability in patients with diabetes mellitus type 2

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Introduction: Our study aimed to investigate the changes of heart rate variability (HRV) and blood pressure (BP) response after different stimuli in patients with diabetes mellitus (DM) type 2.

Methods: Twenty patients with DM type 2 (age range 45–67 years) and 10 presumed healthy age and sex matched controls were included in the trial. All underwent simultaneous non-invasive BP and short-term heart rate (HR) monitoring at rest and after cold stress, deep breething (DB) and head-up tilt (HUT) with subsequent calculation of the time and frequency parameters of HRV. The effetcs of the different stimuli on the HRV and the BP were compared.

Results: In the patients with DM the HR at rest was significantly higher in comparison to controls, while the BP values were slightly increased. Parallel decrease of total power (TP), low frequency spectral power (LF) and of mean R-R and mild increase of low frequency-high frequency ration (LF/HF) were established.

The HUT and the DB caused decrease of BP and it was stronger in the diabetic patients. The cold stress induced predominating in the controls increase of BP. After the three stimuli increase of the examined HRV frequency parameters in the control subjects was observed. This increase was less pronounced in the DM patients after the cold stress and DB. The HUT provoked decrease of HF and TP, while LF and LF/HF remained unchanged.

Conclusions: The assessment of the impaired HRV after different stimuli is useful for the estimation of the cardiac autonomic control in DM.

Disclosure: Nothing to disclose.

PP1034

Cardiac autonomic regulation in myopia students

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PP1035

Sympathetic skin response in children with iron deficiency anemia

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Cerebrovascular diseases 1

PP1036

New inflammatory predictors for cerebral ischemic stroke: echocardiographic epicardial fat thickness and neutrophil to lymphocyte ratio

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Introduction: There are no reports on the relationship between epicardial fat thickness (EFT) in patients with ischemic stroke. The aim of our study was to evaluate EFT and Neutrophil/lymphocyte ratio (NLR) in patients with ischemic stroke (İS) in order to investigate a potential relationship between new inflammatory predictors and ischemic stroke.

Methods: The study included 38 patients with ischemic stroke and 47 age- and sex-matched healthy controls in this cross-sectional study. Echocardiographic assessments of the EFT were measured according to previously published methods. Total and differential leukocyte counts were measured by an automated hematology analyzer.

Results: Mean EFT was 4.86 ± 0.68 and 5.95 ± 1.14 mm in control and stroke groups, respectively. EFT of the İS patients was high compared with control subjects. The mean NLR of the İS patients was significantly higher than that of the control group. For all possible confounding factors between the two groups was not statistically significant difference. Spearman's correlation analysis revealed mild correlations between EFT and NLR.Multivariate multinomial logistic regression analysis revealed a relationship between EFT and the cerebral ischemia stroke.

Conclusions: this study showed, for the first time, that increased EFT is associated with cerebral ischemic stroke. Echocardiographic EFT was correlated with NLR value. NLR and echocardiographic EFT are cheap and readily available markers that may be useful in determining the risk of İS patients.

Disclosure: Nothing to disclose.

PP1037

Atrial electromechanic delay and left atrial mechanical function in stroke patients

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Introduction: The aim of this study was to determine whether atrial electromechanical delay (EMD) as measured by tissue Doppler imaging (TDI) was prolonged in patients with ischemic stroke.

Methods: A total of 30 patients with ischemic stroke and 30 healthy controls participated in the study. Cerebral infarcts of probable embolic origin were diagnosed via imaging and were confirmed by neurologist evaluation according to the American Heart Association (AHA), Lausanne Stroke Registry, and modified Oxfordshire Community Stroke Project guidelines. Active and passive left atrial (LA) emptying volumes and fractions were calculated. Intra- and interatrial EMD were measured via TDI.

Results: Increased left atrial (21.36 ± 10.38 ms versus 12.73 ± 5.79 ms, $p < 0.05$), right atrial (13.66 ± 8.62 ms versus 9.63 ± 6.79 ms, $p < 0.05$), and interatrial EMDs (35.03 ± 9.95 ms versus 22.36 ± 7.95 ms, $p < 0.05$) were observed in stroke patients as compared to controls. Active LA emptying volumes, active LA emptying fraction, passive LA emptying fraction, and passive LA emptying volumes were similar between controls and stroke patients ($p > 0.05$). Total LA emptying volumes were significantly increased in stroke patients as compared to healthy controls (33.19 ± 11.99 ms versus 27.72 ± 7.38 ms, $p = 0.038$).

Conclusions: Interatrial and intraatrial delays may be novel predictors of ischemic stroke.

Disclosure: Nothing to disclose.

PP1038

PAF related ischemic stroke: clinical, radiological, ecocardiographical findings

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Introduction: Atrial Fibrillation is the most common aetilogic factor of stroke but there is no definite data PAF-related ischemic stroke prevalence. We prospectively evaluated clinic, radiologic, thransthorasic echocardiography (TTE) findings and their association with stroke outcome in patients with PAF-related ischemic stroke.

Methods: We studied 48 patients who were diagnosed PAF from our cohort of 588 patients with ischemic stroke. Our clinic's ischemic stroke aetiology workup included ECG, continuos monitoring at stroke unit, carotid ultrasound, TTE, CT, MRI/MRA, 24-h Holter ECG. Patients's characteristics included age, sex, prior history of ischemic stroke, history of congestive heart disease and coronar artery disease and cardiovascular risk factors. For all patients we calculated CHADS2, CHA2DS2VASc, HAS-BLED scores and mRS. Functional independence and good clinical outcome was assessed as mRS 0–1 in the 3rd month.

Results: Among our study population; the mean age was 69.04 ± 10.407. mRS score at 3-month 0–1 was 37 patients, mRS score 2–3 was 6 patients, mRS score 4–5 was 4 patients and only one patient died. CHADS2VASc score ($p = 0.048$), NIHSS ($p = 0.0001$) were significantly related with good clinic outcome at 3-month. There were no significant differences with vascular risk factors and follow-up at 3-month. The patients with left atrium size was higher then 40 mm, functional dependence at 3-month was significantly increased ($p = 0.008$).

Conclusions: Our data showed PAF is related mild stroke outcome at 3-months and rapid regression of neurologic state. Also we could say that the diameter of left atrium could be a marker for stroke outcome.

Disclosure: Nothing to disclose.

PP1039

Case report: familial spontaneous cervical artery dissection and ischemic stroke in two 40-year-old sisters

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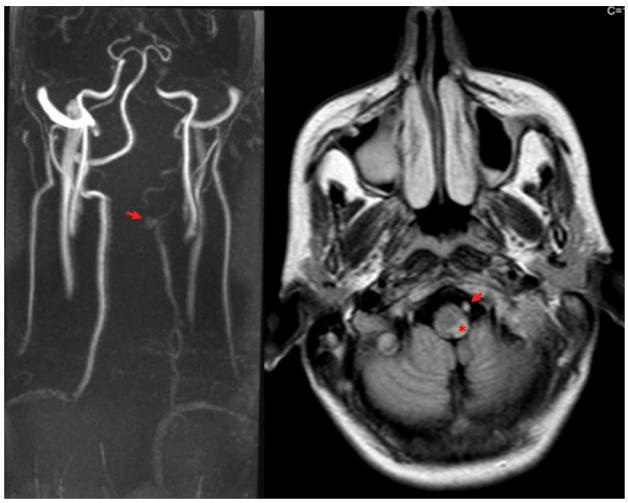
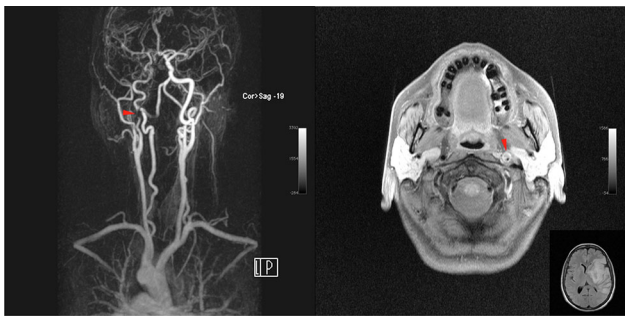
Introduction: Familial spontaneous cervical artery dissection (FsCAD) is a very rare occurrence, with very few cases published in the literature. We present the case of two sisters with a spontaneous cervical artery dissection and ischemic stroke at a young age.

Case report: *Patient A* (2007): A 39-year-old woman, with no relevant medical history, was brought in with a sudden onset of headache, vomiting and vertigo, after a cephalic rotation movement. The head CT scan showed an intraluminal thrombus in the left vertebral artery. The angioMRI showed a left vertebral artery dissection and cerebellar stroke.



Patient B (2013): A 41-year-old woman, the sister of patient A, with previous history of migraine and use of oral contraception, experienced a sudden onset of aphasia and right hemiplegia. No trauma (minor or major) was reported. The head CT scan showed a massive left hemispheric stroke, and the angioMRI confirmed a left internal carotid artery dissection.



Further tests were normal in both cases. There was no family history of vascular disease at a young age. Both sisters were examined by Dermatology and both observations were deemed unremarkable.

Conclusions: FsCAD is a very rare finding and its aetiology remains largely unknown, with the role of ultrastructural changes in the dermal connective tissue and of the genetic mutations being the primary focus of the investigation. The available data suggests a genetic influence, but a solid gene candidate hasn't yet emerged from published studies. Further investigation is required in order to better understand this rare condition.

Disclosure: Nothing to disclose.

PP1040

The impact of malnutrition on stroke management in tertiary hospitals in Turkey

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Introduction: Stroke is a major health problem and leads to a significant financial burden. Concomitant malnutrition may adversely affect stroke prognosis and increase management costs. The study aimed to describe current daily practice for stroke management in patients with or without malnutrition in terms of diagnosis, treatment and follow-up.

Methods: Neurologists with experience on stroke management from 8 tertiary centers filled out a questionnaire including questions about diagnosis, treatment and follow-up of stroke patients. Management algorithms, with specific focus on malnutrition, were developed based on the expert opinion provided by the participants.

Results: Among patients admitted to the emergency department with a diagnosis with stroke, a mean(SE) of 76.4(7.5) % are hospitalized, while others are discharged for a further work-up in outpatient-setting. Of the hospitalized patients, 39.2(7.7) and 41.7(8.9) % are followed in intensive-care(ICU) and normal unit(NU), respectively. Malnutrition prevalence at first admittance and incidence during hospitalization and follow-up are given in Table 1. Patients with malnutrition were more likely to experience longer hospitalization durations (Table 2). The mean(SE) mortality rate at first hospitalization is 10.3(2.9) %; among survivors, mortality rate during 1-year follow-up is 14.2(3.7) %. Expected complications during 1-year follow-up are given in Table 3.

Malnutrition prevalence or incidence	Rate (%)*
Prevalence at admission	7.8 (3.6)
Incidence in intensive care unit	7.1 (4.8)
Incidence in normal ward after ICU	2.6 (2.5)
Incidence in only normal unit**	0.9 (0.6)
Incidence during 1-year follow-up	6.8 (1.4)
	Mean(SE)
Time to malnutrition during 1-year follow-up (month)	4.4 (0.5)

*Results are given as mean(standard error) of ratio

** Patients who are directly admitted to normal unit without intensive care unit admission

ICU: intensive care unit

Hospitalization duration (day)	No Malnutrition*	With Malnutrition*
Intensive care unit*	10.6 (2.9)	18 (4.6)
Normal unit after ICU	5.2 (0.7)	10.2 (1.8)
Only normal unit**	5.5 (0.7)	10.3 (1.5)

*Results are given as mean(standard error)

** Patients who are directly admitted to normal unit without intensive care unit admission

ICU: intensive care unit

Complication (%)	No Malnutrition*	With Malnutrition*
Acute hemorrhage	4.8 (1.3)	6.2 (1.5)
Deep vein thrombosis	3.9 (1.1)	5.6 (1.4)
Infections	8.3 (2.0)	17.4 (3.7)
Pressure wound	2.6 (0.8)	25.9 (11.3)
Psychiatric complications	10.9 (2.4)	23.7 (5.4)
Recurrent cerebrovascular events	6.9 (1.0)	7.8 (1.2)
Recurrent vascular events	5.9 (1.1)	7.3 (1.1)

*Results are given as mean(standard error) of ratio

Conclusion: The results of this analysis revealed current management patterns of stroke in tertiary hospitals in Turkey. Malnutrition seems to be an important risk factor which contributes to poor prognosis after stroke.

Disclosure: This study was sponsored by Abbott Nutrition Turkey.

PP1041

Baloon angioplasty for venous sinus stenosis in an idiopathic intracranial hypertension case

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Objective: The idiopathic intracranial hypertension (IIH) condition is well defined with intractable headaches, visual obscurations and papilledema as dominant features, mainly affecting obese women. With the development of magnetic resonance (MR) technics and widespread use of cerebral digital subtraction angiography (DSA), a significant number of IHH patients found to have associated with nonthrombotic dural venous sinus stenosis were reported. This has led to a renewed interest in endovascular stenting and angioplasty as a treatment for IIH in patients nonresponsive to medical treatment. We present a case without known risk factors for IIH and nonresponsive to treatment.

Case: A 19-years-old woman presented with headache and diplopia. She was diagnosed with IIH since 5-years old and nonresponsive to lumbar cerebrospinal fluid drainage or acetazolamide treatment. MR venography showed thin calibration of transverse sinus. Venous phase of DSA also revealed 50 % stenosis of transverse sinus, 50 % stenosis of left proximal sigmoid sinus and 90 % stenosis of its distal part leading to obstruction of left transvers sinus outflow and direction of left hemisphere drainage to the anterior region. Balloon catheter dilatation of the left sigmoid sinus was performed.

Conclusion: The venous sinus disease in the etiology of IIH may probably be underestimated. In patients with IIH venous sinus stenosis should be evaluated with MR venography and DSA. In patients with venous sinuses lesion who experienced medical treatment failure, endovascular treatment can be considered as a treatment of choice due to its lower complication rate.

Disclosure: Nothing to disclose.

PP1042

The phosphatidylinositol-3 kinase/Akt pathway mediates melatonin's neuroprotective activity after focal cerebral ischemia

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Introduction: Apart from its metabolic functions, melatonin is a potent neuroprotective molecule owing to its antioxidative actions. However, the roles of melatonin receptors and signalling in the neuroprotective effects of melatonin after cerebral ischemia remain unknown.

Methods: With the use of MT1/2 knockout mice and AKT pathway inhibitor wortmannin, we evaluated the effects of melatonin on functional recovery, brain injury, edema formation, signaling pathways resulting from ischemic brain injury.

Results: Here, we show that the infarct volume and brain edema do not differ between melatonin receptors 1/2 knockout ($mt\text{-}1/2^{-/-}$) and wild-type (WT) animals, but melatonin treatment decreases infarct volume in both groups after middle cerebral artery occlusion. We also demonstrate that melatonin treatment decreased activations of CREB, ATF-1, and p38 phosphorylation in both $mt\text{-}1/2^{-/-}$ and WT mice, while p21 and JNK1/2 were reduced only in melatonin-treated WT animals in the ischemic hemisphere. In addition, we observed that melatonin treatment increases AKT phosphorylation after cerebral ischemia and the inhibition AKT with wortmannin reverses neuroprotective action of melatonin after 30 and 90 min of focal cerebral ischemia. Furthermore, melatonin treatment improved grip strength of the contralesional paretic forelimb and motor coordination, which was associated with improved spontaneous locomotor activity and exploration behavior.

Conclusions: We provide evidence that the absence of MT1/2 has no unfavorable effect on ischemic brain injury and the neuroprotective effects of melatonin appear to be mediated through PI3K/Akt. Furthermore, the robust functional improvement encourages proof-of-concept studies with melatonin in stroke patients.

Disclosure: Nothing to disclose.

PP1043

Atrial fibrillation and heart failure: additional factors for cognitive disturbances

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Introduction: Atrial fibrillation (AF) is an important and independent risk factor for cerebrovascular diseases and vascular dementia.

Aim: To evaluate the severity of cognitive dysfunction and compare frequency of mild cognitive impairment in patients with heart failure and AF.

Methods: 218 consecutive patients (mean age 70.1 ± 0.65 years; 57 % Women) with AF without previous embolic events were consecutively admitted. The patients have been classified into three groups: 1—with HF I (NYHA) 8.3 %, 2—HF II 61.9 %, 3—HF III–IV 29.3 %, and according to echocardiography data in 2 subgroups with EF < 40 % (46.2 %) and >40 % (53.8 %).

Results: The mean MMSE score was 26.2 ± 2.8. MMSE scores <26 were found in 46.3 % (101/218) of participants. Patients with advanced HF III–IV (NYHA) had more frequent cognitive difficulties (75.4 vs. 37 vs. 11.1 %, $p < 0.05$).The MMSE score was associated with left ventricular ejection fraction in a non-linear correlation, cognitive performance was significantly lower in subjects with left ventricular ejection fraction of <40 %. Brain CT has shown lacunar or ischemic changes in 52 % of patients with cognitive disturbances. Anticoagulation rate in patients with MMSE <de 24 was only 16 %, with an optimal level of anticoagulation (INR 2.0–3.0) in 8 % of cases.

Conclusions: Advanced chronic heart failure, advanced age and low ejection fraction could be considered important factors for cognitive impairment in patients with AF and underuse of anticoagulation treatment may be considered both a cause and consequence of it.

Disclosure: Nothing to disclose.

PP1044

Recurrent venous thrombosis in a patient with inflammatory bowel disease: options and failures of current treatment

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Background: Cerebral venous thrombosis (CVT) is an infrequent cause of stroke, more common in women and young adults. Major risk factors are prothrombotic conditions, hormonal therapy, and pregnancy/postpartum. Chronic inflammatory diseases confer additional risk.

Case report: Thirty-seven year-old female with migraine with aura and ulcerative colitis (UC) under immunosuppression. Contraception with hormonal intrauterine device. She presented with proximal deep venous thrombosis (DVT) of the left lower limb in March 2013 and was started on warfarin. One month later, under adequate anticoagulation, she repeated left DVT and pulmonary thromboembolism. An inferior vena cava filter was placed and warfarin was switched to rivaroxaban 10 mg/bid. In August 2013 she had UC flare with persistent diarrhea and dehydration, followed by right popliteal DVT. Rivaroxaban was suspended and weight-adjusted enoxaparin initiated. Two weeks later constant, non-pulsatile, right-sided headache started, worsened by supine position and Valsalva maneuver, with partial response to analgesics. Fever, neurological signs or other symptoms were absent and she was admitted to the ER one week later for persistent complaints. General and neurological examinations were normal. Brain MRI with venography revealed CVT of the right lateral and superior sagital sinus. After the acute phase rivaroxaban 20 mg/id was reintroduced. Headache subsided and no hemorrhagic events occurred.

Conclusion: Dehydration during UC flare may contribute to CVT. Treatment failure with rivaroxaban can be attributed to poor intestinal absorption and/or unapproved dosage. Treatment options for recurrent events under anticoagulation in patients with compromised intestinal absorption aren't described in the literature, therefore an individual approach is crucial.

Disclosure: Nothing to disclose.

PP1045

Deep cerebral venous thrombosis presenting with brain stem hemorrhage

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Introduction: Cerebral venous thrombosis constitutes 0.5 % of the cerebrovascular diseases. In some patients it can be presented with a slight headache, whereas some patients have focal neurologic deficits and fewer patients will present with coma. The prognosis of the disease is becoming less severe as the awareness of the diagnosis, neuroimaging techniques and the development of effective treatments increases over the last 10 years.

Case: 49-year-old female patient was admitted to emergency department with headache, confusion and weakness of the left side. Her blood pressure was 120/80 mmHg and had drowsiness, left hemiplegia and left Babinski reflex. Brain CT was performed with the preliminary diagnosis of cerebrovascular disease, hemorrhage in the right mesencephalon was detected. Antiedema treatment was begun. The haematological parameters tested for the etiology of intracranial hemorrhage were within normal limits and brain CT angiography were normal. The size of the lesion on CT was found to be increased in the control brain CT. Brain MRI and MR venography was performed in the patient whose hemorrhage etiology have not found yet and have atypical clinical features. Acute infarct was seen around the hemorrhagic lesion, and deep cerebral venous thrombosis detected in the MR venography. Warfarin treatment was given subsequent to low molecular weight heparin treatment. She discharged with neurological sequelae of left hemiparesis.

Conclusion: Cerebral venous thrombosis should always be considered in the differential diagnosis in patients with atypical cerebrovascular disease.

Disclosure: Nothing to disclose.

PP1046

Dural arteriovenous fistula and concomitant cerebral sinus thrombosis: "The chicken or the egg?"

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Introduction: The relationship between dural arteriovenous fistulas (dAVF) and cerebral sinus thrombosis (CST) is complex and literature covering this topic is scarce.

Methods: Here we report a patient who developed CST with documented pre-existing dAVF.

Results: A 29-years-old woman developed a pulsatile tinnitus in 2008 and work-up identified a type-I dAVF. Feeding arteries comprised branches from the left external carotid and vertebral arteries draining into the left sigmoid sinus. In 2008 and 2009 she underwent endovascular treatment with partial occlusion of the dAVF. In 2013 she presented to our emergency department with acute onset left-sided headache and was diagnosed with CST affecting superior sagittal, left transverse, left sigmoid sinus, and partially the right transverse sinus. She was treated with intravenous heparin followed by subcutaneous low molecular weight heparin (LMWH). Oral contraceptives were discontinued; no other risk factors for CST were identified. Headache markedly improved and the tinnitus resolved. A follow-up MRI showed nearly complete reperfusion of the cerebral sinuses. Catheter angiography after 1 month demonstrated spontaneous occlusion of the pre-existing vertebral artery fistula. A small middle meningeal artery-fistula was embolized. She was continued on LMWH until now and further management will be decided after a follow-up MRI.

Conclusions: It is not uncommon to find that dAVF and CST develop together. So far, CST was mainly considered as the primary event that causes venous hypertension and subsequently the development of dAVF. However, the case reported here supports the hypothesis that dAVF may trigger the development of CST.

Disclosure: Nothing to disclose.

PP1047

Hemispheric hyperperfusion secondary to internal carotid artery dissection using arterial spin labeling: a case report

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Introduction: Arterial Spin Labeling sequence (ASL) is a non invasive Magnetic Resonance (MR) perfusion method for measuring cerebral blood flow (CBF) by using arterial water as a tracer. The ASL CBF map can reveal parenchymal CBF abnormalities such as hypo- or hyperperfusion. We report the ASL findings in a patient with internal carotid artery dissection (ICAD) and severe headache.

Case report: A 44-year-old man was hospitalized for neck pain, Horner syndrome and a cranial nerve palsy (XII). MR images including angiography showed a left ICAD extending to the intrapetrous segment. DWI was normal. The patient had severe persistent headaches. The ASL performed 9 days after admission showed a marked hyperperfusion of the left hemisphere in the left ICA territory (mean increase CBF on left *vs.* right frontal lobe: +100 %, mean increase CBF on left *vs.* right temporal lobe: +70 %) and in the Posterior Cerebral Artery territory (mean increase CBF on left vs. right occipital lobe: +30 %). The Trans-Cranial Doppler ultrasound examination only revealed a slight acceleration of the left MCA velocity (90 vs. 80 cm/s).

Conclusions: Hemispheric hyperperfusion ispsilateral to the ICAD has been already described with perfusion computed tomography and perfusion-weighted MR imaging with gadolinium. It was here documented non-invasively with ASL. The mechanism is unclear since the hyperperfusion is not restricted to the carotid territory. We suspect that autoregulation mechanisms may be impaired by lesions of pericarotid sympathetic and neuro-peptide fibers. The relationships between the hyperperfusion and the severe headache of the patient remain to be explored.

Disclosure: Nothing to disclose.

PP1048

ASL sequence can be used to monitor slow flows within the artery in vertebral dissection: a case report

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Introduction: Arterial Spin Labeling sequence (ASL) is a non invasive Magnetic Resonance (MR) perfusion method for measuring cerebral blood flow (CBF) by using arterial water as a tracer. The ASL CBF map can reveal parenchymal CBF abnormalities and high signal intensity representing slow flow in vessels (arterial transit artifact). We report the correlation between ASL and ultrasound Doppler (USD) findings in a patient with vertebral artery dissection.

Case report: A 40-year-old man reported neck pain during the last week and sudden left hemiparesthesia. The Magnetic Resonance Imaging (MRI) including angiography showed a left vertebral artery dissection from V1 to V4 without DWI abnormality. The ASL showed a marked cerebellar hypoperfusion in the left Postero-Inferior Cerebellar Artery territory and an arterial low flow transit artifact at the level of the V4 portion of the left vertebral artery. The USD confirmed the left vertebral dissection (starting from the initial segment V1) and showed a very low flow in the V4 portion of the vertebral artery (V4). The symptoms disappeared on aspirin. The MRI at day 13 showed the persistence of the left vertebral dissection, the improvement of the left cerebellar ASL hypoperfusion and the disappearance of the low arterial flow transit artifact of the left V4 vertebral artery. The USD showed an obstruction of the left vertebral from V1 to V3 and a reversed flow in V4.

Conclusions: ASL can identify cerebellar CBF hemodynamic abnormalities and low arterial flow in vertebral dissection.

Disclosure: Nothing to disclose.

PP1049

Oral anticoagulation in patients with non-valvar atrial fibrillation attended for ischemic stroke: lessons from daily clinical practice

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Introduction: To assess the degree of anticoagulation (AC) of patients with non-valvar atrial fibrillation (NVAF) and admitted for ischemic stroke (IS) in clinical practice.

Methods: We studied all the patients admitted for IS within the last 2 years. Patients with IS and treated with AC for NVAF were compared with a control group of patients with NVAF and without stroke. The degree of AC was assessed by measuring the INR (international normalized ratio) and TTR (time in therapeutic range) in the last year.

Results: We reviewed 594 IS patients, mean age 71.2 years (SD 12) years, 52 % were male. Of these, 42 (7 %) were patients with NVAF and treated with AC. The control group consisted of 90 patients. We found no statistical differences related to age and sex between groups: IS vs Control: 73.9(11) vs. 75.6 (9) y, male 42.9 % vs. 50 %. The risks for stroke or bleeding were similar in both groups using the CHA2DS2-VASc and HAS-BLED scores: 4.4 vs. 4.3 and 2.7 vs. 3.1, respectively. The TTR was similar in both groups 6.3 m/y vs. 7 m/y (p non significant), however we found differences related to mean INR 2.4 (0.4) vs. 2.5 (0.2), respectively ($p = 0.005$).

Conclusions: The occurrence of IS in patients with NVAF and AC is relatively common and accounts for nearly 1 in 10–15 cases of IS. As long as we only found a slight difference in the INR between groups it is likely that other factors could explain this higher stroke risk.

Disclosure: Nothing to disclose.

PP1050
Ischemic stroke presenting with lower limb monochorea/ballism

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Introduction: Involuntary movements during the acute stage of stroke are uncommon, hemichorea/ballism being the most commonly reported. Vascular chorea has been most frequently associated with thalamic and lenticular ischemic lesions, although other locations have been described, including the subthalamic nucleus (STN).

Case report: A 77-year-old woman with no vascular risk factors was admitted due to sudden onset of nausea, vomiting and involuntary movements of the right leg. On neurological examination, she had incomplete left ptosis, horizontal binocular diplopia on upward and rightward gaze, and choreic movements of the right lower limb that did not allow walking (NIHSS 4). Brain MRI showed an infracentrimetric area of ischemia involving the left anterior STN/substancia nigra/red nucleus. Aspirin and statin were started. Laboratorial work-up, cervical ultrasound, transcranial Doppler and cardiac investigation were unrevealing and Stroke was attributed to Small Vessel Disease. Amissulpride 200 mg tid and diazepam 5 mg tid improved choreic movements. After 2-months of follow-up she only had very mild choreic movements of the right leg.

Conclusion: In only 7 cases has monochorea been reported as part of the initial presentation of stroke. The present case is the only one with ischemic involvement of the STN. The exclusive involvement of the lower limb due to an infarction of the antero-medial STN is in accordance with the known somatothopic organization of the STN.

Disclosure: Nothing to disclose.

PP1051
Posterior fossa ischemia in patients with vertebral artery hypoplasia

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PP1052
Role of internal jugular vein valve incompetence in idiopathic intracranial hypertension

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PP1053
Efficiency of anti edema therapy at acute stroke

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PP1054
Tachycardia as a negative prognostic factor for stroke outcomes

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PP1055
Vascular parkinsonism due to anterior cerebral artery territory infarction

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PP1056
Prevalence of cerebrovascular disease risk factors among patients under 55 years of age with acute cerebrovascular disease in Albania

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PP1057
The quality of treatment of transient ischemic attack (TIA) in Guba-Khachmaz region of Azerbaijan

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PP1058
Reological parameters in patients with intracerebral hemorrhage

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PP1059
Peculiarities of neurological deficit recovery in patients with posterior circulation ischemic strokes in 1-year period of follow up

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PP1060
The relationship of mean platelet volume with acute ischemic stroke

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PP1061
Brain CT findings in first episode depression in older adults

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PP1062

Age-modified hemorheological indices in cardioembolic stroke

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PP1063

Cerebral vascular accident revealing Imerslund-Gräsbeck syndrome

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PP1064

Cerebral thrombophlebitis and ulcerative colitis

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PP1065

Pathomorphology of atherothrombotic ischemic stroke

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PP1066

Evaluation of the young ischemic stroke paitents: single center experience

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PP1067

Clinical and radiological recovery of a patient after hyperbaric oxygen therapy who develop delayed encephalopathy after carbonmonoxide intoxication

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PP1068

Posterior fossa stroke: the epidemiological, clinical features and its prognosis

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PP1069

Effective mechanical thrombectomy in a patient with hyperacute ischemic stroke associated with cardiac myxoma

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PP1070

Ability to participate in a community in patients with stroke who walked with and without assistive devices

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PP1071

A case with akinetic mutism and paratonic rigidity after bilateral anterior cerebral artery infarct

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PP1072

The blood pressure level during and 24 h after i.v. thrombolysis and stroke outcome

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PP1073

TIA as unique symptom of internal carotid artery dissection: a 6 years review

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PP1074

The effect of oral health on carotid-intima media thickness in sub-types of ischemic stroke

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PP1075

Cerebral infarction due to isolated protein S deficiency

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PP1076

Familial cerebral cavernous malformations

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PP1077

Analysis of ischemic stroke in a young population of Uzbekistan

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PP1078

The Babinski sign and its variants in the XXI century: a matter of consistency

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Introduction: The plantar reflex is an integral part of the neurological exam, and its importance seems untouched, notwithstanding increasingly reliable means of detecting pyramidal tract lesions. Its reliability however, remains an issue. Few studies have adressed this and compared the plantar reflex lesser-known variants regarding intra-observer and inter-observer agreement.

Methods: 62 patients were analyzed. The Babinski, Chaddock and Oppenheim reflexes were classified (extensor, flexor, equivocal) by three different observers, recorded and reclassified by the same observers months later. Kappa statistics was used for intra and interobserver agreement for all reflexes and for which duo of variants had the highest agreement between observers. A Wilcoxon test (exact) for the paired data [significance level (α) 0.05] was used for differences between the results obtained at different points in time and between reflexes.

Results: Intraobserver agreement was highest for the Oppenheim with a median kappa value of 0.35, followed by the Babinski (0.34) and Chaddock (0.29). No statistically significant differences were found. Interobserver agreement was highest for the Babinski with a median kappa 0.29, followed by Chaddock (0.23) and Oppenheim (0.13).

Plantar reflex variant	Interobserver agreement*	Intraobserver agreement*
Babinski	0,29	0,34
Chaddock	0,23	0,29
Oppenheim	0,13	0,35

Table 1: Interobserver and intraobserver agreement of plantar reflexes (values given as kappa statistics)

The difference between these was statistically significant. The Babinski–Chaddock combination had the highest median kappa value (0.32), but no statistically significant differences were found.

Plantar reflex variant	Babinski	Chaddock	Oppenheim
Babinski	-	0,32	0,20
Chaddock	-	-	0,23
Oppenheim	-	-	-

Table 2: Interobserver agreement of reflex combinations (values given as kappa statistics)

Conclusions: Consistency remains a drawback of the plantar reflex. Intra-observer agreement seems highest for the Babinski and Oppenheim; for inter-observer the Babinski fared better than the Chaddock and Oppenheim. When two reflexes are elicited, the Babinski–Chaddock combination appears to be the most reliable.

Disclosure: Nothing to disclose.

PP1079

Clinical trial subjects consent process: challenges utilising legally authorised representative (LAR) consent and patient assent within global clinical trials

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Introduction: Multiple neurological conditions pose challenges within the global clinical trial setting pertaining to attaining timely and reliable consent by legally authorised representatives (LAR) with or without patient assent. The key challenges pertain to: adherence to regulatory and ethics requirements; trial site resource; reticence and concern of patient relatives to be legally authorised representatives; timely completion of consent process critically impacting trauma trial eligibility and protocol requirements.

Methods: Over 50 global clinical studies were reviewed conducted by Quintiles since 2008, focusing on identified operational issues and subsequent implemented mitigation strategies. Quintiles has developed an internal, proprietary database using de-identified, aggregated data from many sources. All references will be fully blinded for sponsor details and investigational product details.

Results: Key critical issues pertained to; relatives concern and reticence; regulatory & ethics board processes that impact study start up & timely enrolment. General consistencies and best practices for implementing the LAR consent process were noted. Additionally, there were considerable variations in handling LAR consenting between the different states in the US and between different regions in the same country. Clear differences in type & impact of these challenges were seen between neurological conditions.

Conclusions: Global data demonstrates large regional variations in regulatory & ethics committee positions on the LAR consent process. The challenges associated with the LAR consent process is further exacerbated by the unique operational issues at a site, physician, patient and patient's relative level according to type of neurological indication. This data analysis will ensure more realistic future operational delivery models.

Disclosure: Nothing to disclose.

PP1080

Central nervous system toxicity of local anaesthetics: levobupivacaine and bupivacaine in spinal anaesthesia

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Introduction: Systemic toxicity of local anaesthetics may occur as a consequence of unwanted intravascular or intrathecal injection, or after the administration of an excessive dose of these drugs. Systemic toxicity of local anaesthetic drugs primarily involves the central nervous system (CNS) and then the cardiovascular system. Usually, the CNS is more susceptible to the action of local anaesthetics than the cardiovascular system. Initial signs of CNS toxicity are usually excitatory and include shivering, muscle twitching, and tremors, which are produced by a preferential block of inhibitory central pathways. These signs of CNS excitation are followed by generalized CNS depression with hypoventilation, respiratory arrest and generalised convulsions.

Methods: A prospective, double-blind, randomised study with 60 ASA grade I–II patients aged 18–65 years awaiting knee arthroscopy under spinal anesthesia was performed. There were two patient groups which received 12.5 mg of isobaric bupivacaine or 12.5 mg of isobaric levobupivacaine. The characteristics of sensory and motor blockade and side effects were recorded.

Results: Sensory ($p = 0.018$) and motor blockade onset ($p = 0.003$) was faster in the bupivacaine group. It took less time to regain maximum motor blockade in the bupivacaine group ($p = 0.014$). Moreover, bupivacaine regained a greater sensory blockade ($p = 0.008$). Sensory and motor blockade duration were similar in both groups. Side effects were infrequent and minor: one patient in the bupivacaine group and one patient in levobupivacaine group had shivering. The symptoms were resolved completely during the first 24 h.

Conclusions: Despite some studies providing evidence that levobupivacaine is less neurotoxic than bupivacaine, we found no differences between both agents at equivalent doses.

Disclosure: Nothing to disclose.

PP1081

Cooperation between Europe and Africa for training neurologists since 50 years: successes, weaknesses, opportunities and challenges

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Many reports emphasize the insufficiency of personnel in Clinical and basic Neurosciences in Africa. These last decades, great efforts are done for improving the number and the quality of trained Staff for Africa. After the era of colonization, the cooperation has increased, leading to more training programs with ex-colonies. 50 years after, several specialists have been trained in Europe, then progressively and locally in Africa where a dozen of training sites exist nowadays. In the same period, the phenomenon of brain drain has retained 150 to 200 native African Neurosciences professionals in European countries for various reasons. Those who went back to Africa or have been trained on site, face daily challenges, frustrations and some miraculous results, regarding the scarcity of human and material means. The gap is still huge. The numbers are various and are: In North Africa and the Republic of South Africa, there is now, one neurologist and/or psychiatrist for 200,000. For the rest of the continent the ratios range from one neurologist for 500,000 to 5,000,000 people. For Sub-Saharan Africa, 540 million people are managed with 75 EEG machines, 65 CT scanners and 22 MRIs. Local and international initiatives are also described in this report which demonstrates that, with originality and cooperation, we can make the difference. A SWOT analysis also seeks ways of strengthening a sustainable cooperation between Europe and Africa for Neurosciences fields.

Disclosure: Nothing to disclose.

PP1082

Does neurology residency prepare one for clinical practice? An EAYNT survey

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Introduction: The transition from a resident to a neurologist is challenging and requires skills beyond theoretical knowledge. We aimed to determine the perceptions of residents and junior neurologists regarding the adequacy of their training for clinical practice.

Methods: An anonymous paper-based survey developed by officers of the European Association of Young Neurologists and Trainees. It was distributed to the 120 participants of a Neurology Course in 2013 organized by the European Federation of Neurological Societies. The domains surveyed included perceptions regarding overall preparation for clinical practice, quality of supervision and teaching, guidance to obtain practical skills. The rating was performed on a 5 point scale (0 = unsatisfied; 4 = very satisfied).

Results: Eighty-eight (73 %) returned the survey. The median work experience was 4 years, 45 % had the national board certification. Only 52 % of the respondents were generally satisfied with the neurology training they received. The respondents indicated many deficiencies in the curricula. Almost 42 % reported that they had not received the adequate skills to manage neurological emergencies. Almost 70 % of the respondents were not taught sufficient neurophysiology skills. Nearly 87 % were not satisfied with the available research opportunities during residency.

Conclusions: Our study indicates that there are major gaps in residency curricula in the European Union (EU) and neighboring countries. An EU-wide core curriculum for residency training with common paths devoted to aquisition of practical skills and preparation for future clinical work was defined by the Union of European Medical Specialists. Adoptions of the European core curriculum on the national levels are eagerly awaited.

Disclosure: Nothing to disclose.

PP1083

Regulation of HIF prolyl hydroxylase 2 by gingerol in preventing prion protein-mediated neuronal toxicity

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Introduction: Prion disease is one of the progressive conditions, and it is a fatal brain disease that affects both human and domestic animals. PrP (106–126) retains the neurotoxic properties of the entire pathological PrPsc and it is generally used as a reasonable model to study the mechanism of prion diseases. Our previous studies have shown that HIF-1α is involved in the gingerol-mediated protection of neuron cells.

Methods: The Hypoxia Inducible Factor (HIF) mediates cellular adaptations to low oxygen. Prolyl hydroxylase 2 (PHD2) is oxygen sensor that hydroxylate the HIF alpha-subunit, promoting its proteasomal degradation in normoxia. We have hypothesized and investigated that gingerol inhibits the activity of PHD2, and prevents the HIF-1α protein proteasomal degradation, thereby prevents the occurrence of PrP (106–126)-induced neuronal apoptosis.

Results: Briefly, our results indicated that gingerol prevents the occurrence of PrP (106–126)-induced neuronal apoptosis via HIF-1α up-regulation mediated by inhibiting of PHD2 activity in normoxia. Moreover, the protective effect of gingerol against PrP (106–126)-induced neuronal apoptosis was involved in the upregulation of the expression of PrPc protein.

Conclusions: In conclusion, our results indicate that gingerol has a therapeutic potential for prion disease because its inhibitory effect on the catalytic activity of PHD2 might be of clinical benefit.

Disclosure: Nothing to disclose.

PP1084

Lactoferrin-mediated inhibition of prolyl hydroxylase 2 prevents prion protein-mediated neuron cell death

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Introduction: Prion disorders are associated with the conversion of normal cellular prion protein (PrPc) to the abnormal scrapie isoform of prion protein (PrPsc). Recent studies have shown that expression of normal PrPc is regulated by hypoxia-inducible factor1 alpha (HIF-1α), and that lactoferrin increases full-length PrPc on the cell surface. Lactoferrin is an 80 kDa iron-binding glycoprotein with various biological activities including iron chelating ability.

Methods: HIF-1α and the associated ubiquitin–proteasome pathway are regulated by HIF prolyl-hydroxylases 2 (PHD2). We hypothesized that lactoferrin regulates PHD2 expression and enzymatic activity, and the PHD2 regulation promotes HIF-1α stabilization and prevention of neuronal cell death mediated by prion protein (PrP) residues (106–126).

Results: Lactoferrin protects against PrP (106–126)-induced neurotoxicity by the induction of PrPc expression via strengthening of HIF-1α stabilization in neuronal cells. Futhermore, lactoferrin promotes HIF-1α stabilization through down-regulation of the PHD2 protein and inhibiting the PHD2 activity.

Conclusions: These results demonstrated that lactoferrin prevents PrP (106–126)-induced neurotoxicity via the up-regulation of HIF-1α stabilization which determined by PHD2 expression and enzymatic activity. In addition, these findings suggest that possible therapies such as PHD2 inhibition, or promotion of lactoferrin secretion, may have clinical benefits in neurodegenerative diseases, including prion disease.

Disclosure: Nothing to disclose.

PP1085

Patient career involved care

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Introduction: Here we involve the own patients' careers to participate in their patients own care in the acute stage during the initial days of their hospital stay after an ultra short training and meticulous selection instead of waiting without management aiming at: (1) Better commitment from the patient career if they were well selected. (2) Reduce burden upon the available nursing staff in the ward by the careers assistance. (3) Improving the quality doesn't always necessitate spending more money. (4) Improving the home care of the patient after hospital discharge by creating experienced careers. (5) Zero cost.

Methods: Comparative study between two groups of patients each of them was formed of 5 patients.Group one including patients only, Group two including patients and involvement of their carer in the acute management.

Results: Group 2 including the patients and their carer showed a better outcome as regard activity of daily living, shorter hospital stay and less financial burden than group 1 including the patients only.

Conclusions: Overall prognosis of patients whom their careers were heavily involved in their relative's plan of management from the start can represent an outlet for the limited resources in the developing countries.

Disclosure: Nothing to disclose.

PP1086

Prevalence and predictors of burden in caregivers of people with chronic neurological disease

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PP1087

Seizure and severe hyponatraemia in drug abusers: a clue to synthetic cannabinoids consumption?

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PP1088

Coincidence of ischemic stroke and lead poisoning: a case report

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PP1089

Abstract withdrawn

PP1090
Adherence to stroke treatment pathway reinforced by stroke education program

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PP1091
Telemedicine: is tele-EEG, tele-electrophysiology and telecytology possible: a feasibility study

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PP1092
Biomedical ethics in Russian neurology: successes and problems

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PP1093
Cognitive, extrapyramidal and proprioceptive dysfunction after glyphosate: surfactant herbicide exposure

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PP1094
Knowledge and awareness regarding Parkinson's disease in general population: truth and prejudice

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PP1095
Impact of the implementation of the European Working Time Directive in burnout levels of trainee neurologists: longitudinal study

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PP1096
Awareness about pain management in Greece

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Headache and pain 1

PP1097
Efficacy of Botulinum toxin-A treatment in chronic migraine: First middle east experience

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Introduction: BoNT-A is approved for prophylactic treatment of CM. We aimed to assess the efficacy and safety of Botulinum toxin-A (BoNT-A) in the treatment of chronic migraine (CM).

Methods: This open-label prospective study included 40 CM patients. Each patient received 100 units of BoNT-A following fixed site fixed dose protocol. Patient's headache was assessed by their headache dairy and recording Headache Impact test (HIT-6) at baseline and 4th, 8th and 12th weeks following BoNT-A injection. Adverse events (AEs) were monitored. For willing patients, BoNT-A injection was given and they were assessed at 3 months interval.

Results: After BoNT-A treatment, there were reduction in all parameters (headache frequency and severity, analgesic consumption and HIT-6 score) by 35–40 % at 4th weeks, 41–45 % at 8th weeks and 39–42 % at 12th weeks post treatment. At 4th week, 62.5 % of patients achieved good response while, 37.5 % indicating no alteration in their headache frequency and severity. At 8th weeks and 12th weeks post treatment 30, 25 %, respectively, were found to have no response to treatment. Five patients (12.5 %) experienced mild and short lasting AEs. There was 60–70 % improvement of variables after repeated injections.

Conclusions: BoNT-A is effective and well tolerated therapy in the prophylaxis of CM.

Disclosure: Nothing to disclose.

PP1098
THE rs1835740 variant on 8q22.1 in episodic and chronic migraine

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Introduction: The first genome-wide association study (GWAS) has identified the migraine susceptibility variant rs1835740. The rs1835740 variant has no significant influence on the clinical expression of migraine with aura and migraine without aura. rs1835740 is possibly involved in glutamate homeostasis, which plays a crucial role in migraine chronification. The aim of the study was to evaluate the rs1835740 variant prevalence in episodic and chronic migraine.

Methods: 143 patients with migraine (ICHD-III-beta criteria, 2013) were included; all those patients applied to specialized University headache clinic in Moscow region. 97 patients had episodic migraine (EM), 46 had chronic migraine (CM). The age of patients was 41.5 ± 12.5 years. DNA was prepared from blood samples using Magna DNA Prep 200 kit (Isogene Lab. ltd, Russia). Real-time PCR allele discrimination was performed with the qPCRmix-HS kit (Evrogen, Russia). Primers and probes were synthesized by DNA Synthesis, LLC (Russia). Amplification, detection, and data analysis were performed with a CFX-96 real-time detection system (Bio-Rad, USA).

Results: The prevalence of CC genotype of rs1835740 was 78.5 % in EM and 79.6 % in CM, p = 0.8; the prevalence of CT genotype was 20.3 % in EM patients and 20.5 % in CM patients, p = 0.9; the prevalence of TT genotype 1.3 % in EM and 0 % in CM, p = 0.4.

Conclusions: We did not observe significant difference in the rs1835740 variant prevalence among patients with episodic and chronic migraine. We noticed possible lower prevalence of the rs1835740 variant in Russian migraine patients compared with those in West-European population.

Disclosure: Nothing to disclose.

PP1099

Is oral lornoxicam effective in the treatment of acute migraine attacks? A randomized-controlled study

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Objective: To evaluate the effectiveness of lornoxicam (LNX) in the treatment of acute migraine attacks in adults.

Materials and methods: Forty-four volunteers suffering from acute migraine attacks without aura were enrolled in a prospective, randomized, double-blind, placebo-controlled study lasting equally to the time needed for the occurrence of 4 attacks. Patients were asked to take orally one of the tablets from the blister (Placebo/LNX) given for the study and one more tablet if the headache persisted for three hours. Maximum two tablets per day were allowed. If the headache persisted despite the use of the two tablets, eletriptan 40 mg was permitted at least an hour after the second tablet. The severity of headache was evaluated before taking the drug and afterwards at the 15th, 30th, 60th, and 90th min and at the 2nd, 3rd, 6th, 12th, and 24th h with a yes/no questionnaire. Satisfaction was assessed with a rating system of 5 points (1–5).

Results: Thirty-three placebo and 87 LNX tablets were depleted for a total 120 number of attacks. No tablets were taken for the rest 56 attacks. No statistically significant differences were found between two groups regarding both the severity of pain and treatment satisfaction. In the LNX group, drug related dizziness (n = 1), stiff neck (n = 1), fatigue (n = 1) and suspicious drug related fever (n = 1) and epilepsy seizure (n = 1) side effects were observed.

Conclusion: No significant differences regarding safety and effectiveness in treating acute migraine attacks were found between the LNX and placebo groups.

Disclosure: Nothing to disclose.

PP1100

A case of migraine with aura presenting transient visual field loss in visual field test

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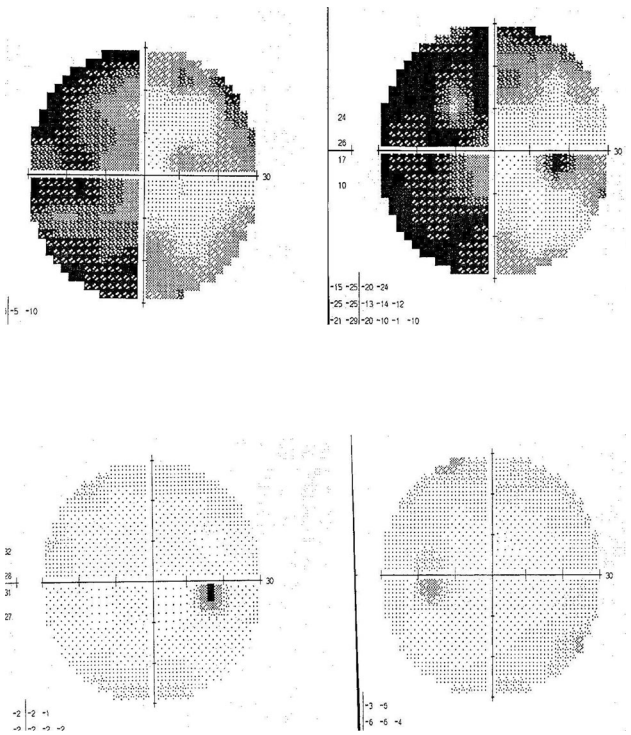
Introduction: Migraine with aura accounts for 10 % of all migraine cases and more than one third of migraine patients have visual symptoms. Aura symptoms are difficult to be detected with laboratory methods. In the literature, aura detected by laboratory methods are rare. We present a case of migraine with aura presenting with visual aura which then confirmed by visual field test.

Case report: A 21-year-old female patient applied for the complaints of pulsatile, severe headache and blurred vision. She had headache for a long time and a family history of migraine. In the examination, no abnormality except for left homonymous hemianopsia. Left homonymous hemianopsia was detected in visual field test (Figure 1). Visual field test repeated on the third day following disappearance of pain was found to be normal (Figure 2).

Conclusions: The pathophysiology of migraine with aura has been subjected to several studies, but a well-accepted mechanism hasn't been established yet. Various opinions have been proposed and some of them have been partially confirmed. However, most of the views put forward are based on cortical spreading depression described by Leão.Why the characteristics of aura differ from attack to attack and why pain is localized unilaterally/bilaterally? Similar questions remain unanswered. We are of the opinion that identification of aura symptoms with laboratory methods in such way that is more objective and evaluation of these findings with the characteristics of resulting pain would make contribution to the better understanding of the pathophysiology of migraine in the future.



Disclosure: Nothing to disclose.

PP1101

Lacosamide as a therapeutic option in a refractory canial neuralgia: results in a series of 20 cases

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Introduction: Lacosamide is a third-generation antiepileptic drug that enhances slow inactivating state of voltage-gated dependent sodium channels. It has been proposed to be useful in the management of neuropathic pain and has been used in small series or isolated cases of cranial neuralgia. We aimed to evaluate its effectiveness in a series of patients with cranial neuralgia refractory to treatment.

Methods: Patients attended in two outpatient headache offices in tertiary hospitals (January 2013–January 2014). Cranial neuralgias diagnosed accordingly to ICHD-III criteria. We have offered lacosamide treatment to patients unresponsive to at least two oral

therapies, one of them carbamazepine. Initial dose of 50 milligrams twice daily and it was increased when necessary at weekly intervals by 100 milligrams/day. We gathered demographic and nosological characteristics. Response was grouped into complete (pain free), partial (reduction in severity or frequency of pain of at least 50 %), or no response.

Results: 20 patients (11 females and 9 males), mean age 60.6 ± 15.2 years (range 24–85).16 of them (80 %) diagnosed of classical trigeminal neuralgia. Previously unresponsive to antiepileptic drugs apart from carbamazepine (16 cases, 80 %, range 1–6 drugs), antidepressants (12, 60 %),or peripheral nerve blocks or surgery(4, 20 %). Lacosamide final dose of 230 ± 96.5 milligrams (100–400); discontinued due to side effects in 3 cases (15 %). A complete response was achieved in 7 patients (35 %) and a partial effect in 6 (30 %).

Conclusion: According to our experience, lacosamide is a potentially effective treatment in refractory cranial neuralgia. Further research is needed to confirm these preliminary findings.

Disclosure: Nothing to disclose.

PP1102

Pain management by means of spinal anesthesia with isobaric levobupivacaine or bupivacaine

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Introduction: Local anaesthetics are used for regional anaesthesia during surgery and for postoperative pain management. The choice of local anaesthetic is determined by matching the patient's anaesthetic and/or analgesic requirements with the pharmacological properties of specific agents.

Methods: A prospective, double-blind, randomised study with 60 ASA grade I–II patients aged 18–65 years awaiting knee arthroscopy under spinal anesthesia was performed. There were two patient groups which received 12.5 mg of isobaric bupivacaine or 12.5 mg of isobaric levobupivacaine. The characteristics of postoperative visual analogical scale (VAS), rescue analgesia and patient satisfaction were recorded.The scale to evaluate patient satisfaction was as follows: excellent (no intraoperatory pain at all), good (slight intraoperatory discomfort with no need for analgesia), fair (pain that required further analgesia with nonsteroidal anti-inflammatory drugs—NSAIDs) and poor (pain that required NSAIDs and opioids). Postoperative pain was recorded every 30 min using a visual analogical scale (VAS) ranging from 0 (no pain at all) to 10 (maximal pain). If the pain score at rest was ≥ 4, dexketoprofen 50 mg/8 h I.V. and paracetamol 1 g/6 h I.V. were administered.

Results: Statistically significant differences were found between both groups for the time [in min; median (range)] to require analgesic drugs after spinal anaesthesia [bupivacaine 297 (146–444), levobupivacaine 247 (184–436)]. Patient satisfaction was 82.1 % excellent and 17.9 % good in Group B, and 80.6 % excellent and 19.4 % good in Group L ($p = 0.883$).

Conclusions: Isobaric bupivacaine and levobupivacaine are analogous anaesthesias for the pain control in knee arthroscopy and both are well-tolerated. However for bupivacaine a longer post-operative painless period was achieved.

Disclosure: Nothing to disclose.

PP1103

Abstract withdrawn

PP1104

Intravenous theophylline relieves post lumbar punction headache promptly

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Introduction: Post lumbar puncture headaches (PLPH) occur in 10–30 % of the patients following lumbar puncture. Epidural blood patch, intravenous hydration, bed rest, theophylline, caffeine, hydrocortisone and pregabalin are the options for the treatment. There are limited numbers of reports pointed out to the efficacy of theophylline in PLPH. We aimed to reveal the time period for onset of the effect of ıntravenous theophylline for relieving PLPHs.

Methods: PLPH patients were included in this study. Patients who had central nervous system infections and malignancies, intracranial haemorrhage, hydrocephalus, intracranial hypertension, convulsions, hypertension, cardiac arrhythmia and those older than 65 years were excluded. Patients were given 200 mg intravenous theophylline (200 mg theophylline in 100 mL 5 % dextrose) infusion over 40 min as indicated in the literature. VAS's were questioned at 0, 30 and 60 min after beginning of the infusions while in sitting positions. Seven patients were included in the study.

Results: Mean age 38.4 year. All of the patients reported decrease of pain. None of them have had a side effect. Mean VAS values at 0, 30 and 60 min were respectively as; 7.2, 3.8 and 2.8. Percentages of VAS decreases between 30–0 min and 60–0 min were respectively as; 47.2 and 61 %.

Conclusions: We found that ıntravenous theophylline rapidly and effectively relieves PLPHs. We concluded that intravenous theophylline is an easy, rapid, effective and safe treatment. To the best of our knowledge, this is the first study demonstrating the time period of the effect of theophylline for relieving PLPHs.

Disclosure: Nothing to disclose.

PP1105

Ophthalmoplegic migraine or multiple cranial mononeuropathy? The diagnostic challenge of a controversial disorder

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Introduction: Ophthalmoplegic migraine is a rare disorder of recurrent migrainous headache with ophthalmoparesis whose pathogenesis is unknown. Whether it should be classified as a migraine variant or painful ophthalmoplegic neuropathy is still debated.

Case report: Fifty years-old female, with history of migraine without aura in her youth, admitted in 2007 for throbbing left orbital and hemicranial headache, with ipsilateral ptosis and ophthalmoparesis, consistent with oculomotor nerve palsy. The investigation, including brain MRI, MR angiography, viral serologies, vasculitis investigation and CSF cytochemical examination, was negative. Symptoms gradually resolved. In 2011 she had a right peripheral facial palsy. In 2013 she was again admitted for tightening right

orbital and periorbital headache, accompanied by photophobia, phonophobia and, 2 days later, diplopia. A right ptosis, mydriasis and ophthalmoparesis were present, consistent with oculomotor nerve palsy. A detailed investigation was again conducted: brain MRI and MR angiography; serum analysis for viral serologies and inflammatory disorders; CSF analysis including cytochemical, microbiological, PCR for neurotropic viruses, *M. tuberculosis* and *Borrelia,* protein electrophoresis. All of it was negative with the exception of newly diagnosed glucose intolerance. The patient was started on prednisolone. There was a progressive and complete clinical improvement. Nine months later, she remains asymptomatic.

Conclusion: In the present case, criteria for ophthalmoplegic migraine are fulfilled. However, the diagnosis of glucose intolerance in the second episode and the occurrence of a peripheral facial palsy amidst episodes, are findings that, although feeble, open the possibility of a multiple mononeuropathy, conferring additional uncertainty to an already challenging entity.

Disclosure: Nothing to disclose.

PP1106

Rupture of an arachnoid cyst as unusual cause of thunderclap headache

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Objectives: The term 'thunderclap headache' refers to a headache with sudden onset and maximum intensity from the beginning. Subarachnoid haemorrhage (SAH) is the most common and severe cause of thunderclap headache, although there are many others, including primary forms. Its appearance constitutes a real alarm symptom which forces a broad differential diagnosis, given its important morbidity and mortality. We present an extremely infrequent cause of thunderclap headache.

Methods: 39-year-old man came to the Emergency Room complaining of 72 h, continuous, very intense, holocraneal headache of sudden onset, with pulsatile-stabbing quality, that increased with cephalic movements and did not response to usual analgesics (acetaminophen and NSAIDs). As a precedent, he referred banal trauma 4 days earlier. Systemic, neurological and ophthalmological exploration were normal.

Results: Cranial CT showed a large left fronto-temporo-parietal arachnoid cyst, expanding over the cerebral parenchyma, with midline displacement. Brain MRI showed rupture of the cyst wall to the subdural space and bilateral subdural hygromas. The patient progressed favourably with conservative treatment with corticoids and common analgesics, reason why surgical treatment was rejected.

Conclusions: The symptomatic presentation of arachnoid cysts in this age group is unusual. Its break is very infrequent and an extraordinary cause of thunderclap headache. Its differential diagnosis goes clearly beyond SAH. Neuroimaging tests are essential to distinguish the different possible aetiologies.

Disclosure: Nothing to disclose.

PP1107

Headache as the leading neurological sign of cavernous sinus thrombosis: a case report

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Introduction: Headache is the most frequent symptom in cerebral venous thrombosis (CVT), and usually the first. However, it has rarely been reported as the only symptom of CVT.

Methods: We report one patient with isolated headache in the present observation at the neurology department in Mahdia-Tunisia.

Results: A 65-year-old male presented with bifrontal headache and fever of sudden onset. In the neurology exam, we noted: Ptosis, chemosis and cranial nerve palsies (III, V, and VI). Cerebral Magnetic Resonance Imaging (MRI) showed a cavernous sinus thrombosis with sinusitis and ethmoiditis. Treatment includes prolonged courses (2 weeks) of two antibiotics and anticoagulation with heparin. The back pain was reduced significantly.

Conclusions: Cavernous sinus thrombosis is a multifactorial condition with gender-related specific causes, with a wide clinical presentation. The cause is usually from a spreading infection in the nose, sinuses, ears, or teeth. Staphylococcus aureus and Streptococcus are often the associated bacteria. Cavernous sinus thrombosis symptoms include: decrease or loss of vision, chemosis, exophthalmos (bulging eyes), headaches, and paralysis of the cranial nerves which course through the cavernous sinus. This infection is life-threatening and requires immediate treatment, which usually includes antibiotics and sometimes surgical drainage. Prognosis depends on the early detection. Correcting the cause, generally the complications can be prevented.

Disclosure: Nothing to disclose.

PP1108

Evaluation of aqueduct CSF flow dynamics with cine phase contrast MRI in patients with idiopathic intracranial hypertension

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Introduction: We aimed to determine whether there is a difference between the patients with idiopathic intracranial hypertension and control group concerning the parameters of CSF flow dynamics at aqueduct level through cine phase contrast MRI, and whether medication taken by these patients has led to any changes in FKS MRG findings.

Methods: There were 10 chronic patients diagnosed with IIH and receive treatment, 10 acute patients who receive no treatment, and a control group of 10 healthy volunteers admitted to this study. Quantitative analysis of CSF flow was made based on the axial images acquired through phase contrast MRI technique at the level of aqueductus. Among these three groups, average peak velocity (cm/s), average velocity (cm/s), forward flow volume, backward flow volume (ml), net forward flow volume (ml), flow rate values of the flow passing through the aqueductus and their aqueductal area were compared.

Results: It was found that there was a difference between IIH patient group who participated in the study and the control group in terms of peak velocity and the peak velocity decreased in patients.

Conclusions: Concerning IIH, a decrease during the transfer of venous blood out of cranium probably because of some venous system problems will decrease the venous compliance and this will lead to an increase in intracranial pressure. It is considered that the reason for the decreases in flow velocity and the flow rate passing through the aquaductus of the patients receiving treatment can be related with CSF production decrease due to treatment.

Disclosure: Nothing to disclose.

PP1109

Cerebral venous sinus thrombosis after spinal anasthesia in a patient with three different risk factors

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Introduction: Cerebral venous sinus thrombosis (CVST) is an uncommon disease characterized by clotting of blood in cerebral venous, or dural sinuses, and cortical veins. It is a rare but potentially fatal cause of acute neurological deterioration related to pregnancy, oral contraceptives, neoplasm, surgery, puerperium, systemic diseases, dehydration, and coagulopathies. There are a few reports of patients with CVST after a lomber punction (LP). However multiple etiological factors could be seen at the same time in some patients. We presented a 36-year-old female patient who has three different risk factors for trombosis and developed intracranial hypotension induced CVST after spinal anesthesia.

Case report: A 36-year-old female was performed rectal surgery with spinal anesthesia for adenocarcinoma. Immediately after surgery the patient had a severe, throbbing, orthostatic headache. She was using oral contraceptives for 8 years. Neurological examination was normal except for diplopia and left abducens nerve paralysis. Fundus examination revealed bilateral papilledema. Magnetic resonance imaging (MRI) of the brain revealed common pachymeningeal contrast enhancement and right transverse sinus thrombus. Patient was treated with heparin and warfarin. At the end of the first week drastic reduction in headache was observed.

Conclusion: While the diagnosis of CVST is confirmed, it is essential to determine the etiology of the disease. Urgent treatment, planning for the duration of treatment and finally, avoiding further thromboembolic events are the main objectives of the management. It is worth emphasizing that the etiology of CVST is multi-factorial, therefore more than one etiology should be considered.

Disclosure: Nothing to disclose.

PP1110

Headache attributed to aeroplane travel: a new therapeutic approach?

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The Headache attributed to aeroplane travel (AH) is a recently described headache disorder that appears exclusively in relation to airplane flights. Its diagnostic criteria have been published in the International Classification of Headache Disorders 3beta. AH is characterized by the sudden onset of a severe head pain, mainly during the landing phase. Secondary causes must be ruled out. Airplane travel is a very frequent experience, with more than 3.3 billion seats offered annually on commercial flights with an occupancy of 70 % (Potasman et al. 2008). Therefore it is believed AH to become a common and relevant condition. Less than half of the AH cases described used medications for preventing the attack. Simple analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) and nasal decongestants have been used as prophylactic therapy. A complete or partial benefit was achieved in about 50 % of patients (Mainardi et al. 2012). A complete response of AH to triptans has been previously reported (Ipekdal et al. 2011). A 38 year-old migrainous woman suffers from AH in about 75 % of her flights. As prophylactic treatment, in her last three air travels, she took a long acting triptan (frovatriptan) before take-off and a NSAID (dexketoprofen 25 mg) 20 min before landing. As results, AH did not appear. Indeed, she complained of AH attack in her last flight, when she took only dexketoprofen before landing, but not triptan before take-off. This case report should indicate the combination of a long-term triptan with NSAID as a new possible therapeutic approach for preventing AH attacks.

Disclosure: Nothing to disclose.

PP1111

Migraine aura-triggered seizure or headache associated with epilepsy?

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Introduction: Migraine aura-triggered seizure, which is defined as the evolution of a migraine attack to a seizure, is a complex and controversial entity by some authors. Few cases have been described.

Clinical case: We report the case of a young 23 year old woman with a history of migraine lasting for 5 years and who has never had epileptic seizures, who presented 3 times at night vigils, some visual manifestations of migraine with aura which rapidly changing to a generalized tonic–clonic seizure. The cerebral MRI was normal, waking EEG was normal, but during sleep few spike-wave in central and parietal right areas were observed. After introduction of sodium valproate, we observed a total cessation of seizures, and a decrease in migraine attacks.

Discussion: A continuum between migraine and epilepsy, two conditions that can go interrelated due to changes in cortical excitability can be found at certain privileged observations. Diagnosis "migraine aura triggered seizure" was chosen because migraine meets the criteria for migraine with aura, seizures occur at least 1 h after the migraine with aura and sodium valproate was effective.

Conclusions: In our own opinion, it is a case of migraine aura triggered seizure, but this rare entity whose diagnosis is difficult, remains a challenge for the clinician, who must make sense of things as much as possible.

Disclosure: Nothing to disclose.

PP1112

The prevalence of premonitory symptoms in migraine

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Introduction: The International Classification of Headache Disorders defines premonitory symptoms as symptoms preceding and forewarning of a migraine attack by 2–48 h, occurring before the aura in migraine with aura and before the onset of pain in migraine without aura. Prevalence rates of patients reporting one or more premonitory symptoms range between 33 and 79 % in clinic-based studies. The aim of our study was to evaluate the occurrence and characteristics of premonitory symptoms, and compare them between two migraine subtypes-with and without aura.

Methods: A multicenter study under the auspices of Serbian Headache Society was conducted in four headache centers in Serbia. Using a structured questionnaire, we retrospectively studied the prevalence of 16 predefined premonitory symptoms in 321 patients with episodic migraine.

Results: The mean age of patients was 38.48 ± 12.24 years, 87.9 % were women, and 25.8 % of them had migraine with aura. At least one premonitory symptom was reported by 263 patients (81.93 %). The most frequently reported symptoms were bad mood (61.4 %), fatigue (60.7 %), irritability (55.7 %), stiff neck (55.0 %) and concentration problems (54.1 %). The mean number of premonitory symptoms per subject was 3.3. Migraine subtype had no effect on the mean number of symptoms per individual, and did not influence the number of symptoms that were always or occasionally associated with migraine attack. Anxiety was significantly more often reported in migraine with aura patients ($p = 0.008$).

Conclusions: Premonitory symptoms are frequently reported by migraine patients. Anxiety preceding the attack seems to occur more frequent in migraine with aura.

Disclosure: Nothing to disclose.

PP1113

Tension type headache and headache attributed to cervical myofascial pain: tenoxicam vs myorelaxants efficacy

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PP1114

Abstract withdrawn

PP1116

The financial crisis has an impact in headaches: preliminary experience of the emergency department of Greek terziary clinic

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PP1117

Visual and motor cortex excitability in migraine: a preliminary study

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PP1118

Transdermal electrical stimulator reduces pain in tension-type headache and prevents the development of medication-overuse headache

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PP1119

Personality traits and mood disorders in the patients with medication overused headache versus the patients with episodic migraine

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PP1120

The efficacy of greater occipital nerve blockade in chronic and episodic migraine

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PP1121

Occipital neuralgia that gave complete response to greater occipital nerve blockade

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PP1122

Association among psychiatric condition, sleep and migraine

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PP1123

The effectiveness of Botulinum toxin A on MIDAS scores in chronic migraine patients

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PP1124

Greater occipital nerve blockade in cervicogenic headache associated with whiplash injury: two case reports

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PP1125

Migraine and sinus headache's; sinus CT findings

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PP1126

Gastric carcinoma presenting with isolated headache

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PP1127

Abstract withdrawn

PP1128

Trigeminal neuralgia prior to lateral medullary infarction

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PP1129

OnabotulinumtoxinA treatment for chronic migraine and concomitant temporomandibular disorders

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PP1130

Abstract withdrawn

PP1131

Behavioral effect of DNQX, AMPA receptor antagonist, on repetitive spreading depression phenomenon

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PP1132

Indomethacin responsive headache-chronic paroxysmal hemicrania insted of chronic cluster headache

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PP1133

Perceptual changes in trigeminal neuralgia

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PP1134

Medication overuse headache as a frequent cause of chronic daily headache: a case series

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PP1135

Efficacy of biofeedback-based heart rate variability in the treatment of tension type headaches in adolescents

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PP1136

Indomethacine-responded hemicrania with Horner syndrome

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PP1137

Cinnarizine for the prophylaxis of migraine associated vertigo: a retrospective study

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PP1138

Abstract withdrawn

PP1139

The results of correction of depressive and anxiety disorders with Tenoten in patients with chronic low back pain syndrome

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PP1140

Confusional migraine without amnesia in an adult

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PP1141

Case report: A prevertebral and intraspinal epidural abscess in the cervical spine following generalized furunculosis

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RI of cervical vertebrae Axial postcontrast]
[MRI of cervical vertebrae STIR after 1 week]
Disclosure: Nothing to disclose.

PP1142
Post coronary angiography headache

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PP1143

Abstract withdrawn

Infection and AIDS

PP1144
Multiphasic disseminated encephalomyelitis associated with *Campylobacter jejuni* infection

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Introduction: Acute disseminated encephalomyelitis (ADEM) typically occurs as an isolated post-infectious phenomenon. If a relapse occurs shortly after the ADEM presentation in association with steroid withdrawal, the term multiphasic disseminated encephalomyelitis (MDEM) is used.
Case study: Female, 26 years old, presented with progressive paraparesis developing within a week. She also reported diarrhoea 3 weeks before. Neurological examination showed dysarthria, tetraparesis, ataxia and pyramidal signs, without encephalopathy. Cranial MRI showed multiple bi-hemispheric white matter lesions with enhancement. Spinal MRI, CSF and neurophysiological studies were unremarkable. The titer of anti-*Campylobacter jejuni* antibodies in serum was extremely high and anti-GM2 antibodies were positive, while other infectious and autoimmunity studies were negative. Oral corticotherapy with gradual tapering was started with complete remission of neurological signs. After 3 months, when the patient was completing weaning of steroids, a clinical relapse occurred. MRI revealed absence of new lesions but an area of restricted diffusion in one of the previous lesions, without abnormal enhancement. Corticotherapy was restarted with slower tapering protocol. At 10 month follow up the patient remains asymptomatic on 5 mg prednisolone. MRI showed pronounced regression of prior lesions.
Conclusions: Difficulties still exist in distinguishing ADEM and MS at the initial clinical episode. *C. jejuni* infection has been related to different neurological syndromes linked with antiganglioside antibodies. To our knowledge, only four cases of ADEM associated with Campylobacter were previously described. We report a case of MDEM associated with *C. Jejuni* and anti-GM2 antibodies that extends the spectrum of neuroimmunologic complications of *C. jejuni* infection.

Disclosure: Nothing to disclose.

PP1145
Brain abscess with *Listeria monocytognes* following Rituximab infusion for *Pemphigus vulgaris*

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Introduction: Immunocompramized patients have more risk to develop meningitis or rarely brain abscess due to Listeria monocytogenes.

Objective: To report an immunocompromised patient who had brain abscess following two doses of Rituximab infusion. Up to our knowledge, such case has not been reported in the literatures.

Case report: A 50-year-old, lady, diagnosed with pemphigus vulgaris and diabetes who have been on prednisolone and azathioprine for about 4 years. She presented with headache, low grade fever and left sided weakness, 2 weeks after receiving the second dose of Rituximab infusion. Her MRI revealed enhancing space occupying lesion with multiple small vacuoles and vasogenic oedema at the right temporo-parietal area. Blood culture yielded *Listeria monocytogenes*. Brain biopsy resulted in necrotic tissues with pus and inflammatory cells. She recovered after 6 weeks course of empirical antibiotics with Ampicillin and Gentamycin.

Conclusion: Brain abscess with listeria is a risk that should considered when adding Rituximab therapy to a patient who already immunocompromised.

Disclosure: Nothing to disclose.

PP1146
A sinister cause of cavernous sinus thrombosis

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Presentation: A 44-year-old lady with poorly controlled type 1 diabetes mellitus presented with left-sided facial pain. She was treated with metronidazole for a tooth abscess but represented 1 week with headache and facial drooping.
Examination: On examination she had chemosis and complete ophthalmoplegia of her left eye with an unreactive pupil. She had reduced sensation in all branches of the trigeminal nerve and had a left lower motor neurone facial palsy. There were no abnormal findings in the limbs.
Results: Blood tests revealed elevated inflammatory markers. An MRI brain revealed expansion of the left cavernous sinus with no enhancement with contrast. She was diagnosed with cavernous sinus thrombosis and treated with anticoagulation and antibiotics. A CT head revealed non-enhancing left-sided turbinates consistent with the "black turbinate sign" associated with invasive mucormycosis.
Management: Antifungal therapy was commenced She underwent surgical debridement and biopsy which revealed necrotic nasopharyngeal tissue and fungal culture confirmed mucormycosis. She developed right-sided limb weakness and a repeat CT head revealed a right-sided pontine infarct and a new left cerebellar artery aneurysm. 9 days after initial presentation she developed low GCS. A CT head revealed acute subarachnoid haemorrhage and the patient died shortly after.
Conclusion: Mucormycosis is a rare but serious fungal infection which must be considered in patients with diabetes and facial sinus infection. Aggressive surgical debridement and antifungal therapy are required but despite these measures, fatality is very common. This poster will review the literature on the diagnosis and management of cerebral mucormycosis.

Disclosure: Nothing to disclose.

PP1147

Migrenous headache and hemispheric cerebral, progressiv, oedema in a young woman: a challenging case

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Introduction: We report a 32-year-old woman with progressive migrainous headache evolving from 9 months with no other medical complaints. Repeated neurological examination, fundoscopies was normal and NSAID just ameliorate for short time the headache. Progressive evolution *determined neuroimaging* investigation. Repeated (3 weekly) dynamic computed tomography revealed an increasing left hemispheric oedema. Patient developed newly diagnosticated focal motor right seizure and slightly right hemiparesis. MRI showed multifocal T2-high lesions mainly in the cerebral white matter, in the left hemisphere, and partly in the cerebral cortex. No gadolinium enhancement was found. CSF examination revealed that the cell count was slightly increased (8/mm^3, protein level (41 mg/dl), and IgG index (0.4) were normal. Encephalitis was evoked but the MR spectroscopy *raise* the *possibility* of cerebral low grade glioma. Than, a brain biopsy was necessary and revealed demyelinating pathology: demyelinating plaques involving the subcortical U-fibers with sparing of the cortex and deep gray matter. These findings were consistent with progressive multifocal leukoencephalopathy. Her symptoms were subacutely progressive, and she developed akinetic mutism 2 month after seizure onset. Polymerase chain reaction (PCR) was positive for JC virus.

Disclosure: Nothing to disclose.

PP1148

Progressive multifocal leukoencephalopathy in a patient with adrenal cortical tumor

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Introduction: Adrenal cortical tumors can present with Cushing's syndrome accompanied with central obesity, buffalo hump, moon face, striae, weight gain, hypertension and diabetes mellitus but also immunosuppression due to hypercortisolism. We report about a man from Bangladesh with neurofibromatosis type 1 who developed dysarthria, confusion, central facial paresis and right-sided limb weakness over a one-month period during the workup for Cushing's syndrome.

Methods: CT abdomen showed an 80 × 60 × 80 mm contrast enhancing tumor in the right adrenal gland with compression of the vena cava and the right liver lobe consistent with an adrenal cortical carcinoma. An initial cranial CT suggested cerebral infarctions lacking clinical correlation. A following MRI of the brain showed bilateral high signaling diffuse T2 and FLAIR white matter changes with involvement of U-fibers that corresponded to Progressive Multifocal Leukoencephalopathy (PML). The cerebrospinal fluid analysis revealed no cell elevation but there was a significantly raised albumin quote. Only 200 JC virus copies/ml were found. An initially low CD4+ and CD8+ count rose after the total resection of the right adrenal gland to normal levels. An attempt to treat with mefloquine was discontinued due to rapid deterioration.

Results: After an initial post-operative neurological deterioration, the patient's condition stabilized 2 months post-operative, now being wheelchair dependent, in the need of 24 h assistance, percutaneous endoscopic gastrostomy tube and using monosyllabic communication. The patient suffers of epilepsy.

Conclusions: This presented case is the first reported association of an adrenal cortical tumor induced hypercortisolism and PML.

Disclosure: K. Fink received travel compensation for a consulting assignment from BiogenIdec.

PP1149

Cerebellar form of progressive multifocal leukoencephalopathy in a patient with pulmonary sarcoidosis

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Introduction: Progressive multifocal leukoencephalopathy (PML) is a demyelinating disease of the central nervous system caused by JC virus reactivation that occurs nearly exclusively in immunocompromised patients, particularly in those who are HIV positive. We report a rare case of cerebellar form PML in a patient with pulmonary sarcoidosis.

Case report: A 25-year-old-man was admitted with gait and speech disturbances that developed over 2 months as well as pulmonary sarcoidosis from 4 years prior without therapy. Neurological examination findings revealed ataxic gait, scanning speech, horizontal nystagmus and incoordination in all extremities. Blood tests showed elevation of angiotensin-converting enzyme and lysozyme, while the percentage of T lymphocytes, especially the CD4 subset, was decreased with a normal CD4/CD8 ratio. HIV-1, and -2 antibodies and a tuberculin skin test were negative. Chest CT revealed bilateral hilar lymphadenopathy. Magnetic resonance imaging (MRI) of the brain demonstrated fluid-attenuated inversion recovery high signal intensity in the bilateral middle cerebellar peduncles extending into white matter. Despite steroid and immunoglobulin therapy, tetraplegia and eye movement impairment developed, and he became lethargic and locked-in syndrome. PML was diagnosed following PCR detection of JC virus DNA in cerebrospinal fluid. Abnormal lesions shown by MRI gradually spread to the pons, medulla, thalamus, and finally subcortical white matter of the frontal lobe after 6 months.

Conclusions: This case supports the hypothesis that a CD4/CD8 ratio shift in sarcoidosis with lack of JC virus-specific cytotoxic cells facilitates PML development. PML should be considered in sarcoidosis patients with white matter lesions.

Disclosure: Nothing to disclose.

PP1150

The chameleon and master of all mimics: a case of neurosyphilis presenting as an HSV encephalitis

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Introduction: Neurosyphilis is thought to be almost extinct in the non-HIV population. It has been reported infrequently in the literature as a clinical and radiological mimic of HSV encephalitis.

Methods: A highly illustrative case of neurosyphilis presenting as a presumed viral/HSV encephalitis is described with a review of the literature.

Results: A 67-year-old White British gentleman presented with a week's history of drowsiness, confusion, sweats and olfactory hallucinations with associated poor appetite, nausea and vomiting. He was sweaty and confused with poor attention and perseveration. There was visible focal and complex partial seizure activity. An MRI brain showed right medial temporal lobe signal change. A CSF showed 90 white cells, 90 % lymphocytes with a raised protein of 0.90. He was treated with aciclovir for presumed HSV encephalitis. The CSF viral PCR was negative. A repeat CSF showed 51 white cells, 80 % lymphocytes and protein 1.12 and negative PCR. He developed an erythematous maculopapular rash over his trunk. A screen for autoimmune and paraneoplastic encephalitis and was negative. A serum VDRL result was later received and was positive with an RPR of 1:128 and a positive TPPA with a titre of 1:1280, consistent with a diagnosis of recent treponemal infection. CSF VDRL serology was positive. He was treated for 21 days with high dose IV penicillin.

Conclusions: Neurosyphilis has been identified as presenting as HSV-like temporal encephalitis. We recommend VDRL testing as standard in such PCR-negative presentations, regardless of retroviral status as all the reports are in HIV-negative individuals.

Disclosure: Nothing to disclose.

PP1151

Early progressive multifocal leukoencephalopathy in a patient with common variable immunodeficiency syndrome reversed under mirtazapine and mefloquine treatment

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Introduction: Demonstration of reversal of progressive multifocal leukoencephalopathy (PML) in a patient with common variable immunodeficiency syndrome (CVID), consisting of severe hypogammaglobulinemia and CD4+ T lymphocytopenia, during treatment with mirtazapine (30 mg/day) and mefloquine (250 mg/week) over a 12 months period.

Methods: Regular clinical examinations including Rankin scale and Barthel index, nine hole peg and box and block tests, Berg balance and 10 m walking tests, and Montreal Cognitive Assessment (MOCA). Laboratory diagnostics included complete blood count and JC virus (JCV) count in cerebrospinal fluid (CSF). The non-coding control region (NCCR) of JCV, important for neurotropism and neurovirulence, was sequenced. Repetitive high-resolution MRI was performed to investigate brain lesion load.

Results: Barthel (60–100 points) and Rankin (4–2) scores, performances in nine hole peg (300–52 s) and box and block (7–35 pieces) tests, and gait stability and walking speed improved. MOCA showed a slight but stable cognitive impairment. JCV disappeared over 3–5 months from 2,568 to 0 copies/ml. The NCCR showed genomic rearrangement. Over time, JCV with NCCR rearrangements were detected that rather resembled the archetype sequence. Cerebral MRI lesion load decreased (8.54–6.31 cm^3) and brain atrophy became apparent.

Conclusions: The patient with congenital CVID who contracted PML with rapidly worsening neurologic deficits at age of 56 years showed improvement followed by stabilization under continuous mirtazapine and mefloquine treatment over the course of 1 year. This was paralleled by JCV clones with lower replication capability before JCV could not be detected anymore.

Disclosure: Nothing to disclose.

PP1152

Encephalic complications of sinusitis about 13 cases

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Introduction: Sinusitis can cause multiple encephalic complications, which although they are exceptional, can be threatening for life and functional prognosis.

Observations: We report 13 cases of adolescents aged from 13 to 19 years, who presented a not treated sinusitis, complicated by cerebral abscesses in 6 cases, cerebral empyema in 4 cases, 2 cases of encephalitis and 1 case of cerebral thrombophlebitis. The germ highlighted in four cases was Haemophilus influenzae. For other cases cultures were negative (probably caused by antibiotic taken earlier). All patients were HIV negative, and patients who presented suppurative collections received neurosurgical treatment with good outcome for 8 of them, and 5 patients died. Patients with encephalitis and cerebral thrombophlebitis received antibiotics for 45 days with good outcome.

Results: Intracranial suppurations from ORL origine are caused in 87 % of cases to sinusitis, they are certainly caused to the late arrival of patients in our hospitals because they often come at the stage of complications. Our patients come an average 14 days after the onset of symptoms, which is consistent with the literature where some come after 1 month.

Conclusions: Sinusitis is a disease requiring treatment early, thus avoiding serious complications which are frequent in our country because of the late arrival of patients in hospitals.

Disclosure: Nothing to disclose.

PP1153

Flaccid paraplegia: a consequence of medula spinal compression lymphoma with a HIV patient

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A case of a 56 year old HIV-positive patient with ALCL who had abnormal spinal cord compression syndrome is presented. One of the major late manifestations of the underlying disease in patients with infection by the human Immunodeficiency (HIV) is the occurrence of lymphoma. Two main types of lymphoma are Hodgkin's lymphoma HL and non - Hodgkin's lymphoma NHL. 56-year-old man, family-healthy, asked for doctor's help because of subfebrile conditions that lasted for 20 days, constant pain in the muscles of arms and legs. After a routine examination by internist, performed laboratory blood tests, he was treated as likely flu situation. Fifteen days later, he felt a general weakness and severe pain in the lumbar region of the spine.

Due to continuous subfebrility hospitalized at the Clinic of Infectious Diseases. During hospitalization gradually leg weakness and numbness occured that progressed to flaccid paraplegia. All laboratory test repeated. Among other tests, ELISA and "Western Blot" were done and were positive. Antiviral therapy was included. RTG of thoracolumbosacral spine was normal. Magnetic resonances imaging (MRI) of the thoracolumbar spine showed heterogeneous ventilation on spine vertebrae at different levels of the thoracolumbar spine and extradural soft tissues of T10–L1 which made cord compression. The patient undergone surgery and laminectomy and extradural mass was removed. It was histologically confirmed that extradural mass corresponds ALCL. After that, therapy was conducted (cyclophosphamide, doxorubicin, vincristine and prednisolone) and followed by radiotherapy. Currently, patient is in generally stable condition, with flaccid paraplegia.

Disclosure: Nothing to disclose.

PP1154

Invasive brain aspergillosis following alemtuzumab therapy

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Introduction: Despite its remarkable efficacy, alemtuzumab therapy can be accompanied by serious complications, including cytopenia and subsequent infections. Fungal infections are mainly evident during the post-treatment phase. These infections are also common within patients suffering from hematologic malignancies.

Case report: A 74-year-old female in remission of B cell chronic lymphocytic leukemia, submitted to alemtuzumab and intravenous steroids developed apathy and functional dependence progressing over 5 months. She was admitted to the hospital due to a subacute right hemiparesis. Neurological examination revealed a drowsy patient, right oral myoclonic movements, right homonymous hemianopia, and severe right hemiparesis. Analytic work-up and head CT were unremarkable, with the exception of mild elevation of D-dimers. Electroencephalogram was compatible with grade 2–3 encephalopathy. CSF samples were normal, with no identifiable bacteria, fungi or neoplastic cells, normal immunophenotyping and negative JC virus PCR. She continued worsening presenting fluctuant mental status. A second head CT showed a non-enhancing hypodensity in the right occipital lobe. Brain MRI revealed multiple hyperintense T2-signal lesions. She entered in septic shock due to ischemic colitis. Post-surgery, the patient suffered an extensive fatal left temporo-parieto-occipital hemorrhage. At post-mortem, fungal hyphae were identified in some of the brain lesions and *Aspergillus* was also identified in lungs.

Conclusions: Invasive pulmonary aspergillosis and cytomegalovirus reactivation are the two most commonly seen opportunistic infections in alemtuzumab therapy. Intracranial Aspergillus infection corresponds to 10-20 % of all cases of invasive aspergillosis and remains a challenging diagnosis, especially due to its non-specific clinical presentation and uncommon fungus growth in CSF.

Disclosure: Nothing to disclose.

PP1155

Listerial brainstem encephalitis: a case report

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Introduction: *Listeria monocytogenes* is a common cause of meningitis in well defined risk groups including newborns, elderly people and patients with immunosuppression. Brainstem encephalitis accounts for only 5–10 % of Listerial central nervous system infections and is observed prevailingly in middle-aged healthy adults. We report the case of a 57-year-old woman with Listerial encephalitis.

Methods: Case report.

Results: A 57-year-old woman was admitted with headache, fever, diplopia, hypesthesia on the right side of the face, slight cerebellar ataxia, mild dysarthria and dysphagia. Magnetic resonance imaging (MRI) revealed T2-hyperintense lesions and small areas of nodular enhancement reflecting microabscesses predominantly in brainstem and cerebellum, furthermore thalamus and basal ganglia. Cerebrospinal fluid (CSF) analysis showed pleocytosis of 58 leucocytes/µl with lymphocytic predominance. With isolating *Listeria monocytogenes* from blood culture the diagnosis could be confirmed. The patient was treated with ampicillin and trimethoprim/sulfametrol intravenous for 3 weeks, followed by oral treatment with amoxicillin/clavulanic acid for 2 weeks. The patient's neurological condition subsequently improved and she could be discharged with full recovery. MRI controls revealed a noticeable decrease of the lesions.

Conclusions: Listerial encephalitis is a rare and severe infection of the brainstem with a high mortality. Diagnosis can be difficult, because the CSF analyses often show mild, nonspecific abnormalities and CSF cultures have a low sensitivity, misleading to diagnosis of viral or autoimmune encephalitis. As an early treatment is crucial for a favorable outcome, empirical treatment with appropriate antibiotics for Listeria should be administered in every patient with brainstem encephalitis.

Disclosure: Nothing to disclose.

PP1156

Acute encephalomyelitis revealing a neurotoxocariasis

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Background: Toxocariasis is a parasitic zoonosis caused by larvae of Toxocara canis or Toxocara cati. Most human infections are thought to be subclinical or self-limited. Clinical involvement of the central nervous system is exceptional.

Observation: A 62-year-old woman with a history of hereditary multiple exostosis has presented with acute left side weakness with facial palsy. Examination noticed left flaccid hemiparesis, left peripheral facial palsy, left trigeminal nerve impairment and a thoracic sensory level (T8). Blood count revealed hypereosinophilia. Brain and spine MRI showed multiple spinal lesions (T5–T7 and T10–T12) with central nodular contrast enhancement, a pontine lacune and periventricular hyperintense lesions. CSF analysis showed 6 cells per millimeter and normal proteins. Toxocariasis serologies were positive in plasma and CSF. Intravenous Albendazol treatment (15 mg/kg/d) was initiated associated to corticoids with clinical improvement and spinal lesions regression on control MRI.

Discussion: Neurotoxocariasis can result in varying neurological manifestations: encephalitis, strokes, meningitis and myelitis. The diagnosis of neurotoxocariasis is based on several findings: high serum titers of T-canis antibodies, eosinophilia in blood and/or CSF, clinical and radiologic improvement, as well as the normalization of the CSF parameters during antihelminthic therapy. In the literature, angiographically documented reports describe cerebral vasculitis involving small vessels occlusion and resulting in brain infarcts.

Albendazol is considered as the treatment of choice. Corticosteroids are sometimes added to reduce the acute inflammatory and immunologic manifestations.

Conclusion: To our knowledge, this is the second reported case of toxocaral encephalomyelitis. Neurotoxocariasis should be considered in every central neurological syndrome associated with eosinophilia.

Disclosure: Nothing to disclose.

PP1157

Bilateral syphilitic optic neuritis: an alert to human immunodeficiency virus co-infection

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Introduction: Syphilis is an infection with high incidence and prevalence worldwide. The involvement of the central nervous system (CNS) can occur at any time after the initial infection with *Treponema pallidum*. Despite the broad spectrum of CNS manifestations described in syphilitic infection, the ocular involvement, especially if bilateral, is uncommon.

Methods: Case report.

Results: A 52-year-old man noticed decreased central vision in his left eye (LE). Three days later he noticed similar event in the right eye (RE). He reported weight loss of 10 kg in 5 months and previous maculopapular eruption on the soles. On evaluation, he had visual acuity 1/10 in LE and 6/10 in RE, optic disc oedema and relative afferent pupillary defect in LE, bilateral central scotoma (more pronounced in LE) and normal brain magnetic resonance imaging. Laboratory tests showed positive serum Venereal Disease Research Laboratory (VDRL) and *Treponema pallidum* Haemagglutination as well as HIV-1 infection. Cerebrospinal fluid (CSF) showed lymphocytic pleocytosis, elevated protein levels and positive VDRL. These results confirmed the diagnosis of neurosyphilis with bilateral involvement of the optic nerves and HIV-1 co-infection. He was treated with intravenous penicillin G (14 days), with improvement of visual field defects, visual acuity and CSF changes, keeping follow-up in Infectiology.

Conclusion: Optic neuritis is a rare ocular manifestation of neurosyphilis. Accordingly, its occurrence, especially if bilateral and in accordance with previous case reports, should lead to the prompt investigation of concomitant infections, in particular, HIV co-infection.

Disclosure: Nothing to disclose.

PP1158

Unusual MRI findings in an HIV positive adult with *Epstein-Barr* virus meningoencephalitis

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Background: *Epstein-Barr* virus (EBV) is ubiquitous within the general population.EBV infection is associated with multiple neurological complications, usually meningoencephalitis, being the most prevalent *opportunistic viral infection* among *HIV* infected patients.

Clinical case: A 40-year-old HIV1-positive female patient, undergoing antiretroviral therapy (ART) and poorly controlled due to treatment non-compliance (detectable viral load and CD4+ lymphocytes below 200 cells/μL), was admitted for progressive headache and cognitive and behavioral changes for the previous month. Apart from confusion and mild neck stiffness, the neurological examination was otherwise normal. Cerebrospinal fluid (CSF) analysis showed mild lymphocytic pleocytosis and increased protein content. MRI revealed prominent bilateral calcifications of basal ganglia and dentate nucleus (already seen in a previous CT-scan from 3 months prior to admission), and de novo diffuse brain swelling and abnormal T2 hyperintensity of the caudate nucleus' head. EBV serology was compatible with remote or reactivated infection and CSF polymerase chain reaction for EBV was highly positive, therefore establishing the diagnosis of EBV meningoencephalitis. Calcium-phosphorus abnormalities and other infectious causes were ruled out. There was a gradual recovery after reintroducing ART.

Conclusion: This case highlights atypical imaging aspects of EBV meningoencephalitis in adults: basal ganglia T2 hypersigna—observed in EBV encephalitis in children—and noticeable bilateral grey nuclei calcifications - common in pediatric acquired AIDS and described in children with chronic active EBV infection. We wonder if these unusual findings can be attributed to EBV infection alone or if they might be related to the coexistence of EBV and HIV.

Disclosure: Nothing to disclose.

PP1159

Fulminant neurosyphilis and concurrent acute HIV infection presenting with new onset seizures

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Syphilis can coexist with HIV infection. Rarely both concurrent infections are diagnosed in their acute phase. Syphilis can extend to the central nervous system usually after longer period of time. It can present with seizures and focal neurological findings. We report a rare case of hyperacute neurosyphilis, with central nervous involvement in less than three weeks from infection, and concurrent HIV presenting as a fulminant picture. Twenty-four-year-old man without past medical history presented with abdominal pain, fever, vomiting and diarrhea for the past week. On exam had splenomegaly and inguinal adenopathy, later confirmed by CT abdomen—retroperitoneal and inguinal areas. Abdominal lymphadenopathy, massively elevated LDH and fever raised the suspicion of a non-Hodgkin lymphoma. Biopsy of an inguinal node and labs reveal instead an acute HIV and concurrent syphilis infection. Patient reported an unprotected sexual encounter three weeks prior. HIV-1 RNA copies/ml was over seven million. RPR high titer was positive in the blood. HIV had B genotype. Lymphocytic panel was consistent with an acute HIV infection. Early during the hospital stay had a generalized seizure. On Levitiracetam were no recurrent seizures nor abnormal electroencephalogram. MRI brain with contrast had no areas of abnormal enhancement. Spinal tap revealed elevated CSF protein and positive VDRL. Negative toxoplasma antibodies were found in blood and CSF, as well as Cryptococcus antigen. Central nervous involvement with syphilis usually takes longer from the inoculation, however massive infection can shorten the interval. Concurrent HIV in the acute phase contributed to the clinical lymphadenopathy.

Disclosure: Nothing to disclose.

PP1160

Abstract withdrawn

PP1161

"Idiopathic" facial nerve palsy in hepatitis C infection

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Objective: Acute idiopathic facial nerve palsy (Bell's palsy) is the most common cause of facial paralysis, caused by inflammation of the facial nerve, not seldom after a viral prodrome. Viruses associated with Bell's palsy are for example: HSV, mumps, EBV, CMV, HIV, Influenza, Coxsackie. Until fairly recently, acute or chronic hepatitis C infection (HCV) had not been implicated in Bell's palsy. We present a patient with chronic hepatitis C, who developed Bell's palsy during treatment with peginterferon-alfa (PEG-IFN-alfa).

Case report: A 49-year-old man presented with rightsided facial palsy since 3 days, which begun after he noticed pain behind his right ear. He had no recent illnesses, no headache or fever. His medical history revealed chronic HCV, for which he used PEG-IFN-alfa and Ribavirin since 6 weeks. Examination showed a facial palsy, House-Brackmann grade IV. He had no skin rash, vesicles or erythema. Medication was discontinued and three weeks later he had improved to House-Brackmann grade II.

Results: Quantitative HCV RNA: <12 IE/ml (2–2013: 2.9×10^6 IE/ml); genotype 3A Serology for Lyme, HIV, syphilis was negative.

Conclusion: PEG-IFN-alfa, together with Ribavirin, is the current treatment of choice for chronic HCV. Our patient presented with a peripheral facial nerve palsy while on peginterferon-alfa for chronic HCV. More than ten similar cases have been reported in the literature, so there seems to be an association between peripheral facial nerve palsy and chronic hepatitis C virus infection treated with interferon therapy. The underlying mechanism, however, is still poorly understood.

Disclosure: Nothing to disclose.

PP1162

Aphasia, somnolence and recurring fever episodes caused by tuberculous encephalitis

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Introduction: A 79-year-old woman with recurring fever episodes, aphasia and somnolence was admitted. The lady reported about some cardiac problems and lung tuberculosis in the childhood and a history of several recent hospital stays because of the symptoms.

Methods: Case report.

Results: The preceding examinations included X-ray and computed tomographic scans of diverse body parts, a scintigram, transthoracal and transoesophageal echocardiography, pleura puncture, bronchoscopy, gastroscopy, bone marrow biopsy and laboratory tests without any relevant result. Nevertheless, in a magnetic resonance imaging of the cerebrum multiple contrast medium enhancing lesions could be seen. The analysis of the cerebrospinal fluid showed a increased cell count (195/3 per µl), lactat (4.4 mmol/l) and total protein (171 mg/dl) an a discrete decrease of glucose levels (38 mg/dl) without an evidence of malignant cells. A polymerase chain reaction and culture of the cerebrospinal fluid finally detected *Mycobacterium bovis* ssp bovis. The gamma interferon test was positive. *Mycobacterium bovis* ssp bovis was also found in the urine. Initially, we started an antibiotic therapy according to the guidelines with Isoniazid, Ethambutol, Pyrazinamid and Rifampicin and later changed to Moxifloxacin according to the antibiogramm because of a primary resistance of Pyrazinamid. We added Vitamin B6 and steroids. The vigilance and speech improved lightly but stayed bedridden. Finally, she died due to complications after four months.

Conclusions: In summary we report about a lady with encephalitis by bovine tubercle bacilii as a post primary reactivation with prolonged detection. This was caused by the rarity of this disease in Western Europe these days.

Disclosure: Nothing to disclose.

PP1163

An aggressive case of PCR negative varicella zoster virus induced transverse myelitis

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Introduction: Varicella zoster virus (VZV) infection is usually a mild and self-limiting disease. It has been reported that a primary infection can have a more severe clinical course in adulthood. In temperate regions such as Europe the vast majority of the population is seroconverted to VZV by adolescence. However tropical regions experience different age related VZV seroprevalence patterns.

Case report: We report a case of an immune competent 42-year-old female from Surinam who developed a complete tetraplegia with respiratory failure several days after a varicella virus primo infection. MRI of the spine depicted no abnormalities at first. Analysis of the cerebrospinal fluid showed a mild pleiocytosis; VZV DNA was not detected by PCR. However VZV IgG antibodies were positive. Repeat MRI of the spine 10 days after admission showed a diffuse increased signal intensity throughout the spinal cord from C2 to T4 level with cord expansion and swelling. A treatment with intravenous acyclovir and steroids was started eventually followed by five cycles of plasmapheresis without neurological improvement.

Conclusion: It is important to stress that VZV induced myelitis as a primary infection can have an extremely aggressive course in immune competent patients. A negative VZV-PCR in the CSF does not exclude the diagnosis, and anti-VZV IgG antibodies should be routinely examined as well.

Disclosure: Nothing to disclose.

PP1164

Acute human T-lymphotropic virus type 1_ associated myelopathy: a rare case successfully treated with intravenous pulse methylprednisolone

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PP1165

Abstract withdrawn

PP1166

Paradoxical tuberculosis-associated immune reconstitution inflammatory syndrome of central nervous system

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PP1167

Cerebral toxoplasmosis as first manifestation of AIDS

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PP1168

Herpes encephalitis: a case report

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Movement disorders 1

PP1169

Reliability of administrative data for the identification and follow-up of cohorts of Parkinson's disease patients

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Introduction: Parkinson's disease (PD) is an health public problem worldwide. Administrative data are useful for epidemiologic and health services studies. Our aim was to define procedural algorithms to identify PD patients (on regional basis) using administrative data.

Methods: We built a priori two algorithms, respecting privacy laws, with theoretical increasing specificity for PD including: (1) PD hospital discharge diagnosis; (2) PD specific exemption; (3) minimum two separate prescriptions an antiparkinsonian drug. The two algorithms differed for drugs included. The sensitivities were tested on an opportunistic sample of 319 PD patients from the databases of 5 regional Movement disorders clinics.

Results: The estimated prevalence of the Tuscany PD population was 0.58 % for algorithm 1 and 0.34 % for algorithm 2. On the sample-cohort algorithm 1 correctly identified 291 PD patients (sensibility = 91.2 %), and algorithm 2 242 PD patients (sensibility = 75.9 %).

Conclusions: We produced two reproducible algorithms presenting theoretical increasing specificity with good sensibility in pinpoint PD patients on the base of administrative data. This may represent a low-cost strategy to reliably follow up diagnostic and therapeutic healthcare pathways.

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PP1170

Cerebellar abnormalities in clinical practice of dystonia

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Introduction: The role of the cerebellum in dystonia has been controversial. We have come across some patients with focal cervical or segmental dystonia who have cerebellar involvement in terms of radiological features or clinical signs. Based on this observation, and the questions regarding the role of cerebellum in dystonia, we planned to study cerebellar involvement on imaging and clinical examination in patients with cervical dystonia.

Methods: Using a structured questionnaire, we documented clinical characteristics including—age, sex, clinical examination including cerebellar features on examination, MRI features and genetic tests available in patients with cervical dystonia.

Results: From 398 with late onset cervical dystonia, 198 had neuroimaging available for review. Of these 30 (15 %) patients had some abnormality of either the imaging or on examination suggesting cerebellar dysfunction. The mean age of these patients was 44.1 years. 27 (13.6 %) had cerebellar abnormalities on MRI and 18 (9 %) had cerebellar signs on examination (Table 1).

The four clinical groups of cerebellar involvement with dystonia.

Group	Characteristics	Number of patients in the group (n)	Number of patients with abnormal imaging of cerebellum	Number of patients with cerebellar signs on examination	Mean age (years)	Male:Female
Group 1	Cervical dystonia with incidental cerebellar atrophy	7	7	0	50.5	3:4
Group 2	Cervical dystonia with cerebellar lesions+	9	9	4	39.8	4:5
Group 3	The syndrome of (predominantly cervical) dystonia and cerebellar ataxia	12	10	12	36.6	2:10
Group 4	Inherited ataxias presenting mainly with dystonia	2	1	2	17.7	3:2
Total		30(15%)	27(13.6%)	18 (9%)	44.1	12:21

Group 1 and 3 have been tested negative for SCA 1,2,3,6,7 and 12.

Conclusions: Though larger studies may be needed to confirm this, the findings from this study, support the role of cerebellum in dystonia and suggest that it may be clinically relevant. Evidence from studies looking at cerebellar neurophysiology, functional neuroimaging and pathology, support the idea that there may be overt clinical or radiological cerebellar involvement in dystonia.

Disclosure: Nothing to disclose.

PP1171

Polygraphic investigation of spontaneous swallows in Parkinson's disease

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Introduction: Spontaneous swallows (SS) in patients with Parkinson's disease (PD) were not systematically studied particularly by using polygraphic recording systems.

Method: We studied 27 PD patients and 22 controls. Polygraphic recording consisted of surface electromyography of submental, orbicularis oris and oculi, masseter muscles, a laryngeal and nasal sensor for respiration, electroencephalogram, electrooculogram and electrocardiogram.

Results: We studied 27 PD patients and 22 controls. Polygraphic recording consisted of surface electromyography of submental, orbicularis oris and oculi, masseter muscles, a laryngeal and nasal

sensor for respiration, electroencephalogram, electrooculogram and electrocardiogram. SS frequency rate was very variable and *arrhythmic* in both normal and PD patients during wakefullness and slow wave sleep. In PD patients, the number of SS per minute increased when compared to normal controls (0.95 vs 0.6 SS/min) during wakefullness. SS frequency rate was decreased significantly in PD patients during slow wave sleep (4.0 vs 2.0 SS/min).

Conclusion: Dysphagia plus frequent coughing occurs in all stages of PDA novel finding was the salvo type of consecutive swallow bursts with more than 4 SS in PD patients. Decrease of SS at the slow wave sleep and salvo type swallow bursts were the major findings in patients with PD. We conclude that this finding might be related to the delayed triggering of accumulated SS at the pharyngeal spaces and this can be due to insufficient sensory inputs to the central nervous system.

Disclosure: Nothing to disclose.

PP1172

Vertebrobasilar insufficiency in patients with idiopathic Parkinson disease

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Introduction: Gait and postural disturbances are one of the most disabling features of idiopathic Parkinson's disease (iPD). Pedunculopontine nucleus has been indicated to have important role in modulation of gait while degeneration of neurones in pedunculopontine nucleus may lead to postural instability in iPD. Our goal was to investigate the presence of vertebrobasilar insufficiency on transcranial ultrasound (TCS) as an indirect indicator of postural disturbances in iPD.

Methods: We examined 125 patients with idiopathic PD (83 males and 42 females, mean age 64.7 $\pm$ 13.3). Clinical stage of disease was assessed by Hoehn & Yahr Scale (H&Y score 1–5). TCS was performed on Rimed four view using suboccipital window. According to the age scale we estimated vertebrobasilar insufficiency at peak systolic velocity (PSV) up to 20 cm/s.

Results: There were 65 patients with H&Y score $\geq$3 (Group A) and 60 patients with H&Y score $\leq$3 (Group B). In Group A mean disease duration was 13.94 years and vertebrobasilar insufficiency was detected in 50 patients (76.92 %). In Group B mean disease duration was 8.5 years while vertebrobasilar insufficiency was detected in 31 patients (51.66 %).

Conclusions: There is a strong correlation between vertebrobasilar insufficiency, disease duration and clinical stage. We found that vertebrobasilar insufficiency is more frequent in patients with postural disturbances. Our results indicate the importance of transcranial sonography in determination of vertebrobasilar insufficiency as indirect sign of postural instability in iPD.

Disclosure: Nothing to disclose.

PP1173

Clinical variability and genetic delineation of PKAN disease among four Saudi families

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Background: Pantothenate Kinase Associated Neurodegeneration (PKAN) is an autosomal recessive disorder with basal ganglia iron accumulation and genetic background. Its characteristic features are progressive dystonia, rigidity, speech regression, psychiatric manifestation and pigmented retinopathy.

Method: Review of clinical and radiological findings in patients with features suggestive of PKAN disease in a tertiary care referral center in Saudi Arabia. Screening for mutation in (PANK2) gene were done.

Result: 12 patients (6 male, 6 female) of four different families with positive consanguinity were studied. The main age of onset was 5 year (range 1–13). Initial manifestations were speech regression and gait disturbance in majority of patients. Average age of speech regression is 2 years after onset and was noted in more than 80 % of patients. Asymmetrical focal dystonia with loss of postural reflexes leading to loss of ambulation within 3 years after onset was observed in 70 % of patients. 5 patients passed away during 5 years of follow up. Radiological studies showed iron deposition in medial Globus Pallidi. Four novel mutations in PANK2 gene were identified in 4 families, one in each (p.256P>L, mutation on exon 6 1231G>A, mutation on exon 3 c.682G>T, and deletion of exon 1–6 of PANK2 gene).

Conclusion: The association of different mutations in PANK2 gene unraveling the clinical variability of PKAN, all identified mutations were novel and will add to the spectrum of all PANK2 known mutations.

Disclosure: Nothing to disclose.

PP1174

Musician dystonia as the initial presentation of Parkinson's disease

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Introduction: Dystonia in PD is often a manifestation of wearing-off or levodopa-induced dyskinesia. It may be a presenting sign of young-onset PD (YOPD), usually in the lower limbs, but musician dystonia has not yet been reported.

Results: A male guitar music teacher of 42 years-old, with history of depression since the age of 32, treated with sertraline, presented with difficulty in relaxing his 4th and 5th right fingers on playing the guitar. Symptoms started when he was 41, followed by involvement of the contralateral hand on the same task. Six months later, he noticed some difficulties while typing on the keyboard's computer. He denied hyposmia, symptoms suggesting REM sleep behaviour disorder and dysautonomic features. Neurological examination showed the presence of bilateral palmomental reflex, facial hypomimia, normal tonus of limbs, grade 1 rest tremor of right upper limb (RUL) with postural exacerbation, and dystonia of RUL on playing the guitar, characterized by extension of the middle finger and flexion of right 4th and 5th fingers. A grade 1 bradykinesia was noted on his right hand; gait and pull test were normal. Copper and iron metabolism were normal, and there were no acantocytes. DaTSCAN® showed a marked striatal dopaminergic depletion, more prominent on the left side. He was

started on ropinirole with improvement of both dystonia and tremor. We are awaiting the result of PARK-2 genetic test.

Conclusions: We report the first case of a musician dystonia as the initial manifestation of PD. YOPD may manifest as a task-specific dystonia.

Disclosure: Nothing to disclose.

PP1175

Transcranial magnetic stimulation treatment for dystonia

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Introduction: We aimed to investigate the efficacy of repetitive transcranial magnetic stimulation (rTMS) for the treatment of patients with dystonia.

Methods: We used a round TMS coil and a device with a maximum value of magnetic induction—2.2 Tesla. Treatments were administered in 10 daily sessions over 2 weeks. The magnetic field set equal to or slightly above the motor threshold according to individual tolerance and reached 0.5–1.0 Tesla. We used 10 rTMS sessions delivered at 0.8–1 Hz in the series to the C1 and C7 vertebrae location simultaneously. Series duration was 5 s, interval between pulse trains—5 s, session duration 6–8 min. We treated 58 patients with segmental and generalized forms of dystonia. The control group consisted of 30 patients with generalized and segmental dystonia forms. Degree of dystonia was assessed scale Burke-Fahn-Marsden.

Results: We have seen positive changes in 42 (72.4 %) patients in the form of improved gait, reducing tremor of the limbs. The parameters scale Burke-Fahn-Marsden decreased from 25 [17, 32] to 19 [15, 29] points. ($P < 0.05$). No adverse events were observed. 30 Hz rTMS was well tolerated except by one patient who wished to terminate the study due to facial muscle stimulation.

Conclusions: These results support the notion that the modulation of the prefrontal cortex can alleviate the core symptoms of dystonia, and suggest that rTMS can be used in the treatment of patients generalized and segmental forms of dystonia.

Disclosure: Nothing to disclose.

PP1176

Handicap in Parkinson's disease with levodopa-induced motor complications

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Introduction: Handicap has rarely been assessed in Parkinson's disease (PD). Our aim is to study handicap in PD patients with severe levodopa-induced motor complications (MC).

Methods: Handicap was assessed before surgery in PD patients submitted to DBS, using the London Handicap Scale (LHS) (0 = maximal handicap; 1 = no handicap). DBS evaluation also included a levodopa challenge test, total UPDRS off and on, Schwab & England scale (SE) off and on, Hoehn & Yahr (HY) staging off and on, AIMS scale for dyskinesia off and on, patients' diaries of MC, and formal neuropsychological and psychiatric testing.

Results: 71 patients (males 59.5 %), mean age 61.5 years (SD 7.36) and mean disease duration 14.6 years (SD 5.53). UPDRS I median score was 2, while part II off and on was 21 and 8, respectively. UPDRS III median score was 42 off and 19 on (mean improvement in levodopa challenge test 59.78 % (SD 19.94)), while median part IV score was 9. Mean SE was 50 % off and 90 % on. Off mean duration was 4.6 h (SD 3.1) and the duration of on with troublesome dyskinesias was 2.9 (SD 2.9). LHS mean total score was 0.56 (SD 0.14). Higher scores in UPDRS II on and UPDRS III off, morning dystonia, worse score in SE on and shorter on without dyskinesias were independently associated with higher handicap.

Conclusions: Handicap was moderate. Severity of motor symptoms in off, functional disability in on and duration of good on state are the determinants of handicap in PD patients with severe MC.

Disclosure: Nothing to disclose.

PP1177

Circadian aspects of fatigue syndrome in patients with Parkinson disease

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Introduction: Fatigue syndrome's (FS) prevalence among patients with PD varies between 40 and 70 %. Many PD patients suffer from FS both in the morning and evening. This fact can reflect circadian rhythms changes in PD patients. Other nonmotor problems can induce the vicious circle.

Objective: To define circadian aspects of FS in PD patients.

Methods: 80 PD patients with FS were studied. MDS UPDRS, PD's fatigue scale (PFS), FS's diary were applied. Patients with PFS score >3.3 were included in the study. Middle age of the patients was 64.5 ± 6.5. PD's stage: 2.6 ± 0.5, disease's duration: 5.9 ± 4.04.

Results: According to FS diary 47 % patients experienced escalation of FS in the evening, in 18 % of patients severity of FS didn't vary significantly during the day, 35 % patients marked the most disabling state in the morning. After treatment's optimization more physiological FS fluctuations occurred: 94 % patients noted relief of FS in the morning with it's gradually growth to the evening. 6 % patients didn't notice any changes. Such changes were valued positively by all patients. PFS's analysis showed that most changes happened in 10, 14, 16 points. Such effect developed at the end of the 2nd week after treatment's adjustment.

Conclusions: PD is characterized with certain rhytmicity. Patients with FS are more prone to circadian disturbances. Our study shows that dopaminergic adjustment influences periodic phenomenon FS, alleviating it, makes it more physiological. Whether dopaminergic drugs act through direct influence on FS, or their action is realized through improvement of non-motor symptoms needs further investigation.

Disclosure: Nothing to disclose.

PP1178

Symptomatic copper deficiency in Wilson's disease patient treated with zinc sulphate

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Introduction: Wilson's disease (WD) is caused by excess of copper that leads to copper accumulation and needs life-long decoppering treatment. However, overtreatment with anti-copper agents may cause copper deficiency which may present with neurologic and hematologic symptoms. We report WD patient with copper deficiency during zinc sulphate therapy.

Case report: A 37-year- old woman with presymptomatic WD diagnosed in 1998, treated with zinc sulphate was admitted to our clinic in 2013 because of paraesthesias in the fingers and toes for 3 months. Her neurological examination was normal. She had leucopenia (WBC 2.9 $\times$ 10^9/L, normal range 4.5–10.5 $\times$ 10^9/L). Serum ceruloplasmin 0.92 mg/dl (normal range 25–45), copper serum concentration <5 μg/dl (normal range 70–140), urinary copper excretion 11 μg/24 h (normal range 0–50) were markedly decreased. MRI of cervical spine showed linear increased T2 signal lesion in the posterior column of the cervical cord. Somatosensory evoked potentials showed impaired conduction in the dorsal column. Electromyography didn't show neuropathy. Vitamin B12 level was in normal range. Liver function tests were normal. Zinc sulphate was withdrawn. Within 1 month leucopenia resolved completely. Serum ceruloplasmin (5 mg/dl) and serum copper concentration (20 μg/dl) 6 months later were higher than in previous tests. Urinary copper excretion was still low (12.5 μg/24 h). MRI of cervical spine 6 month later demonstrate marked improvement. Nine months after interruption in anti-copper treatment, d-penicillamine instead of zinc sulphate was introduced.

Conclusion: Copper deficiency as result of anti-copper treatment may cause neurological and hematological signs. Treatment must be regularly monitored.

Disclosure: Nothing to disclose.

PP1179

Cognitive disorders in patients with early stages of Parkinson's disease

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Introduction: Parkinson's disease (PD)—one of the most frequent neurodegenerative diseases.

Objectives: To determine the influence of cognitive disorders on quality of life and daily activities on PD patients in early stages.

Methods: 80 patients with PD on the early stages were included (male: female = 29: 51). 26,9 % of our patients had 1–1.5 stage of modified H&Y scale, 40.2 %—2nd and 32.9 %—2.5 stage. The average age was 59 $\pm$ 8 years; the mean duration of the disease—3.1 $\pm$ 2.7. The mixed form of PD predominated overothers (62.2 %). We used Hoehn and Yahr scale modified by Lindvall to assess PD severity (Hoehn M., Yahr M., 1967, O. Lindvall, 1989); cognitive disorders—Monreal cognitive assessment scale (MOCA, Nasreddine M.D., 2004); assess affective disorders—Hamilton Rating Scale—(M. Hamilton, 1959, 1999); to assess the quality of life—a questionnaire Boer (Boer A.G. et al. 1996) and the PDQ-39 (Peto V. et al. 1995).

Results: Cognitive impairment in 37.5 % cases had cortical-subcortical nature, and they included bradifreniia, short-term memory failure, disorders due to false interpretation of the task, impulsive decisions, perceptual disturbances. Quality of life (PDQ-39) were 38.8 $\pm$ 23.3; on (Boer)—137.6 $\pm$ 29.5. There was a positive correlation of cognitive disorders with quality of life ($r = 0.0094$) and affective disorders ($r = 0.0015$).

Conclusions: Cognitive disorders in the early stages of the disease significantly deteriorate the quality of life and daily activities of patients with PD.

Disclosure: Nothing to disclose.

PP1180:

Phenotypic variability of PINK1 gene alteration in patient with early onset parkinsonism

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Introduction: Mutations in Parkin are the most frequent genetic cause of autosomal recessive early onset parkinsonism (AREP). Mutations in the PINK1 gene account for only 1–4 % of early-onset cases. Our objective is to define genotype and phenotype relationships of patient with atypical AREP.

Case and results: The 49-year-old gentlemen had a 2 years history of tremor, dystonia and difficulty to walk with rigidity at the bilateral lower limbs. His dystonic symptoms progressively worsened. He has not been responded to levodopa and biperiden. His mother and uncle had Parkinson disease in family history. Brain and spinal MRI revealed no abnormalities. The patient was screened for Parkin, PINK1 gene mutations. All exons and exon–intron boundaries of Parkin (PARK2) and PINK1 (PARK6) genes of this patient was subjected to HDA analysis followed by direct sequencing of detected variants. Two missense alterations were determined in this patient. One of them was V380L in Parkin gene. It was identified as SNP. Additionally, it had any pathogenic effect related with the disease according to SHIFT and HSF programmes. The other of alteration was N521T in PINK1. It was also identified as SNP. Although it had any pathogenic effect related with the disease according to SHIFT, this alteration might important about splicing mechanism according to HSF.

Conclusions: Clinically, PINK1-linked PD cases have a slow progression and a good and sustained response to L-Dopa. In contrast to usual phenotypic forms, we report a PINK 1 gene alteration case that has an atypical beginning and clinical features.

Disclosure: Nothing to disclose.

PP1181

Abstract withdrawn

PP1182

Myoclonic tremor of the head after spasmodic torticollis surgery

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Introduction: Myoclonic tremor of the head is a rare disorder with unknown etiology. There are few cases described with tremor which appears after spasmodic torticollis surgery.

Case report: We present the case of a 56 years old woman who was diagnosed in 1996 with right spasmodic torticollis. In the family, her mother presented essential tremor with involvement of the head. In 1996, the patient underwent right selective C1–C3 anterior rhizotomy and right intrarahidian sectioning of spinal nerves. In 1997, the initial surgery was followed by stretching and elongation of right sternocleidomastoid muscle. After the two procedures, there was a major improvement of spasmodic torticollis.

Two years ago, the patient developed rest "no–no" type tremor of the head, that is continuous, irregular, with a myoclonic component. The tremor is aggravated by emotion and disappears during sleep. The tremor worsened during the last 5 months in the context of depression. There was no medication for depression At physical exam, there can be noted the myoclonic tremor of the head, right hemiface hypertrophy, atrophy of right sternocleidomastoid muscle. Treatment with beta blocker (Propranolol) was initiated with mild improvement.

Conclusions: tremor appearing long time after surgery for cervical dystonia is encountered rarely and its management is difficult.

Disclosure: Nothing to disclose.

PP1183

Evaluation of the factors affecting psychosocial functioning of patients with Parkinson's disease

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Introduction: Considering the influence of different motor and non-motor features of Parkinson's disease (PD), it is important to evaluate psychosocial functioning of the patients. We aimed to assess determinant factors of psychosocial activity in PD patients using the Scales for outcomes in Parkinson's disease-psychosocial questionnaire (SCOPA-PS).

Methods: 110 eligible subjects with idiopathic PD filled up a number of questionnaires during a face-to-face interview and clinical examination. PD-related characteristics including disease duration (time passed from diagnosis), and measures of disease severity were recorded. In addition, fatigue severity scale (FSS-Per), hospital anxiety and depression scale (HADS), Parkinson's disease quality of life questionnaire (PDQ-39) and SCOPA-PS questionnaire were also used.

Results: Higher Hoehn & Yahr stage ($r = 0.34$, $P < 0.001$) and lower Schwab & England ADL scale ($r = -0.55$, $P < 0.001$) were significantly correlated with the total score of the SCOPA-PS questionnaire. All of the domains of PDQ-39 were directly correlated with the SCOPA-PS score as well as anxiety ($r = 0.64$, $P < 0.001$), depression ($r = 0.71$, $P < 0.001$) and fatigue ($r = 0.35$, $P < 0.001$). Multivariable regression analysis showed that anxiety ($P = 0.020$) and depression ($P < 0.001$) scores, cognition ($P = 0.047$), stigma ($P < 0.001$) and mobility ($P = 0.003$) domains of the PDQ-39 questionnaire independently affected psychosocial functioning.

Conclusions: Our findings show that patients with more severe PD have more serious problems with their psychosocial functioning. Although both motor and non-motor domains of PD have been shown to be important factors, psychiatric problems such as depression, anxiety and stigma together with fatigue have more prominent independent effect on psychosocial activity of PD patients.

Disclosure: Nothing to disclose.

PP1184

Restless abdomen syndrome

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Introduction: We present a patient with restlessness in the upper abdomen starting at rest and in the evening hours.

Case report: A 64-year old man comes for an examination due to an internal tickling sensation under the diaphragm. The sensations are present in a lying position, at rest, usually in the evening, when lying down to bed. The symptoms disturb his sleep and disappear when he gets up and starts moving. Some years ago he had similar problems in the lower extremities which spontaneously disappeared.

Results: The neurological examination was normal. We excluded possible secondary causes which might cause restless legs (RLS) symptoms. The level of ferritin and thyroid hormones were normal. Urea, creatinine, glucose and liver enzymes were normal as well. CT of abdomen and thoracic spine was normal. Ultrasound of abdomen during the symptoms did not show any abnormal movement of the diaphragm. Treatment with gabapentin (400 and 800 mg in the evening) did not have any significant effect. We checked the responsiveness to dopaminergic therapy. After administering levodopa/benserazide (200/50) the symptoms disappeared. After the patient received pramipexole 0.54 mg significant decrease in unpleasant sensations and normalization of sleep occurred.

Conclusions: So far 3 similar cases were described in literature [1]. Regarding the typical course of symptoms and responsiveness to medication, which helps relieve RLS syndromes, we have concluded that our patient has a phenotypic variant of RLS at another location.

References

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Disclosure: Nothing to disclose.

PP1185

Impairment of the cerebral cortex in patients with pure hereditary spastic paraplegia

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Introduction: Hereditary Spastic Paraplegia (HSP) is a clinically and genetically heterogeneous disorder characterized by progressive spasticity and weakness of the lower limbs caused by neurodegeneration of the corticospinal tracts in the spinal cord. We investigate possible changes in the cerebral cortex in patients with pure HSP and their relationship with clinical impairment.

Methods: Twenty-one patients with pure HSP (10 with SPG4 mutations) and 18 aged-matched healthy controls were recruited. We assessed patients' clinical impairment using the Spastic Paraplegia Rating Scale (SPRS). Data were acquired with a 1.5 T MRI scanner. The protocol included a T1-weighted high-resolution brain image. Data were processed using Freesurfer software. A region of

interest (ROI) -based analysis of the precentral and postcentral gyri was performed. Mean Cortical Thickness, Cortical Volume, Surface Area and White Matter Volume underneath gyrus of each ROI were measured. Univariate general linear model with "group" as a fixed factor and Intracranial Volume as a between-subject continuous covariate was performed. We also explore the correlation between these measurements and SPRS scores and disease duration.

Results: In HSP patients precentral gyri and right postcentral gyrus were significantly thinner and Cortical Volume was significantly reduced in bilateral postcentral giry and right precentral gyrus. SPRS scores and duration of the disease correlated with reduced Cortical Volume, Surface Area and White Matter volume in right precentral gyrus.

Conclusions: We found cortical impairment involving primary motor and sensory areas in patients with pure HSP. Changes in precentral gyrus are more pronounced in advanced stages of the disease.

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PP1186

Modifying effect of ceruloplasmin polymorphism on iron chelation response in Parkinson's disease

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Introduction: In Parkinson's disease (PD), excess iron is detected primarily in the substantia nigra (SN), where dopaminergic neurons are exposed to high levels of reactive oxygen species. Excess labile iron can enhance neuronal death by Fenton reaction. By oxidation of iron, ceruloplasmin allows iron transportation between blood and cells. Ceruloplasmin metabolism disturbances may increase brain iron overload. Our aim was to evaluate the interaction between iron chelation response on clinical, biological and MRI parameters and the ferroxidase activity in relation with the ceruloplasmin polymorphism D544E.

Methods: A pilot, double blind, placebo-controlled randomized clinical trial with a 6-month delayed-start paradigm, was set in 40 patients on stabilized dopamine regimens with deferiprone. Effects of deferiprone were analyzed according to the ceruloplasmine genotypes, on motor UPDRS, MRI R2* sequences (indirect assessment of iron overload) and blood iron metabolism.

Results: Early-start patients (n = 19) compared to delayed start patients (n = 18) (37/40 completed) responded significantly earlier and sustainably to treatment in both SN iron deposits (R2* MRI) and motor UPDRS. The AT group (n = 5) had a greater clinical improvement, an greater increase in ceruloplasmin levels and a greater reduction of R2* value as compared with AA group (n = 32).

Conclusions: A moderate iron chelation regimen that avoids changes in systemic iron levels may constitute a therapeutic modality for all PD patients but with a higher benefit in patients carrying the AT polymorphism. Lower ceruloplasmin activity may be at higher risk of iron metabolism dysfunction and may require stronger iron chelation.

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PP1187

Camptocormia treatment by the continuous subcutaneous infusions of apomorphine

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Background: Camptocormia may be present as a rare idiopatic dystonic disorder, or much more frequently as a symptom of the complicated stage of Parkinson's disease (PD). Reported prevalence rates range from 3 % to 17 % in PD. Camptocormia poorly respond to both manipulation with dopaminergic treatment or deep brain stimulation.

Methods: In the last 4 years, we had to manage five patients suffering from Parkinson's disease who developed camptocormia. All five patients were treated with L-DOPA and dopamine agonists at the time when camptocormia appeared. None of the patients improved following the manipulation of treatment or botulinum toxin injections into affected trunk muscles. The diagnostic apomorphine challenge test was performed in all five patients. In the case of a positive response the treatment with continuous subcutaneous infusions of apomorphine was initiated.

Results: The camptocormia improved in all patients at the 4 week of continuous apomorphine treatment, and this effect remained stable. One patient died after 3 years of the initiation of apomorphine treatment; in other 4 patients the mean duration of stable response is 1.8 years.

Discussion: Virtually no controlled studies have been performed in camptocormia to establish safety, tolerability and efficacy of any treatment. There are only a few case reports and retrospective studies which reported the experience with different treatments. Our experience is that the apomorphine hydrochloride in the form of continuous subcutaneous infusions can be successfuly used for the treatment of camptocormia in the late stage od Parkinson's disease.

Disclosure: Nothing to disclose.

PP1188

Malignant syndrome in Parkinson's disease without antiparkinsonian treatment withdrawal: a case report

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Malignant syndrome is a rare complication occurring during the course of drug treatment for Parkinson's disease. It resembles neuroleptic malignant syndrome and is characterized by hyperthermia, consciousness disturbance, autonomic dysfunction and elevation of serum creatine kinase. Malignant syndrome is a potentially fatal condition and awareness of this condition is imperative for prevention and treatment. The commonest precipitating factor is dopaminergic drug withdrawal or dose reduction. We report a patient with Parkinson's disease (PD) who developed Malignant syndrome despite continuation of anti-parkinsonian drugs. A 60-year-old male with a 6-year history of PD presented with wearing-off symptoms. He experienced two episodes characterized by hyperthermia (up to 42 degree C), altered sensorium, tachycardia, and severe dyskinesia. Elevated serum creatine kinase (up to 86472 U/L), acute renal impairment and hyponatremia (122 mEq/l) were observed. Treatment of intravenous fluid infusion, external body cooling and dantrolene sodium were effective. Finally, significant improvement was achieved. Malignant syndrome should always be considered in a patient with PD who presents with unexplained changes in consciousness with hyperpyrexia.

Disclosure: Nothing to disclose.

PP1189

The effect of subthalamic nucleus deep brain stimulation on motor symptoms of familial Parkinson's disease patients

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Introduction: The frequency of familial Parkinson's disease (PD) and consanguinity is higher, and also parkin mutations are common in Turkey. Because of the levodopa responsiveness of parkin-linked parkinsonism may different from sporadic PD we investigated the motor improvements in PD patient groups with or without family history after subthalamic nucleus (STN) deep brain stimulation (DBS).

Methods: We evaluated 59 consecutive PD patients (32 male, 54.2 %) in this prospective study. Family history of PD and parental consanguinity of the patients were noted. The severity of clinical symptoms were measured using Unified Parkinson's Disease Rating Scale (UPDRS) II and III; and dopaminergic treatment dosage calculated as levodopa equivalent dose (LED) before and on the sixth of the STN DBS.

Results: The mean age was 53.93 ± 10.06 and the mean disease duration was 14.09 ± 6.88 years. Nineteen patients (32.2 %) have a family history of PD and 17 patients (28.8 %) have parental consanguinity. The mean age was younger and the mean disease duration was longer in familial PD patients. After STN DBS mean 55.15 %; 57.55 %; and 50.02 % reduction found on UPDRS part II; III scores, and LED respectively. We found no statistical difference on UPDRS II, III scores and LED between familial and sporadic PD patients before and after STN DBS.

Conclusions: Our study suggest that clinical outcomes of STN DBS may not be better in familial PD than the sporadic disease.

Disclosure: Nothing to disclose.

PP1190

Assessment of serum uric acid level in essential tremor

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Introduction: Decreased serum uric acid has been associated with neurodegenerative diseases such as Parkinson's disease (PD) in the elderly. Several studies suggest that there may be a link between PD and Essential tremor (ET) which is thought to be a neurodegenerative disease. Serum uric acid level and its relationship with prognosis in ET patients has not been addressed.

Methods: Subjects with ET were evaluated for motor disability and cognitive dysfunction using the validated Standardized Mini-Mental State Examination (SMMSE). Individuals with dementia, depression or other neurodegenerative disorders were excluded, as were subjects on uric acid-lowering therapy or with serious illnesses such as severe anemia, chronic renal failure, hepatic disease or active or ongoing cardiovascular or cerebral vascular disease.

Results: One hundred and sixteen subjects (52 patients and 64 controls well matched in comparison of age and sex) were enrolled. Uric acid level was similar between the groups. Uric acid level correlated to age, ET starting age, cholesterol level and creatinine level ($p < 0.05$).

Conclusions: There was reasonable epidemiological evidences to support a link between ET and these neurodegenerative diseases, but we did not find any difference between uric acid levels of patients and controls in statistical analysis.

Disclosure: Nothing to disclose.

PP1191

Clinical features of idiopathic and secondary paroxysmal dyskinesias

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Introduction: To define better the phenotype of idiopathic and secondary paroxysmal dyskinesias (PxDs), which are a challenging group of disorders characterized by recurrent episodes of involuntary movements. PxDs include paroxysmal kinesigenic (PKD), paroxysmal nonkinesigenic (PNKD) and paroxysmal exertion-induced (PED) varieties.

Methods: We reviewed 21 (8 men/13 women) cases with respect to attack characteristics, aetiology, family history and treatment response.

Results: Our population consisted of 12 patients with idiopathic PxD (5 men/7 women) and 9 with secondary PxD (3 men/6 women). Nine patients belonging to three pedigrees had a familial PxD (PKD in two and PED in one). Mean age at onset of idiopathic PKD cases was 8 years (range 5–16 years), much earlier than PED cases (25 years). Most subjects with idiopathic PKD (75 %) had daily attacks lasting between 30 and 60 s, whereas in the three PED cases the usual duration of the episodes was 15 min. Attack distribution varied widely, and most experienced pure dystonia rather than choreodystonic movements. All PKD patients in whom antiepileptics were tried showed a dramatic improvement of dyskinetic episodes. One PED case responded very well to levodopa. Mean age at onset of secondary forms was much later (46 years). Eight cases had PNKD and one had PKD. Causes included vascular lesions, multiple sclerosis, toxoplasma encephalitis (in one HIV patient), endocrine disorders and some drugs such as neuroleptics, alcohol and fluoxetine.

Conclusions: Keep in mind the variable phenomenology and the spectrum of causes associated with PxDs can afford a more accurate diagnosis and early intervention.

Disclosure: Nothing to disclose.

PP1192

Cognitive correlates of apathy in pre-symptomatic and early stage Huntington's disease

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Introduction: Apathy is core feature of Huntington's disease (HD). Frequency/severity of apathy increases along disease progresses and should be recognized from the pre-symptomatic stage. However, little is known about the neural substrates of apathy in HD and its implications over cognition.

Objectives: (a) To delimitate the frequency/severity of apathy in pre-symptomatic gene carriers at "mid and near" time to onset and in early-stage HD; (b) to study the impact of apathy over cognitive performance.

Methods: N = 39 pre-HD patients (UHDRS < 4; TFC > 11) classified into mid (n = 24) and near (n = 15) to onset and n = 49 early-HD (UHDRS > 4; TFC > 8) participated. The Problems System Behavior Scale was used to assess depression, irritability, psychosis, apathy and executive dysfunction. The FAS, Trail Making A&B, SDMT and Stroop were used to obtain different measures of cognitive performance.

Results: Depression, irritability and apathy were significantly present from the "mid-time to onset" stage but just apathy followed a linear increase along stages. Severity of apathy significantly correlated with Stroop interference, SDMT and semantic fluency while no correlations were found for other neuropsychiatric symptoms. Motor score correlated with the same items than apathy plus TMT A&B.

Conclusions: In HD, clinical meaningful symptoms of apathy are still present from the pre-symptomatic stage and strongly correlate with cognitive measures of medial-frontal cortex functioning, semantic processing and visuo-motor integration and speed, similarly than motor symptoms that also correlates with measures of DLPFC functioning. In HD apathy and motor symptoms shares similar, but not equal neurocognitive substrates.

Disclosure: Nothing to disclose.

PP1193

The autosomal-dominant familial parkinsonism in a remote area of the Czech Republic

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Objective: To assessment the base of inheritance in families with autosomal-dominant parkinsonism.

Backround: In the epidemiological study carried out in an isolated population of South-Eastern Moravia in Czech Republic, a surprisingly high prevalence of parkinsonism was found, which differed from the published prevalence rates in other European countries.

Methods: On the basis of detailed genealogical examination of all individuals with confirmed parkinsonism the pedigrees were compiled and the DNA analysis of probands from each pedigree was subsequently initiated. For this, the massive parallel sequencing method using Ion Torrent technology was used.

Results: Three large pedigrees with an autosomal-dominant inheritance pattern of parkinsonism were identified. Using DNA sequence analysis, which was focused on the gene loci in which have been mutations associated with PD described, none of the previously described mutations was found. In all so far examined probands was detected mutation (rs 1352879) that occurs generally in the population in very low frequency and the presence of which has in Europe never been reported.

Conclusion: The mapping of relevant gene loci (in which the causal mutations related to PD phenotype have been described) in the other samples is conducted. The most interesting mutation (rs 1352879) will be searched for its functional characteristics and possible relationship to the mechanism of disease. If necessary, the mapping will be extended to other loci alternatively in other chromosomes.

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Disclosure: Nothing to disclose.

PP1194

POLG1-related progressive external ophthalmoplegia and levodopa-responsive parkinsonism

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Introduction: POLG1 mutations have been associated with a wide phenotypic spectrum, including inherited parkinsonism usually in combination with progressive external ophthalmoplegia (PEO).

Methods: To describe two cases of idiopathic parkinsonism and POLG1 mutations.

Results: *Patient 1*: A 64-years-old man, with a prior 6-years history of PEO, dysphagia, dysarthria and axonal sensory neuropathy, presented with right-dominant parkinsonian features at age 56, along with right foot dystonic movements. DaTscan demonstrated a bilaterally reduced dopamine uptake in the corpus striatum. POLG1 sequencing identified the substitutions P648R and W585X. At 8 years follow-up of parkinsonian syndrome, the patient presented a sustained dopaminergic response, with a decrease of 16 points in the MDS-UPDRS-III score (54 % improvement) after a 300 mg L-dopa challenge test. *Patient 2*: A 66-years-old woman, with a prior 20-years history of PEO, dysphagia, facial diparesis, axonal sensory neuropathy and proximal myopathy, presented, at age 60, with left-dominant postural tremor and bradykinesia, along with left foot dystonic posturing. There was an autossomal dominant familial history of PEO. Reduced striatal ^{123}I-ioflupane uptake was seen in the right putamen and caudate on DaTscan. POLG1 sequencing revealed the substitutions T251I-P587L, in cis-orientation, and W486X. At 3 years follow-up of parkinsonian syndrome, she presented a sustained dopaminergic response.

Conclusions: The identification of POLG1 mutations in cosegregation with parkinsonism has provided valuable insights into the molecular underpinnings of neurodegenerative parkinsonism. Analysis of POLG1 gene seems to be an appropriate step in the diagnostic workup of patients with mendelian transmission of parkinsonism, especially in the presence of neuromuscular syndrome.

Disclosure: Nothing to disclose.

PP1195

Pallidal iron accumulation in Huntington's disease

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Introduction: Brain iron deposition has classically been observed in Neurodegeneration with Brain Iron Accumulation syndromes, but may also be associated with a variety of neurodegenerative disorders, including Huntington's disease (HD).

Methods: To describe a case of HD with pallidal iron accumulation since the early stage of disease progression.

Results: A 35-years-old man presented with progressive cognitive decline, general restlessness and behavior changes, with irritability, repetitive behaviors and lack of self-care at 34. There was a familiar history of psychiatric disease. Examination revealed impairment of executive functions, generalized hyper-reflexia, delayed initiation or slowing of voluntary saccades and gaze impersistence and distractibility, hands postural and kinetic tremor, choreic movement, affecting predominantly the trunk and occasionally the face, cervical dystonia, and sporadic distal choreodystonic movements. Magnetic resonance disclosed bilateral hypointensity over the globus pallidus at T2-weighted image, slight atrophy of striatum and parietal and cerebellar cortex, and left temporal fusiform gyrus cytic formation. Peripheral neurophysiologic examination revealed myopathic changes in deltoid and quadriceps femoris muscles. Laboratorial study was normal (including serum caeruloplasmin and urinary copper levels, acanthocytosis in peripheral blood and erythrocytes Kell antigens determination). Sequencing of the HTT gene identified an expanded allele with 45 CAG repeats and a normal allele with 15 repeats.

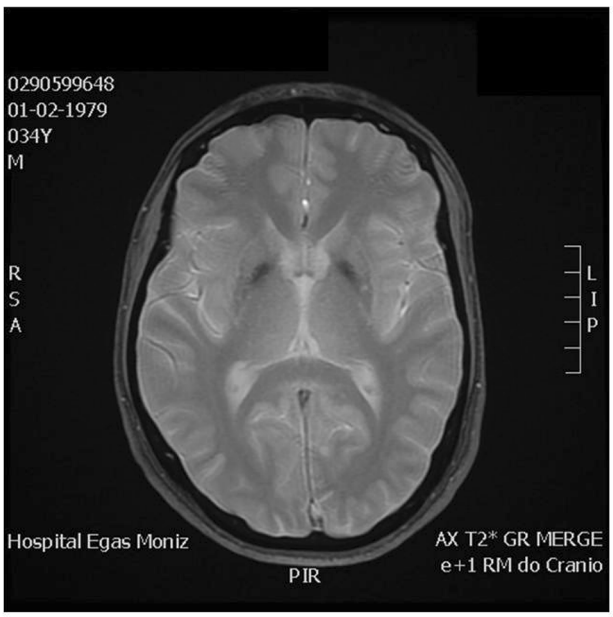

Fig. 1 Pallidal iron accumulation with bilateral hypointensity over the globus pallidus at T2-weighted image.

Conclusions: Pallidal iron deposition in earliest stages of HD may suggest the iron may be a causal factor in the neuronal degeneration process. If the pallidal iron accumulation has a predictive or prognostic value in HD remains under discussion.

Disclosure: Nothing to disclose.

PP1196

REM sleep behavior disorder and autonomic dysfunction in Parkinson's disease

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PP1197

Vascular pathology causing late onset generalized chorea: case report

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PP1198

Abstract withdrawn

PP1199

Hospital admissions in Parkinson's disease: causes, duration and mortality

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PP1200

Risk factors progression cognitive disorders in Parkinson's disease

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PP1201

Marin-Amat syndrome: case report and review of the literature

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PP1202

The burden of non-motor symptoms in Parkinson's disease

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PP1203

Spectrum of hyperkinetic movement disorders in psychiatric emergency

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PP1204
Aspects of cognitive impairment in a patients group with Parkinson's disease

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PP1205
Evaluation of VEMP in idiopathic Parkinson disease patients

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PP1206

Abstract withdrawn

PP1207
Neck pain as common manifestation of Parkinson's disease

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PP1208
Risk factors for Parkinson disease

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PP1209
Corticobasal degeneration: clinical characteristics and management strategies of 26 Egyptian patients

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PP1210
Dyslipidemia increases or reduces the risk of Parkinson disease: a cohort of 86 patients

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PP1211
Movement disorders associated with aphasia in early ischemic strokes: study of two cases

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PP1212
Psychiatric manifestations in patients with functional dystonia

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PP1213
Botulinum toxin type-A injections for oromandibular dystonia

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PP1214
Atypical forms of Parkinsonism plus syndromes

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PP1215
Myasthenia gravis as a cause of dropped head syndrome in Parkinson's disease; autoimmunity or coincidence?

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Multiple sclerosis and related disorders 1

PP1216
No evident disease activity (NEDA) in the AFFIRM study: association with brain atrophy and functional outcomes

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Introduction: Analyses were conducted to investigate relationships between 'no evident disease activity' (NEDA) and brain atrophy and functional status in patients with relapsing-remitting multiple sclerosis (RRMS).

Methods: NEDA was defined as no relapse, no 12-week sustained Expanded Disability Status Scale (EDSS) progression, no gadolinium-enhancing lesions, and no new/enlarged T2 lesions over 2 years. Percentage changes in brain parenchymal fraction (BPF) over the second year of study, changes from baseline to 2 years in Paced Auditory Serial Addition Test-3 (PASAT), Timed 25-Foot Walk (T25FW), and 9-Hole Peg Test (9-HPT), as well as rates of confirmed EDSS improvement (12-week sustained decrease of $\geq$1.0 point) were compared in combined natalizumab- and placebo-treated patients from the AFFIRM study.

Results: Overall, 242 of 904 patients (27 %) had NEDA over 2 years. Patients with NEDA had smaller median percentage decreases in BPF than patients with disease activity (-0.15 vs -0.28 %; $P = 0.0055$). NEDA was associated with better outcomes from baseline in PASAT scores (median change 2.00 with NEDA vs 1.00 without NEDA; $P = 0.0005$), T25FW (median change 0.00 s with NEDA vs 0.20 s without NEDA; $P < 0.0001$), and 9-HPT (median change -0.73 s with NEDA vs -0.24 s without NEDA; $P < 0.0001$). Rates of EDSS improvement were greater in patients

with NEDA than in patients with disease activity (36.9 % vs 22.6 %; hazard ratio 1.918 [95 % confidence interval: 1.374–2.678]; $P = 0.0001$).

Conclusions: NEDA was significantly associated with less brain atrophy, more disability improvement, and better outcomes in cognitive function, walking speed, and upper extremity function in patients with RRMS.

Disclosure: Study Supported by: Biogen Idec Inc. RAR has received honoraria or consulting fees from Biogen Idec, Genzyme, and Novartis and has received research funding from the National Institutes of Health, National Multiple Sclerosis Society, Genzyme, and Novartis. EF has received compensation from Biogen Idec, Genzyme/Sanofi, and Novartis for consulting services and received research funding from the National Institutes of Health, Biogen Idec, and Genzyme/Sanofi. AG has received compensation from Acorda, Biogen Idec, Genzyme/Sanofi, GW Pharma, Mylan, Novartis, Teva, and Vaccinex for consulting services and financial support for research activities from Acorda, Avanir, Biogen Idec, EMD Serono, Genzyme/Sanofi, Novartis, Ono, Roche, Sun Pharma, Takeda, and Teva. JTP has received consulting fees and honoraria from Acorda, Biogen Idec, Genzyme, Novartis, and Teva and research support from Biogen Idec and Roche. AP and SB are employees of Biogen Idec.

PP1217

Quantitative electroencephalography in clinically isolated synrdome and relapsing remitting multiple sclerosis: correlation with cognitive functions

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Introduction: In this study, we aimed to evaluate cognitive impairment in clinically isolated syndrome (CIS) and relapsing-remitting MS (RRMS) using quantitative electroencephalography (QEEG) and neuropsychological tests.

Methods: We included 30 CIS, 30 relapsing-remitting MS patients and 34 healthy subjects as controls to the study. Patients were in remission for at least 8 weeks and did not have depression and did not take any drug. In QEEG frequency and interhemispheric coherence were calculated with Fast Fourier Transform (FFT) method in artifact free 36 s epoch of the EEG. Neuropsychological tests assessing attention, executive functions, working memory and visual memory were performed for all subjects.

Results: In RRMS group we detected decreased beta coherence in the frontal regions and decreased delta, teta and beta coherences in the central and parietal regions. We also detected increased delta coherence in the temporal regions of the RRMS patients. However, there was no difference between groups in terms of spectral power analysis. Neuropsychological tests revealed a decreased attention speed in CIS group and RRMS patients had a lower performance in executive functions, information processing speed, attention, working memory and visual memory. There was a correlation between decreased interhemispheric central beta and occipital theta, alpha and beta coherences and executive dysfunction in RRMS patients.

Conclusions: Although QEEG is a sensitive and objective method to evaluate cognitive impairment in RRMS group, it is not able to show early cognitive impairment in CIS.

Disclosure: Nothing to disclose.

PP1218

Effects of siponimod (BAF312) alone and when combined with propranolol on absolute lymphocyte count decrease and recovery in healthy subjects

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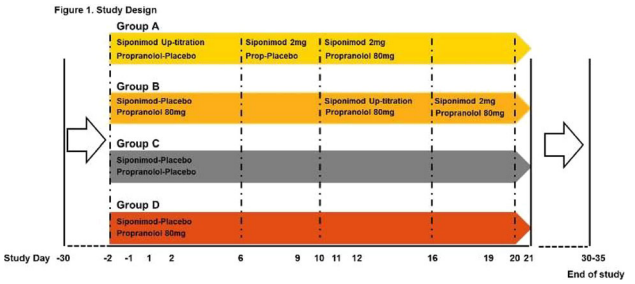
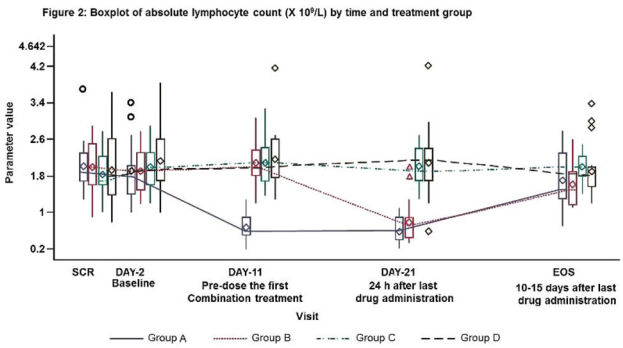
Introduction: Siponimod (BAF312) is a selective sphingosine-1-phosphate ($S1P_{1,5}$) receptor modulator under development for secondary progressive multiple sclerosis. We evaluated the pharmacodynamic effects of siponimod 2 mg (therapeutic dose) on absolute lymphocyte counts (ALC) and subsequent recovery following treatment discontinuation.

Methods: This was a randomised, double-blind, placebo-controlled study for 20 days in 76 healthy adult subjects with four treatment arms: propranolol 80 mg (10 days) on top of siponimod 2 mg steady state (Group A), siponimod 2 mg (10 days) on top of propranolol steady state (Group B), propranolol (Group C) and placebo (Group D).



ALC was measured at baseline, Day 11, Day 21, and end of study (EOS) visit (Day 30-35). ALC was evaluated as a secondary endpoint.

Results: In Group A, mean ALC was decreased to 36 % (0.69×10^9/L) at Day 11 and 31 % (0.60×10^9/L) at Day 21 of pretreatment levels (1.92×10^9/L). In Group B, mean ALC was 2.10×10^9/L at Day 11 compared to 1.91×10^9/L at baseline. At Day 21, mean ALC in Group B was 0.79×10^9/L (41 % of pretreatment levels). At EOS in group A and B, ALC recovered to normal levels for all except one subject (Group A). No significant change in ALC was observed in Group C or D.



[Figure 2]

Conclusion: Siponimod 2 mg at steady state led to mean ALC decrease to approximately 30–40 % of the pretreatment levels and was not altered by propranolol co-administration. ALC recovered to normal levels after treatment discontinuation.

Disclosure: Shibadas Biswal, Florine Polus, Atul Pawar, Uday Kiran Veldandi, and Eric Legangneux are employees of Novartis. This study was funded by Novartis Pharma AG.

PP1219

Optical coherence tomography versus visual evoked potential: which is more sensitive in detecting optic neuritis of neuromyelitis optica?

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Introduction: Detection rates of optic neuritis (ON) by optical coherence tomography (OCT) or visual evoked potential (VEP) are varying according to the number of attack or disease severity in multiple sclerosis (MS) and neuromyelitis optica (NMO). The aim of this study was to evaluate the utility of OCT and VEP for detecting and discriminating ON between MS and NMO.

Methods: We performed a cross-sectional study of 109 patients with at least 1 clinical ON episode at least 6 months prior (74 NMO and 35 MS patients).

Results: The sensitivity of OCT after ON was 57.6 % and VEP sensitivity was 61.9 %. For the investigation of disease specific findings without effect of cumulative damage by number of attacks, we focused on one episode ON (33 MS eyes vs 60 NMO eyes). For unaffected eyes, the sensitivity of VEP tends to be higher in MS (18.8 %) than NMO (4.3 %) ($p = 0.056$) with no difference in the sensitivity of OCT. In one episode ON, the sensitivity of OCT was significantly higher in NMO (50.0 %) than MS (21.2 %) ($p = 0.007$) with no difference in the sensitivity of VEP. The abnormal OCT in one episode ON may suggest more possibility of NMO (odds ratio = 2.36; 95 % CI, 1.17–4.76).

Conclusions: The sensitivity of VEP and OCT are not different in ON. However abnormal VEP in unaffected eye may be useful for the detection of subclinical ON in MS and abnormal OCT in one episode ON presents 2.4 times more possibility of NMO than MS.

Disclosure: This study was supported by Korea Research Foundation grant funded by Korea Government (KRF 20109-0067502).

PP1220

Safety of alemtuzumab by treatment course in patients with active relapsing-remitting multiple sclerosis

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Introduction: Alemtuzumab, as 2 annual treatment courses, demonstrated superior efficacy versus subcutaneous interferon beta-1a with consistent, manageable safety in treatment-naive relapsing-remitting multiple sclerosis (RRMS) patients and those who relapsed on prior therapy. In the CARE-MS studies, approximately 20 % of patients received a third alemtuzumab course in year 3. This report examined safety by course in the alemtuzumab clinical program.

Methods: In the 36-month, phase 2 CAMMS223 (NCT00050778) and 24-month, phase 3 CARE-MS I (NCT00530348) and CARE-MS II (NCT00548405) core studies, active RRMS patients received alemtuzumab 12 mg/day intravenously on 5 consecutive days at baseline and 3 consecutive days 12 months (24 months in CAMMS223) later. All studies included an extension (NCT00930553) with patients receiving as-needed alemtuzumab re-treatment.

Results: 919, 894, and 167 patients received 1, 2, and 3 annual courses of alemtuzumab 12 mg over 3 years, respectively. Proportions of patients with adverse events (AEs; 94.7, 89.3, 92.2 %), serious AEs (11.5, 8.6, 11.4 %), and infections (58.8, 53.0, 54.5 %) were similar after each course. Infusion-associated reactions were less prevalent after first course. Thyroid AE incidence was greatest in year 3, although this is unlikely due to administration of a third course since it was also observed during year 3 in patients not receiving a third course.

Conclusions: These data suggest that additional courses of alemtuzumab treatment were not associated with an increase in risk for AEs including infections. Robust patient education and long-term monitoring enabled early detection and treatment of autoimmune disorders.

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PP1221

Idiopathic recurrent transverse myelitis: a multiple sclerosis variant or a different identity?

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Introduction: Recurrent transverse myelitis (RTM) is a common presentation of Multiple Sclerosis (MS) and can be the only manifestation of the disease. When MRI criteria for MS diagnosis are not satisfied and other causes are excluded, Idiopathic Recurrent Transverse Myelitis (RTM-I) is assumed, but it remains in question if this is a MS variant or an independent entity.

Objective: To determine whether RTM-I can be distinguished from RTM-MS on the basis of clinical manifestations and complementary exams.

Methods: Retrospective analysis of clinical charts of patients followed at the Demyelinating Disorders Consultation with RTM as major manifestation. Patients with Neuromyelitis Optica (NMO), NMO spectrum disorders and systemic autoimmune diseases were excluded. Two subgroups were defined: RTM-MS (MS MRI criteria fulfilled), RTM-I (remaining patients).

Results: 38 patients included, 22 RTM-MS, 16 RTM-I. Median follow-up time: 92.2 ± 65.9 months. Regarding the first episode, the RTM-I group had more frequently motor involvement (75vs.40.9 %, $p = 0.039$), incomplete recovery (81.25 vs.22.73 %, $p = 0.002$), and prolonged recovery (81.25 vs.45.5 %, $p = 0.028$). The initial brain MRI was abnormal in 50 % of both groups, only fulfilling MS MRI criteria in the RTM-MS group. Oligoclonal bands (OB) in the cerebrospinal fluid (CSF) were less common in RTM-I (31.3 vs. 81.3 %, $p = 0.005$). No significant difference was found in terms of gender, age, number of recurrences or final EDSS score.

Conclusions: MTR-I seems to be an entity distinct from MS, differing in its clinical presentation with motor involvement

preponderance and worse recovery, and in paraclinical studies with absence of OB in CSF and MRI lesions atypical for MS.

Disclosure: Nothing to disclose.

PP1222

Fampridine improves gait parameters, balance test and functional independence measurement (FIM) in multiple sclerosis

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Introduction: Multiple sclerosis (MS) is an inflammatory demyelinating disease of the central nervous system (CNS) that is prevalent among young adults and usually leads to chronic disability. Ambulation is important to patients with MS, and they perceive it as a major issue for their health. Clinical trials have demonstrated that dalfampridine improves walking ability among patients with MS. We aimed to evaluate this drug's efficiacy on gait parameters, balance test, functional independence measurement retrospectively.

Methods: Datas collected from 20 patients who have MS (15 women, 5 men; aged, 32-61 years) diagnosis and have been following by Kocaeli university department of neurology and also had been assessed about gait difficulties by department of physical medicine and rehabilitation before and after one month treatment of 4-aminopyridine (AP) between 2011 and 2012. In this retrospective pretest–posttest (one group) designed study, disease activity, temporal-spatial gait parameters (which were collected with computerized gait analysis), Berg-Balance test and functional independence measurement (FIM) data sanalyzed by using Wilcoxon test.

Results: We found significant difference at temporal- spatial gait parameters regardingcadence, stridelength, double supportand walking speed ($P < 0.05$). Berg-Balance test results was also significantly betterafter treatment with 4-(AP) ($P < 0.05$). Beside there was no siginficant change with FIM results ($P > 0.05$).

Conclusions: Although we could not confirm about an improvement at functional independency, Dalfampridine seems as an effective treatment for gait and balance imperfections for MS patients.

Disclosure: Nothing to disclose.

PP1223

Rituximab experience in neuromyelitis optica: data from a single center in Turkey

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Introduction: Rituximab, an anti-CD20 monoclonal antibody has been suggested as an agent for neuromyelitis optica (NMO) by EFNS guidelines. To date, variable results with this treatment have been reported. We would like to present our experience with rituximab in NMO spectrum diseases.

Methods: NMO patients who received rituximab were selected from our database. Age at disease onset, duration of disease, clinical attack rate and Expanded Disability Status Scale (EDSS) scores before and after the treatment were recorded.

Results: Seven patients were included (Median age: 33, all females). Median age at disease onset was 23 years (range 12–49) while median duration of disease was 3 years (0–39) at the time of rituximab treatment. Main reason for switching patients to rituximab was either treatment failure or intolerance with steroids or other immunosuppressants. Median clinical attack rate was 2 attacks/patients/year (range 1–3) before treatment, which was 1.5 attacks/patients/year (range 0–3) after treatment. CD20 levels were below 3 % during attacks. Median EDSS score was 8.0 before (range 2–8.5) and after (range 2–10) after rituximab at the end of follow up (median: 23 months, range 7–25). Post-treatment EDSS scores and attack rate was not available for one patient. Two patients were not analyzed since they were on RTX for less than a year.

Conclusions: Rituximab, despite CD20 depletion, could not perform a significant decrease in clinical–radiological attack rate or EDSS scores. In patients with already worsening disease and with lack of adequate response to other immunosuppressants, rituximab may not be able to achieve remission.

Disclosure: Nothing to disclose.

PP1224

Spastic paraparesis associated with anti-aquaporin-4 antibodies in a patient infected with hepatitis C virus

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Introduction: Hepatitis C virus (HCV) infection is associated with several neurological manifestations, considered to result from neuroimmunological dysregulation, sometimes associated to interferon-alpha treatment. We report a case of a patient with spastic paraparesis, positive anti-aquaporin-4 antibodies (anti-AQP4 Ab) and non-treated HCV infection.

Case report: A 48-year-old woman, with a previous diagnosis of non-treated hepatitis C, presented with a 10-year history of progressive gait disturbance, attributed to Primary Progressive Multiple Sclerosis. She had an irregular clinical follow-up. Neurological examination disclosed a grade 4 spastic paraparesis, hyperreflexia in lower limbs, right positive Hoffmann sign, bilateral Babinsky sign and spastic gait only possible with bilateral support. Brain MRI showed an asymmetric, bilateral pontine and left mesencephalic hyperintense signal in T2/FLAIR, with no gadolinium enhancement. Spinal MRI was normal. Visual evoked potential revealed bilateral prechiasmatic conduction delay. Blood tests showed positive anti-HCV antibody with a viral load of 4,517,000 IU/mL and a positive anti-AQP4 Ab with cell-based assay test (1/1024). Cerebrospinal fluid (CSF) analysis was normal, with no oligoclonal bands. The patient started IV methylprednisolone followed by oral prednisolone, interferon-alpha and ribavirin. There was a slight clinical improvement 2 weeks later.

Conclusions: We present a case of optic and brainstem demyelinating disorder associated with anti-AQP4 Ab. There are 5 case reports describing association between HCV infection and central nervous system (CNS) demyelination with positive anti-AQP4 Ab, 3 patients previously treated with interferon-alpha. Anti-AQP4 Ab should be tested in patients infected with HCV and CNS demyelination.

Disclosure: Nothing to disclose.

PP1225

Vestibular evoked myogenic potentials in evaluation of brainstem involvement in multiple sclerosis

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Introduction: The aim of this study was to determine the usefulness of vestibular evoked myogenic potentials (VEMP) in the brainstem involvement in multiple sclerosis (MS).

Methods: 50 healthy controls (group 0), 50 MS patients without (group 1) and 50 MS patients with (group 2) clinical signs of brainstem involvement were enrolled. Age, gender, Expanded Disability Status Scale (EDSS) score and brainstem functional system score (BSFS) were collected from all patients. Ocular (oVEMP) and cervical VEMP (cVEMP), using acoustic clicks of 1 ms duration, intensity of 130 dB SPL and 1 Hz stimulation frequency, were performed in all participants and differences in latencies and amplitudes were analyzed between three groups.

Results: Group 1 showed statistically significant prolonged N10 and P13 oVEMP latencies bilaterally in comparison to group 0 (all p values < 0.0001). In group 2 in comparison with group 0 statistical significance was reached for bilateral oVEMP latencies (all p values < 0.0001) and following cVEMP latencies: waves N23 SCM right and left and left P13 SCM ($p = 0.003$, $p = 0.016$ and $p = 0.018$, respectively). There were no significant differences between groups 1 and 2 (all p values >0.177). No conduction block was identified in group 0, while conduction block in at least one explored wave was observed in 5 subjects (10 %) in group 1 and 17 subjects (34 %) in group 2, reaching statistical significance $p = 0.004$.

Conclusions: VEMP is a reliable method in detection of symptomatic and asymptomatic brainstem involvement in MS and it is superior to clinical examination in detection of brainstem lesions.

Disclosure: Nothing to disclose.

PP1226

Intermittent symptomatic atrioventricular block during fingolimod initiation

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Introduction: Fingolimod is an oral sphingosine-1-phosphate receptor modulator used for the treatment of relapsing-remitting form of multiple sclerosis (RRMS). Although the drug is safe, certain side effects exist, with cardiac conduction abnormalities and elevation of liver enzymes being the most severe.

Case presentation: A 47-year-old female patient with RRMS developed an intermittent, symptomatic Weckenbach type of atrioventricular block 5 h after the first dose of fingolimod that lasted 5 h and resolved completely. The same reaction occurred after the second dose of the drug, which was discontinued. Magnetic resonance imaging showed demyelinating lesions in the cerebral hemispheres, at C6-C7 and C7-C8 vertebral levels and one gadolinium-enhancing lesion at T1-T2 level. Evaluation of the patient's autonomic nervous system (ANS) function was performed by reviewing heart rate variability (HRV) from the holter's R-R intervals and applying modified Ewing's Tests, namely orthostatic, sustained handgrip and deep breathing test. Frequency domain analysis of HRV showed increased parasympathetic activity expressed as high frequency component and decreased sympathetic tone expressed as low frequency, implying ANS abnormalities (Fig. 1B). In Ewing tests, whereas the patient reacted normally to both orthostatic (heart rate and blood pressure response) and deep breathing tests, she could not increase diastolic blood pressure during sustained hand-grip, suggesting impaired cardiac sympathetic activity.

Conclusion: Expression of this particular arrhythmia might be related to ANS dysfunction due to demyelinating lesions in the upper thoracic spinal cord that have been previously associated with myocardial ischemia and arrhythmias, possibly augmented by the parasympathetic effect of the drug.

Disclosure: E.Andreadou received research grants from Biogen, Merck-Serono, Novartis and Sanofi-Aventis as well as lecture fees from Teva. M.E. Evangelopoulos received consulting and lecture fees from Biogen, Novartis and Teva. M. Anagnostouli received research grants from Biogen, Merck-Serono, Novartis and Teva. C.Kilidireas received research grants from Biogen, Novartis, Teva and Merck-Serono Gerakoulis S, Gialafos E, Grigoriou A and Haina V have nothing to disclose.

PP1227

Spatial QRS-T angle is increased in MS patients possibly due to ANS dysfunction

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Introduction: Widening of ECG derived spatial QRS-T angle (sQRS-Ta) has been predictive of cardiovascular events in the general population. However, its significance in MS patients is not known.

Methods: sQRS-Ta was derived from the baseline resting 12 lead ECG of randomly selected 125 patients, aged 41.08 ± 12.22 years old. Mean duration disease was 4.08 ± 5.8 years and they were compared with sex and age adjusted healthy subjects. All participants were free of cardiac abnormalities with at least an ejection fraction of >50 % at echo. The presence of left ventricular hypertrophy (LVH), diastolic dysfunction of left ventricle (DD) as well as demographics related to therapy and comorbidities were noted. Exclusion criteria were the presence of coronary artery disease, arterial hypertension and diabetes mellitus. Heart rate, QRS duration, QT and QT corrected were calculated. 85 patients with established MS, were screened for the incidence.

Results: sQRS-Ta was wider in MS group compared to healthy one(17.61 ± 10.93 vs 13.03 ± 5.97, $p < 0.001$and was not associated with the age, the presence of DD or LVH, thyroid disease, smoking and/or obesity. Heart rate,QRS duration, QT and QT corrected were not different among groups. sQRS-Ta is correlated with QRS duration ($p = 0.01$, $r = 0.229$).

Conclusions: Ventricular repolarization heterogeneity, as reflected by wider sQRS-Ta is common in MS. Possible mechanism is Autonomic Nervous System dysfunction which is common in MS patients.

Disclosure: Nothing to disclose.

PP1228

Delayed-release dimethyl fumarate and relapses requiring intravenous steroid use and MS-related hospitalizations: integrated analysis of the phase 3 DEFINE and CONFIRM studies

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Introduction: To evaluate the effect of delayed-release dimethyl fumarate (DMF) in reducing the number of relapses requiring intravenous (IV) steroids and MS-related hospitalizations in relapsing-remitting MS (RRMS) patients, a pre-specified integrated analysis of the Phase 3 DEFINE and CONFIRM studies was conducted.

Methods: Eligibility criteria included age 18–55, RRMS diagnosis (McDonald criteria), and EDSS score 0–5.0. Patients were randomized and received treatment with placebo, delayed-release DMF 240 mg twice (BID) or three times daily (TID), or glatiramer acetate (CONFIRM only), for up to 2 years. Numbers of relapses requiring IV steroids and MS-related hospitalizations were tertiary endpoints in DEFINE and CONFIRM.

Results: The integrated analysis included a total of 2,301 patients, including 771, 769, and 761 in the placebo and delayed-release DMF BID and TID groups, respectively. At 2 years, compared with placebo, delayed-release DMF reduced the annualized rate of relapses requiring IV steroids by 48 % (BID; rate ratio [95 % confidence interval]: 0.519 [0.425–0.635]; $P < 0.0001$) and 50 % (TID; 0.501 [0.408–0.614]; $P < 0.0001$), and reduced the annualized rate of MS-related hospitalizations by 34 % (BID; 0.660 [0.472–0.921]; $P = 0.0146$) and 47 % (TID; 0.529 [0.372–0.752]; $P = 0.0004$).

Conclusion: Delayed-release DMF significantly reduced the number of relapses requiring IV steroids and MS-related hospitalizations, suggesting benefits with regard to patient burden and health economic savings due to decreased resource utilization. These findings further support the efficacy results of DEFINE and CONFIRM.

Disclosure: Study supported by Biogen Idec, Inc.

PP1229

Natalizumab in spinal relapsing-remitting multiple sclerosis

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Introduction: Multiple sclerosis (MS) with spinal involvement is associated with poor prognosis. The aim of this study was to evaluate the efficacy of natalizumab (NTZ) in patients with spinal relapses.

Methods: Multicenter, retrospective study with prospectively collected data. Relapsing-remitting (RR)-MS patients treated with NTZ for ≥1 year following a spinal relapse (SR) defined as spinal patients (S–P), were compared to a matched control group free from SR ≥ 2 years prior to NTZ treatment (non-spinal patients, NS-P). Patients received quarterly neurological evaluation and yearly brain MRI. Study endpoints were mean annualized relapse rate (ARR), disability progression (measured by expanded disability status score [EDSS] score), cumulative probability of EDSS progression (of at least 1 point if EDSS ≤ 5.5 and 0.5 points if EDSS > 5.5), and new brain T2 and gadolinium enhancing lesions at year 1 and after a mean of 3 years as well as the severity of qualifying SR.

Results: 220 NTZ-treated patients were screened of which 68 S–P and 68 NS-P were included. Mean ARR was similar between groups at one year (S–P: 0.06; NS-P: 0.06; $p = 0.89$) and after a mean of 3 years (S–P: 0.06; NS-P: 0.07; $p = 0.48$). Mean EDSS increase and radiological parameters at 1 and 3 years were similar in S–P and NS-P as well. SR qualifying for NTZ were more disabling than non-SR ($p = 0.02$).

Conclusions: Up to 3 years, NTZ treatment had a similar efficacy in S–P and NS-P. Attacks qualifying for NTZ treatment were more disabling in S–P compared to NS-P.

Disclosure: Dr. Zecca reports personal fees from Biogen—Dompé, personal fees from Teva, personal fees from Genzyme, personal fees from Novartis, personal fees from Merck Serono, personal fees from Bayer Shering, outside the submitted work. C. Kamm has nothing to disclose. G. C. Riccitelli has nothing to disclose. M. Heldner has nothing to disclose. M. Caporro has nothing to disclose. Dr. Gobbi reports personal fees from Biogen - Dompé, personal fees from Teva, personal fees from Genzyme, personal fees from Novartis, personal fees from Merck Serono, and personal fees from Bayer Shering.

PP1230

Clinical efficacy of delayed-release dimethyl fumarate in relapsing-remitting MS (RRMS) patients with highly active disease: integrated analysis of the phase 3 DEFINE and CONFIRM studies

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Introduction: To assess the clinical efficacy of delayed-release dimethyl fumarate (DMF) over 2 years in RRMS patients with highly active disease at baseline, a post hoc analysis of integrated data from the Phase 3 DEFINE and CONFIRM studies was conducted.

Methods: Eligibility criteria included age 18–55 years, RRMS diagnosis (McDonald criteria), and EDSS score 0–5.0. Patients were randomized and received treatment with placebo ($n = 771$), delayed-release DMF 240 mg twice (BID; $n = 769$) or three times daily (TID; $n = 761$), or glatiramer acetate (CONFIRM only; $n = 350$), for up to 2 years.

Results: 136 patients met criteria for highly active disease (defined as ≥2 relapses in the year prior to entry into DEFINE/CONFIRM and ≥1 gadolinium-enhancing lesion at baseline), including 48, 45, and 43 in the placebo and delayed-release DMF BID and TID groups, respectively. In these patients, at 2 years, ARR was reduced significantly by delayed-release DMF BID (rate ratio [95 % confidence interval]: 0.397 [0.222–0.710]; $P = 0.0018$) and borderline significantly by delayed-release DMF TID (0.599 [0.353–1.015]; $P = 0.0570$). The proportion of patients relapsed was reduced significantly by delayed-release DMF BID (hazard ratio [95 % confidence interval]: 0.368 (0.190–0.712; $P = 0.0030$) but not TID (0.696 [0.388–1.250]; $P = 0.2254$). There was no significant effect of delayed-release DMF on time to sustained 12-week disability progression. Other definitions of highly active will also be examined.

Conclusions: These findings suggest that delayed-release DMF 240 mg BID demonstrates clinical efficacy in RRMS patients with highly active disease. However, due to the small sample size, the results should be interpreted with caution.

Disclosure: Study supported by: Biogen Idec, Inc.

PP1231

Catastrophic rebound after natalizumab treatment discontinuation

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Introduction: Natalizumab (NTZ) is a very effective drug for the treatment of relapsing-remitting multiple sclerosis (RRMS). In some patients discontiunation is needed due to the risk of progressive multifocal leukoencephalopathy (PML). After discontinuation severe clinical and radiological worsening has been described in some patients.

Methods: From a cohort of natalizumab treated patients, 25 patients were switched to fingolimod, those who had a rebound after discontinuation were selected. Clinical and magnetic resonance imaging (MRI) data were collected. Our aim is to describe the clinical and radiological characteristics these patients before and after the rebound.

Results: Four patients were included, disease duration 9.325 years; mean time with NTZ of 3.1 years; all patients were positive for JCV. In the 3 following months after discontinuation all patients started with fingolimod. Despite the treatment, after stopping the patients started with neurological deterioration (mean 4.15 months with multifocal involvement: 75 % presented with motor disturbances, 50 % cognitive impairment, and 25 %seizures. The average worsening in EDSS was of 2.75 points [1.5–5 points]. The MRI showed anincrease in T2 and gadoliniumlesions on MRI, with a mean of 21 enhancement-lesions [11–45]. All patients received 5 daysof intravenous metylprednisolone, and one patient required plasmapheresis. After the rebound 3 patients continued with fingolimod, only one patient restarted NTZ.

Conclusions: Discontinuation of NTZ treatment can trigger a severe rebound with a marked clinical and radiological worsening. A close monitoring and a short washout period is recommended after drug withdrawal.

Disclosure: Nothing to disclose.

PP1232

Intractable hiccup in multiple sclerosis treated by plasmatic exchanges

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Introduction: Intractable hiccups is rarely described with inflammatory disease; seen specifically in neuromyelitis optica (NMO), hiccups is possible in multiple sclerosis (MS).

Observation: A 28-year-old man was admitted to paraparesis associated with hiccups and vomiting. Brain MRI showed T2 and FLAIR hyperintensities; medular MRI was normal. Lumbar puncture identified an inflammatory liquid with oligoclonal bands. With a high dose of corticosteroids, spastic paraparesis was improved. A diagnosis of MS was made and a mitoxantrone treatment was started. Intractable hiccups was noted 2 monthes later. A new brain MRI revealed T2 weighted hyperintensities in the area postrema. Serum neuromyelitis optica antibodies (NMO Ab) were negative. Hiccups was persistant after symptomatic treatment. Finally the patient benefited from plasmatic exchanges (EP). After 2 courses of 4 EP associated with Gabapentine, hiccups and vomiting disappeared, without relapse.

Discussion: Hiccups and vomiting are more often seen in NMO. Associated with many locations, they are mainly described in medulla oblongata; this area, including the area postrema, has a high aquaporine 4 expression (AQP4). However, hiccups and vomiting are rarely describe in patients suffering from MS. Thus, the clinical and cerebral MRI involvement in our patient allowed us to make this diagnosis of MS. Hiccups and vomiting are thus resistant and validate our discussion of the advantages of EP, with excellent results.

Conclusion: Hiccups and vomiting in inflammatory diseases need to be discussed regarding NMO but they can also reveal MS. These symptoms are resistant to classic treatment, but can respond to EP.

Disclosure: Nothing to disclose.

PP1233

Delayed-release dimethyl fumarate and freedom from measured clinical and neuroradiologic disease activity in relapsing-remitting multiple sclerosis (RRMS) patients: integrated analysis of DEFINE and CONFIRM

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Introduction: To evaluate the effect of delayed-release dimethyl fumarate (DMF) on the proportion of RRMS patients with no measured clinical and/or neuroradiologic disease activity, a post hoc analysis of integrated data from the Phase 3 DEFINE and CONFIRM studies was conducted.

Methods: The integrated analysis included treated patients randomized to placebo or delayed-release DMF 240 mg twice (BID) or three times daily (TID). Absence of clinical disease activity (no relapses and no EDSS progression over 2 years) was analyzed in the intent-to-treat (ITT) population. Absence of neuroradiologic (no new/enlarging T2 and no gadolinium-enhancing lesions over 2 years) and overall disease activity (no measured clinical or neuroradiological disease activity over 6 months, 1 year, or 2 years) were analyzed in the MRI cohort.

Results: A total of 2,301 patients (1,046 in the MRI cohort) were included. At 2 years, in the delayed-release DMF BID and TID vs placebo groups, the proportions of patients with no measured clinical disease activity were 69 % and 71 % vs 53 %; the proportions with no measured neuroradiologic disease activity were 34 % and 35 % vs 20 %; and the proportions with no measured overall disease activity were 23 % and 23 % vs 11 % (all $P < 0.0001$). Results for overall disease activity at 6 months and 1 year (MRI population) and at

2 years (patient subgroups stratified by age, gender, treatment history, prior relapses, and baseline EDSS score) will also be presented.

Conclusions: Delayed-release DMF significantly increased the proportions of RRMS patients free of measured clinical, neuroradiological, and overall disease activity.

Disclosure: Study supported by Biogen Idec, Inc.

PP1234

Nitric oxide synthases gene polymorphisms and multiple sclerosis

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Background: Although the role of nitric oxide (NO) in the pathogenesis of inflammation at multiple sclerosis (MS) is well documented, main of the studies are focused only on inducible nitric oxide synthase (iNOS) isoform as the high-output producer of NO. In the animal model, the level expression of iNOS correlates with severity of clinical sign. Expression of iNOS was also observed in active plaques in MS patients. A positive correlation between plasma and cerebrospinal fluid levels of nitrates/nitrites and clinical disease activity and MS course has been found.

Objectives: The aim of the study was to investigate the association between −2447 C/T and −1026 G/T iNOS polymorphism, −786T/C endothelial nitric oxid synthase (eNOS) polymorphism and -5266C/T neuronal nitric oxid synthase (nNOS) polymorphism and multiple sclerosis.

Methods: We genotyped a total of 90 unrelated patients (23 men, 67 women) with definitive MS according to McDonald criteria and 53 healthy controls matched for age and sex. Genotyping was perfomed using PCR with restriction analysis. Genotype frequencies were compared by Chi square and Fisher's exact tests.

Results: We observed no remarkable differences in genotype or allele distribution in the case–control comparison for all study polymorphisms (nNOS : $Pg = 0.52$, $Pa = 0.82$, eNOS: $Pg = 0.28$, $Pa = 0.69$, iNOS −1026G/T : $Pg = 0.81$, $Pa = 0.56$, iNOS −2447C/T : $Pg = 0.87$, $Pa = 0.9$).

Discussion: Our results did not confirm an association between genetic variations in iNOS gene and susceptibility to multiple sclerosis (althought some previous studies did), neither in eNOS and nNOS genes.

Disclosure: Nothing to disclose.

PP1235

Natalizumab increased the probability of clinically important confirmed walking speed improvement in AFFIRM

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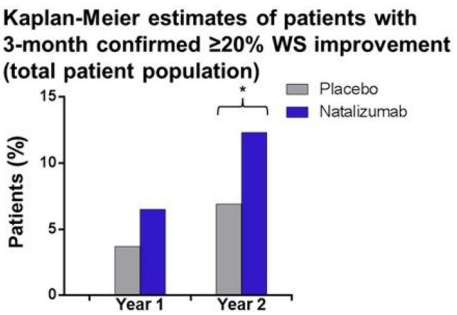
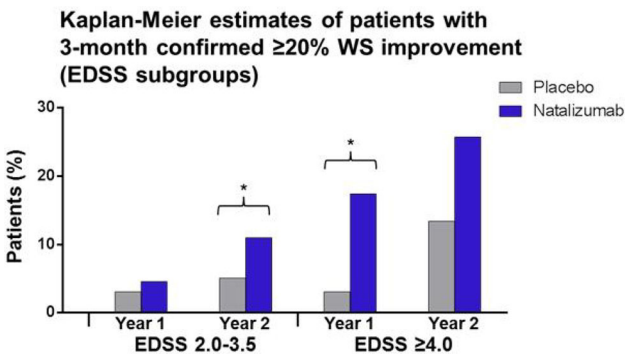
Introduction: Treating walking impairment is important to MS patients. A post hoc analysis of the AFFIRM trial was performed to assess the effects of natalizumab on walking speed (WS) improvement.

Methods: WS was calculated from timed 25-foot walk assessments. Kaplan–Meier estimates of patients with 3-month confirmed ≥20 % WS improvement from baseline were compared between natalizumab (N = 613) and placebo (N = 301) groups at years 1 and 2 of AFFIRM with subgroups defined by baseline Expanded Disability Status Scale (EDSS) scores. Patient-reported physical functioning, assessed by SF36-Physical Component Summary (PCS), was compared between those with and without ≥20 % WS improvement.

Results: Natalizumab significantly increased the probability of ≥20 % WS improvement at year 2 by 78 % ($P < 0.05$) (Fig. 1) and at year 1 by 5-fold in the subgroup with EDSS ≥4.0 ($P < 0.05$) (Fig. 2). Similar trends were observed across all subgroups. Regardless of treatment, patients with ≥20 % WS improvement over 2 years had a 2.7-point mean improvement in SF36-PCS, while patients without 20 % WS improvement had a 0.3-point mean worsening ($P < 0.01$). Of all patients with ≥20 % WS improvement over 2 years, 24 % had ≥1-point EDSS improvement.

Conclusions: In AFFIRM, natalizumab increased the probability of confirmed ≥20 % WS improvement for relapsing-remitting MS patients. Treatment effects were larger for patients with higher EDSS. The association between 20 % WS improvement and physical quality of life supports the clinical meaningfulness of this measure. The disparity between 20 % WS and EDSS improvement suggests that this outcome captures treatment effects distinct from those measured by EDSS.





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PP1236

Cognitive evolution in Tysabri (natalizumab): treated multiple sclerosis patients

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Introduction: Cognitive dysfunction affects 40–60 % of MS patients and progresses over time. Natalizumab has shown to be superior to placebo in preserving cognitive function for the first 2 years of therapy. The objectives are to understand the impact of natalizumab on cognition beyond two years of therapy and investigate whether baseline characteristics are predictive of clinical response.

Methods: This is a single-center, 24-month, observational study. Sixty-three patients treated with natalizumab were assessed prior to monthly infusions using the Cogstate battery and SDMT. The Beck depression questionnaire was also administered at baseline and every 4th month prior to infusion. Patient demographics, MS treatment history, EDSS, MSSS, and natalizumab treatment duration were collected at baseline. Patients with cognitive impairment from other causes were excluded. A linear mixed model was conducted with time on natalizumab (4 years, $n = 12$) as a between-subjects factor, time point as a within-subjects factor, and age, EDSS, type of MS and number of prior drug treatments as covariates. The current data are from the 12-month interim analysis.

Results: Irrespective of time on natalizumab, significant improvements were observed in executive function ($p < .0001$), verbal memory ($p < .0001$), and working memory ($p < .0001$), whereas processing speed ($p = .19$) and attention ($p = .15$) remained unchanged. Only one patient had clinically meaningful decline, defined as a decline of 1 or more standard deviations over three consecutive months on two or more Cogstate tests.

Conclusions: Interim analysis suggests that natalizumab can preserve cognitive function and the ability to learn beyond two years of continuous therapy.

Disclosure: Study supported by an unrestricted grant from Biogenidec. Brian Harel, Adrian Schembri and Joanne Gale are employees of Cogstate.

PP1237

Sexual dysfunction in patients with MS

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Introduction: MS may reduce the QoL of patients. One component of QoL is sexual satisfaction. Sexual function remains understudied among patients with MS in Ukraine.

Aim: To investigate the sexual function in patients with RRMS depending on treatment type, disease duration and frequency of attacks.

Methods: 90 patients suffering from RRMS were examined, 50 women and 40 men aged 18–35 years. The Female Sexual Function Index (FSFI) for women and The Male Sexual Quotient exam (MSQE) for men were used to assess sexual function. SF-36 questionnaire was used to assess the QoL, and Back Depression Scale to assess depression. Patients were divided into groups according to their treatment; the number of attacks per year; the duration of disease; by sex.

Results: Sexual satisfaction was generally higher in women than in men ($p = 0.013$). No significant differences in sexual satisfaction were found among the groups of patients receiving disease-modifying therapy and treatment-naive among both men and women ($p = 0.101$). Intensity of sexual dysfunction was clearly correlated with the number of attacks per year ($p = 0.002$) and with disease duration ($p = 0.003$). Sexual dysfunction was correlated with depression ($p = 0.012$) and with reduced QoL ($p = .015$).

Conclusions: Sexual dysfunction can be considered as one of the symptoms of MS, requiring medical attention and leading to reduced QoL of patients. Intensity of sexual dysfunction depends on the number of attacks per year and disease duration. Depression can be both a cause and a consequence of sexual dysfunction and patients with MS.

Disclosure: Nothing to disclose.

PP1238

Delayed-release dimethyl fumarate and health-related quality of life (HRQoL) in relapsing-remitting multiple sclerosis (RRMS) patients according to prior therapy: integrated analysis of DEFINE and CONFIRM

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Introduction: To evaluate the effect of delayed-release dimethyl fumarate (DMF) on HRQoL in RRMS patients with a history of treatment with interferon beta-1a/1b or glatiramer acetate (GA; prior ABCRE subgroup) or no prior MS treatment (treatment-naïve subgroup), a post hoc analysis of integrated data from the Phase 3 DEFINE and CONFIRM studies was conducted.

Methods: Eligibility criteria included age 18–55 years, RRMS diagnosis (McDonald criteria), and EDSS score 0–5.0. Patients were randomized to placebo ($n = 773$), delayed-release DMF 240 mg twice (BID; $n = 773$) or three times daily (TID; $n = 761$), or GA (CONFIRM only; $n = 360$), for up to 96 weeks (2 years). HRQoL was assessed using the Physical and Mental Component Summary (PCS/MCS) scales of the Short Form-36 version 1.

Results: In the prior ABCRE subgroup, there were 208 placebo patients and 196 delayed-release DMF BID patients. In the treatment-naïve subgroup, there were 377 placebo patients and 380 delayed-release DMF patients. The remaining patients had a history of non-ABCRE MS treatment. At Week 96, in the prior ABCRE subgroup, mean changes from baseline in PCS and MCS scores were significantly improved with delayed-release DMF BID vs placebo (PCS, $P = 0.0006$; MCS, $P = 0.0173$). In the treatment-naïve subgroup, mean changes from baseline in PCS but not MCS scores were significantly improved with delayed-release DMF BID vs placebo (PCS, $P = 0.0132$; MCS, $P > 0.05$). Results for delayed-release DMF TID will also be presented.

Conclusions: Delayed-release DMF demonstrated similar benefits on HRQoL over 2 years in patients with prior ABCRE treatment or no prior MS treatment.

Disclosure: Study supported by: Biogen Idec, Inc.

PP1239

Quantifying cognitive deficits in multiple sclerosis: an extensive evaluation of a short version of Rao's Brief Repeatable Battery (BRB)

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Introduction: Cognitive impairment is frequent in Multiple Sclerosis (MS) and may be economically monitored by the Brief Repeatable Battery (BRB; Rao 1990). Even a short version of the BRB may be highly accurate. Subtests examining cognitive processing speed, working memory and long-term memory, have been shown to display high sensitivity and specificity (Portaccio et al. 2009). To date, the latter observations rely predominantly on data testing sensitivity and specificity of a BRB subtest with respect to cognitive impairment detected by the entire BRB. In contrast, studies which use more extensive neuropsychological assessments as refined indicators of verified cognitive impairment are sparse.

Methods: Sensitivity and specificity of BRB subtests were examined in 110 MS-Patients in relation to cognitive impairment determined in a subsequent extensive neuropsychologic diagnostic procedure (2.5 h duration). The latter involved computerized tests, which addressed the cognitive domains relevant for BRB subtests.

Results: Intercorrelations of BRB subtests and computerized tests of the extensive procedure were highly significant (all p-values <.01). Sensitivity (range: 47–58 %) and specificity (range: 86–87 %) of BRB subtests resembled findings of previous work. When subtests were combined, sensitivity increased to 80 %, while specificity dropped to 52 %.

Conclusions: High sensitivity and specificity of BRB subtests could be confirmed with regards to an extensive diagnostic procedure for the first time. While these attributes were observed for separate subtests, the combination of subtests may foster sensitivity at the expense of specificity when considering extensively validated psychological impairment.

Disclosure: Authors of the current work received support from Bayer Vital GmbH, Biogen Idec GmbH, Boehringer Ingelheim Pharma GmbH, Genzyme GmbH, MEDA Pharma GmbH, Merck Serono GmbH, Novartis Pharma GmbH, Sanofi-Aventis GmbH and Teva GmbH.

PP1240

Peginterferon beta-1a may improve recovery following relapses: post hoc analyses of the pivotal phase 3 ADVANCE study in patients with relapsing-remitting multiple sclerosis

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Objective: To determine whether subcutaneous peginterferon beta-1a (PEG-IFN; 125 μg) every 2 (Q2W) or 4 (Q4W) weeks improved recovery following relapses (RfR) during year 1 of the ADVANCE study, and to examine the relationship between functional systems scores (FSS) during a relapse and following 3-month sustained disability progression (SDP).

Methods: SDP due to incomplete RfR was defined as onset of 3-month SDP ($\geq$ 1.0- or $\geq$ 1.5-point increase in Expanded Disability Status Scale score, from respective baseline scores of $\geq$ 1.0 or 0.0, confirmed after 12 weeks) within 180 days of a relapse. Simultaneous FSS worsening was defined as $\geq$ 1 point change caused by a relapse, with the same FSS being part of the SDP.

Results: Overall, n = 55 experienced SDP associated with relapses; n = 57 experienced SDP not associated with relapses (fewer on PEG-IFN versus placebo). Relapse severities were not different between groups. Approximately 90 % with SDP had $\geq$1 FSS with simultaneous worsening during the preceding relapse; evident in 87 % within 15 days of the most recent relapse (most frequent in pyramidal [55.3–55.7 %]). Q2W and Q4W reduced the proportion of patients experiencing SDP due to incomplete RfR versus placebo by 56 % (p = 0.012) and 41 % (p = ns), respectively. Following a recent relapse, a lower proportion receiving Q2W (13.6 %) and Q4W (15.2 %) had SDP versus placebo (19.6 %); indicating relative reductions in risk of SDP following any relapse of 30 and 22 %, respectively.

Conclusions: PEG-IFN, compared with placebo, significantly improved RfR. Approximately half of patients with SDP in Year 1 of ADVANCE did not have an associated relapse.

Disclosure: Study sponsored by Biogen Idec Inc. (Cambridge, MA, USA). BCK: honoraria from Bayer Schering, Biogen Idec Inc., Merck Serono, Novartis, Roche, Sanofi Aventis, and Teva Neurosciences, and financial support for research from Bayer Schering, Biogen Idec Inc., Merck Serono, and Teva; TFS: consulting fees from Biogen Idec Inc., Novartis, Teva Neuroscience, Genzyme and Accorda; SDN: consulting fees from Biogen Idec Inc. and Genzyme; SS, SH, XY, BS: employees of Biogen Idec Inc.

PP1241

Factors influencing clinically-meaningful physical deterioration in patients with relapsing-remitting multiple sclerosis: results from the ADVANCE study

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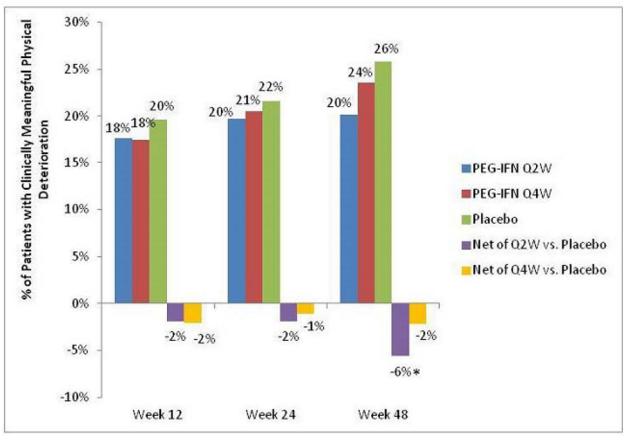
Objective: ADVANCE, a Phase 3, randomised, double-blind study, showed superior effects of peginterferon beta-1a (PEG-IFN) 125 μg every 2 (Q2 W) and 4 (Q4 W) weeks over placebo at 1 year in patients with relapsing-remitting multiple sclerosis (RRMS). This analysis investigated the influence of treatment and disease factors on clinically-meaningful physical deterioration (CMPD) as assessed by the Multiple Sclerosis Impact Scale (MSIS-29).

Methods: The MSIS-29 was assessed at baseline, 12, 24, and 48 weeks. A $\geq$ 7.5-point increase from baseline, obtained from literature, was used to define CMPD in the MSIS-physical subscale. A repeated measures logistic regression model was used to assess the impact of treatment, baseline, and time-dependent predictors, and interaction terms of treatment and predictors on the risk of experiencing CMPD. Significant factors at $p < 0.1$ were retained in the final model, unless they were clinically meaningful.

Results: Data from 1,508 patients were included in the analysis. Compared to placebo, the proportions of patients with CMPD were consistently lower with PEG-IFN treatment, especially with the Q2 W regimen at Week 48 (Fig. 1). Relapses and disability progression were found to be the main factors influencing CMPD (Table 1). The odds of experiencing a CMPD caused by disability progression tended to be lower with PEG-IFN than with placebo (Table 1).

Conclusions: Relapses and disability progression are the key contributors to CMPD. PEG-IFN treatment incurred no additional risk of CMPD and may have the potential to lower it by reducing the risks of these events, as well as the impact of disability progression.

Figure 1 Proportions of patients with clinically-meaningful physical deterioration at each assessment



*Significance at p≤0.05

Table 1 Factors Influencing Clinically-Meaningful Deterioration in MSIS-Physical Scale

Variable	Estimate (Odds Ratio)	95%CI
Time (visits)	1.01	1.00 – 1.02
Baseline score	0.99	0.98 – 1.00
Age	1.06	1.04–1.08
Cumulative number of relapses since randomisation*	2.19	1.59–3.01
Last relapse <29 days from assessment*	4.07	2.14–7.75
PEG-IFN Q2W vs. placebo	0.84	0.56–1.25
PEG-IFN Q4W vs. placebo	0.95	0.64–1.42
Confirmed disability progression if on PEG-IFN Q2W*#	2.93	0.95–9.02
Confirmed disability progression if on PEG-IFN Q4W*#	2.34	0.78–6.98
Confirmed disability progression if on placebo*#	4.20	1.76–10.05

*Indicating time-dependent covariates; #Indicating interaction effects

Disclosure: Study sponsored by Biogen Idec Inc. (Cambridge, MA, USA). SG, AA, IP: employee of Evidera which receives funding from Biogen Idec Inc.; EK and BS: employees of Biogen Idec Inc.; GP: owns Biogen Idec Inc. stock.

PP1242

Cortical activation changes following botulinum toxin treatment of leg spasticity in multiple sclerosis

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Background: Botulinum neurotoxin (BoNT) treatment affects multiple levels of the sensorimotor system and can relieve spasticity of lower limbs caused by multiple sclerosis. The aim of our functional magnetic resonance study was to evaluate cortical activation changes following botulinum-toxin treatment of leg spasticity in multiple sclerosis.

Methodology: Four patients (1 man, 3 women, mean age 46.5, SD 9.3 years) with multiple sclerosis affected with leg spasticity were studied. Patients performed repeated knee extension-flexion movements during brain functional MRI which was acquired in three sessions: before and 4 and 12 weeks after BoNT treatment into the spastic muscles. The change of leg spasticity was assessed using the Snow scale.

Results: BoNT treatment decreased leg spasticity across the group. fMRI pre-BoNT treatment showed extensive bilateral task-related activation of frontoparietal sensorimotor cortical areas, whereas post-BoNT treatment caused retraction to midline and contralateral sensorimotor cortex. Third examination after 12 weeks of BoNT treatment showed re-expansion to a similar extent as seen in the pre-BoNT session.

Conclusions and relevance: This pilot study suggests that relief of leg spasticity may be associated with temporary partial normalization of activation in primary and association sensorimotor cortical areas. Spasticity may be contributing to the documented compensatory over activation of the sensorimotor system in multiple sclerosis.

Disclosure: Nothing to disclose.

PP1243

Cognitive dysfunction and the relationship with fatigue and depression in primary Sjögren syndrome

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Introduction: There are few studies that demonstrate cognitive dysfunction in primary sjögren syndrome. The cognitive deficits were on attention, information processing, executive function and memory. The aim of this study is to determine the prevelance cognitive dysfunction and the relationship with fatigue and depression in PSS.

Methods: An evaluation was made with 33 cases in between July 2011 and August 2013, and 20 control cases with similiar demographic characteristics and education levels. The clock drawing test, COWAT, PASAT, BNT, SDLT, AVLT, BJLOT and RCFT were administered. Depression was defined by using Hamilton Depression Scale and Beck Depression Inventory. SF-36, EQ-5D and FSS were applied in order to evaluate daily life activities, health status and fatigue.

Results: We detected a decrease in the test performance in COWAT, PASAT, SDLT, AVLT and BJLOT. It was determined that there was an impairment in the test performance of attention, information processing, short-term and long-term memory, and visual-spatial perception ($p < 0.05$). There was an increase in the severity of fatigue and a decrease in daily life activities when compared to healthy controls ($p < 0.05$).

Conclusions: Cognitive dysfunction defined in primary sjögren syndrome was described with fronto-subcortical dysfunction. White matter anomalies detected in MRI and a hypoperfusion demonstrated by SPECT in frontal, parietal, cingulate and hippocampal areas were found to be correlated with an impairment in executive function and visual-spatial perception. The administration of the detailed neuropsychological tests is useful in identifying subclinical and clinical cognitive dysfunction.

Disclosure: Nothing to disclose.

PP1244

Investigation of ceralifimod's (ONO-4641) cardiac effects

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Introduction: We assessed the effects of ceralifimod (ONO-4641), a selective, sphingosine-1-phosphate receptor-1 and -5 agonist, on

cardiac rate and conduction at four dose levels, compared with placebo and fingolimod.

Methods: A total of 144 healthy volunteers were randomized to ceralifimod (ONO-4641; 0.01, 0.025, 0.05 or 0.10 mg), placebo, or fingolimod (0.5 mg) once daily for 14 days. Twenty-four-hour 12-lead Holter monitoring was performed at pre-dose (Day -1) and Days 1, 2, 4, 7 and 14 to determine heart rate (HR), PR interval and further electrocardiographic parameters at serial time points and as averaged hourly HRs (hHR).

Results: Ceralifimod (ONO-4641) showed a dose-dependent decrease in resting HR and hHR. On Day 1, the largest mean decrease from baseline HR was −3.0 bpm, −3.6 bpm, −5.3 bpm at 6 h post-dose with ceralifimod 0.01, 0.025, 0.05 mg, respectively, and -9.4 bpm at 7 h after dosing with ceralifimod 0.10 mg compared with -12.2 bpm at 7 h in the fingolimod group. In the placebo group, all mean HR changes from baseline were positive. Exposure effect analysis on Day 1 showed that the effects were concentration dependent. Throughout the study, overall maximum negative chronotropic effects occurred on different days depending on dose, being more pronounced and occurring earlier for higher doses. Treatment effects on PR interval were low, with the largest mean increases from time-matched baseline generally below 5 ms compared with 9 ms for fingolimod on Day 1.

Conclusions: Ceralifimod (ONO-4641) caused dose-dependent cardiac effects, which were, at the highest dose of 0.10 mg, slightly less pronounced than those of fingolimod 0.5 mg.

Disclosure: Study supported by: EMD Serono, Inc., Rockland, Massachusetts, USA, a subsidiary of Merck KGaA, Darmstadt, Germany.

PP1245

Evaluation of atrioventricular blocks and sinus pauses at re-initiation of siponimod (BAF312) treatment after variable periods of discontinuation from continued drug therapy

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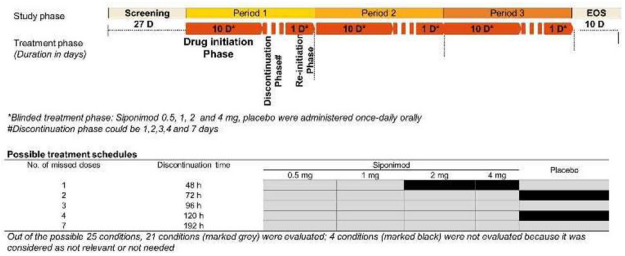
Introduction: Siponimod (BAF312) is a selective sphingosine 1-phosphate ($S1P_{1,5}$) receptor modulator currently in development for the treatment of secondary progressive multiple sclerosis. We investigated the incidence of atrioventricular blocks (AVBs) and sinus pauses (SP) at re-initiation of siponimod treatment after variable periods of discontinuation from continued therapy in healthy subjects.

Methods: Siponimod doses 0.5–4.0 mg, and placebo were evaluated in combination with drug discontinuation periods: 48–192 h.

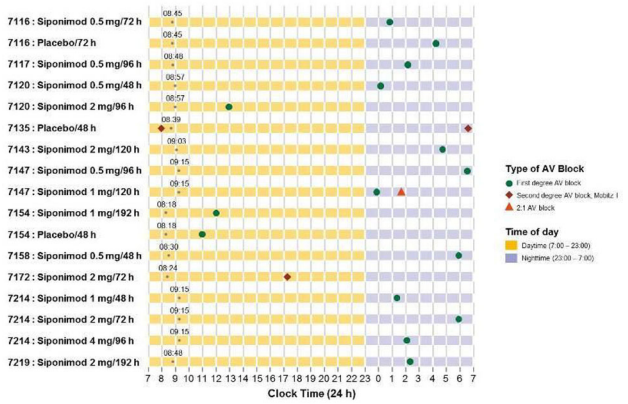
Figure 1: Study design



A 12-lead Holter ECG was recorded starting 1.5 h before and until 24 h after single-dose re-initiation. AVBs (degree) and SPs (defined as RR > 2 s) were summarized by dose level, discontinuation period, and by resting (11:00 PM to 07:00 AM [8 h]) and non-resting hours (remaining 16 h).

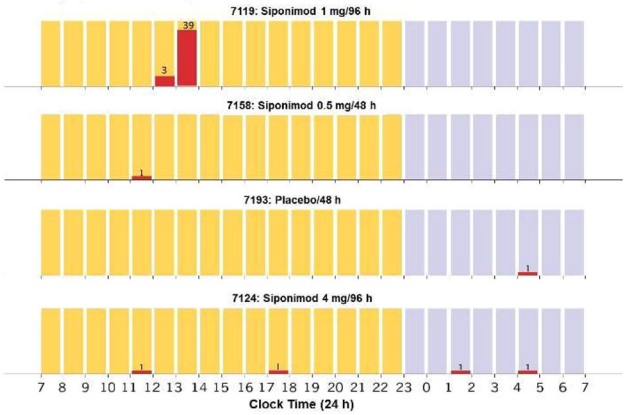
Results: 138 subjects were enrolled and 117 were evaluated. After single dose re-initiation, first-degree AVBs were detected in 15 subjects (13 siponimod, 2 placebo) with no clear dose/discontinuation periods pattern; 80 % occurred during resting hours. Second degree AVBs (4 events) were reported in 3 subjects (dose/discontinuation periods: 2 mg/72 h, 1 mg/120 h and placebo/48 h); 2 events occurred during resting periods.

Figure 2: Summary of AVBs on placebo conditions, by subject number, dose group and discontinuation periods



SPs were observed in 4 subjects (0.5 mg/48 h, 1 mg/96 h, 4 mg/96 h and placebo/48 h); in 2 subjects only during daytime, 1 subject during resting hours only and 1 subject in both periods. The longest duration of RR was 2.26 s.

Figure 3: Number of sinus pause events (RR > 2 s) occurring within hourly interval over 24-hours, by subject number, dose groups and discontinuation periods



All detected AVBs and SPs were asymptomatic.

Conclusions: The majority of AVBs were observed during significantly shorter resting periods, which are associated with increased vagal tone known to increase the PR interval. AVBs and SPs were asymptomatic and not considered to be of clinical relevance.

Disclosure: This study was funded by Novartis Pharma AG. Eric Legangneux, Kasra Shakeri-Nejad, Vassilios Aslanis, Alexandros Sagkriotis, Bruno Brendani, Rhett Behrje are employees of Novartis.

PP1246

Differential methylation pattern of promoter of Fas death receptor in multiple sclerosis patients depending on response to IFN beta therapy

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Introduction: IFN beta (IFNb) is one of the most important first-line treatments in multiple sclerosis (MS). Clinical trials demonstrate the beneficial effects of IFNb. However, individual response is highly heterogeneous and 30–50 % of patients are considered non-responders or suboptimal responders to this treatment. One of the mechanisms of action of IFNb involves upregulation of FAS expression in antigen-specific T lymphocytes and increment of apoptosis of these cells. Apoptosis via Fas/Fas ligand may be related with the shutting-off of the immune response by in situ elimination of autoreactive lymphocytes, becoming an essential mechanism in the regulation of the inflammatory reaction. IFNb treatment may affect the epigenetic regulation of gene expression of apoptosis related genes. Our aim in the present study was to analyze the epigenetic variations (methylation) accompanying IFNb treatment in the Fas gene in peripheral lymphocytes from MS patients regarding the response to this drug.

Methods: Fifty IFNb treated MS patients have been included. Response to treatment was established by clinical criteria: occurrence of 1 relapse or an increase of 0.5 point in the EDSS after one year of treatment compared with the year prior to IFNb therapy. Analysis of DNA methylation was performed by bisulfite method.

Results: Methylation pattern of a CpG island located in the Fas promoter was significantly increased in non-responder MS patients.

Conclusions: In non-responders patients, IFNb treatment leads to a hypermethylation of Fas promoter which might be related to defects in apoptosis, with a consequent decrease in the remove of autoreactive T cells by apoptosis.

Disclosure: Fernández O has received honoraria as consultant in advisory boards, and as chairmen or lecturer in meetings, and has also participated in clinical trials and other research projects promoted by Biogen-Idec, Bayer-Schering; Merck-Serono, Teva, Novartis, Almirall and Allergan.

Peripheral nerve disorders 1

PP1247

POEMS syndrome: case report of rare clinical presentation with pathological spinal fracture

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Background and purpose: POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy and skin changes) is a rare multisystemic disease, which belongs to plasma cell dyscrasia (monoclonal plasma cell proliferative disorder, almost always λ). Bone fractures in patients with POEMS syndrome are rarely described in literature. They are caused by bone lesions, which can be osteosclerotic, osteolytic with sclerotic shaft or "soap bubble" vision lesions. The aim of this article is to present a rare clinical presentation of POEMS syndrome in a woman with spinal fracture, probably as manifestation of osteosclerotic myeloma.

Case report: We have presented a rare clinical case of a female patient with pathological fracture of the thoracic vertebra. Our patient has developed spontaneous asymptomatic vertebral fracture that was initially misdiagnosed as hemangioma, but later histological result has lead us to the possibility of plasmacytoma. Serum protein electrophoresis and immunofixation revealed evidences of monoclonal gammopathy (λ light chains).

Conclusions: In patients with chronic and progressive demyelinating polyneuropathy of unknown origin, with systemic manifestation of organs, skin and endocrine glands should always be thinking of monoclonal plasmacytoma. We report a patient with POEMS syndrome with an extremely rare clinical manifestation.

Disclosure: Nothing to disclose.

PP1248

Neurogenic claudication-mimic due to severe aortoiliac disease

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Introduction: Symptoms arising from lumbar stenosis and arterial occlusive disease can demonstrate similarities that present a considerable diagnostic challenge. We experienced an atypical case of patient mimicking neurogenic claudication, whose symptom arose from severe aortoiliac occlusive disease.

Methods: Case report.

Results: A 48-year-old male had exertional bilateral pelvic pain and claudication for 3 months. He complained of severe aching and burning sensation around his buttock and thighs. After about 200 ~ 1,000 meter walking, he experienced pain in the gluteal region, followed by paresthesia and sensory loss. These sensory symptoms were not correlated with dermatome. Pulses of bilateral femoral, posterior tibial and dorsalis pedis arteries were weak. At rest, the right and left ankle/brachial indexes (ABI) were reduced. When he walked about 200 m, bilateral dorsalis pedis pulses were not observed. After 5 min of rest, weak pulses of dorsalis pedis arteries reappeared. The CT angiography revealed long segmental chronic thrombotic occlusion involving the distal abdominal aorta and both common iliac arteries. After a successful aorto-biiliac bypass operation, he could walk remarkably long distance without pain and sensory symptoms.

Conclusions: Many cases with claudication have typical manifestation of whether vascular or neurogenic type. But there exists a widely unknown third type of intermittent claudication, which causes leg pain with any muscular effort similar to the vascular type. In the future, by evaluating the clinical symptoms and physical examination in such cases, it can shed a light on the clinical marker of diagnosing neurogenic claudication mimic due to peripheral arterial disease.

Disclosure: In conclusion, we report a patient with peripheral arterial disease and neurogenic claudication mimicking symptom which resolved completely after a successful vascular surgery.

PP1249

The time course of pseudo-conduction blocks in a patient with vasculitic neuropathy

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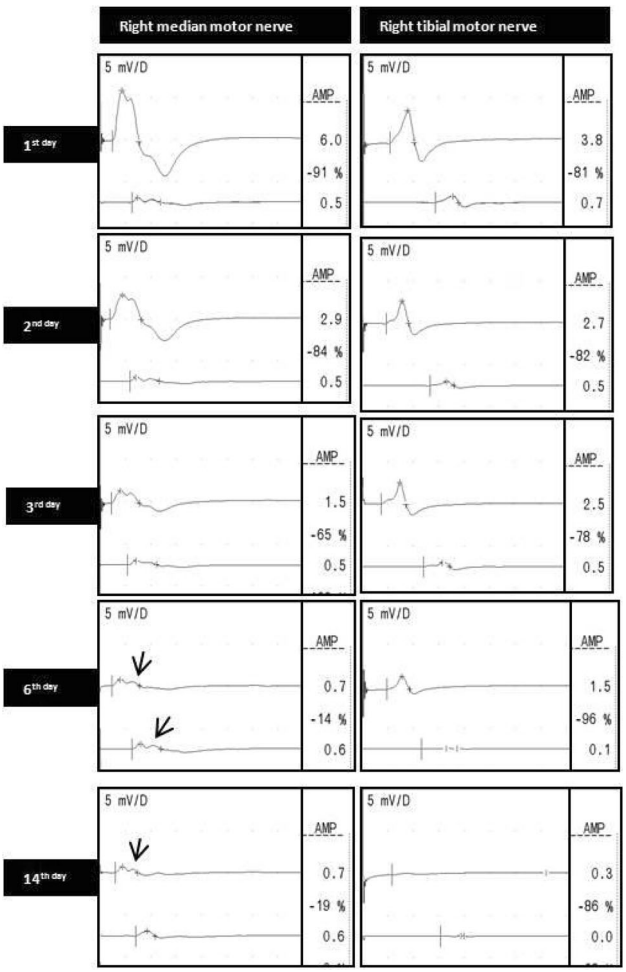
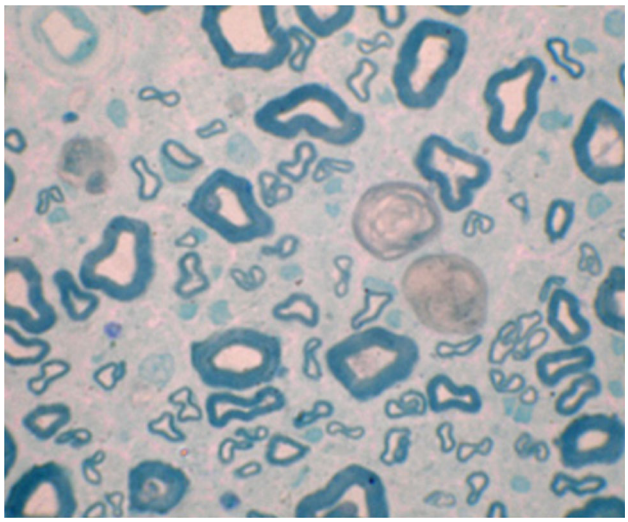
Introduction: "Pseudo-conduction block" can be an early and warning electrophysiological finding of vasculitic neuropathies (VN). Here we report the time course of pseudo-conduction block in a VN patient.

Patient: Fifty-six-year-old female referred because of burning and weakness in hands and feet for 2 months. The neurological examination revealed asymmetric, multifocal motor weakness more prominent on the right hand with thenar atrophy. There was asymmetrical sensation loss in all modalities. Biceps, triceps reflexes were diminished whereas patella and Achilles reflexes were absent. Antinuclear antibody titer was 1/320, C-reactive protein and p-ANCA were highly positive.The cerebrospinal fluid examination was normal. First electrophysiological examination showed asymmetric axonal neuropathy. Also there were significant drops in the amplitude/area of compound muscle action potentials (CMAP) evoked by proximal electrical stimulation relative to distal stimulation at ulnar and tibial nerves. Initially these findings were suggestive for motor conduction blocks. We repeated electrophysiological examination during the following 5 days. Motor conduction blocks at these nerves were resolved, proximal and distal CMAP amplitudes became similarly low (Fig. 1). Finally we decided these findings as pseudo-conduction blocks.The sural nerve biopsy showed perivascular inflammation and active axonal degeneration (Fig. 2). Although nerve biopsy findings were not diagnostic for VN, clinical and laboratory findings strongly suggested a polyarteritis nodosa type vasculitis due to systemic lupus erythematosus.

Conclusion: Although motor conduction blocks generally suggest acquired demyelinating neuropathies, it might be an earlier evidence of Wallerian degeneration. Serial nerve conduction studies are helpful to distinguish these two entities.





Disclosure: Nothing to disclose.

PP1250

Three families with hereditary amyloid polyneuropathy with three different mutations

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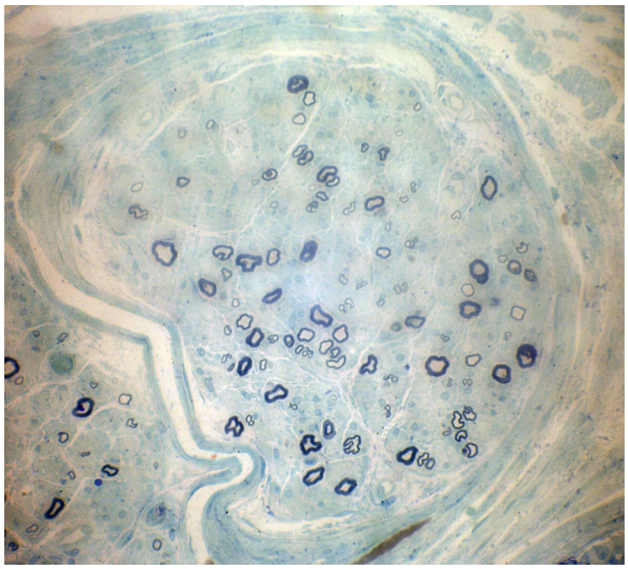
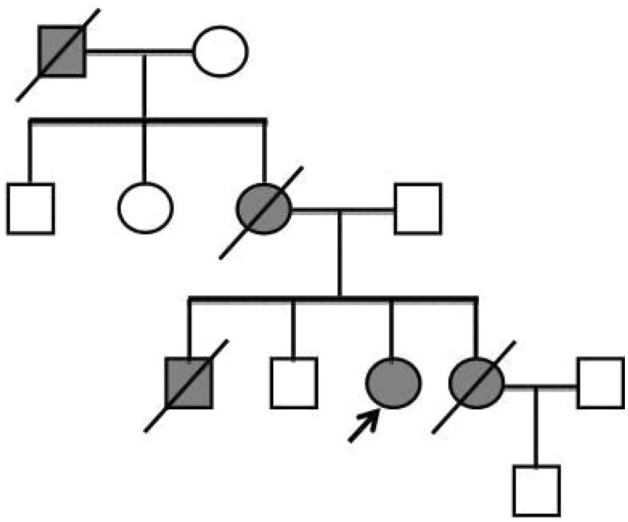
Introduction: Transthyretin (TTR)-related hereditary amyloidosis is a rare autosomal dominant systemic disorder which can present with progressive, axonal sensory, autonomic or motor neuropathy called familial amyloidotic polyneuropathy. We report cases from three families with clinical and nerve biopsy findings.

Case presentations: *Case 1*: 54-year-old man presented with numbness in his hands and feet for 2 months. The neurological examination revealed glove-stocking sensation loss and diminished Achilles reflexes. Routine laboratory tests were normal. Three months later, his examination showed bilateral weakness in lower extremities. Electrophysiological examination showed mixed neuropathy prominent in sensory nerves. The nerve biopsy revealed moderate fiber loss (Fig. 1). Congo-red staining failed to demonstrate amyloid. Amyloid polyneuropathy was always suspected but the genetic analysis was not available at that time. The Val30Met mutation could be determined after 19 years when his son suffered from burning in the feet who is on tafamidis treatment now. *Case 2*: 18 year-old female referred because of constipation, orthostatic hypotension. His father got the diagnosis of hereditary amyloidosis with Thr49Ser mutation on TTR gene due to autonomic symptoms and heart failure; died at the age of 38. Her neurological examination was normal except minimal vibration loss. *Case 3*: 30 year-old female admitted with heart failure, progressive leg weakness, incontinence and orthostatic hypotension. She had 4 relatives including her sister with familial amyloidosis (Fig. 2). The genetic analysis showed Glu54Lys mutation. She did not have any improvement despite three months tafamidis trial.





Conclusion: We present three families with variable clinical features due to three different mutations.

Disclosure: Nothing to disclose.

PP1251

Small fiber neuropathy in patients with chronic graft-versus-host disease after allogeneic hematopoietic stem cell transplantation: preliminary results of a prospective study

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[1]Department of Neurology; [2]Department of Hematology; [3]Department of Pediatric Hematology and Oncology, Medical School University of Zagreb, Clinical Hospital Centre Zagreb, Zagreb, Croatia; [4]Experimental Transplantation & Immunology Branch, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD, USA

Introduction: Neurologic complications in chronic graft versus host disease (cGVHD) after hematopoietic stem cell transplantation (HSCT) may include peripheral neuropathy. A significant number of cGVHD patients experience painful muscle cramps and neuropathic pain (NeP). Small fiber neuropathy (SFN) may be the cause of NeP and it can be diagnosed with quantitative sensory testing (QST).

Methods: Ten patients with cGVHD were examined and QST was performed (Pathway CHEPS). The patients also filled the Pain Detect questionnaire with final goal to diagnose the NeP and to validate the NeP treatment.

Results: Six out of 10 patients reported pain and muscle cramps at the time of presentation and 4 of them met the criteria for NeP according to Pain Detect questionnaire. In all patients with NeP the QST disclosed affection of C and A-delta fibers (elevated threshold for pain, heat and cold sensation). In five non-NeP patients QST showed affection of only A-delta fibers.

Conclusion: Neuropathy in cGVHD may have various causes and patterns. SFN may be the cause of NeP. According to our preliminary results, it is possible that A-delta fibers in cGVHD are affected first, in the period before NeP, while the affection of C and A-delta fibers presents later, after patients develop NeP. Neurologic complications and pain in cGVHD may have major impact on the functional status, quality of life and long term outcomes of cGVHD patients. Early recognition and proper diagnostics of SFN and NeP may contribute to the better treatment of pain in cGVHD patients.

Disclosure: Nothing to disclose.

PP1252

Severe motor neuropathy with monoclonal gammopathy and high titers of antibodies against GM1 and GD1b gangliosides: response to treatment

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Introduction: Neuropathy associated with monoclonal protein (MP) and antibodies against gangliosides (Ab-G) GM1 GD1b asialo GM1 present with severe motor neuropathy. We hereby report.

Methods: A 75 year old male presented subacute diffuse motor neuropathy. Electrophysiological study (EDX) revealed a mixed pattern. Nerve biopsy disclosed rare signs of demyelination. IgIV and steroids were inefficient. Plasma exchanges (PE) stabilized temporarily symptoms. Immunologic testing revealed an IgM lambda MP with monoclonal expansion in the blood and bone marrow, and positive Ab-G. In spite of treatment associating Cyclophosphamide, Fludarabine and Rituximab, the patient developed tetraplegia and died.

A 67-year-old male presented chronic multifocal motor neuropathy. EDX revealed demyelinating signs without conduction blocks. Protein level was 0,91 g/L in CSF. Nerve biopsy disclosed rare signs of demyelination. IgIV were inefficient. PE and steroids allowed improvement with relapse at weaning. Immunological testing revealed an IgG kappa MP and Ab-G. After 6 pulses of cyclophosphamide a severe relapse occurred with tetraplegia and respiratory failure, leading the patient to ICU. Treatment associating Rituximab and PE improved the patient's condition 4 months later regaining walking with aid and no respiratory assistance.

Results: In both cases presentation was that of a disabling motor neuropathy with MP and similar Ab-G profile. Disease resisted to different treatments, chemotherapy was undertaken because of the severity of neuropathy and hypothesis of an immunological or infiltrative mechanism.

Conclusions: In the setting of severe motor neuropathy, testing for MP and Ab-G is important to adapt specifictreatment and reverse dramatic course.

Disclosure: Nothing to disclose.

PP1253

Deletion of ADAM10 in axons impairs axonal outgrowth and remyelination in the PNS

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Introduction: An emerging body of evidence suggests that disintegrin and metalloproteinases (ADAMs) play an essential role in primary development and myelination of the peripheral nervous system (PNS). ADAM10 is a membrane-anchored metalloproteinase with both proteolytic and disintegrin characteristics. Previous in vitro studies propose that during the process of myelin formation, ADAM10 is highly upregulated and appears to be critically involved in axonal outgrowth that is a requirement for myelination in the PNS.

Methods: To further address the importance of ADAM10 in these processes in vivo we generated a cell specific Cre-loxP-mediated knockout model of ADAM10 either in myelin-forming Schwann cells (P0-cre, ADAM10$^{-/-}$) or in motor neurons (Mnx-cre,ADAM10$^{-/-}$). We performed a sciatic nerve crush, which is widely accepted as a valid model for peripheral nerve regeneration. To determine the level of clinical impairment continuous clinical and electrophysiological examination was conducted. To quantify the degree of post-traumatic axonal degeneration and remyelination semi-thin sections were generated.

Results: Under physiological conditions P0-cre, ADAM10$^{-/-}$ as well as Mnx- cre, ADAM10$^{-/-}$ did not present with any clinical, electrophysiological or histological phenotype when compared to wildtype mice. However, traumatic peripheral nerve lesion by sciatic nerve crush revealed a significant reduction of nerve fibres, especially of small calibre fibres in Mnx- cre, ADAM10$^{-/-}$ mice.

Conclusion: Our data suggest that axonal ADAM10 is important for neuronal outgrowth and thus represents a prerequisite for successful regeneration and consecutively remyelination. ADAM10 might play a crucial role in the interaction between axons and Schwann cells during the process of remyelination.

Disclosure: Nothing to disclose.

PP1254

Efficacy and tolerability of different brand of IVIg in the maintenance treatment of chronic immune mediated neuropathy

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Introduction: Treatment with high dose intravenous immunoglobulin (IVIg) is effective in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) and multifocal motor neuropathy (MMN). Not all brand of IVIg are however licensed for their use in these neuropathies. We now analysed the efficacy and tolerability of different brand of IVIg in the maintenance treatment of CIDP and MMN.

Methods: We reviewed the reports of six patients with CIDP and seven with MMN treated with IVIg from 2009 to 2013. Two patients with CIDP and two with MMN started ex novo their treatment while 9 continued the treatment initiated 2–169 months before (mean 45). In all patients we measured the MRC score in the six most affected muscles before each infusion, the monthly dose and brand of IVIg and adverse events.

Results: Patients were treated with IVIg for 25–60 months (mean 48) with a monthly dose of 70 g (range 20-160 g including starting dose). Patients were treated with IgVena, Gammagard, Kiovig and Flebogamma for a variable period of time. Minor and transient side effects were equally observed with each therapy. Two MMN e two CIDP patients increased the monthly dose for disease progression but this was not related to the change in IVIg. No variation in the MRC sumscore and in IVIg dose was observed in the other patients despite the change of IVIg.

Conclusions: Chronic maintenance treatment with IVIg in our patients with MMN and CIDP was not associated with a different tolerability or efficacy despite the use of different brands of IVIg.

Disclosure: Nothing to disclose.

PP1255

Acute intermittent porphyria (AIP) presenting as acute neuropathy, a laboratory and genetically confirmed observation

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Introduction: AIP is an inherited metabolic disorder and one of the main differential diagnosis for acute motor neuropathy.

Methods: Case report.

Results: A 32-years old previously healthy female patient presented with recurrent heavy abdominal pain. Antibiotics and analgesics had been given without success. The patient lost weight and developed general weakness. The patient presented with progressive proximal symmetrical flaccid tetraparesis (BMRC 3 prox., 4 dist.), normal DTR, no sensory loss. She reported general hyperalgesia and diffuse pain. Severe tachycardia was considered to be a sign of autonomic involvement. The tetraparesis progressed within 4 days (BMRC 1 prox., 2 dist.). The combination of abdominal symptoms and neuropathy suggested AIP, hematin therapy was initiated. Over 2 months the patient gradually recovered (BMRC 3 prox., 4 dist.). Findings:

- 24-h urine analysis: porphyrin (3,300 μg; <150 μg), aminolevulinic acid-U (90 mg/l; <10 mg/l) and porphobilinogen (142 mg/l; <1.7 mg/24 h)
- Genetic examination: confirmation of AIP (mutation c.973C > T). Family history for AIP negative.
- NCV: mild axonal neuropathy with preserved sensory conduction velocities. F-waves preserved.
- EMG: no denervation.
- SSEP, MEP, cerebral MRI: normal.

Conclusions: This is a case report of a family negative AIP presenting with an acute motor neuropathy and abdominal symptoms. Abdominal pain is often the initial symptom followed by symmetric or asymmetric neuropathy with proximally accentuated tetraparesis. Also a diffuse pain syndrom, autonomic symptoms, mental state changes and seizures are reported. The duration of an attack may be days to weeks, usually with a complete recovery.

Disclosure: Nothing to disclose.

PP1256

Guillain–Barre syndrome associated with rapid immune reconstitution following autogeneic hematopoietic stem cell transplantation

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Introduction: A patient followed for Hogdkin disease (HD) presented a Guillain-Barré syndrome (GBS) after hematopoietic stem cell

transplantation (HSCT). In this context, a post transplant immune reconstitution is discussed.

Observation: A 21 years old man, followed for HD with recurrence at 18 months, enjoyed an autologous HSCT. After 57 days, the patient presented neurologic trouble with tetraparesia, abolition tendon reflexes and facial diplegia. Acute polyradiculoneuropathy was confirmed by electromyogram; cerebrospinal fluid (CSF) examination revealed normal cell count, elevated protein levels at 2.1 g/l. No cell lymphoma was found. No tumor or infectious argument was otherwise founded. Plasma exchange (PE) were made before a neurological worsening, complicated by acute respiratory distress syndrome and autonomic dysfunction with cardiac arrest recovered. Thereafter, 5 monthly courses of intravenous immunoglobulin (IVIG) were performed to clinical improvement. Unfortunately this development was hampered by mechanical respiratory complication that led to the death of the patient, the 237th day of evolution. The final diagnosis of GBS, occurred in a context of post transplant immune reconstitution in a patient treated for LH, was retained.

Discussion: With a frequency of less than 1 %, GBS is a rare complication of HSCT. The literature review collects 31 cases, 10 occurred after autograft. The average installation time is 7 weeks, so that chemical toxicity can not be discussed. Etiopathogenic mechanisms remain obscure.

Conclusion: GBS is possible after HSCT indicated for the treatment of LH. Despite the use of immunomodulatory treatment, the prognosis is dark for 1/3 of cases.

Disclosure: Nothing to disclose.

PP1257

Two cases with different involvement of hypoglosseal nerve

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Introduction: Isolated hypoglossal nerve palsy is rare and may be due to an intracranial or extracranial space - occupying lesion, head and neck injury, carotid artery dissection, vascular abnormality, idiopathic, infection, autoimmune disease or neuropathy and vaccination. We report two cases of isolated unilateral XII th nerve palsy one of them cause proved to craniocervical trauma and other one due to local infection.

Methods: *Case 1*: 54 years old woman had admitted with hypoglossal atrophie and paralysis. Cause of palsy appeared to be cervical trauma to hypoglossal nerve. Her cranial MRI and other radiologic investigation were normal. Her lingual electromyographic investigation revealed acut, sub-acut partial axonal damage at the right side. Her findings were lost after 3 months. *Case 2*: We report a 48-year-old woman who presented with headache spreading from servical to the head and dysphonia. The left side of the tongue was atrophic and deviated to the left side on protrusion and fasciculations were noted. Cranial and neck MRI revealed that a lesion at the inferior of canalis hypoglossus next to foramen jugularis. Concentric needle electromyography of the left side revealed fibrillation and positive sharp waves with decreased recruited motor units.

Results: Their outcome were good.

Conclusions: In the hypoglosseal palsy, all possible causes must be thought. Two cases prognosis were good which one of them using antibiotherapy, other one spontaneously.

Disclosure: Nothing to disclose.

PP1258

Neurotoxic chemotherapy in Charcot-Marie-Tooth disease: a case series

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Introduction: Disabling peripheral neuropathy (PN) is a major dose-limiting side effect of many chemotherapeutic agents (CA). The main risk factors are the type of chemotherapy and the cumulative dose. Pre-existing neuropathy, especially Charcot Marie Tooth (CMT) neuropathy is a generally accepted risk factor and can determine early and severe chemotherapy-induced neuropathy. This study reports 9 patients with CMT, all treated for cancer and worsened after "safe dosages" of CA.

Methods: Review the last 15 years of patients with cancer and clinical and electric evidence of CMT in the neurological clinic of the Salperière hospital. Nine patients have been collected and have received CA.

Results: All patients have family history, clinical history and electrophysiologic studies compatible with CMT. Five patients have a demyelinating pattern and the last 4 an axonal pattern. Most patients presented with previously unsuspected CMT (8 of 9). Five patients received vinca alcaloides and 4 taxanes. Five patients had a mild clinical improvement after treatment discontinuation.

Conclusions: PN is a major side effect in patients with cancer receiving CA. Pre-existing CMT neuropathy is often unknown. Regarding our case series, CMT with axonal neuropathy pattern is as risky as demyelinating one. Vinca alcaloides and Taxanes seem to be the most dangerous CA for deterioration or revealing CMT. Even if CMT is a quite rare condition, prior to use CA, it seems relevant to screen for family history or clinical signs of CMT and refer to a neurologist if necessary.

Disclosure: Nothing to disclose.

PP1259

Report of two unusual cases of unilateral isolated hypoglossal nerve palsy

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Introduction: Isolated hypoglossal nerve palsy is a rarely seen condition. Here, we present two unusual cases of hypoglossal nerve palsies subsequent to dental complications.

Cases: Patients were female (21 and 35 years old, respectively). They both had a history of difficulty in swallowing, disturbed speech and loss of volume on the right half-side of their tongues. The second patient had also diagnosis of bruxism and trigeminal neuralgia. Oral pantogram of the first patient showed a small exostosis on the apex of the right bottom impacted wisdom tooth with a surrounding radiolucency suggesting inflammation around it. Removal of the tooth resulted in the improvement of function of the hypoglossal nerve. The second patient had a history of full mouth dental reconstruction for the last 18 months. Oral pantogram showed radiolucency suggesting inflammation that lies under the right bottom dental bridge. Removal of the dental bridge resulted with improvement of both trigeminal neuralgia and function of the hypoglossal nerve.

Conclusion: Inflammation around the hypoglossal nerve or itself during its course from the angle of the mandible through the sublingual region may result with the injury of this cranial nerve. Therefore, the physicians coming across with isolated hypoglossal nerve palsy should consider the possible unusual dental causes as the differential diagnosis.

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Disclosure: Nothing to disclose.

PP1260

Significance of ultrasound muscle echointensity in diagnosis of carpal tunnel syndrome

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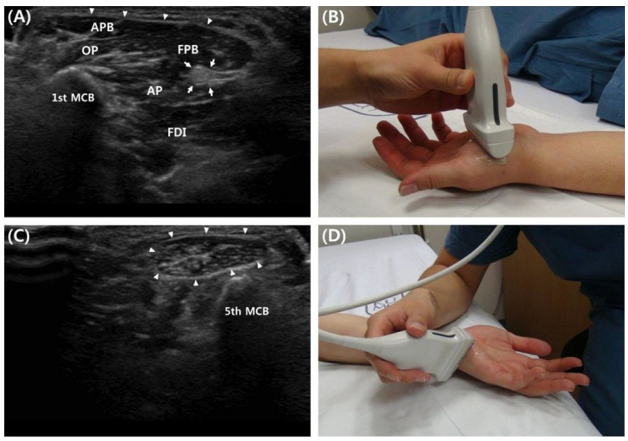
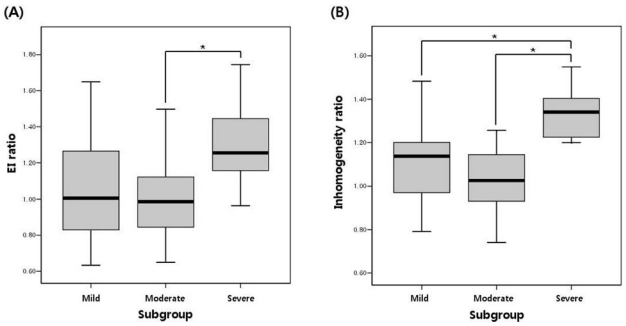
Introduction: High echointensity (EI) of muscles in ultrasonography (US) is suggested as evidence of secondary muscle damage resulting from neuropathy. We performed this study to investigate reliability of new ultrasonographic measurement to evaluate secondary muscle changes resulting from carpal tunnel syndrome (CTS).

Methods: Forty-five hands from 30 patients with CTS and 20 hands from 11 normal healthy subjects were recruited. The hands of patients were divided into three subgroups based on the Canterbury grading. Transverse US images of thenar and hypothenar muscles were obtained.



A region of interest (ROI) was drawn to analyze EI of the muscles and mean EI and standard deviations of EI in the ROI were calculated. To avoid the influence of possible differences in muscle EI between individuals, ratios of thenar muscle to hypothenar muscle were used for statistical analysis. The ratio of mean EI was named the EI ratio, and the ratio of the standard deviation was termed the Inhomogeneity ratio.

Results: The EI ratio was significantly higher in the patient group compared with the control group ($p = 0.044$), whereas the inhomogeneity ratio was not significantly different. Comparison among the three subgroups of patients showed significant differences in both EI ratio ($p = 0.045$) and inhomogeneity ratio ($p = 0.014$).



The presence of denervation potentials in EMG showed a very strong correlation with EI ratio ($p = 0.000$).

Conclusions: The new ultrasonographic method to detect secondary muscle damage resulting from neuropathy was proven to be effective. Both EI and inhomogeneity ratios measured by US could be diagnostic parameters for CTS.

Disclosure: Nothing to disclose.

PP1261

Ulnar nerve instability around the elbow in healthy subjects: ultasonographic and electrophysiologic findings

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Introduction: Ulnar nerve (UN) instability during elbow flexion may be a potential cause of ulnar neuropathy, which might be related with snapping of medial triceps muscle. This study is designed to evaluate the relationship between ulnar nerve instability and snapping of the medial triceps muscle during elbow flexion using ultrasonography and nerve conduction study (NCS) of the UN.

Methods: Forty-two elbows of 21 healthy subjects were recruited. Dynamic ultrasonography was performed in three positions of the elbow: extension, 90 degree flexion, and full flexion. The horizontal distance from the apex of medial epicondyle (ME) to the margin of ulnar nerve and medial triceps muscle (ME_UN and ME_TB, respectively) were measured. The ulnar nerve instability was classified into three types according to the degree of movement: no dislocation, subluxation and dislocation. Ulnar NCS was done.

Results: In 90 degree elbow position, no dislocation and subluxation were 35 (83.3 %) and 7 elbows (16.7 %), and in full flexion, no dislocation, subluxation and dislocation (47.6 %), 17 (40.5 %), and 5 elbows (11.9 %). Pearson correlation coefficients between UN instability and snapping of medial triceps muscle in 90 degree and full flexion of elbow were 0.547 and 0.781 (p-value, <0.001), respectively.

Conclusions: Ulnar nerve instability is increased with elbow flexion, which might be related with the snapping of median triceps muscle. It is important to recognize ulnar nerve instability during elbow flexion as a potential cause of ulnar neuropathy, and also to perform the ulnar motor NCS considering the ulnar nerve instability.

Disclosure: This study was supported by a Korea University grant (K1326792).

PP1262
Case report: acute inflammatory demyelinating polyneuropathy with bilateral extensor plantar reflexes

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PP1263
A helping hand

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PP1264
Searching for an etiology for mononeuritis multiplex

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PP1265
A severe chronic form of ("A")MSAN during pregnancy

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PP1266
Electrophysiological study of the sciatic nerve in spontaneously hypertensive rats: is there a gender difference?

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PP1267
Study of late responses' parameters in carpal tunnel syndrome

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PP1268
Livedoid vasculopathy associated with peripheral neuropathy successfully treated with warfarin

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PP1269
Guillain Barré syndrome following acute brucellosis: a case report

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PP1270
Recurrent severe Guillain Barré syndrome: a case report

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Introduction: Guillain–Barre Syndrome (GBS) is known to be monophasic, recurrence of GBS is uncommon.

PP1271
Ulnar nerve entrapment neuropathy at the elbow: relationship between the electrophysiological findings and neuropathic pain

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PP1272
A case of rhabdomyolysis presenting as unilateral hemiplegia

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PP1273
Neuralgic amyotrophy: a specific cause of bilateral shoulder pain

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PP1274
Post-irradiation neuromyotonia of the hypoglossal and spinal accessory nerves

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Cerebrovascular diseases 2

PP2001

Quality of life in patients after spontaneous subarachnoid hemorrhage

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Introduction: Favorable outcome and reduced quality of life (QoL) in survivors after spontaneous subarachnoid hemorrhage (SAH) is well documented in literature, therefore the aim of this study is to evaluate level of disability and QoL after spontaneous SAH, and compare QoL in surgical and non-surgical patients.

Methods: The research is a cross-sectional study of 92 patients (50 patients with surgically treated aneurysmal SAH, 42 patients with conservatively managed spontaneous SAH). Functional outcome was evaluated by modified Rankin Scale (mRS), QoL was measured with SF-36 in 3 months' period after discharge from hospital.

Results: In surgically treated patients' group mean age was 46.7 (31 male, 19 female); in conservatively managed patients' group mean age was 54.7 (26 male, 16 female); by mRS good outcome had 62 and 57 % patients, respectively. The mean Physical Health and Mental Health scores of SF-36 were 46.18 ± 12.06, 46.30 ± 10.49 and 47.85 ± 5.91, 41.90 ± 4.97, respectively. In both groups significantly low scores in emotional role (RE) were reported, also in physical role (RP) in conservatively managed patients' group. In surgically treated patients' group mean scores of components of SF-36 were lower in elderly (>51) and in poor-grade patients (H&H > 3), especially in domains of Physical Functioning, RP and RE, also General Health and Vitality. There was statistically significant correlation between mRS and physical and mental components of SF-36 ($p \leq 0.05$).

Conclusions: Survivors after spontaneous SAH despite having good outcome suffer from lower QoL, especially in emotional sphere; hence more attention should be paid to emotional disorders after SAH resulting in improving QoL in such patients.

Disclosure: Nothing to disclose.

PP2002

Red blood cells aggregation in rat model of thromboembolic stroke

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Introduction: Microvascular blood flow appears to play pivotal role in ischemic stroke contributing to restoration of oxygen supply, neuroprotection and prognosis. Blood rheology characterizes blood flow in microvessels and might be essential in stroke pathology. The aim of the study was to evaluate the hemorheological disturbances in rat model of thromboembolic stroke (TS).

Methods: Male Wistar rats were underwent TS ($n = 9$) or false surgery ($n = 10$). After 24 h infarct size was assessed by 7-T MRI (BioSpec 70/30, Bruker, Germany); neurological examination (McGrow scale, Benderson scale, sensorimotor tests) was conducted and kinetics of spontaneous aggregation and disaggregation of red blood cells (RBC) in shear flow was evaluated by light reflection technique (LADE, RheoMedLab, Russia).

Results: Infarct size correlates to the severity of neurological deficit ($r = 0.67$, $p < 0.05$), which in turn correlates to the rate of initial RBC aggregate formation ($r = 0.78$, $p < 0.05$). Hydrodynamic strength of RBC aggregates was found to be decreased in TS group (36.84 [30.97; 46.42] 1/s comparing to 41.88 [43.83; 54.77] 1/s, $p < 0.05$).

Conclusions: Increased rate of initial RBC aggregate formation may contribute to the disturbances of blood flow in microvessels. Lowering of strength of RBC aggregate in TS probably relates to compensatory reaction. Further investigation will allow shedding light on the issue of microvascular blood flow impairment in ischemic stroke.

Disclosure: Nothing to disclose.

PP2003

Abstract withdrawn

PP2004

Cerebral venous thrombosis due to neurobrucellosis

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Introduction: Brucellosis is considered to be the most widespread zoonosis in the world. Nervous system involvement is rare. We report a case of neurobrucellosis.

Case report: A 20-year-old man was admitted to the hospital with a 2-month history of headache and two episodes of seizures. He also presented neck pain and fever. The patient lived in a rural area and he reported the ingestion of raw sheep milk. Examination on admission revealed neck stiffness. Cerebro spinal fluid (CSF) findings revealing a lymphocyte pleocytosis and an increased protein level. The results of agglutination titers for Brucella species were significantly elevated in both serum and CSF. Cerebral magnetic resonance imaging revealed cortical thrombosis in the left temporal and occipital lobe. Intravenous heparin was started and a therapy with Rifampicin, Doxycycline was instituted.

Discussion: Neurobrucellosis may lead to a variety of clinical manifestations and imaging abnormalities that mimic other neurologic diseases. The most common presentation is as a typical meningitis or meningo-encephalitis. Brucella can involve cerebral venous sinuses causing pseudotumor cerebri-like symptoms. Cerebral venous thrombosis may occur as a complication of brucellar meningitis. The vascular insult is likely due to an inflammatory process of the venous system. There are only a few cases reported in the literature. The outcome is favorable if treatment is started early and continued for an adequate period.

Conclusions: Neurobrucellosis may appear with different clinical manifestations. Since brucellosis in an endemic zoonotic disease in Tunisia, neurobrucellosis should be considered in the differential diagnosis of patients presenting with a cerebral venous thrombosis.

Disclosure: Nothing to disclose.

PP2005

Smoker's paradox in ischemic stroke: independent association or simple coincidence?

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Introduction: It is still unclear whether pre-stroke tobacco smoking may independently improve prognosis after stroke. We aimed to evaluate the association between smoking, patients' profile and short-term outcome in acute ischaemic stroke.

Methods: This is a retrospective analysis of consecutive patients admitted to our stroke center between June 1995 and September 2011. Data were prospectively collected in a detailed registry. Patients were categorized as: (1) current-smokers, who smoked at least occasionally within 5 years before stroke onset); (2) past-smokers, who stopped smoking more than 5 years before stroke onset; (3) never-smokers. Basic comparisons between particular groups were preceded by an overall test for significance.

Results: We identified 983 (26 %) current-smokers, 622 (17 %) past-smokers and 2121 (57 %) never-smokers. Those three groups significantly differed in age (63, 73, and 78 years, respectively), burden with major vascular risk factors, presence of pre-stroke disability (15, 21, and 29 %) and predominant stroke etiology (large artery atherosclerosis, cardioembolism or large artery atherosclerosis, and cardioembolism). Baseline neurological deficit was more severe in never-smokers (NIHSS 7, 7 and 10). Unadjusted logistic regression showed that compared to never-smokers, both current-smokers and past-smokers were less likely experience in-hospital death (OR 0.49, 95 % CI: 0.38–0.63 and OR 0.64, 95 % CI: 0.49–0.85, respectively). They were also more likely to achieve good outcome at discharge (OR 1.84, 95 % CI: 1.48–2.15 and OR 1.73, 95 % CI: 1.44–2.07). However, those associations were not confirmed in a multivariable analysis.

Conclusions: Smokers may achieve better outcome after ischaemic stroke. However, this paradox is not a causal association but rather depends on age and comorbidities.

Disclosure: Nothing to disclose.

PP2006

Production of pro-inflammatory cytokines in patients with progressive cognitive deficit after subarachnoid hemorrhage

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Introduction: The aim of study was to evaluate the state of systemic inflammatory response in patients 1 year after aneurismal subarachnoid hemorrhage (SAH) with prominent decline in cognitive function.

Methods: Total number of 32 patients after non-traumatic SAH and 10 healthy volunteers were included in the study. Cognitive status was assessed by Montreal cognitive assessment (MoCA). Cut off point for progressive cognitive deficit (PCD) was estimated as MoCA score after 1 year of SAH onset less than 19 points or MoCA score decline more than 9 points. IL-1β, IL-6, IL-17 and CRP were estimated in blood plasma by the ELISA-method. Patients were tested at discharge from the hospital and 1 year after disease onset.

Results: PCD one year after SAH was determined in 15.6 % of patients. Concentration of IL-1β, IL-6 and CRP in patients with PCD did not differ from patients without PCD 1 year after SAH. CRP concentration was higher in both groups while compared to control group at initial examination ($P < 0.05$) and 1 year after SAH onset ($P < 0.05$), however no significant differences between groups with mild and prominent cognitive decline were found. In group with PCD significant increase in IL-6 and IL-17 production at initial examination as well as increased IL-17 production 1 year after SAH onset were found [OR: 4.01 (95 %, CI 1.27–11.40; $P = 0.02$)].

Conclusions: PCD after one year SAH was associated with increased production of IL-17 and IL-6 in early recovery period and delayed increase in IL-17 production 1 year after disease onset.

Disclosure: Nothing to disclose.

PP2007

Platelet function and risk factors of resistance to acetylsalicylic acid used in the prevention of stroke

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Introduction: The aim of the study was to evaluate the prevalence of resistance to acetylsalicylic acid (ASA), used for prevention of stroke, including the assessment of risk factors associated with ASA resistance (AR).

Materials and methods: 340 patients taking ASA and 46 healthy volunteers were enrolled in the study. Patients were divided into the following groups: 1 (acute phase of stroke), 2 (chronic phase of stroke), 3 (patients without stroke, but with high cerebrovascular risk; SCORE > 10 %). Platelet function was assessed by impedance aggregometry method in the whole blood using a multi-channel platelet function analyzer (Multiplate®, Dynabyte).

Results: The prevalence of AR ranged from 35 % (acute phase of stroke) to 44 % (patients without stroke). AR was slightly but insignificantly higher in patients with diabetes mellitus. The following risk factors for AR were determined: ASA dose ≤100 mg/daily, taking ASA >1 year, heart rate >70 beats/min, smoking, taking ACE inhibitors and nitrates, haematocrit >40 %, platelet count $>300 \times 10^3$, LDL concentration >3.5 mmol/l. The probability of the critical event was significantly higher for diabetic patients with AR (OR 4.78; $p = 0.04$). For the remaining patients with AR the risk for a critical event was higher but insignificantly.

Conclusions: The study confirmed the occurrence of AR in many patients taking ASA for stroke prevention. Risk factors for AR are as follows: low ASA dose, longer time of ASA therapy, higher heart rate, nicotinism, usage of some drugs, higher haematocrit and platelet count, abnormal LDL. The laboratory AR established by impedance aggregometry increases the risk for clinical AR.

Disclosure: Nothing to disclose.

PP2008

The sex hormone ratios and risk of acute cerebral infarction

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Introduction: Sex hormones may be associated with higher incidence of clinically significant stroke or stroke related events. Elucidating the impact of sex hormones on the cerebral vasculature is important for understanding male–female differences in stroke and various conditions. The aim of the present study was to assess the role of sex hormone ratio in acute ischemic stroke.

Methods: Between January 2011 and December 2013, a total of 154 patients with acute cerebral infarction or transient ischemic attack, and 132 control subjects were included in this study. Sex hormones including estradiol, estrogen, testosterone, free testosterone and progesterone of all patients were investigated. We analyzed sex hormone ratio of these patients.

Results: In men, compared with control group, estradiol/testosterone (E/T) ratio and estradiol/free testosterone (E/T free) ratio were significantly elevated in the stroke patient group. ($P = 0.036$ and $P = 0.024$). On the contrary, there were no evidence for an association between ischemic stroke and E/T, E/T free ratio in women.

Conclusions: Sex hormones may play a complicated role in determining the risk of stroke. In this study, higher E/T or E/T free ratio were associated with ischemic stroke in men. Other sex hormone ratios were not related with acute ischemic stroke. These findings support the hypothesis that increased estradiol and reduced testosterone were associated with ischemic stroke, particularly in men.

Disclosure: Nothing to disclose.

PP2009

Neuroprotective effects of amlodipine besylate on oxidative stress-injured neural stem cells

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Introduction: Hypertension is the main risk factor for various neurological diseases. Amlodipine besylate (AB), a Ca^{2+} antagonist and widely-used antihypertensive drug, has been reported to reduce oxidative stress. In this study, we examined the neuroprotective effects of AB on oxidative stress-injured neural stem cells (NSCs) with a focus on the phosphatidylinositol 3-kinase (PI3K) pathway.

Methods: We treated primary cultured NSCs injured by H_2O_2 with several concentrations of AB. The viability of NSCs was measured by trypan blue staining and LDH assay, and apoptosis was investigated by TUNEL and DAPI staining. To evaluate the effects of AB on proliferation of NSCs we performed BrdU labeling and colony formation assays. The level of free radical production was also checked. We confirmed the effects of AB on intracellular signaling proteins by western blot analysis.

Results: After treatment with H_2O_2, the viability of NSCs decreased, but co-treatment with AB restored the viability of H_2O_2-injured NSCs. H_2O_2 increased free radical production and apoptosis in NSCs, while co-treatment with AB attenuated these effects. NSC proliferation decreased upon H_2O_2 treatment, but that combined treatment with AB restored proliferation. Western blot analysis showed that AB treatment increased the expression of cell survival-related proteins linked with the PI3 K pathway, but decreased the expression of cell death-related proteins.

Conclusions: Our results suggest that AB restores H_2O_2-inhibited viability and proliferation of NSCs by inhibiting oxidative stress and activating the PI3 K pathway.

Disclosure: Nothing to disclose.

PP2010

In-hospital mortality among stroke patients admitted to hospital on weekends as compared with weekdays

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Introduction: The purpose of present investigation was to compare in-hospital mortality of patients admitted for stroke during weekdays and those admitted during weekends. The study was conducted in the Department of Neurology, Split University Hospital Split (DNSUH).

Methods: Data were analyzed for 3.868 consecutive stroke patients admitted to DNSUH from January 2005 to December 2010. Inclusion criteria were known outcome, whether it was death or discharge to home care or in some rehabilitation centers. Exclusion criteria were incomplete medical records and the unknown outcome. The main outcome measure was mortality from stroke.

Results: 2.899 patients were hospitalized on weekdays and 969 on weekends. Percentage of deaths was 22.84 % on weekdays and 23.84 % on weekends ($P = 0.412$). The highest mortality was observed in patients admitted on Friday (25.49 %), but there was no statistically significant difference compared to the other days of the week ($P = 0.515$). There was no difference in mortality over the weekend in relation to the type of stroke: ischemic (20.57:21.36; $P = 0.623$) or hemorrhagic (43.00:39.69; $P = 0.524$), or in relation to the age of patients divided in four age groups ($P = 0.482$, $P = 0.116$, $P = 0.724$, $P = 0.815$).

Conclusion: In conclusion, the in-hospital mortality of patients with stroke admitted to DNSUH during weekend was the same compared with stroke patients with a weekday admission. Of predictors for in-hospital outcome, timing of admission had no significant influence on mortality.

Disclosure: Nothing to disclose.

PP2011

Incidence of admission hyperglycemia and relationship to the functional outcome of acute ischemic stroke patients

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Introduction: Hyperglycemia (HG) occurs in up to 60 % of stroke patients without known diabetes. HG after acute stroke is associated with larger infarct volumes and cortical involvement, and with poor functional outcome. It is common practice in stroke units to reduce blood glucose levels exceeding 180 mg/dl (10 mmol/l). The aim of this study was to investigate the incidence of HG and the relationship to the functional outcome of acute ischemic stroke patients.

Methods: We analyzed 114 adult nonconsecutive patients (age: median 66.2 years, 61 % men) with first ischemic stroke ever. HG is defined as a blood glucose level above 110 mg/dl. Functional outcome at 90 days was assessed using the modified Rankin Scale (mRS). A poor outcome was defined a mRS score ≥ 2.

Results: Admission glucose level >110 mg/dl was found in 69 patients (60.5 %). A level between 110 and 179 mg/dl in 48 (69.6 %) and a level >180 mg/dl in 21 (30.4 %) patients. mRS score ≥ 2 was found 53 (76,8 %) patients with HG, in 15 (71.4 %) patients with glucose level >180 mg/dl. mRS ≥ 2 was found in 24 (53.3 %) normoglycemic patients.

Conclusions: Despite small number of patients our findings suggest that the incidence of admission HG is high and associated with poor functional outcome, and it is consistent with literature data. Aggressive hyperglycemic control in ischemic stroke remains still a controversial and challenging problem.

Disclosure: Nothing to disclose.

PP2012

Profile and management of stroke patients in eastern Democratic Republic of Congo

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Introduction: Stroke is one of the leading causes of adult death and disability worldwide. In the sub-Saharan Africa, despite prevailing infectious diseases, non communicable diseases such as cerebral stroke have progressively become important, but poorly documented.

Methods: This observational pilot study, the first carried in Bukavu (eastern part of the DRC), aimed at characterizing stroke patients (SP) and matched controls, mainly regarding cardiovascular risk factors (CVRF). It consecutively included 31 SP admitted at the reference provincial hospital among which 19 could be compared to age- and sex-matched controls.

Results: Stroke patients were predominantly males and young. Brain imaging was poorly available, revealing mostly hemorrhagic stroke. The main recorded CVRF were high blood pressure (HBP), BMI, total cholesterol, LDL, triglycerides, low HDL and regular alcohol consumption. Females were more frequently affected by CVRF related to body fat excess. Only HBP was associated to increased risk of strokes. Stroke outcome was comparable to that of other African reference centers.

Conclusions: Our study further emphasizes on the important role of high blood pressure in mostly young stroke patients in Africa, while body fat excess appears to be predominant in women. Though, our findings need still to be confirmed by larger studies. The role of other CVRF like psychological stress should be evaluated in this war-torn region, as well as alcohol consumption and diabetes, which supposedly have high prevalence in the region.

Disclosure: Nothing to disclose.

PP2013

Evaluation of dementia syndrome in post stroke patients

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Aim: The assessment of post stroke dementia and its correlation with clinical and imaging data.

Methods: We studied the charts of 237 stroke patients followed up at the neurology unit, ambulatory, Tirana. They are presented at least 3 months after the first or recurrent stroke. Diagnosis of dementia was made according to the DSM IV criteria. All patients underwent a detailed neurological examination. HIS score was applied. CT, MRI of the brain is requested. Patients who had previous history of dementia, impairment of communication after stroke were excluded from the study. SPSS 17.0 program was applied for data analyze.

Results: The mean age is 67, 5 (± 5, 9) years old. There are 71 females and 166 males. We analyzed the data of 67 (28 %) patients of them who met criteria for dementia. 40 patients of them had 4-7 in HIS score. 27 patients had > 7 in HIS score, 0 patients had < 4 in HIS score. There is a statistically significant correlation between post stroke dementia and ages of patients, level of education, cardiovascular diseases, diabetes. There is a statistically significant correlation between PSD and multiple and subcortical vascular lesions. No significant correlation between post stroke dementia and subtype of stroke, carotid stenosis, hypertension, hypercholesterolemia, between subtypes of post stroke dementia and vascular risk factor is found.

Conclusions: This study suggests that dementia syndrome is most frequent in stroke patients with multiple and subcortical vascular lesions. Multiple vascular risk factor are more predictive for post stroke dementia.

Disclosure: Nothing to disclose.

PP2014

Risk factors of hemorrhagic transformation and parenchymal hematoma in patients with ischemic stroke

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Introduction: Hemorrhagic transformation (HTf) and parenchymal hematoma (PH) are complications of ischemic stroke. The aim of the study is to clarify the risk factors of HTf and PH in hospitalized patients with ischemic stroke, not treated with thrombolysis.

Methods: A total of 149 patients with acute ischemic stroke were included in this study in four months period. The diagnosis of ischemic stroke was made by diffusion weighted MRI. HTf and PH were detected with brain CT within 1 week after diagnosis of ischemic stroke.

Results: HTf and PH were observed in 41 patients (27.5 %) (18 female, 23 male). Obesity (BMI > 30) (41.4 %), hypertension (73.1 %) diabetes mellitus (31.7 %), coronary artery disease history (31.7 %) and recurrent stroke history (31.7 %), smoking (43.9 %) were noted according to percentage values. None of them was treated with anticoagulant drugs and 48.7 % of patients were under antiagregant drugs treatment before ischemic stroke. Large and small artery atherosclerosis (41.4 %) and cardio embolism (39 %) were the most common etiological factors. We began antiagregant treatment to 17 % of patient, combination of antiagregant and low-dose unfractionated heparin treatment to 56 % of patient and anticoagulant treatment to 27 % of patient after ischemic stroke. HTf was detected in 80,5 % of patients and PH was detected 19,5 % of them.

Conclusion: Our study suggests that the significant risk factors of HTf and PH were hypertension, obesity and smoking. Cardio embolism was the most common etiology in PH.

Disclosure: Nothing to disclose.

PP2015

Recurrent PRES or something mimicking it?

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Posterior reversible encephalopathy syndrome (PRES) is characterized by headache, seizures, altered consciousness and visual disturbances. Magnetic Resonance Imaging (MRI) shows vasogenic edema with signal changes on T2 and FLAIR, located in the parieto-occipital lobes. Precipitating factors are hypertension, hypercalcaemia, uraemia, immunosuppressants, infection (HIV) and autoimmune diseases. Recurrence of PRES is uncommon, ranging between 3.8 and 8 %.

A 76-years-old man presented in May 2012 with a single generalized seizure without other neurological symptoms. MRI showed vasogenic edema predominantly in the right parieto-occipital lobe. He received prednisolon 100 mg/day for 6 days. MRI after 3 weeks showed remission of the lesions. CSF was normal. MRI after 3 months revealed relapse of the edema. He got diagnosis for PRES and antihypertensive treatment was initiated. In December 2013 he was re-admitted with

confusion, headache and vomiting. High blood pressure was observed (180-210/70-90).His clinical status returned to his baseline over 9–10 days as the blood pressure was gradually lowered.

Routine blood investigations were negative, including se-calcium, ACE, ANA, ANCA-C, ANCA-P, immunoglobulins, M-component, HIV, and paraneoplastic antibodies. Brain MRI disclosed new bilateral but now predominately left-sided parietal, frontal and temporal signal changes without contrast enhancement and normal MR angiography. CSF examination showed slightly elevated protein (0.72) and IgG (0.74). Flow cytometry was normal. Brain biopsy was performed; histological diagnosis is pending but will be presented at the congress.

Here, we present a patient with three PRES-like radiological relapses where atypical PRES are suspected but PRES mimicking lymphoma can neither exclude until the histological confirmation.

Disclosure: Nothing to disclose.

PP2016

Intra-arterial tissue Plasminogen Activator in acute ischemic stroke

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Introduction: The 'Hyper dense Middle cerebral artery (MCA) sign' on plain CT scan of brain in acute ischemic stroke, indicates acute thrombotic occlusion of MCA.

Objective: We evaluated the serial progression of this sign on follow-up CT/MRI and its effect on recanalization and clinical outcome after intra-arterial thrombolysis with tissue Plasminogen Activator (tPA).

Materials and methods: Thirty-three acute ischemic stroke patients who were treated with intra-arterial tPA 9 12–18 mg) within 6 h of symptom onset were enrolled in this study. Recanalization status was evaluated using the thrombolysis in myocardial infarction (TIMI) flow grade on digital subtraction angiography immediately after thrombolysis. Baseline clinical parameters and clinical outcome were reviewed.

Results: A positive Hyper dense MCA sign was detected in 39 %. The mean TIMI grade was higher in the patients with a positive sign 2.8 vs 1.1, respectively ($p < 0.005$). A history of Atrial fibrillation was significantly higher in the patients with hyper dense MCA sign. In 86 % of patients with the positive sign, the sign disappeared on follow-up CT/MRI, and disappearance of the sign was well correlated with complete recanalization on follow-up CT/MR angiography in 22/28(79 %) patients. This sign was not associated with a favourable functional outcome 30 later.

Conclusions: The Hyper dense MCA sign is indicative of acute thromboembolic occlusion and predicts the immediate effectiveness of intraarterial thrombolysis. There was good recanalization rate of 79 %. The appearance of this sign was not associated with a favourable clinical outcome after thrombolysis.

Disclosure: Nothing to disclose.

Clinical neurophysiology

PP2017

The patients with A waves and no F waves

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Introduction: If A and F waves are not properly recognized and differentiated, one can falsely identify an A wave as an F wave and evaluate the examination as normal at the early stages of the disease. As a result the early markers of an acquired polyneuropathy may be eluded by mistake. In this study we evaluated the electrodiagnostic results of the patients with detectable A waves and no F waves.

Methods: The patients referred to our EMG laboratory in Istanbul Education and Research Hospital between January 2010 and September 2013 were evaluated retrospectively.

Results: 64 patients who had A waves in their electrophysiological examinations, were included. We diagnosed 41 patients with polyneuropathy, 7 with radiculopathy. Two patients had normal examinations. 36 of them had A waves but didn't have F waves in their peripheral nerves. The electrophysiological diagnosis of the patients were motor demyelinating polyneuropathy in 9, sensorymotor demyelinating in 13, sensorymotor axonal in 6, sensorymotor mixed in 4, multifocal motor in 2. The last 2 patients had chronic radiculopathy, 28 had demyelinating features in their examinations. We found 59 nerves in 36 patients displaying these features. The nerves without F wave but detectable A waves were tibial ($n = 22$), peroneal($n = 20$), median ($n = 9$) and ulnar nerves ($n = 8$).

Conclusions: Demyelinating polyneuropaties may present with A waves and no F waves. Early diagnosis and treatment is important and we must pay attention to the recognition and detection of the A waves for early treatment strategies.

Disclosure: Nothing to disclose.

PP2018

High-frequency navigated repetitive magnetic stimulation in the treatment of central post-stroke pain

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Introduction: The aim of our study was to assess the efficacy of high-frequency repetitive navigated transcranial magnetic stimulation (rTMS) and the cortical excitability changes in patients with central post-stroke pain (CPSP) before and after stimulation.

Methods: Five patients (3 males, 2 females; age, 59.8 ± 8.4 years with a mean duration of CPSP of 71.9 ± 46.0 months) were included and underwent 10 sessions of high-frequency rTMS (10 Hz; stimulation, 2 s; rest, 58 s) over the motor hotspot of the abductor pollicis brevis muscle in the primary motor cortex of the affected hemisphere with 80 % of motor threshold. A Visual Analogue Scale (VAS) was used to evaluate the pain intensity. In addition, we assessed the motor-evoked potential (MEP) amplitude, MEP latency, motor threshold at rest, magnetic field strength at the stimulation point, and squared motor cortical area before and after stimulation.

Results: Four of 5 patients showed an evident VAS score reduction after the stimulation (7.0 [6.0; 8.0] before, 2.0 [1.0; 5.0] after, $p = 0.03$). We observed a decrease in MEP amplitude and squared cortical area and an increase in motor threshold and magnetic field strength. Differences were not significant after statistical data manipulation; this was probably due to the small number of patients. There were no significant changes in MEP latency. The analgesic effect of rTMS persisted for 3 months.

Conclusions: These findings showed the efficacy of high-frequency rTMS in the treatment of CPSP. Our neurophysiological findings represent decreased cortical excitability after rTMS sessions.

Disclosure: Nothing to disclose.

PP2019

Pathological findings of multimodal evoked potentials in leber hereditary optic neuropathy

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Introduction: Leber hereditary optic neuropathy (LHON) is the most common mitochondrial disorder characterized by acute or subacute painless loss of central vision. However, neurophysiological findings confirm wider systemic involvement in LHON. The aim of the study was to examine function of different sensory pathways using multimodal evoked potentials—transcranial magnetic stimulation (TMS), visual (VEP), brainstem auditory (BAEP) and somatosensory (SEP) evoked potentials.

Methods: The study included 10 patients and 13 asymptomatic family members who were diagnosed with LHON after detailed medical examination and molecular-genetic confirmation. VEP was performed in all subjects, BAEP and SEP in seven, while TMS was used in six of them.

Results: Pathological VEP with prolonged P100 latencies and decreased or low amplitudes was found in all probands. Three asymptomatic family members had decreased amplitudes with normal P100 latencies. In all probands, in whom it was performed, BAEP was pathological with interpeak latencies (IPL) prolongation IPL I–V and IPL I-III. Furthermore, in 9 family members BAEP showed IPL I–V prolongation, among which 5 had IPL I-III prolongation. Additionally, MEPs evoked by TMS were altered, while SEP was pathological only in one patient who had a delay of cortical evoked responses and prolonged central conduction time.

Conclusions: Pathological findings of multimodal evoked potentials, particularly BAEPs and MEPs, may confirm widespread involvement of central nervous system in LHON.

Disclosure: Nothing to disclose.

PP2020

Sensitivity of OCT and VEPs in multiple sclerosis

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Objectives: To evaluate the relative value of optical coherence tomography (OCT) and visual evoked potentials (VEPs) in assessing visual involvement in patients with multiple sclerosis (MS).

Methods: Cross-sectional study of 121 consecutive subjects with MS. Of 242 eyes, 166 had no previous history of optic neuritis (ON), 22 had a single recent ON episode (<3 months); 54 had chronic ON (at least 1 episode >3 months before). All patients underwent assessment of EDSS, visual acuity (VA), OCT retinal nerve fiber layer (RNFL) thickness and VEP.

Results: In eyes with recent ON, the sensitivity of OCT was 5.6 % considering only RNFL thickness increase, 38.9 % considering also RNFL reduction, with a higher sensitivity of VEP (77.3 %; McNemar $p < 0.0001$ and 0.02). In eyes with chronic ON, no significant difference was found between OCT (68.5 %) and VEP (81.5 %) sensitivity (VEP/OCT 88.9 %). In asymptomatic eyes, VEPs had a higher sensitivity (31.7 %) vs OCT (19.9 %; $p = 0.005$); VEP/OCT combined detected abnormalities in 39.2 %. In this subgroup, VEP score and global RNFL thickness were significantly correlated with EDSS, disease duration, not with VA.

Conclusions: The present findings confirm a higher sensitivity of VEPs in the subacute phases of optic neuritis and in asymptomatic eyes. This discrepancy fades off after more than 3 months from the ON episode. Finally, the correlation with disability and DD favours the usefulness of both techniques in monitoring MS patients, to be verified through longitudinal studies.

Disclosure: Part of this work was financially supported by Merck Serono S.A., Geneva, Switzerland. Merck Serono is the biopharmaceutical division of Merck KGaA, Darmstadt, Germany.

PP2021

Ipsilateral motor evoked potentials to transcranial magnetic stimulation in right- and left hemisphere stroke

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Introduction: In previous studies transcranial magnetic stimulation (TMS) have demonstrated ipsilateral motor evoked potentials (iMEPs) after stimulation the unaffected as well as the affected hemisphere in the chronic stage of stroke. Whether there is difference between right (RH) and left (LH) hemisphere lesion in ishemic stroke patients is unclear. This study aimed to address this question.

Methods: This study investigated iMEPs elicited by TMS in 94 right-handed patients with hemiparesis after ischemic stroke in the middle cerebral artery territory (49 with RH and 45 with LH lesion) and 20 healthy right-handed subjects.

Results: We recorded iMEP in 2 control subjects (10 %) on the left side only after stimulation LH. In stroke patients, stimulation the unaffected hemisphere revealed differences between RH and LH: 71,4 % patients with RH lesion have iMEPs and only 28,6 % patients with LH lesion. iMEPs were also observed after stimulation the affected hemisphere: in 37,7 % patients with RH lesion and in 62,3 % with LH lesion.

Conclusions: These data identify different neurophysiological features of the right and left cerebral hemispheres in chronic stroke patients. Higher levels of activating processes in the left dominant hemisphere retained under lateralized hemispheric pathology. The contribution of the left and right hemispheres of the adult brain to recovery after stroke are discussed.

Disclosure: Nothing to disclose.

PP2022

Time to sustained remission of pseudobulbar affect (PBA) episodes after treatment with dextromethorphan and quinidine

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Introduction: PBA is a neurological condition characterised by frequent, uncontrollable, disruptive laughing and/or crying episodes, which can cause embarrassment and impair social function. PBA occurs secondary to neurological diseases/injury affecting brain areas coordinating emotional expression. The primary goal of PBA treatment is to reduce the number and/or severity of episodes. Dextromethorphan and quinidine (DMQ [NUEDEXTA®]) was shown to be efficacious in reducing PBA symptoms, with approximately 50 % of patients achieving a complete remission defined as no PBA episodes during the last 14 days of a controlled clinical trial. DMQ is the only approved PBA treatment (US and EU). An ad hoc analysis

assessed the mean time to entering a sustained remission in pivotal trial patients.

Methods: Phase 3, randomised, double-blind, placebo-controlled, multicenter study in adults with PBA secondary to amyotrophic lateral sclerosis or multiple sclerosis. Sustained remission was defined as remaining PBA-free after having at least 14 days without PBA episodes. Data are reported for patients receiving the twice-daily dextromethorphan hydrobromide 30 mg/quinidine sulphate 10 mg (DMQ-30) dose vs placebo (equivalent to 23/9 mg DMQ base, the highest EMEA-approved dose).

Results: Differences from placebo emerged early, and were significant by week 2 (DMQ-30 11.8 % vs placebo 7.3 %; $P = 0.04$, Chi square). Cumulative remission rates increased steadily and remained significantly greater at endpoint for DMQ-30 (47.3 %) vs placebo (29.4 %; $P = 0.006$, Chi square).

Conclusion: Almost half of patients taking DMQ-30 for PBA entered remission at the pivotal trial endpoint. Significant differences from placebo emerged at 2 weeks and persisted at trial endpoint.

Disclosure: Drs. Formella, Siffert, and James are employees of Avanir Pharmaceuticals, Inc.

PP2023

Sympathetic and cardiovascular changes induced by sodium oxybate treatment in patients with narcolepsy and cataplexy

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Introduction: Sodium oxybate (Xyrem) is effective on many narcolepsy symptoms but it may also induce a systemic hypertension with an unclear mechanism. Previous animal studies suggest that the cardiovascular responses elicited by sodium oxybate involve the activation of central sympathetic pathways. The aim of this study was to elucidate the sympathetic involvement in systemic hypertension induced by Xyrem.

Methods: We studied 4 hypocretin-deficient narcolepsy and cataplexy male patients who underwent microneurographic recording of muscle sympathetic nerve activity (MSNA) from the peroneal nerve with monitoring of blood pressure (BP) and heart rate (HR). The recording was made before and 6 months after Xyrem treatment (6 gr/die).

Results: Before Xyrem treatment resting data were (mean ± DS) 68 ± 19 bursts/100 (b/100) heart beats (HB) and 44 ± 13 burst/min for MSNA, 116,5 ± 14 mmHg for systolic and 72 ± 17 mmHg for diastolic BP, 64,2 ± 3,5 beats/min for HR. After 6 months of Xyrem both MSNA and BP increased (mean ± DS 81 ± 16 b/100 HB and 52 ± 10 b/min for MSNA, 153 ± 26 and 95 ± 14 mmHg for systolic and diastolic BP, respectively) whereas HR showed no significant change (64.5 ± 5.5 beats/min).

Conclusion: These preliminary data suggested that BP elevation induced by Xyrem could be due to a sympathetic hyperactivity although this conclusion must be supported by additional data.

Disclosure: Nothing to disclose.

PP2024

Central motor conduction time in patients with spinocerebellar ataxia type 3

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Introduction: Although corticospinal pathway is also affected in spinocerebellar ataxia type 3 (SCA3), few studies have measured the relationship of this affection with intensity of cerebellar signs. Generally, central motor conduction time (CMCT) was normal up to advanced stages of the disease (Arpa et al. 2000).

Methods: CMCT of right (R) and left (L) upper limbs (UL-CMCT) and lower limbs (LL-CMCT) were measured in 15 patients (median SARA: 12, range: 2-26.5) with SCA3 following methods in Santiago-Pérez et al. 2007. Median, range and absolute frequency of altered CMCT were calculated. Spearman's rho coefficients of correlation between CMCT and total and each item's SARA score were used to measure how related CMCT are with cerebellar signs.

Results: A prolonged RUL-CMCT was found in 4 of 14 patients (median: 5.2 ms range: 3.23–10 ms); a prolonged LUL-CMCT in 5 of 15 (median: 5.4 ms range: 3.9–10 ms); a prolonged RLL-CMCT in 4 of 15 (median: 12.1 range: 7.5–19.7 ms); a prolonged LLL-CMCT in 3 of 15 (median: 12.5 range: 9.8–18.3 ms). CMCT are poorly correlated with total SARA score (Spearman's rho: RUL: −0.150, LUL: −0.040, RLL: 0.194, LLL: 0.386) and with particular SARA items.

Conclusions: Although corticospinal abnormalities can occur in SCA3, they are not related with cerebellar signs. This could indicate that neurodegeneration in corticospinal tract and in cerebellum progress in different paces and that are influenced by distinct mechanisms.

Disclosure: Nothing to disclose.

PP2025

The cutaneous silent period in essential tremor

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Introduction: The pathogenesis of essential tremor (ET) still remains unclear. The cutaneous silent period (CuSP) is a spinal inhibitory reflex primarily mediated by A-delta nerve fibers. To date, CuSP has not been studied in patients with ET. The aim of this study was to evaluate the changes in CuSP in patients with ET.

Methods: Seventeen patients with ET were compared with 15 age- and sex-matched controls. The individuals were evaluated based on the nerve conduction study (NCS) recorded from both upper and lower extremities and CuSP (latency and duration) recorded from the right thenar muscle evoked by electrical stimulation of the digital cutaneous nerve of the right index finger.

Results: There were not any significant differences in NCS and CuSP latency between patient and control groups. The CuSP duration prolonged in ET patients compared to healthy controls.

Conclusions: Elongation in the duration of the CuSP in patients with ET may suggest insufficient inhibition in the intermediate spinal inhibitory neurons which generate CuSP, cortical hypersensitivity or abnormality of the cortical inhibitory mechanisms. Further studies with larger series are needed to understand the potential pathophysiological mechanisms underlying ET.

Disclosure: Nothing to disclose.

PP2026

Does peripheral small fibre neuropathy accompany psoriasis? Utility of the cutaneous silent period

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Introduction: The neurogenic inflammation in the pathogenesis of psoriasis has been previously discussed. Moreover, the concomitant occurrence of peripheral large nerve neuropathy has been reported in several psoriatic patients. The aim of this study was to investigate the possible peripheral small nerve fibre neuropathy existance in psoriasis.

Methods: Fifteen patients with psoriasis vulgaris were compared with 15 age- and sex-matched controls. The patient and control groups were compared in terms of nerve conduction studies (NCS), CuSP latency and duration in both upper and lower extremities.

Results: There were not any significant differences in NCS between patient and control groups. CuSP latencies in both upper and lower extremities were determined to be prolonged in patients compared to controls.

Conclusions: This is the first study that suggests the possible peripheral small nerve involvement in patients with psoriasis.

Disclosure: Nothing to disclose.

PP20207

How anticipation modulates programmed responses to kinematic stimuli

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Introduction: Kinematic stimuli may trigger voluntary or reflex responses. In some situations subjects are exposed to unexpected body or limb displacements to which they have to react, e.g. construction workers on slippery surfaces at risk of falling. Here we explore how kinematic stimuli modulate voluntary and reflex responses according to the state of a subject's anticipation.

Methods: Nine healthy subjects were suspended in a Lokomat system and were exposed to unexpected passive left knee flexion at three angular velocities randomly presented (6, 60, 240°/s). In some intermingled trials subjects were informed to expect a 240°/s left knee movement. Subjects were asked to perform a right wrist extension as soon as they felt their leg move (conditions: 6-React, 60-React, 240-React-unexpect, 240-React-expect, respectively). We recorded EMG activity from orbicularis oculi and sternocleidomastoid muscles to assess possible startle responses, from left quadriceps muscle to obtain stretch reflexes, and from wrist extensors to assess reaction time.

Results: Reaction time was shorter for 240-React-unexpect and 240-React-expect than for 6-React and 60-React conditions. Furthermore, most 240-React-unexpect trials showed startle responses as evidenced by orbicularis oculi and/or sternocleidomastoid EMG activity. Reaction time was shortest when startle activity was present or when the stimulus was expected. In contrast, stretch reflex latency in quadriceps was longer when the stimulus was expected than unexpected, irrespective of accompanying startle activity.

Conclusions: Anticipation may differentially modulate subjects' voluntary and reflex responses to kinematic stimuli.

Disclosure: Nothing to disclose.

PP2028

An atypical Guillan-Barré syndrome associated with hepatitis B infection

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Introduction: Clinical or subclinical acute demyelinating neuropathy that does not full-fill the criteria of a Guillain-Barré syndrome (GBS) may complicate hepatitis. We report a case of atypical GBS with hepatitis B infection. CaseA 40-year-old healthy man was admitted to the hospital with acute onset bilateral facial palsy and bilateral lower and upper limb weakness, numbness and pain. His complaints were progressed during 3–4 weeks. His physical examination was normal. On neurological examination he had bilateral peripheral facial palsy. Muscle weakness was present in left shoulder abduction (4/5), right hip flexion (4/5) and left toes (4/5). All deep tendon reflexes were hyperactive. Results of routine laboratory tests were normal except for slightly elevated liver enzyme. On serological evaluation HBsAg, Anti HBc total, Anti HBe were positive, Anti HBs, Anti HBc IgM, HBeAg, Anti HCV and HIV Ag/Ab were negative. Cytochemical analysis of cerebrospinal fluid was normal. Blood and urine immunefixation electrophoresis were normal. On electrodiagnostic examination all sensory nerve responses were absent; there were significant slowing of distal latencies and F wave latencies in all motor nerve responses. The compound muscle action potential (CMAP) amplitudes were low and we detected abnormal temporal dispersion in left median and bilateral tibial nerves. Sural nerve biopsy was normal. He recovered spontaneously.

Conclusions: Atypical clinical presentation of GBS may occur and HBV infection could be responsible of it. Because early diagnosis and timely administration of intravenous immunoglobulin or plasma exchange improve the degree of neurologic recovery, gastroenterologists should be aware of this association.

Disclosure: Nothing to disclose.

PP2029

Using photosensor for precise recording of the stimulus onset during N400 event related potentials registration

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Background: Extracting event-related potentials (ERP) from multichannel EEG recordings requires precise synchronization between stimulus presentation and EEG recording system.

Objective: The aim of this study was to develop a photosensor for a precise recording of stimulus onset during N400 ERP registration.

Materials and methods: The sample consists of 15 healthy subjects who were visually presented with 104 semantically congruent or incongruent word pairs. ERPs were obtained by averaging EEG data registered with the 21 channel digital EEG system (impedance <5kOhm, bandwidth 0.1–30 Hz). Synchronization between stimulus presentation and EEG recording system was obtained using specially developed photosensor which was placed on the stimulus presentation screen and connected to the EEG bipolar channel. EEG signal was processed by ERPLAB software. Photosensor's sensitivity and response time were measured.

Results: Photosensor was made using silicon NPN phototransistor in hermetically sealed package with base terminal and glass lens. It was sensitive to changes in light intensity on the screen. Measured sensitivity was 0.2 uV/lux with constant response time (<1 ms). ERPs were extracted by averaging EEG data based on precise timing information which was recorded as a spike at one of the EEG channels. A statistically significant difference in the N400 ERP component amplitude was registered between the semantically congruent and incongruent trials in the interval ranging from 300 to 400 ms after the stimulation ($p < 0.05$).

Conclusion: This research demonstrates a successful utilization of photosensor for a precise recording of the stimulus onset during N400 ERP registration.

Disclosure: Nothing to disclose.

PP2030

Electrophysiological study of SCA and FRDA patients

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Introduction: The aim of our study is to examine the bioelectrical activity of nerves and muscles in spinocerebellar (SCA) and Friedreichs' ataxia (FRDA) patients according to a standardized protocol, in order to obtain information about the severity and distribution of peripheral nerve involvement.

Methods: We examined 18 genetically diagnosed, older than 18 years of age SCA and FRDA patients. Control group was formed by 31 age-matched healthy individuals. We performed sensory and motor conduction studies, F responses, needle EMG of proximal/distal muscles, and motor unit number estimations (MUNE) of distal muscles to upper and lower extremities of both groups. Descriptive statistics and group comparisons were done for each recorded parameter.

Results: All sensory responses were low in amplitude ($p < 0.01$) in patients as well as sensory conduction velocity was slow ($p < 0.05$) for ulnar nerve. Median and peroneal motor amplitudes were also low ($p < 0.01$). Median, peroneal ($p < 0.01$), ulnar, and tibial ($p < 0.05$) motor conduction velocities were significantly slow. MUNE in m. abductor pollicis brevis and m. tibialis anterior muscles were significantly lower in patient group than healthy individuals ($p < 0.01$). Needle EMG evaluation revealed neurogenic involvement in 1/3 of patients.

Conclusions: Polyneuropathy is frequent in SCA and FRDA patients. Sensory nerves in lower extremities were predominantly involved however, signs of motor dysfunction were also notable. MUNE can provide quantitative information about motor nerve fiber and/or motor neuron involvement. Clinical and electrophysiological findings of peripheric polyneuropathy syndrome were more striking in atactic patients with proven genetic defect.

Disclosure: Nothing to disclose.

PP2031

High frequency paired associative stimulation modulates the corticospinal excitability in human subjects: an EEG study

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Introduction: Objective of our study is to evaluate the effects of a rapid paired associative stimulation (rPAS) on the corticospinal excitability on M1, observing the modulation of the MEP amplitude and of the absolute EEG-power, and their correlations, as expression of cortical synaptic strengthening/weakening.

Methods: We tested on 12 healthy subjects the effect of three PAS conditioning protocols (25 ms, 15 ms and sham ISI) on the MEP amplitude and the absolute EEG-power, and their specific correlations, 30′ after the end of the protocols.

Results: We found after PAS25 ms a MEP amplitude increase correlated to a global reduction in α/β-EEGpower and increase in θ/δ. After PAS15 ms a MEP amplitude decrease correlated to a global increase in α/β-EEGpower and reduction in θ/δ. No changes were found after rPASsham.

Conclusions: Looking at these modulations and correlations, it's conceivable that the effects of PAS25 ms could be expression of cortical synaptic potentiation. On the contrary the effects of PAS15 ms could mean cortical reset. The modulation could be dependent from cortical GABAergic, glutamatergic and cholinergic circuitries. Beyond the purely neurophysiological aspects, our protocol could be interesting in neuro-rehabilitation, taking account of the effective, quick and persistent modulation of cortical oscillatory activity at bi-hemispheric level.

Disclosure: Nothing to disclose.

PP2032

F wave duration as a diagnostic tool in primitive restless legs syndrome

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Introduction: Restless legs syndrome (RLS) is a frequent condition, but its pathophysiology is not completely understood. The dopaminergic system has a primary role and some studies have highlighted a condition of spinal hyper-excitability. The aim of our study is to explore this hypothesis through the electrophysiological evaluation of patients affected by primitives RLS.

Methods: 15 women affected by primitive RLS and 17 age-matched females (controls) were selected. All subjects underwent ENG evaluation to exclude any secondary causes of lower limb paresthesias and to evaluate spinal excitability. We considered three parameters:the amplitude and the duration of F waves (FWD) of the tibial and ulnar nerves plus the ratio between FWD and the duration of the corresponding compound muscle action potential (FWD/CMAPD).

Results: None of the subjects (both RLS and controls) showed alterations in nerve conduction velocities. Compared to the control group, significantly higher values were found in RLS patients for the mean FWD for both ulnar ($p < 0.05$) and tibial ($p < 0.01$) nerves and

for the mean FWD/CMAPD ratio average ($p < 0.001$), while not significant differences were found for the mean Amplitude.

Conclusions: The results of our study indicate a widespread spinal motoneuronaI hyper-excitability. Such condition could be mainly due to an altered modulation within the interneuronal system. Presently, RLS diagnosis is based exclusively on clinical criteria. The FWD/CMAPD ratio can help to shed light on the pathogenesis of RLS, is easily obtainable and can represent an instrumental diagnostic tool especially in cases of evening lower leg discomfort of unclear interpretation.

Disclosure: Nothing to disclose.

PP2033

Spontaneuos periodic hypothermia: differential diagnosis and treatment of a very rare condition

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Introduction: Spontaneous preiodic hypothermia, described as recurrent episodes of temperature lower than 35 °C, has been linked to the agenesia of corpus callosum (Shapiro syndrome), as a result of central nervous system pathology that affects thermorregulator structures. They have been seldom described without associated systemic or brain lesions. The spontaneuos periodic hypothermia with hyperhidrosis is one of these cryptogenic situations, with not yet understood physiopathology and which diagnostic difficulty is patent in this case report.

Case description: JPG, 66 years-old male, was admitted because of daily recurrent episodes of hypothermia, lasting from minutes to hours, sometimes reaching the 32 °C. This had begun a month and a half before. The episodes were usually morning, beginig with profuse sweating, followed by hypothermia and mild bradicardia. After this, the patient became drowsy and prostated. The patient had similar episodes years before, with auto-resolution. He didn't present other significant antecedents. We excluded hormonal, cardiac, toxic, tumoral and infectious comorbilities. After different speciality evaluations and several ineffective medications after, the diagnosis of spontaneous periodic hypothermia syndrome was made and the patient was treated with clonidine, which after dose titulation was effective.

Conclusion: The spontaneous periodic hypothermia syndrome in adults is a very rare condition, with about 50 escribed cases in literature, both in children and adults. Despite its unknown physiopathology, it might be related with hypermelatoninemia. It is strange and probably underdiagnosed but treatable disease.

Disclosure: Nothing to disclose.

PP2034

Part of brainstem dysfunction on migraine's course assessment

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Introduction: Diagnostic and estimation of migraine's severity may be determined by detecting of brainstem condition, which turn from including into process of Blink Reflex (BR) segments. The goal of our study was to access of brainstem dysfunction part on migraine's course assessment.

Methods: There were fifty patients with migraine observed: 21 with migraine with aura (MA) and 29 with migraine without aura (MWA). All patients have a frequent migraine's attacks and have not any medicament treatment on moment of examination. BR was obtained bilaterally during interictal period by electrical stimulation of r. supraorbitalis n. trigemini. Latency, durations and amplitudes of R1 and R2 components of BR were analyzed.

Results: Hyperexcitable BR was determined at 86 % of patients ($n = 43$). That type of BR has an early R1 component registration (latency of R1 less than 9.0 ms), short R2 latency (less than 26 ms), prolonged R1 and R2 duration (more than 8.8 and 39.9 ms accordingly), R3 complex registration and normal amplitudes. Only seven subjects had normal parameters and at five of them were registrated R3 components. Hyperexcitable BR appearance correlates with aura presence in clinic picture ($r = 0.65$, $p = 0.032$). Signs of hyperexcitable BR asymmetry with R1 and R2 abnormalities in contralateral of hemicrany side prevalent at patients with MA ($r = 0.34$, $p = 0.033$).

Conclusions: Migraine's patients with severe attacks have the brainstem dysfunction. For subjects with MA characterized hyperexcitable BR with R1 and R2 abnormalities asymmetry in contralateral of hemicrany side. Parameters of BR are a prognostic criterion to determine of migraine course.

Disclosure: Nothing to disclose.

PP2035

Clinical-neurophysiological particularities of brainstem condition on hemispheric stroke into estimation of Cortexin* effectivity

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Introduction: Significant condition to prognose of vascular catastrophes is integrity of brainstem. The aim of our study was to detect of neurophysiological criterion of brainstem dysfunction on acute hemispheric stroke patients and to estimate of neuroprotection strategies effectivity.

Methods: There were investigated ninety seven patients with acute hemispheric stroke and twenty seven patients with chronic cerebral ischemia. Clinical and neurophysiological methods were used: auditory brainstem, somatosensory (SSEPs), optical (OEPs), endogenous (P300) evoked potentials and Blink Reflex (BR), NIH scale.

Results: In acute stage of hemispheric stroke received signs of brainstem conducting abnormalities in rostral and caudal parts by evoked potentials data: SEPs, OEPs and BR components latencies increasing continued until 21 day after stroke start. Patients had 6 ($4 \div 7$) points of NIH. Including the Cortexin into treatment program led to acceleration of clinical and neurophysiological restoration tempos to seventh day compared to basis therapy ($P < 0.005$). That fact evidenced about prevention the progression of conduction block on mesencephalic level. In that conditions SEPs parameters recovery testified to reversibility of thalamo-cortical dysfunction. BR components latencies and durations normalized to seventh day. Similar effect was detected about latency and amplitude of P300 ($P < 0.05$). Towards seventh day patients had 3 ($2 \div 4$) points Of NIH, to 21 day—less than 1 point ($P = 0.003$).

Conclusions: Evoked potentials characteristics are indicators of brainstem dysfunction on hemispheric stroke. Comparative estimation of Cortexin effectivity contrast to basis therapy whereas including that medication accelerated reduction of brainstem dysfunction and normalized clinical condition under NIH data.

Disclosure: Nothing to disclose.

PP2036

The situation of the EEG in a developing Country, Egypt

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Introduction: EEG is the most important investigation in all types of epilepsies; providing that it was properly performed and carefully interpreted in the context of a well-described clinical setting. This work aims at high lightening the situation of the EEG service in a developing country.

Methods: All consecutive EEG reports from 1,232 patient done over a year at 3 locations were retrospectively reviewed. The following data were evaluated; EEG findings, clinical indications, requesting physician specialty, age of the patient, duration of the record, state of the patient whether awake or asleep, and the cost of the procedure.

Results: EEG in a developing country besides being ordered mainly by neurologists and neurosurgeons; it was noticed to be ordered by other specialties in a significant percentage. Striking enough overt continuous seizures/movements and witnessed seizure without return to baseline was not the main indication for ordering an EEG from all physicians including neurologists and neurosurgeons. The majority of the EEGs undergone for children at the school age or below were done during induced sleep using chloral hydrate. Routine short term EEG remains the most common type of EEG ordered in Egypt compared to long term video/sleep EEG. The Concept of the continuous EEG monitoring for an ictal recording is having many limitations in a developing country some of them are financial and others are related to the professional awareness about its usefulness.

Conclusions: More awareness is required as regard the indications and value of all types of EEG in a developing country.

Disclosure: Nothing to disclose.

PP2037

A new recording muscle for repetetive nerve stimulation technique: occipitofrontalis

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PP2038

The patients with multiple A waves

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PP2039

Current approaches to diagnosis of sensorineural hearing loss at children and meaning auditory evoked potentials at this

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PP2040

Variation of median nerve latencies values after phalen maneuver

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PP2041

Dextromethorphan/Quinidine (DMQ) treatment significantly increased percentage of days free of pseudobulbar affect (PBA) episodes in a phase 3, randomised, placebo-controlled trial

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PP2042

Dextromethorphan/Quinidine for treatment of pseudobulbar affect: analysis of treatment-related adverse events

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PP2043

Multimodal evoked potentials in monitoring the course of multiple sclerosis

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PP2044

EEG response to different odors in healthy individuals: a promising tool for objective assessment of olfactory disorders

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PP2045

Prevalence of accessory deep peroneal nerve in refferred patients to an electromyografy lab

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PP2046

Intracranila metallic body artifact in routine scalp EEG

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PP2047
Effects of acupuncture at DU 20 point on electroencephalogram

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PP2048
Using occipitofrontalis muscle at repetitive nerve stimulation in myastenia gravis patients

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PP2049
Visual and somatosensory evoked potentials in vitamin B12 deficiency

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Epilepsy 1

PP2050
Down syndrome and late onset myoclonic epilepsy in Down syndrome: investigation of EPM1 gene mutations in two cases

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Introduction: Trisomy 21, alias Down syndrome (DS), is a relatively common genetic condition with an incidence dependent on maternal age. Senile myoclonic epilepsy is being increasingly recognized as a late onset complication in elderly patients with Down syndrome in association with cognitive decline. This specific syndrome bears some broad clinical and EEG similarities to the progressive myoclonic epilepsies, particularly Unverricht-Lundborg disease (ULD). Interestingly, both EPM1 gene for ULD and amyloid precursor protein *(APP)* gene, which is implicated in Alzheimer Disease are both located on chromosome 21. Our aim was to find out a shared pathogenetical mechanism for clinico-electrophysiological similarities in these different genetic syndromes.

Methods: Two patients aged 53 and 58 years, with a history of 4 years of late onset myoclonic epilepsy, were included in the study. After obtaining written informed consent from their legal custodian, blood samples were taken. Dodecamer repeats and other possible EPM1 mutations on the chromosome 21 were investigated after isolation of DNA from their blood samples.

Results: Epileptiform abnormalities on the frontal regions with generalized slowing were found on their EEG recordings. Their myoclonic seizures were partially controlled under valproate and levetiracetam treatments. We could not find any dodecamer repats and point mutations after genetic analysis.

Conclusions: Our study did not show any mutations of EPM1 gene on chromosome 21 but did not exclude a shared genetic mechanism in these syndromes. Extra genes on the third copy of chromosome 21 or epigenetic factors may play role in this distinct type of epilepsy in DS.

Disclosure: Nothing to disclose.

PP2051
Serum natural neurotropic autoantibodies in epilepsy patients

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Objective: To study the levels of autoantibodies (AAB) to brain proteins-antigens (NF-200, GFAP, BMP, and S100β) in blood serum of patients with idiopathic and symptomatic epilepsies.

Methods: We studied 52 patients with epilepsy (main group) at the average age of 36.2 ± 14.7 years old. The main group was divided into 2 groups: I group—38 patients with idiopathic epilepsy, II group—14 patients with symptomatic epilepsy. The control group consisted of 16 healthy subjects. Immunological studies were conducted with ELI-test by immunoenzymatic analysis. The data obtained were processed using methods of variation statistics.

Results: We observed significant elevation of AAB to protein S100β in epilepsy patients, greater in idiopathic epilepsy, compared to control (54.3 ± 10.3; 39.4 ± 10 and 5.8 ± 1.3 CU, respectively, $\eth < 0.001$). The levels of AAB to MBP were high in the first group (14.9 ± 4.9 CU, $\eth < 0.001$), while in the second group were low (2.6 ± 4.3 CU), in comparison with control (8.0 ± 4.7 CU). The levels of AAB to GFAP were higher in symptomatic epilepsy (13.9 ± 7.9 CU, $\eth < 0.001$). Patients with idiopathic epilepsy had higher (22.0 ± 6.7 CU) levels of AAB to NF-200 vs. patients with symptomatic epilepsy (11.4 ± 6.4 CU) ($\eth < 0.001$).

Conclusions: Thus, all groups of epilepsy patients differed from control group by as individual levels, as degree of deviations of the studied immunological parameters. Early-initiated immunotherapy may improve seizure outcome in such patients.

Disclosure: Nothing to disclose.

PP2052
Effect of oxcarbazepine (Oxapine) on cognitive functions in epilepsy

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To study effect of oxcarbazepine on cognitive functions in adult patients with epilepsy.

Material: We studied 48 patients with partial seizures (mean age: 33.8 ± 15.3 y.o.) who had not previously treated with other AEDs. All patients received monotherapy with oxcarbazepine at doses of 300; 600 and 1,200 mg/day. Follow-up was for over 6 weeks. We conducted EEG, assessed cognitive functions by using MMSE scale, test to memorize five words, clock drawing test and test for speech activity. The effectiveness was measured by between-group comparison of patients.

Results: The results were statistically significant in favor of the oxcarbazepine 1,200 mg/day group (on 41.2 and 14.8 %) compared to the oxcarbazepine 300 and 600 mg/day group ($p < 0.0001$). The time to meeting one of the exit criteria was also statistically significant in favor of the oxcarbazepine 2,400 mg/day group ($p = 0.0001$), however, we observed CNS side effects in ≥5 % of patients treated with oxcarbazepine 2400 mg/day. The best results on cognitive functions were observed in the oxcarbazepine 1200 mg/day group. The worse

effect by influence as on seizures, as on cognitive functions was marked in the oxcarbazepine 300 mg/day group.

Conclusions: Treatment with oxcarbazepine should be initiated with a dose of 600 mg/day. If clinically indicated, the dose may be increased by 300 mg/day at approximately weekly intervals to 1,200 mg/day. Most patients were not able to tolerate the 2,400 mg/day dose, primarily because of CNS effects. Oxcarbazepine is effective at a dose of 600–1,200 mg/day and improves cognitive functions in most epilepsy patients.

Disclosure: Nothing to disclose.

PP2053

Epilepsy impairs long-term functional outcome after different stroke subtypes

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Objective: To determine the influence of post-stroke epilepsy on long-term functional outcome in stroke survivors.

Methods: This study is a prospective cohort study among 140 stroke survivors with a first-ever TIA, ischemic stroke, or intracerebral hemorrhagic (ICH) stroke, aged 18–90 years. After a mean follow-up of 10 years, we performed a follow-up assessment that included an evaluation for post-stroke epilepsy and functional outcome. Odds ratios for poor outcome on the modified Rankin Scale (mRS) (score > 2) and Instrumental Activities of Daily Living (IADL) (score < 8) were calculated using logistic regression analysis.

Results: One hundred twelve patients (80 %) with ischemic stroke, 4 patients (2.8 %) with TIA, and 28 patients (20 %) with ICH developed post-stroke epilepsy. Ischemic stroke patients with epilepsy more often had a poor functional outcome than those without, both on the mRS and IADL (mRS score > 2: 24.5 % vs. 9.2 %, $p = 0.001$; IADL < 8: 28.8 % vs. 14.6 %, $p = 0.02$). In this case, epilepsy occurred in 24.5 % of patients with cardioembolic stroke. Epilepsy was not related to functional outcome in patients with TIA and ICH. Multiple regression analysis revealed that epilepsy was an independent predictor of poor functional outcome after ischemic stroke assessed by mRS (mRS score > 2: odds ratio 4.02, 95 % confidence interval 1.33–8.60). In contrast, there was no such relation for IADL.

Conclusions: Epilepsy after stroke is a common problem that negatively affects functional outcome, even more than 10 years after ischemic stroke.

Disclosure: Nothing to disclose.

PP2054

Relatively benign course in the long term follow-up of two cases with epilepsy associated with NMDAR-antibody positivity

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Introduction: Autoimmune encephalitis associated with N-methy-D-aspartate receptor (NMDAR)-antibodies (Ab) usually presents with psychiatric disturbance, seizures, dyskinesias, impaired consciousness and autonomic dysfunction. The majority of the original cases were young women with ovarian teratoma. Although patients presenting with non-paraneoplastic or isolated syndromes have also been documented, their long-term outcomes are not well known.

Methods: The clinical, laboratory and long-term follow-up findings of two NMDAR-Ab positive male patients diagnosed with focal epilepsy of unknown cause were investigated retrospectively.

Results: A 43-year-old male admitted 20 years ago with seizures, subfebrile fever and amnesia. The CSF analyses were unremarkable and EEG showed diffuse slowing. He subsequently developed drug-resistant focal epilepsy and 10 years after these initial symptoms he presented with episodic postictal paranoid psychosis. In the last three years, the seizure frequency has markedly decreased and psychotic symptoms have been completely resolved. The 40-year-old second patient presented with convulsive seizures during sleep with left temporal spikes in the EEG and postictal tachycardia 5 years ago. His focal seizures with autonomic and cephalic aura were controlled with carbamazepine. He had only a depressive episode and cognitive assessment showed slight long term memory deficit with moderate attention disturbance. Both patients had nonspecific white matter lesions on MRI. None of them received immunotherapy due to relatively benign course in the long term follow-up.

Conclusions: Relatively benign long-term course of our patients suggests that NMDAR-Ab is associated with a larger clinical spectrum than previously believed and NMDAR-Ab encephalitis might present with mild and restricted clinical features.

Disclosure: Nothing to disclose.

PP2055

Structural covariance mapping delineates medial and medio-lateral temporal networks in déjà vu

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Déjà vu (DV) is an eerie phenomenon experienced frequently as an aura of temporal lobe epilepsy, and reported commonly by healthy individuals. Neuroscientific investigations are beginning to elucidate the underlying neurophysiological substrates, implicating medial and lateral temporal cortex in both pathological and non-pathological DV. This supports the notion of DV as a memory-based illusion, resulting from acute perturbation of memory-related brain systems. The mechanisms underlying such perturbation remain to be explored in non-pathological DV, however. To address this, the present study builds upon the finding that DV frequency in healthy individuals is related to structural alterations throughout the medial and lateral temporal cortex. Specifically, on the basis of evidence showing that covarying measures of grey matter between two brain regions indexes connectivity between them, we investigated the relationship between DV frequency and structural connectivity among brain structures implicated in non-pathological DV. Structural covariance mapping revealed two patterns of grey-matter covariance: Among the first, comprised primarily of limbic structures and the caudate, correlations in grey-matter volume became increasingly positive with higher DV frequency; the second encompassed medial and lateral temporal structures, among which higher DV frequency was associated with increasingly negative grey-matter correlations.

Comparing these structural findings with a measure of functional connectivity among the same set of brain regions implies that these two covariance patterns reflect two distinct networks. We suggest DV emerges as a result of altered patterns of neural activity within and between these two networks, leading to these distinct patterns of coordinated structural alterations.

Disclosure: Nothing to disclose.

PP2056

Hyperfamiliarity for faces: a rare syndrome

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Introduction: Kraepelin first described the illusion of familiarity in 1890. This disorder, called hyperfamiliarity for faces syndrome (HFFS) is modality-specific and stimulus-specific syndrome in which unfamiliar people or faces seem familiar. Occurs in the absence of psychiatric illness, emotional disorder or cognitive impairment.

Methods: Case report.

Results: A 57 years-old woman, with personal history of achondroplasia, hypertension and dyslipidemia was admitted at the emergency department (EM) with generalized tonic–clonic seizures (GTCS). Over the past 2 days she had been complaining of headaches and memory loss. At admission she was disoriented with an attention deficit and verbal memory impairment. Blood and CSF biochemistry as well as brain CT scan were unremarkable. Acid valproic was started without clinical evidence of seizures relapsing. Since her first day in ward she reported a continuous phenomenon of hyperfamiliarity for faces ("I know everyone"). She underwent brain MRI without change and the EEG showed left temporal paroxysmal activity. Work-up diagnosis of infectious and immune/paraneoplastic encephalitis was negative. The patient was empirically treated with acyclovir and metilprednisolone without benefit. Only after the introduction of levetiracetam she showed progressive remission of HFFS.

Conclusions: The diagnosis of HFFS is based on a selective false familiarity of multiple faces. Although of uncertain aetiology it was identified in patients with epilepsy or GTCS being considered by some authors a post-ictal phenomenon of left temporal lobe seizures. The rarity of HFFS is probably due to the under-recognition of this paramnesia.

Disclosure: Nothing to disclose.

PP2057

Long-term efficacy and tolerability of zonisamide as monotherapy or adjunctive treatment in epilepsy patients: an observational study

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Introduction: Zonisamide (ZNS) is an antiepileptic drug with a broad spectrum of action mechanisms. While ZNS is usually indicated for the adjunctive treatment of partial seizures in Western countries, it is licensed for partial and generalized seizures as monotherapy or adjunctive treatment in South Korea. We performed the present study to evaluate the long-term efficacy and tolerability of zonisamide in clinical practice.

Methods: This is a retrospective, single-center, long-term observational study. A total of 148 patients (82 men, 66 women, aged 14–85 years) who were initiated with ZNS as monotherapy or adjunctive treatment were included. The usual starting dosage of zonisamide was 100 mg/day and optimal-dose adjustments were made according to individual clinical responses. Efficacy and tolerability were analyzed every year during 5-year follow-up.

Results: The overall retention rate was 66.1 % at 1 year and 55.1 % at 5 years follow-up. Patients with monotherapy (70.8 % versus 44.1 %) and generalized seizures (71.6 % versus 48.2 %) were more likely to continue ZNS compared with those with adjunctive therapy and partial seizures. The most common cause of discontinuation was adverse events such as somnolence, skin rash, and gastrointestinal problems.

Conclusions: Our study shows the tolerability and efficacy of ZNS in the treatment of patients with partial and generalized seizures as in monotherapy and adjunctive therapy. The retention rate of ZNS was comparable to those of other antiepileptic drugs including lamotrigine, topiramate, and levetiracetam. Further studies would be necessary to confirm the effect of ZNS in generalized seizure and as monotherapy.

Disclosure: Nothing to disclose.

PP2058

Efficacy and safety of zonisamide in treatment of partial, generalized or combined seizures in adults with epilepsy: a pooled data analysis

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Introduction: The purpose of the study was to evaluate safety and efficacy of Zonisamide in the treatment of partial, generalized or combined seizures in Indian adults.

Methods: This prospective, non-comparative, open-label observational study enrolled 655 patients from 30 centres throughout India. Adult patients with partial, generalized/combined seizures received 100 mg Zonisamide OD as monotherapy/adjunctive therapy for 24 weeks, with 2 weekly dose titration as required. Evaluation was done at 4, 8, 12, 16, 20 and 24 weeks to evaluate safety (adverse events) and efficacy (seizure freedom and responder rate). Efficacy and safety were also assessed using Clinicians Global Assessment of Response to Therapy (CGART) and Patients Global Assessment of Tolerability to Therapy (PGATT), respectively.

Results: Out of 655 patients enrolled, 563 completed the study. Zonisamide was used as first line therapy and first add-on in 20.92 and 59.85 % patients, respectively. A significant decrease in seizure frequency was seen at every follow up visit as compared to baseline ($p < 0.0001$) with maximum change seen at week 24 (mean change from baseline $= -3.98$, 95 % CI -3.39 to -4.57). 24 week seizure freedom and responder rate was seen in 41.22 and 91.15 % patients, respectively. Discontinuation due to adverse effects of drug was seen in only 0.92 % patients. 55.61 % patients showed good response (CGART) and 57.32 % showed good tolerability (PGATT) to Zonisamide therapy at week 24.

Conclusions: Zonisamide is an effective treatment in partial, generalized as well as combined seizures in adults with a good tolerability profile. No new safety signals were observed.

Disclosure: The presenting Author is an employee of Eisai Pharmaceuticals India Private Limited.

PP2059

Bone mineral density in epileptic adolescents treated with antiepileptic monotherapy

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Introduction: Antiepileptic drugs can produce negative influence on bone mineral density in adolescents with epilepsy.

Methods: We evaluated influence of lamotrigin (LTG) and valproate (VPA) on lumbar bone mineral density (BMD L_1–L_4) in adolescents with epilepsy. Lumbar bone mineral density *Z*-score (BMD L_1–L_4 *Z*-score) was measured in 31 adolescents with epilepsy

aged 13-18 years, both genders treated with lamotrigin (n = 15) or valproate (n = 16) monotherapy longer than 1 year. Patient lumbar spine BMD Z-scores values were compared with matched control group values (32 healthy adolescents, both genders). All patients were ambulatory and had similar physical activity and calcium intake. Patients and control group are gender, weight and height matched. For statistical analysis we used software SPSS version 15 (Mann–Whitney *U*-test and Pearson's correlation). Statistical significance was $p < 0.05$.

Results: The lumbar spine BMD Z-score values in epileptic patients treated with lamotrigin were not significantly lower compared with control group values (0.69 ± 0.93 vs. 0.96 ± 0.86; $p = 0.37$; n.s.), as well as in epileptic patients treated with valproate (0.75 ± 0.87 vs. 0.96 ± 0.86; $p = 0.56$; n.s.) Therapy duration had not negative influence on lumbar BMD in both patient groups ($r_{xy} = 0.10$; $p > 0.05$).

Conclusions: Lumbar BMD *Z*-scores were lower in patient group treated with lamotrigin or valproate compared with control, but not significantly, and there were not dependent on therapy duration.

Keywords: Epilepsy, valproate, lamotrigin, adolescents, bone mineral density, Z-score.

Disclosure: Nothing to disclose.

PP2060

No need to record habitual seizures in temporal lobe epilepsy patients with congruent non-invasive interictal EEG and MRI results

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Introduction: To evaluate the need of ictal EEG in epilepsy surgery candidates with unitemporal interictal epileptiform discharges (IED) and MRI detected ipstemporal pathology.

Methods: In the database of our epilepsy monitoring unit 304 patients with temporal lobe epilepsy (TLE) were identified. Based on expert opinion 275 unilateral, 19 bilateral and 10 non-lateralized TLE were defined. Patients with unilateral TLE missing ictal EEG (n = 1) or MRI (n = 3) were excluded. Stochastic calculations were based on 1967 ESP of 275 TLE patients having at least two lateralized ESP.

Results: IED were recorded in 98 % of the unilateral TLE patients. Purely unitemporal IED, consistent with side of TLE in all cases, were present in 61 % of these patients. Ipsitemporal MRI pathology was found in 83 % of these patients. Ictal EEG was consistent with side of TLE in 99 % of these patients. Calculations using mainly binomial distribution and Bayes' Theorem revealed, that in EVM six seizures were needed to receive a concordance greater than 0.9 with a probability greater than 95 %.

Conclusion: Despite of excellent lateralization value (Chi Square, $p < 0.001$) of purely unitemporal IED with ipsitemporal MRI pathology, rare patients (1 %) showed discordant ESP. However, both patients were seizure free after lesion resection. Our data support the view that is not mandatory to record seizures in TLE patients with congruent interictal EEG and MRI. Following stochastic analysis at least six ipsilateral ESP are recommended in case of incongruent data.

Disclosure: Nothing to disclose.

PP2061

Treatment of resistant epilepsy with pyridoxine in an adult patient with spastic tetraparesis and severe learning disability: a case report led discussion of the literature

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Introduction: Pyridoxine-responsive epilepsy is well known in children, here we report that a 29-year-old patient with neonatal onset intractable epilepsy showed a significant clinical improvement with addition of pyridoxine.

Case: She is chairbound due to a spastic quadriparesis, learning disabled and tube fed. She had been treated with numerous antiepileptic drugs from her first few days of life without ever fully controlling seizures, leading to the frequent administration of rectal diazepam and subsequently buccal midazolam in her 20s for frequent clusters and status. A significant reduction in seizure frequency and severity of was obtained after adding pyridoxine to her treatment, subsequent dose reduction caused a re-emergence of seizures severe enough to require midazolam. The use of midazolam fell from "more days than not" to less than monthly.

Discussion: Three main conditions have emerged in the years since pyridoxine dependency was described—the original condition, pyridoxine responsive epilepsy and recent studies suggest vitamin B6 reduction may be linked with long term anti-epileptic treatment but its contribution to chronic AED-resistant epilepsy remains obscure.

Conclusion: Our patient highlights the importance of considering pyridoxine as an adjunctive therapy in chronic AED-resistant epilepsy of adults dating from childhood and the improvement in quality of life for her family and herself due to this intervention. The different entities involving pyridoxine in epilepsy will be discussed in depth.

Disclosure: Nothing to disclose.

PP2062

Epileptic seizures and epilepsy in patients with stroke: a five years study including stroke patients in Kosovo

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Introduction: Some patients after ischemic stoke and hemorrhagic stroke develop a seizure, and a small number go on to develop secondary epilepsy.

The aim of this study was to analyse in detailed storke patients that develope epilepsy and to determine the most affected age group, most affected sex and most affectet patients according to their living place. In addition, we have analyzed distribution between two types of strokes: haemorrhagic and ischaemic.

Methods: This is a retrospective cros sectional study seted in the Neurology Clinic in Kosovo. We have retrospectively included

patients that have been hospitalized in our clinic in a 5 years period, suffering an ischaemic or haemorrhagic stroke.

Results: Out of 3,700 stroke patients (mean age 69.3 ± 6.8 years old, 68.1 % males) included in this study 185 (mean age 67.1 years old) have developed epilepsy. Majority of patients (80.54 %) have sufered an ischaemic stroke, whereas 19.46 % of patients sufered as haemorrhagic stroke. According do geogrophical areas most of the that developed epilepsy lived in rural countries (62.4 %). Furthermore, males were more frequently affected compared to females with 57.1 %.

Conclusions: Only 5 % of patients with haemorrhagic and ischaemic stoke developed epilepsy. Most of the patients affescted were males. In addition, most of them lived in rural rather than in cities. According to etiology, most of the stroke patients associated with epilipsy were ischaemic.

Disclosure: Nothing to disclose.

PP2063

Sexual dysfunction in young men suffering from idiopathic epilepsy

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Introduction: Epilepsy is an important problem of Neurology. Prognosis of epilepsy has been improved during last years: in significant number of patients it became possible to achieve seizure control by taking antiepileptic drugs. It has been noted that antiepileptic drugs can lead to sexual dysfunction, however this problem was not studied in Ukraine yet.

Methods: 124 men with idiopathic epilepsy aged 18-35 years were examined. All patients were on monotherapy: 32 patients took valproates, 31 levetiracetam, 31 topiramate, 30 lamotrigin. The Male Sexual Quotient exam (MSQE) was used for sexual function assessment.

Results: Sexual dysfunction in patients taking valproate was observed in 68.8 %, levetiratsam group: 16.1 %, topiromate group: 35.8 %, lamotrigine group: 36.7 %. The main cause of sexual dysfunction in all groups was reduced or absent libido (90 %, $p = 0.012$). In the group of patients taking valproate erectile dysfunction cases were recorded (53.1 %, $p = 0.015$).

Conclusions: The impact of antiepileptic therapy on sexual function young men should be considered when choosing treatment. Preference should be given to new generation drugs.

Disclosure: Nothing to disclose.

PP2064

Post-stroke epilepsy

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Introduction: Cerebrovascular lesions are the leading cause of epilepsy in the elderly and occurrence of post-stroke epilepsy in different studies ranges between (4.4–42.8 %).

Methods: Examined group consisted of 30 patients (17 male and 13 female) with post-stroke epilepsy; control group consisted of the same number of patients without seizures two years after stroke. Localization of stroke was verified by computed-tomography, and the verification of seizure type was based on self and/or family history. For statistical analysis it was used x^2 test, $p < 0.05$ was considered as significant.

Results: Stroke in right cerebral hemisphere was verified in 73.4 % patients examined, and in 43.4 % of control group ($p < 0.05$). Recurrent stroke was present in 26.6 % (control group 6.6 %). Stroke in frontal lobe was registered in 40 % (control group 13.3 %; $p < 0.05$); temporal lobe in 20 % (control group 16.6 %); parietal lobe in 16.6 % (control group 30 %); without stroke in occipital lobe (control group10 %). Multiple lacunars lesions were found in 23.3 % (control group 30 %). In total sample ($N = 60$) were found significantly more represented at females ($p < 0.05$). Generalized tonic–clonic seizures were represented in 30 % of patients; simple focal in 13.30 %; focal with generalization in 33.33 %; complex focal in 10 %; Jackson (motor) in 13.30 % patients.

Conclusions: Post-stroke epilepsy is more common in patients with stroke localized mostly in right hemisphere in frontal lobe. Epileptic seizures are predominantly focal type, with and without generalization.

Disclosure: Nothing to disclose.

Multiple sclerosis and related disorders 2

PP2065

Abstract withdrawn

PP2066

Comparison of 2005 and 2010 Macdonald MRI criteria for diagnosis of MS: a retrospective study in London

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Objective: Multiple sclerosis (MS) can be difficult to diagnose clinically, however MRI imaging can provide evidence that can support a clinical diagnosis. The Macdonald criteria has been developed to make the diagnosis of MS more uniform and reliable, especially in the context of MRI. It was developed in 2001 and has been revised in 2005 and 2010.The aim of this study was to compare the diagnostic validity of the 2005 and 2010 criteria.

Method: We collected initial MRI images for 38 patients from the MS clinic at the Royal London hospital from 2006 to 2011 who presented with symptoms suggestive of demyelination. Their images were reviewed in terms of dissemination in space (DIS), dissemination in time (DIT) and both DIS and DIT using the 2010 and 2005 Macdonald criteria.

Results: From this study, both criteria showed 100 % specificity in the diagnosis of MS and 100 % positive predictive value. Both showed similar sensitivity 0.53 and 0.66 and negative predictive value of 0.33 and 0.2 in 2005 and 2010 criteria, respectively.

Conclusion: Although this study has a limited number of patients, it did show similarities in both criteria in terms of diagnostic value. However, in the real life clinical setting, the 2010 criteria has advantages over the 2005 criteria in that MRIs do not need to be delayed to be valid for use in diagnostic interpretation-often in the acute setting patients are scanned within a few days and therefore the 2010 criteria allows MRI diagnosis without re-scanning later.

Disclosure: Nothing to disclose.

PP2067

Brain distribution of MS565, an imaging analogue of siponimod (BAF312), in non-human primates

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Introduction: Siponimod (BAF312) is a selective sphingosine 1-phosphate ($S1P_{1,5}$) receptor modulator currently in Phase 3 development for secondary progressive multiple sclerosis. Experimental studies in rats showed that siponimod penetrates into the CNS (4–8 h post-administration) and may result in direct beneficial effects. We investigated the brain distribution and kinetics of siponimod by using an iodine-labeled analogue with similar rat pharmacokinetic properties, [^{123}I]MS565, and single photon emission computed tomography (SPECT) in non-human primates (NHP).

Methods: [^{123}I]MS565 (radioactive half-life of 13.2-h) was administered to 2 adult male rhesus NHPs *(Macaca mulatta)*, as single intravenous bolus. SPECT studies were performed using a MollyQ camera (Neurophysics Inc., Shirley, MA, USA). Brain penetration was assessed by serial dynamic scanning over a 2-day period. The scans were reconstructed and analyzed using PMOD 3.405 software. Standardized uptake values (SUV) were calculated by normalizing for injected activity and body weight. Subsequently, images were co-registered to an MRI template for volumes of interest extraction, time-activity curves generation and brain penetration estimation. Blood samples were taken to determine the radiometabolite concentration in plasma.

Results: [^{123}I]MS565 penetrated NHP brain with highest concentration of 0.008–0.014 %ID/mL at around 24-h post-injection. Peak SUV values were around 0.6–0.8 during day 2 imaging session. Radiotracer metabolism in plasma was slow and at 24-h post-injection $\sim$70 % of parent compound was still present in plasma.

Conclusions: [^{123}I]MS565 is a promising SPECT imaging agent to investigate the potential CNS distribution of siponimod. Whole-body imaging is ongoing to obtain radiation absorbed dose estimates for [^{123}I]MS565.

Disclosure: The study was supported by Novartis Pharma AG. Adriana Tavares, Olivier Barret, David Alagille, Thomas Morley, Caroline Papin, and Gilles Tamagnan received support from Novartis as employees of Molecular Neuroimaging Inc. Ralph P. Maguire, Emmanuelle Briard, and Yves P Auberson are employees of Novartis.

PP2068

Cerebrospinal fluid inflammatory markers in patients with multiple sclerosis

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Introduction: Multiple sclerosis (MS) is an inflammatory-demyelinating disease of the central nervous system (CNS). Autoimmune inflammation is common in the early stages of MS. This stage is followed by the neurodegenerative process. There are an increasing number of studies dealing with biomarkers in CSF and their role in the diagnosis and treatment of MS. We hypothesized that the levels of some markers could be changed in MS in comparison with controls. We studied five inflammatory markers (interleukin-6 (IL-6), interleukin-8 (IL-8), interleukin-10 (IL-10), beta-2-microglobulin, orosomucoid).

Methods: CSF and serum levels of inflammatory markers were assessed in 38 patients with newly diagnosed MS meeting McDonald's revised diagnostic criteria and in 28 subjects as a control group (CG). In the control group were patients with non-inflammatory disease of CNS. The lumbar puncture was indicated from differential diagnostic reasons. In the MS patients, the lumbar puncture was performed at the time of the first clinical symptoms compatible with MS.None of our patients had been treated by corticosteroids before the lumbar puncture.

Results: Levels of beta-2-microglobulin and interleukin-8 in CSF were found to be significantly higher in MS patients in comparison to CG ($p < 0.001$ resp. $p = 0.007$). No differences in other CSF markers (IL-6, IL-10 and orosomucoid) and serum levels of all markers between both groups were found.

Conclusions: The levels of two studied inflammatory markers were found to be increased at the time of first clinical symptoms of MS. Research on the role of inflammatory and neurodegenerative markers in MS should continue.

Disclosure: Nothing to disclose.

PP2069

Previous treatments influence disease activity during fingolimod therapy in multiple sclerosis patients

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Introduction: Fingolimod (FTY) is the first oral drug approved for Relapsing Remitting Multiple Sclerosis (RRMS) patients. In the absence of robust trials, the FTY long-term efficacy and safety profile is still to be determined. The aim of our study is to evaluate clinical and MRI outcomes of MS patients during FTY treatment.

Methods: One hundred and 26 patients treated with FTY for at least 6 months at San Raffaele Hospital MS Centre underwent clinical evaluation and brain MRI at baseline and after 3, 6, 12, 18 months. Sixty-seven patients had been previously treated with immunomodulants (IM), 59 patients with Natalizumab alone or in temporal combination with other treatments (NZ). Baseline group comparisons were performed using Mann–Whitney *U*-test.

Results: Compared to NZ patients, we observed in IM patients a significant greater reduction of the Annualized Relapse Rate (ARR) after 3 ($p = 0.046$), 6 ($p = 0.006$), 12 ($p = 0.001$) and 18 months ($p = 0.0002$) and a significant lower number of Gadolinium enhancing lesions (Gdls) after 3 ($p = 0.0003$), 6 ($p = 0.003$), 12 ($p = 0.002$) and 18 months ($p < .0001$). The ARR and Gdls decreased during the whole follow up in both IM and NZ groups, although NZ patients were significantly more active. Anyway, after only 6 months of FTY treatment, MS activity in NZ patients was also significantly reduced. No EDSS progression was observed in both groups.

Conclusions: FTY was able to control disease activity after both DMT and Natalizumab therapy, although without a complete suppression of MS activity after Natalizumab discontinuation, partly due to the known disease reactivation.

Disclosure: Messina MJ has not disclosures. Rodegher M has not disclosures. Rocca M has received speaker honoraria from Biogen Idec and Symposia International Foundation. Filippi M has received compensation for consulting and/or speaking from Bayer, Biogen Idec, Merck Serono, and Teva. Romeo M has not disclosures. Maida S has not disclosures. Copetti M has not disclosures. Martinelli V has received speaker honoraria or funding for travel expenses from Biogen-Dompé SG, Merck Serono, Bayer Schering Pharma, Novartis, Teva Pharmaceutical Industries and Sanofi-Aventis. Comi G has received compensation for consulting services and/or speaking activities from Novartis, Teva Pharmaceutical Ind., Sanofi, Genzyme, Merck Serono, Biogen Bayer, Actelion and Serono Symposia International Foundation.

PP2070

A demyelinating disorder charachterized by repeated episodes of optic neuritis and brainstem dysfuntions in a girl with anti-MOG positivity

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Introduction: B cells and antibodies are important in Central nervous system diseases (CNS) and antibodies against *Myelin* Oligodendrocyte Glycoprotein (MOG) could be relevant especially in pediatric cases.

Method: case report.

Results: A 16-year-old girl complained a brainstem dysfunction in August and in December 2010. Both times a brain MRI showed T2 hyperintense lesions in brainstem, along the third ventricle, right insula and left thalamus. Oligoclonal bands were absent. Anti-aquaporin antibodies were negative. Both times clinical and radiological abnormalietis disappeared after intravenous steroids. Moreover in October 2010, April and October 2011 she had three episodes of optic neuritis (ON) and every time she recovered with steroids. A diagnosis of multiple sclerosis was made and she started glatiramer acetate in November 2011. She did well till September 2013 when she had a left ON with recovery. In November 2013 she presented another episode of severe brainstem dysfunction. A MRI showed a new T2 lesion involving mainly the right cerebral peduncle, hypothalamic region, and thalamus. Anti-MOG *antibodies were found.* High dose steroid had no benefits. She was then treated with both intravenous cyclophosphamide (3,700 mg) and rituximab (2,200 mg). The following brain MRIs showed a progressive reduction of lesions and she recovered.

Conclusions: In the spectrum of demyelinating disorders we can speculate that there are disease in which anti-MOG could be pathogenetic. Therefore they could be a biomarker to tailor therapy choosing drugs targeting B-cells.

Disclosure: Nothing to disclose.

PP2071

CSF-KFLC in comparison to OCB and Q-IgG

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Introduction: Immunoglobulin G (IgG) oligoclonal bands (OCB) are the most widely used CSF test to support the diagnosis of multiple sclerosis (MS). However, determination of OCB using isoelectric focusing (IEF) on gels followed by immunoblotting is non-quantitative and demands methodological expertise. The disadvantage of the quantitative IgG-index is its low sensitivity. Several studies indicated that elevated kappa free light chains (KFLC) in the CSF might offer a quantitative tool to indicate intrathecal IgG synthesis by achieving a higher sensitivity than IgG-index. We aimed to compare KFLC levels to OCB patterns and IgG-index.

Methods: 331-paired CSF and serum sample were analysed, including 23 MS samples. KFLC and IgG were measured using an automated nephelometer and OCB were detected by isoelectric focusing (IEF) on gels followed by immunoblotting. OCB were classified in five patterns according to Andersson et al.1994.

Results: Q KFLC was significantly elevated in cases with OCB type 2 and 3, that are indicative for intrathecal IgG synthesis, as compared with type 1 ($p < 0.0001$). 91 % of patients with MS showed elevated Q KFLC, 87 % showed positive OCBs and 87 % showed elevated IgG-index.

Conclusion: Our data support the relevance of KFLC as a rapid and quantitative tool to detect intrathecal IgG response and thereby overcoming disadvantages of OCB and IgG-index.

Disclosure: Nothing to disclose.

PP2072

Gray matter involvement in patients with multiple sclerosis; clinical, DTI magnetic resonance imaging, OCT findings

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PP2073:

EEG changes in Dalfampyridine treatment

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PP2074

Effectiveness of magnetic fields in fatigue in multiple sclerosis patients

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PP2075

A prospective study of urinary complications in multiple sclerosis; a multidisciplinary approach, urodynamic findings and treatment options

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PP2076

Two-year interim analysis of quality of life in patients with relapsing-remitting multiple sclerosis (RRMS) treated with delayed-release dimethyl fumarate in the ENDORSE study

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PP2077

Delayed-release dimethyl fumarate and disability assessed by the multiple sclerosis functional composite (MSFC) in relapsing-remitting multiple sclerosis (RRMS) patients participating in the DEFINE study

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PP2078

Teriflunomide in routine clinical practice: design of the TACO study

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PP2079

Abstract withdrawn

PP2080

Abstract withdrawn

PP2081

Abstract withdrawn

PP2082

Efficacy of delayed-release dimethyl fumarate in european patients with relapsing-remitting multiple sclerosis (RRMS): integrated analysis of the phase 3 DEFINE and CONFIRM studies

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PP2083

Effect of delayed-release dimethyl fumarate on health-related quality of life (HRQoL) in relapsing-remitting multiple sclerosis (RRMS) patients with and without measured disease activity

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PP2084

Treatment with interferon beta-1b although persistent aminotransferases elevation

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PP2085

Optimization of multiple sclerosis therapy via high-dose, high-frequency administration of subcutaneous interferon beta-1a: the OPTION study

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PP2086

Abstract withdrawn

PP2087

Impairment of cognitive functions in patients with clinically isolated syndrome: a pilot study

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PP2088

Homocysteine level in experimental model of multiple sclerosis

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PP2089

Abstract withdrawn

PP2090

Treatment of a severe ADEM patient with immunoadsorption

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PP2091

A case of multiple sclerosis presenting as eight and half syndrome

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PP2092

Indicators of the immunological status after high-dosage immunoablative therapy with autologous stem cell transplantation in multiple sclerosis

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PP2093

The prediction of interferon's flu-like syndrome in therapy of multiple sclerosis

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PP2094

Interleukins and the psycho-emotional sphere in patients with multiple sclerosis

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PP2095

Extracranial–intracranial venous structures in patients with relapsing-remitting multiple sclerosis, Doppler sonography, cranial MR venography and selective venography with the evaluation and comparison with healthy controllers

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PP2096

Subjective reports of fatigue and depression in relation to objective measures of motor performance and cognitive functioning in relapsing-remitting multiple sclerosis

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PP2097

Tremor in multiple sclerosis (MS): different patterns of long latency reflexes suggest different underlying pathophysiological mechanisms

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PP2098

Neurofibromatosis type 1 associated to multiple sclerosis

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PP2099

Clinical efficacy sulbutiamine for treatment of fatigue in patients with multiple sclerosis

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PP2100

A composite of real-world practical measures of early disease activity can predict long-term disease outcome in CHAMPIONS

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PP2101
United States multiple sclerosis patients' preferences for injectable treatments

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PP2102
German multiple sclerosis patients' preferences for injectable treatments

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PP2103
Gastrointestinal symptoms in patients with multiple sclerosis

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PP2104
Markers of demyelination in patients with multiple sclerosis and thyroid autoimmune reactivity

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PP2105
Diagnostic value of NMO/AQP4 antibody in assessing idiopathic inflammatory demyelinating CNS diseases (IIDCDs) in Egyptian patients

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PP2106
Female MS patients knowledge of multiple sclerosis and pregnancy relation

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PP2107
Retinal nerve fiber layer thickness and disability in multiple sclerosis patients

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PP2108
Rebound of multiple sclerosis activity after fingolimod therapy discontinuation

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PP2109
Concentration of 25(OH)D3 and calcium and phosphorus metabolism in patients suffering from relapsing-remitting multiple sclerosis

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PP2110
Clinical efficacy of delayed-release dimethyl fumarate in minority patients with relapsing-remitting multiple sclerosis (RRMS): an integrated analysis of the phase 3 DEFINE and CONFIRM studies

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PP2111
Seasonal activity of multiple sclerosis based on magnetic resonance Imaging parameters in Georgia

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PP2112
Limited heart rate effects following siponimod re-initiation after variable periods of drug discontinuation

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PP2113
Interim results of the Swiss post marketing surveillance monitoring quality of life and treatment satisfaction in patients with relapsing-remitting multiple sclerosis (SWISSASCENT)

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PP2114

The importance of nitric oxide and arginase in the pathogenesis of acute neuroinflammation: are those contra players with the same direction?

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PP2115

Exercise-based patient education in people with multiple sclerosis

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PP2116

Paroxysmal dystonia as a manifestation of multiple sclerosis

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PP2117

Indolent progressive multifocal leukoencephalopathy (PML) after natalizumab in relapsing remitting multiple sclerosis (RRMS)

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PP2118

Abstract withdrawn

PP2119

Multiple sclerosis and motherhood choice: an observational study of the Portuguese women

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PP2120

Objective measurement of fatigue in patients with multiple sclerosis—norm values and predictors

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PP2121

Abstract withdrawn

PP2122

Abstract withdrawn

PP2123

Lymphocytopenia after fingolimod therapy confronted with escalated administration against therapy interruption

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PP2124

Sleep disturbances related to multiple sclerosis

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PP2125

Injection-site reactions of serum-free subcutaneous interferon beta-1a in patients with relapsing multiple sclerosis: 2-year interim analysis of a prospective observational study in Spain

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PP2126
Validity and reliability of the Turkish version of the monitoring my multiple sclerosis scale

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PP2127
Health-related quality of life in EU patients with relapsing-remitting multiple sclerosis (RRMS) treated with delayed-release dimethyl fumarate: integrated analysis of DEFINE and CONFIRM

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Thyroid disease in patients with multiple sclerosis during interferon-beta therapy

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PP2130
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PP2135
Large tumor like demyelinating lesions in the brain

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PP2138

microRNAs play a critical role in regulation of an autoimmune demyelination

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PP2139

Comparative analysis of the quality of life in patients with multiple sclerosis of different age groups

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PP2140

Cognitive impairment and glucose cerebral metabolism in relapsing-remitting and progressive multiple sclerosis patients

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PP2141

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The comparison of vitamin D3 levels in spring and autumn in patients suffering from multiple sclerosis

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The impact of interferon beta treatment upon pregnancy in patients suffering from multiple sclerosis

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PP2144

Adhesion molecules and matrix metalloproteinase-9 in patients with multiple sclerosis

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PP2145

Evaluation of sensory and pain perception and mechanisms of central modulation of pain perception in patients with multiple sclerosis

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PP2146

Neuromyelitis optica spectrum disorder (NMOSD) with systemic lupus erythematosus (SLE) in a 47 year-old Filipino: a case report

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PP2147

Effects of 4-aminopyridine on depression in multiple sclerosis patients

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PP2148

Anxiety correlates with fatigue in multiple sclerosis patients

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PP2149

A patient with combined central and peripheral demyelination

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PP2150

Effects of glatiramer acetate on cortical functions and fatigue in multiple sclerosis: a morpho-functional MRI study

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PP2151

Effect of natalizumab on clinical/radiological disease activity and quality of life in a prospective Belgian cohort of relapsing-remitting multiple sclerosis patients

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PP2152
Comorbidity of multiple sclerosis and psoriasis

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PP2153
Thrombotic microangiopathy (TMA) caused by IFN-beta treatment in multiple sclerosis (MS) patient: a case report

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PP2154
Severe rebound of multiple sclerosis activity to the spinal cord after Fingolimod withdrawal

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PP2155
Delayed-release dimethyl fumarate and health-related quality of life in relapsing-remitting MS patients stratified by baseline demographic and disease characteristics: integrated analysis of DEFINE and CONFIRM

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PP2156
Epidemiology of multiple sclerosis in Tuzla-Canton, Bosnia and Herzegovina

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PP2157
Assessment of COgnitioN, FatIgue, Depression, anxiety, AdherENCE in relapsing-remitting multiple sclerosis patients receiving subcutaneous interferon beta-1a: CONFIDENCE study design

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PP2158
Clinical management of patients with relapsing–remitting multiple sclerosis transitioning from natalizumab to dimethyl fumarate

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PP2159
Markers of neurodegeneration in different stages of MS

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PP2160
Multiple sclerosis and panuveitis: a rare association

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PP2161
A case confusing multiple sclerosis and central nervous system graft-versus-host-disease

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PP2162
Demyelination diagnosed during tumor necrosis factor antagonists therapy: coincidence or not?

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PP2163
Effect of bismuth subsalicylate (Pepto-Bismol®) on gastrointestinal tolerability in healthy volunteers receiving oral delayed-release dimethyl fumarate: a randomized, multicenter, double-blind, placebo-controlled, phase 1 study (PREVENT)

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PP2164

Gastrointestinal tolerability of delayed-release dimethyl fumarate in a multicenter, open-label study of patients with relapsing forms of multiple sclerosis (MANAGE)

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Muscle and neuromuscular junction diseases

PP2165

Sustained remission in a case of musk (+) myasthenia gravis treated with IV rituximab as primary therapy

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Introduction: Muscle specific tyrosine kinase (MuSK) antibody positive myasthenia gravis accounts for 50–70 % of seronegative cases. MuSK (+) patients are predominantly women with early, prominent bulbar and respiratory symptoms and poor response to standard therapies. Several reports suggest a role for rituximab, an anti-CD20 monoclonal antibody, in patients who fail conventional immunotherapies. We report our experience with rituximab as first line therapy for a MuSK(+) MG patient.

Methods: The patient is a 29-year-old woman who developed symptoms of bulbar weakness and respiratory insufficiency at age 22. She required recurrent intensive care unit admissions over the next 10 months due to type 2 respiratory failure that resulted in tracheostomy placement. She had minimal limb weakness and remained undiagnosed for the subsequent 4 years. She underwent re-evaluation at age 26.

Results: The clinical examination revealed bilateral ptosis, facial weakness, tongue weakness and atrophy. A tracheostomy was in place and mild proximal weakness in the upper and lower extremities. The repetitive nerve stimulation revealed a 27 % decrement at 3 Hz. EMG and NCS were normal. The acetylcholine receptor antibodies and anti-striated muscle antibodies were negative. Anti-MUSK antibodies were elevated. The patient was treated with intravenous rituximab 375 mg/m^2 weekly for 4 weeks. The patient clinically improved. The tracheostomy was discontinued. She remains asymptomatic off all medications for over 3 years.

Conclusions: Intravenous rituximab may induce sustained remission in MuSK(+) myasthenia gravis even after a single course and may be considered for primary therapy. Ideally a randomized controlled study would interrogate this hypothesis.

Disclosure: Nothing to disclose.

PP2166

Clinical and genetic features of the patients with MNGIE: cohort at the department of neurology, Istanbul Faculty of Medicine

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Introduction: Mitochondrial neurogastrointestinal encephalopathy (MNGIE) is a rare genetic disorder which is characterized by gastrointestinal symptoms, cachexia, ptosis, ophthalmoparesis, neuropathy and leukoencephalopathy. Mutation in the thymidine phosphorylase encoding *TYMP* gene, leads to dysfunction of the catalytic activity of the enzyme causing systemic accumulation of its substrates, that causes mitochondrial DNA instability and dysfunction in oxidative phosphorylation chain. In recent years treatment options urges early diagnosis of this disorder. Here, we present the genetic and clinical features of seven Turkish patients, diagnosed as MNGIE in our clinic.

Methods: Clinical and laboratory findings of seven Turkish patients from four unrelated families diagnosed with MNGIE at the Department of Neurology, Istanbul Faculty of Medicine between 2009 and 2013 were retrospectively evaluated.

Results: Six patients were male, only one patient was female. Mean age of onset was 16.2 $\pm$ 8.35 years. Intra- and inter-familial variability in the age of onset and rate of disease progression were striking. Nausea and vomiting were the most common presenting symptoms which were usually followed by bilateral ptosis and ophthalmoparesis within 2 years. Ptosis was absent in one patient with rapid progression, whereas all other characteristic symptoms were evident. All patients had gastrointestinal symptoms, cachexia, neuropathy and distal muscle weakness. Three patients died due to disease related causes during the follow up. Notably, we described four novel mutations in the TYMP in our patients.

Conclusions: Our data indicates the marked intra- and inter-familiar phenotypic variability in MNGIE as previously described and four novel pathological mutations in TYMP.

Disclosure: Nothing to disclose.

PP2167

Angiogenic factors dynamics during skeletal muscle regeneration

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Introduction: The establishment of a well-organized, stable vasculature is a key process during skeletal muscle regeneration, and a key goal in regenerative medicine. These processes are orchestrated by a large panel of systemic and local signals. However, detailed mechanisms are still unclear.

Methods: Multiplex assay was used to measure level progression of an array of pro-angiogenic growth factors and cytokines during muscle regeneration in animal models. Crush injuries were performed with a forceps on the left gastrocnemius muscle. Muscle and blood samples were collected at specific time-points. Selected factors were further detected in situ, by immunolabelling. The contralateral muscle was used as control.

Results: Significant local and systemic levels were detected for pro-angiogenic, inflammatory cytokines from 24 h up to 2 weeks post-injury. Likewise, the local levels of notorious angiogenic factors like vascular endothelial growth factors A and C and hepatocyte growth factor increased in the 2nd/3rd week post-injury, but were accompanied by high systemic levels compared to fibroblast growth factor 2. Surprisingly, we detected significant tissue levels, peaking at the end of the 1st week post-injury, for a set of angiogenic factors—

amphiregulin, betacellulin, endoglin, follistatin and PLGF-2—that were never taken into account and tested in such an experimental system. The distribution of the interstitial cells involved in their synthesis during muscle regeneration was pointed out by immunofluorescence.

Conclusions: Identification of new angiogenic factors secreted locally during normal regeneration opens a promising perspective for improving skeletal muscle healing after injury or muscle diseases.

Disclosure: Nothing to disclose.

PP2168

Myopathy with muscle hypertrophy as a rare presenting feature of primary amyloidosis

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In systemic amyloidosis, the major sites of clinically important amyloid deposition are in the kidneys, heart, and liver. We report a rare case of primary amyloidosis associated with plasma cell dyscrasia initially presenting with musculoskeletal manifestations.

65-year-old woman was admitted with a 6-month history of difficulties in walking, progressive muscle weakness, stiffness, myalgia and spontaneous muscle overgrowth. Examination revealed visible increase in muscle bulk in the pelvic girdle muscle group and also marked macroglossia. Severe weakness of deltoid, triceps, biceps, iliopsoas and gluteus maximus muscles was confirmed in the absence of reflex or sensory changes. Electromyographic findings and mildly elevated CK levels were compatible with myopathy. Magnetic resonance imaging (MRI) of muscle demonstrated generalized muscle enlargement and patchy edema prominent in pectoralis major, serratus anterior, paravertebral and pelvic girdle muscles.

Muscle biopsy taken from deltoid muscle revealed mild variation in fiber size, accumulation of amyloid in thickened blood vessel walls as well as in muscle fibers with Congo red staining. In further investigations, the diagnosis of systemic AL amyloidosis in association with plasma cell dyscrasia was established. Over 3 months, cardiac, gastrointestinal and visceral involvement was evident. She did not respond to systemic chemotherapy and died of systemic complications of amyloidosis.

This case highlights the importance of investigations for amyloid myopathy in middle-aged patients with progressive myopathy or muscle hypertrophy of unclear cause.

Disclosure: Nothing to disclose.

PP2169

Patient with CASPR2 myasthenic-myotonic syndrome

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48 year old female patient was first admitted in September 2011 when she experienced gradually progressive symptoms of clumsiness in the left hand, periodically diplopia, dysarthria and partial ptosis on the left. In the department of neurology all clinical symptoms resolved by the next day. Blood tests and brain MRI were normal.

In January 2012 patient was referred to the neurology department in West-Tallinn Central Hospital.

Neurological exam demonstrated ptosis on the left, dysarthria, weakness and atrophies of small hand muscles with brisk reflexes and fasciculations in arm muscles, but no pyramidal signs. ENMG revealed subacute neurogenic changes in C8 and Th1 innervated muscles. Extensive clinical workup was unremarkable.

In February 2012 patient was re-admitted as dysarthria, dyspnea and muscle weakness had progressed. Also, weakness and atrophies of small hand muscles, fasciculations in the tongue and shoulder-girdle area were more marked, however no plantar extensor signs were demonstrated. Repeated ENMG confirmed progression with fasciculations and fibrillations in 3 segments and right diplets in frontal muscle. CSF was normal and oligoclonal bands negative.

Anti CASPR2 IgM was positive in low titre (+1:10). Amyotrophic syndrome was diagnosed.

In May 2012 patient's symptoms had stabilised with less fasciculations and weakness, small hand muscle atrophies had subsided. ENMG demonstrated positive changes with no spontaneous activity in limb muscles, large motor units were present diffusely.

Repeated analysis CASPR2 IgM demonstrated higher titer (IgM++ 1:32) than 4 months ago.

The final diagnosis of CASPR2 positive neuromyotonia was made.

Disclosure: Nothing to disclose.

PP2170

Anxiety and depression symptoms in patients with generalized myasthenia gravis

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Introduction: We investigated the symptoms of anxiety and depression in Myasthenia Gravis (MG) patients using practical psychiatric scales and aimed to emphasize the need for clinical awareness.

Methods: Thirty patients (21 women), between 48 and 59 years of age, who were registered in the Neuromuscular Unit in our Neurology Clinic were included in the study. The depression and anxiety symptoms were evaluated using the Beck Anxiety Scale (BAS) and the Beck Depression Scale (BDS). The correlation between these scores and age, gender, disease duration, intensive care unit experience, medications being used and the frequency of admission to a medical center were analyzed using the SPSS statistical program.

Results: The BAS and BDS scores were found to be higher than the normal ranges in >50 of the whole patient group (56 and 60 %, respectively). One third of all the patients required medical psychiatric treatment. The disease duration (RS:0.68 and 0.56, $p = 0.016$ for BAS and BDS, respectively), admission rate (RS:0.66 and 0.46, $p < 0.001$, for BAS and BDS, respectively) and hospitalization (RS:0.64 and 0.48, $p < 0.001$, for BAS and BDS, respectively) were statistically significantly related with the BAS and BDS scores.

Conclusions: Although there is a predictable relationship between psychiatric symptoms and MG, surprisingly few studies have evaluated this correlation. The symptoms of anxiety and depression may easily mask the myasthenic symptoms and leading to delayed diagnosis or misdiagnosis of MG. Furthermore, these symptoms may mimic the myasthenic symptoms and leading to over-treatments for MG. Thus, the use of practical psychiatric scales to evaluate the psychiatric status in routine neurological visits would help in deciding the specific treatment strategies.

Disclosure: Nothing to disclose.

PP2171

Stiff limb syndrome: a case report

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Introduction: Stiff-person syndrome (SPS) is a rare disorder characterized by rigidity of the truncal muscles, painful spasms, and an exquisite sensitivity to external stimuli. Stiff-limb syndrome (SLS) is a rare variant of SPS. We report a SLS in a young woman.

Case report: A 27-year-old healthy woman presented with a sudden onset of spasms of right arm muscles, preceded by sudden movement, loud noise or emotional stress. Her physical examination was remarkable in that her right upper extremity was rigid on passive and active ranges of motion. Movements were severely limited and painful. No paraspinal or axial contractions were palpated. Sensory examination was normal, and there was no extrapyramidal rigidity. EMG testing showed continuous motor unit activity on the upper right arm muscles. Anti-GAD antibody examination was negative. Immunological data and the paraneoplastic antibodies were negative. The patient improved at high doses of clonazepam. She was given also IV immunoglobulin as an adjunctive therapy.

Discussion: SLS is a newly emerging entity presenting focally with rigidity and spasms involving one or more limbs. The distal leg is the most affected. EMG show continuous motor unit activity at rest, but the distribution is very different from SPS. GAD auto-antibody titers are raised in a smaller proportion. SLS can also be paraneoplastic. Response to treatment is partial in SLS in marked contrast with those with SPS. Our patient remains ambulatory.

Conclusion: Only two cases of SLS exhibiting upper limb signs were reported. Our case report illustrates this exceptional variant of SPS.

Disclosure: Nothing to disclose.

PP2172

Val71Ala: a rare transthyretin variant in an American patient and response to liver transplantation

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Introduction: Mutations in TTR cause an autosomal dominant neuropathy, characterized by deposition of insoluble amyloid fibrils in the extracellular space in the nerves and muscles. Liver transplantation is the only treatment option in the USA. Although over 50 TTR mutations have been reported, the Val30Met mutation remains the most common. The Val30Met patients respond well to liver transplantation. A rare Val71Ala mutation was previously described in Europe; however, how these patients respond to liver transplantation is not known. Here, we report the first American patient with the Val71Ala mutation, the clinical characteristics and the response to liver transplantation.

Methods: Case report.

Results: A 42-year-old man of Swedish/Irish descent, presented with a 2-year history of progressive weight loss, weakness/numbness/pain in arms and legs. Examination revealed weakness of distal arms and legs and decreased pin prick sensation up to mid-thighs, and up to the elbows. Vibration sense was absent at ankles and knees, and decreased at wrists. Patellar and ankle reflexes were absent. EMG/NCS revealed a CIDP-like picture. Muscle and nerve biopsies showed amyloid deposits. DNA testing revealed Val71Ala mutation in the Transthyretin gene. 8 months later, the patient underwent a domino liver transplant, following which mild betterment of neurological weakness was reported.

Conclusions: Here we provide the first report of a rare Transthyretin mutation (Val71Ala) as a cause of Transthyretin amyloid neuropathy in an American patient. Our study also provides data to suggest that liver transplantation may be beneficial in the Val71Ala patients, similar to the Val30Met patients.

Disclosure: Nothing to disclose.

PP2173

Both binding and blocking antibodies correlate with disease severity in myasthenia gravis

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Introduction: The purpose of this study was to compare assays of acetylcholine receptor (AChR) binding and blocking antibodies for their ability to the diagnosis of myasthenia gravis (MG) and to estimate the clinical severity of MG patients.

Methods: The patients enrolled in the study had been tested for both binding and blocking antibodies and had disease duration exceeding 2 years since diagnosis. The patients were divided into five main classes by the Myasthenia Gravis Foundation of America (MGFA) clinical classification. Again, the enrolled patients were divided into ocular and generalized group according to MGFA classification. We compared the type and titer of antibodies and the thymus status between the ocular and generalized group.

Results: Thirty-five patients met the inclusion criteria. Of these, 16 patients (47 %) had both blocking and binding AChR antibodies, 11 patients (31 %) had only binding antibodies, and 8 patients (22 %) had only blocking antibodies. By defined clinical classification, the ocular and generalized groups included 10 and 25 patients, respectively. Sixteen patients in the generalized group possessed both AChR antibodies, with the remaining patients displaying only the binding antibody. All the patients with only blocking antibody were classified into ocular group.

Conclusions: Our study demonstrates that MG patients with both binding and blocking antibodies show more severe generalized MG or myasthenic crisis. Patients in the generalized group tend to have higher titers of binding and blocking antibodies. We suggest that both antibodies tests are useful in determining whether the disease will generalize.

Disclosure: Nothing to disclose.

PP2174

Cholinergic transmission of outer hair cell impaired in myasthenia gravis

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Introduction: Nicotinic acetylcholine receptors (nAChRs) are located on outer hair cell (OHC) which is source of otoacoustic emission (OAE), and can be inhibited by alpha-bungarotoxin like muscular nAChR in myasthenia gravis (MG). The classical techniques such as repetitive stimulation, autoantibody, and response to ACh esterase

inhibitor (AChEI) are sometimes not helpful for diagnosis of MG. The purpose of this study is to evaluate OAE for the possible role in diagnosis of MG.

Methods: We performed transient evoked otoacoustic emissions (TEOAEs) and distortion product otoacoustic emissions (DPOAEs) on 30 ears of 15 MG with normal hearing, and on 20 ears of 10 controls.

Results: Mean age was not different. TEOAE were significantly lower in MG (3.41 dB SPL) than in controls (8.69 dB SPL) ($p < 0.01$). DPOAE were lower in MG at higher frequencies between 2,026 and 4,053 Hz ($p < 0.01$). TEOAE and DPOAE were significantly lower in repetitive stimulation positive group and in AChR antibody positive group. TEOAE and DPOAE were correlated with titers of antibody.

Conclusions: The decrease of OAE in MG is probably related to the reduced cholinergic transmission at OHC level. This study supports the role of ACh in the efferent function of OHC, as well as the impaired AChRs on OHC in MG. Furthermore, more reduced OAE in repetitive stimulation positive or AChR antibody positive groups with the correlation between OAE and antibody titer suggests impaired OHC function by AChR antibodies in MG. Consequently, measuring TEOAEs and DPOAEs may be useful in the diagnosis of MG.

Disclosure: Nothing to disclose.

PP2175

Thymoma with or without paraneoplastic Myasthenia gravis- is minimally invasive tumour resection really safe?

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Introduction: Thymomas are malignant tumours, often associated with Myasthenia gravis and treated in neurological context. Complete operative resection is along with radiation and chemotherapy the mainstay of therapy and the most important prognostic factor.

Regarding the surgical procedure no clear guidelines exist. Whilst there is agreement that an en bloc resection of the tumour, the complete thymus and the surrounding mediastinal fat is necessary, the technical approach differs considerably. Most treatment centres choose an open approach through a median sternotomy, but recently many minimally invasive techniques arise. These methods do have advantages, but it remains uncertain, whether they are as safe as the conservative approaches, especially in long term observation.

Here we want to report five cases of tumour recurrence after minimal invasive thymoma resection and discuss the potential mechanism.

Methods: Retrospective data evaluation.

Results: We can present five cases of patients with thymoma +/− myasthenia gravis, with recurrence after a minimally invasive operation. In two cases thymoma and thymus gland were not completely resected but classified as a complete resection. In another case pleural carcinosis emerged years after the specimen pouch ruptured during operation.

Conclusions: We can show that recurrences of thymomas do emerge using minimally invasive techniques and that the occurrence can be related to the operation technique in some cases. Therefore we think that the use of these methods should be carefully considered, having in mind that recurrences of thymomas can occur many years later.

Disclosure: Nothing to disclose.

PP2176

Characteristics features of long-time survived patients with Duchenne muscular dystrophy

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Introduction: The prognosis of Duchenne muscular dystrophy (DMD) has been remarkably improved according to the progress of the respiratory care and cardiac protective therapy. At present, it is possible to prolong over 40 years in Japan. The aim of this study was to clear the clinical characteristics of long-time survived patients with DMD.

Methods: The mean age of death among DMD inpatients was 32.1 years old for the last ten years in our hospital. We investigated clinical features of DMD inpatients survived over 35 years.

Results: Eight of 14 inpatients with clinically diagnosed as DMD were over 35 years old. Four of 8 patients showed deleted exons of the dystrophin gene by MLPA analysis and were picked up. The mean age of 4 patients was 44 years old. They were bedridden because of severe weakness of the skeletal muscles. They had non-invasive positive pressure ventilation all day due to severe respiratory dysfunction. On the other hand, their cardiac involvements were not so damaged. Their ejection fractions measured by ultrasonic echocardiography were 0.18–0.50. They had some medicines for cardiomyopathy, such as angiotensin converting enzyme inhibitor, diuretic, digitalis, and so on. Two patients received oral nutrition and 2 patients required tube feeding. The mean of body mass index was 13.6. Two patients were diagnosed as depressive state or adjustment disorder in spite of mild cognitive dysfunction by psychologist.

Conclusions: We experienced long-time survived patients with DMD. All of them had artificial ventilatory support but their cardiomyopathies were not so severe.

Disclosure: Nothing to disclose.

PP2177

Correctness of referral to the repetitive nerve stimulation test and diagnostic outcome

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Introduction: Repetitive nerve stimulation test (RNST) is a useful method in the diagnosis of diseases of the neuromuscular synapse.The aim of this study was to verify the correctness of indications when referring to RNST and sensitivity of the method in the diagnosis of diseases of the neuromuscular junction (NMJ).

Methods: RNST was performed on 91 referred patients under the suspicion of NMJ disorders. Synergy PIU NCS EMG System was used and test performed on distal n.medianus–m.abductor pollicis brevis and proximal system n.accessorius–m.trapezius at low stimulation frequencies (1–3 Hz). Any decrement in CMAP amplitude of more than 10 % was defined as abnormal. Referral diagnosis was verified after the completion of planned examinations.

Results: After all tests were conducted, of 91 patients sent for RNST (mean age 15.34, SD 9.38), diagnosis of NMJ disorder was confirmed in 61(67 %), out of which 20 with congenital myasthenic syndrome (KMS), and 41 with autoimmune myasthenia gravis (aMG). 55 % of KMS patients and 70.7 % of aMG patients had abnormal RNST, without reaching statistically significant difference (Pearson Chi Square 1.474, $p = 0.225$). Eight (27.6 %) had abnormal RNST on distal system, 16 (55.2 %) on proximal, and 5 on both

systems in the group with aMG. One patient with KMS had abnormal RNS findings on the distal, and the remaining 10 (90.9 %) on the proximal system.

Conclusions: Results suggest high accuracy of the presumed diagnosis before referral to RNST, good sensitivity of the method and continuing need for its use in the diagnosis of NMJ disorders.

Disclosure: Nothing to disclose.

PP2178

Unusual clinical manifestations of hereditary inclusion myopathy

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Introduction: Hereditary inclusion body myopathy (HIBM) is a group of progressive myopathy disorders, which are uncommon in the general world population.

Case 1, 2 and 3: 41-year-old daugter, 70-year-old father and 60-year-old uncle presented bilaterally ptosis, progressive proximal muscle weakness and atrophy in the upper and lower extremities with diminished distal muscle. Blood tests for serum Creatine Kinase (CK) were in normal ranges. EMGs showed myopathic and neurogenic potentials especially in the proximal muscles. Muscle biopsy showed non-enflamatuar myopathic findings with inclusion bodies and rimmed vacuoles.

Case 3 and 4: 36-year-old and 41-year-old sisters presented progressive weakness of the distal leg muscles of the upper and lower extremities with sparing quadriceps muscles. Distal leg muscles of the lower extremities were symmetrically atrophic and deep tendon reflexes were diminished. CK levels were normal. EMGs showed myopathic and neurogenic potentials especially in distal muscles. Muscle biopsy showed non-enflamatuar myopathic findings with inclusion bodies and rimmed vacuoles.

Conclusion: HIBM constitutes a unique group of neuromuscular disorders characterized by adult-onset and a typical muscle pathology including rimmed vacuoles and filamentous inclusions. Clinical presentations of HIBM are variable:

1. An autosomal dominant form where the quadriceps are one of the first muscles to become weak.
2. An autosomal recessive form so-called quadriceps-sparing myopathy.
3. Inclusion body myopathy associated with Paget disease of bone and frontotemporal dementia.

We report 5 cases from 2 families in this study. To our knowledge, ptosis in HIBM is not described earlier.

Disclosure: Nothing to disclose.

PP2179

Breathing pattern and central ventilatory drive in Late-Onset Pompe disease (LOPD)

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Background: Pompe disease is an autosomal recessive disorder characterized by GAA deficiency that results in intra-lysosomal glycogen accumulation mainly affecting skeletal muscles. Respiratory symptoms may represent LOPD onset and have been attributed to diaphragm involvement. Glycogen accumulation has been demonstrated also in peripheral nerves and in the CNS, either in patients or in animal models. Consequently, it has been suggested that there could be a potential neurogenic influence on LOPD patients respiratory dysfunction.

Aim: This study is to determine the breathing pattern and the central ventilatory drive in LOPD patients to better define the pathophysiology of respiratory impairment.

Methods: 15 LOPD patients were studied and compared with a control group of 15 age- and sex-matched individuals.The rate, time, and depth of breathing and inspiratory occlusion pressure in mouth in the first 0.1 s (P0.1) were measured under basal conditions and compared with spirometric and respiratory pressure measurements.

Results: In LOPD patients, respiratory pattern including shallow breathing index and respiratory rate were increased, whereas P0.1 value was decreased ($P < 0.001$).

Conclusions: The respiratory pattern found in LOPD patients has also been documented in other neuromuscular disorders due to respiratory muscle weakness. Conversely, P0.1, that is an expression of the respiratory center output, in LOPD patients resulted decreased whereas in other muscle disorders resulted increased as compensatory event to the muscle weakness. Our data suggest that LOPD patients have a low activity of the respiratory drive, demonstrating that an involvement of CNS contributes to the pathophysiology of the respiratory failure.

Disclosure: Nothing to disclose.

PP2180

The interaction between tropomyosin-related kinase B receptor S and serine kinases modulates acetylcholine release in adult neuromuscular junctions

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We conducted an electrophysiological study of the functional link between the tropomyosin-related kinase B (trkB) receptor signaling mechanism and serine-threonine kinases, both protein kinase C (PKC)

and protein kinase A (PKA). We describe their coordinated role in transmitter release at the neuromuscular junction (NMJ) of the *Levator auris longus* muscle of the adult mouse. The inhibition of the trkB receptor with K-252a results in a significant reduction in the size of EPPs indicating that this receptor may be coupled to ACh release stimulation. We found that the intracellular PKC pathway can potentiate ACh release without the involvement of the trkB receptor function. However the trkB pathway needs an operative PKC pathway to be coupled to the release mechanism and potentiate it. The operativity of trkB is a necessary condition) and one effect of trkB may be PKA stimulation.

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Disclosure: Nothing to disclose.

PP2181

Phenotypic variability of myotonic dystrophy type 2

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Introduction: The aim was to assess manifestations of myotonic dystrophy type 2 (DM2).

Methods: Study comprised 34 DM2 patients and 34 matched DM1 patients (67.6 % females, 53 ± 10 years).

Results: Proximal muscles were similarly affected in both groups, while distal were less involved in DM2 ($p < 0.01$)–ptosis (3 vs. 62 %), mastication weakness (21 vs. 82 %), impaired speech (21 vs. 94 %), swallowing difficulties (15 vs. 38 %), significant sternocleidomastoid and trapezius weakness (56 vs. 100 % and 15 vs. 36 %), handgrip and jaw myotonia (71 vs. 100 % and 38 vs. 97 %). Forced vital capacity <90 % was found in 3 % of DM2 patients and 52 % of DM1 ($p < 0.01$). Differences in EMG findings were not significant—myopathy was present in 93 % of DM2 and 100 % of DM1 patients and myotonia in 90 and 100 %, respectively. Calf hypertrophy was found in 29 % and hand tremor in 38 % of DM2 patients, while were absent in DM1. Severe ECG abnormality was found in 9 % of DM2 and 22 % of DM1 patients ($p > 0.05$) with shorter PQ in DM2 (0.16 ± 0.03 vs. 0.21 ± 0.02, $p < 0.01$). Diabetes was more frequent in DM2 (32 vs. 7 %, $p < 0.01$). Frequency of eye cataract was similar in DM2 and DM1 (82 vs. 97 %, $p = 0.05$).

Conclusions: DM2, compared to DM1, is manifested with older age at onset, less involvement of distal, cranial and respiratory muscles, less pronounced myotonia and cardiac abnormalities. Presence of calf hypertrophy, hand tremor and diabetes is suggestive of DM2.

Disclosure: Nothing to disclose.

PP2182

Enzymatic replacement therapy in patients with late-onset Pompe disease—5-year follow up

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Introduction: Late-onset Pompe disease (LOPD) is progressive metabolic myopathy, affecting skeletal muscles, which, if untreated, leads to serious disability and/or respiratory failure. Enzyme replacement therapy (ERT) improves muscle strength, respiratory function and prevents disease progression. We present a 5-year follow-up of 4 LOPD patients treated with ERT.

Methods: Four patients with LOPD received ERT: two started treatment in 2008, other two in 2010. Patients received recombinant human alpha-glucosidase in dose 20 mg/kg intravenously every two weeks. Physical efficiency was assessed in 6-minute walk test (6MWT). Spirometry was performed to examine FVC and FEV1. Liver enzymes, LDH, CK and CK-MB levels were assessed.

Results: Walking distance in 6MWT increased by average 9 % in the first two years and 21 % in the first 3 years of treatment in two patients with the longest treatment compared to the baseline. Similar changes were detected in spirometry: the biggest FVC increase was observed in two patients with the highest FVC values before treatment, which increased to normal values adjusted for age and sex in 3 years of treatment, that is by 28 and 34 %. In two other patients FVC reached 88 and 76 % of predicted values. ERT didn't affect liver or muscle enzymes levels.

Conclusion: The improvements of exercise tolerance and FVC were observed in all patients in the first 3 years of treatment and were the biggest in patients treated the longest and with the least severe neurological and respiratory symptoms. Early ERT introduction results in higher improvement of respiratory and ambulation functions.

Disclosure: Nothing to disclose.

PP2183

Metabolic syndrome in patients with myotonic dystrophy type 1

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Introduction: Aim was to investigate frequency and features of metabolic syndrome (MetSy) in patients with myotonic dystrophy type 1 (DM1).

Methods: Study comprised 66 DM1 patients (50 % males, 41.9 ± 10.5 years old, with disease duration of 41.9 ± 10.5 years and CTG repeat length of 751.9 ± 280.6). New worldwide consensus criteria for MetSy from 2009 were used.

Results: Components of MetSy were present with following frequencies: hypertriglyceridaemia 67 %, low HDL cholesterol 35 %, hypertension 18 %, central obesity 14 %, hyperglycemia 9 %. MetSy was present in 11 (17 %) of patients, among them 7 (11 %) had three components and 4 (6 %) had four components. Presence of MetSy was not in association with patients gender and age, severity and duration of disease, neither with CTG repeats length ($p > 0.05$). Patients with MetSy had significantly lower total SF-36 score as a measure of quality of life in comparison to patients without MetSy (34.8 ± 21.6 vs. 53.8 ± 23.2, $p < 0.05$).

Conclusions: Although certain components of MetSy are very frequent in patients with DM1, only 17 % of them met the criteria for MetSy. Patients with MetSy had significantly lower quality of life.

Disclosure: Nothing to disclose.

PP2184
Subclinical cardiac involvement in thymomatous Myasthenia gravis

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Introduction: Myasthenia Gravis primarily affects skeletal muscles, however cardiac involvement has been reported in thymomatous MG. We present a case of an MG patient whom cardiac Magnetic Resonance Imaging (cMRI) in accordance to premature ventricular beats (PVC) confirmed the presence of cardiomyopathy and the application of cortisone treatment reversed it.

Methods: A 58-year-old male presented with a two- month history of eyelid ptosis after thymectomy and fatigue induced deterioration of clinical condition which improved at rest. The electrophysiological study showed disorder of the neuromuscular junction and the serum acetylcholine receptor antibodies had a titer of 46 nM (positive titer > 0.6 nM). Pyridostigmine resulted in mild clinical improvement. A thorough cardiac evaluation was performed, including electrocardiogram, cardiac ultrasound, 24 h ambulatory ECG (Holter) and cMRI. ECG and echo didn't show abnormalities related to MG while holter showed moderate number of PVC (>30 beats/h) and one couplet of PVCs. Exercise test was negative for coronary artery disease while enhancement areas in the interventricular septum and in the lateral wall of the LV were seen during the cardiac MRI in T1 sequences indicative of fibrotic process. The patient after the cardiac exams received prednisolone 60 mg/day with clear clinical improvement while the repetitive cMRI was clear with no evidence of gadolinium enhancement.

Conclusions: Although myocardial damage is usually detected long after the diagnosis of MG, in our case, there was concurrent presentation of cardiac involvement and myasthenia process. The combination of cMRI and Holter successfully detected cardiac abnormalities for which the patient received cortisone.

Disclosure: Nothing to disclose.

PP2185
Two cases of myotonic dystrophy type 1 associated with white matter abnormalities of the brain

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PP2186
Duchenne muscular dystrophy in Tunisian children

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PP2187

Abstract withdrawn

PP2188
Miyoshi myopathy: a case report

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PP2189
Course of myasthenia gravis during pregnancy—expirience in Clinical Centre Nis, Serbia

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PP2190
Periodic paralysis: a thyrotoxic periodic paralysis case

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PP2191
Correlations between creatine kinase and blood pressure in repeated measurements

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PP2192
Immunological background of myasthenia gravis

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PP2193

Abstract withdrawn

PP2194
A case of late onset Pompe

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PP2195
Antibodies to acetylcholine receptors in case of myasthenia gravis associated with concomitant autoimmune diseases

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PP2196
Myasthenia gravis as a paraneoplastic syndrome associated with colon adenocarcinoma

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PP2197
Treatment of a seronegative Myasthenia Gravis pacient with complications

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PP2198

Abstract withdrawn

PP2199

Ischemic infarction, sepsis and trombocytopenia after using intravenous immunoglobuline in patient with chronical demyelinizating inflammatory neuropathy

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PP2200

Myotonic dystrophy type 1 as a multisystemic disease—lessons from the Serbian Registry

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PP2201

Electromyographic correlation with clinical severity, antibody levels and treatment response in Myasthenia gravis

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PP2202

Idiopathic inflammatory myopathies—clinical features, complementary investigation and treatment response

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Neuro-epidemiology; Neurorehabilitation

PP2203

Prevalence of Restless Legs syndrome in Trabzon, in the Northeast Black Sea Region of Turkey: associated factors, clinical characteristics and biochemical correlations

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Introduction: The prevalence of RLS in Turkey has been reported at 3.2, 3.4 and 5.5 % in three different population based study conducted in different areas. In this study we aimed to assess the prevalence of RLS in Trabzon and to evaluate associated factors including some biochemical evaluations.

Methods: Face-to-face, home interviews were conducted among a random sample of 3789 adults aged 20 or above. The criteria suggested by the International Restless Legs Syndrome Study Group were used in the assessment of RLS. Individuals responding 'yes' to at least one question were interviewed and examined by neurologists for the definitive diagnosis of RLS. An age- and gender-matched RLS-negative individual from the same district was enrolled in the control group. Blood samples of RLS patients and control subjects were taken to after 12 h fasting to evaluate fasting blood sugars, ferritin, vitamin B12, folic acid, and creatinine.

Results: The prevalence of RLS in the study population was 4.5 %. The prevalence in women was significantly higher than in men and increased with age. RLS was more common in subjects with anemia. Serum ferritin levels were significantly lower in RLS patients than in control subjects. No significant difference was found between the groups in terms of fasting blood glucose, vitamin B12, folic acid, or creatinine.

Conclusions: Our study provides further evidence for the low prevalence of RLS in Turkey compared to the Western countries. Anemia and low serum ferritin level are the major factors associated with RLS in our population.

Disclosure: Nothing to disclose.

PP2204

Knowledge of Tunisian young person's about stroke risk factors, warning signs and treatment

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Introduction: Atherosclerosis is the usual cause of strokes. Primary prevention of this disorder must being in childhood or early adolescence. The aim of this study is to assess knowledge of young person's about stroke and to identify information source.

Methods: We randomly selected 1220 young person's ($18 \leq$ age ≤ 25 years) living in Sousse and performed an open-ended and closed questionnaire about stroke risk factors, warning signs, source of information, and stroke attitude. The survey was carried out during 12 months and administered by medical students.

Results: The mean age was 21.2 ± 2.8 years. Men present 56.1 % of them. Smoking was reported by 28.9 % of the respondents. Brain as the site of stroke was recognized by 52 % of the cases. Only 28.2 % were able to cite three risk factors and 14.2 % said that they do not know anything. Stress and hypertension were the most frequently risk factors identified. Only 13.8 % of the respondents were able to cite three stroke warning signs and 4.4 % don't cite any sign. Positive responses about stroke risk factors and warning signs appear to be more prevalent when using closed-ended rather than open-ended questions. The first action during a stroke attack was going to call emergency services (63.9 %). The most common sources of information were TV, radio in 63.7 % and internet in 47 %.

Conclusions: Knowledge of stroke risk factors and symptoms is poor amongst young people. Our results have important implications for the primary prevention to reduce stroke incidence.

Disclosure: Nothing to disclose.

PP2205

A feasibility study to establish a national registry of neurological diseases in Hungary based on reimbursement databases—stroke as an example

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Introduction: There are considerable geographical differences in the prevalence of neurological disorders. Although the prospective population based study is the gold standard to estimate the epidemiological features of a disease, the analysis of the reimbursement database of a national health insurance fund may be an acceptable approximation in countries with universal coverage and a single payer health insurance system.

Methods: The anonymized database of the National Health Insurance Fund, the single-payer agency offering universal coverage, was analyzed to identify stroke and TIA patients in the population of 131 thousand in 2 districts of Budapest for the period of 2002–2007. The postal codes were used to identify residence, and the ICD-10 codes G45, I61 and I63 were searched to find cases with TIA, intracerebral hemorrhage and ischemic stroke.

Results: During the 6-year period over nine thousand TIA or stroke cases were identified. After excluding those with TIA 4383 cases were left with the diagnosis of intracerebral hemorrhage or ischemic stroke. Of these cases 75 % were hospitalized and 25 % were treated as outpatients. Over 60 % of hospitalized cases were treated at neurological departments. In the outpatient settings 84 % of those with a diagnosis of stroke or TIA were seen by neurologists.

Conclusions: If reimbursement databases are used to approximate epidemiological features of neurological diseases, it is insufficient to search the inpatient databases even for potentially disabling diseases. Limiting the searches to neurological inpatient and outpatient services will also result in underestimation of the number of people affected by neurological diseases.

Disclosure: Nothing to disclose.

PP2206

The impact of the multidisciplinary rehabilitation for multiple sclerosis relapses: a randomized controlled trial

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Introduction: The aim of our study was to evaluate the benefits of administration of intravenous high-dose methylprednisolone (HDMP) combined with multidisciplinary rehabilitation (MDR) of relapse in persons with multiple sclerosis (MS) in order to assess whether combination of steroid therapy with MDR is more beneficial than steroid therapy alone.

Methods: This investigation was conducted as randomized controlled trial at the Clinic of Neurology, Belgrade. MS patients were eligible if they had established diagnosis and relapse requiring application of HDMP. Forty-nine patients were included in the study and randomized to control and treatment groups by simple randomization, and 37 completed the study. Five days, 1 g daily, intravenous MP was administered to all patients. Treatment group additionally received individualized MDR program over a 3-week period. All outcome measures (EDSS, FIM, BDI, FSS and MSQoL-54) were completed on admission, at 1 and 3 months.

Results: No significant changes were detected in the EDSS, BDS, FSS and FIM scores between baseline and 1- and 3-month follow-up scores. Statistically significant improvement in quality of life (QoL) in the treatment group at both time points was detected for both Physical health composite (PHC) and Mental health composite (MHC) scores, and in the control group, only for PHC score. In the treatment group, the analysis of magnitude for changes in QoL has shown sustained large effect size (ES) for both PHC and MHC scores, while in the control group, sustained moderate ES only for PHC.

Conclusions: MDR seems to improve MS relapse outcome.

Disclosure: Nothing to disclose.

PP2207

Measurement of intrathecal IL-6 levels helps diagnosis of neurological disorders

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Background: Interleukin 6 (IL-6) acts as a pro-inflammatory cytokine, and plays an important role in mediator of fever and acute phase response. In neurological disorders, neuro-Bechet disease, central nervous system (CNS) lupus and influenza-associated encephalopathy are reported to elevate intrathecal IL-6 levels, but little is known about other neurological disorders. We analyse the association between intrathecal IL-6 levels and various neurological disorders.

Patients and methods: We retrospectively examined the patients who underwent lumbar puncture in our hospital from April 2012 to March 2013, and classified into eight categories: (1) cerebrovascular diseases, (2) infection of CNS, (3) encephalopathy, (4) epilepsy, (5) inflammatory, demyelinating and autoimmune diseases, (6) peripheral neuropathies, (7) malignant disorders, and (8) others. We analysed the intrathecal IL-6 levels, cerebrospinal fluid (CSF) cell counts, and protein levels.

Results: 155 patients (76 male) were evaluated. Median CSF cell counts in the group of infection of CNS ($n = 30$), encephalopathy ($n = 11$), inflammatory, demyelinating and autoimmune diseases ($n = 23$), and epilepsy ($n = 13$) were 73/mm^3 (interquartile range (IQR) 99.75), 1/mm^3 (IQR 1.5), 2/mm^3 (IQR 4), and 4.2/mm^3 (IQR 11.25) respectively. And median intrathecal IL-6 levels were 113.15 pg/mL (IQR 218.5), 19.7 pg/mL (IQR 24.75), 4.2 pg/mL (IQR 11.25), and 18.8 pg/mL (IQR 60.1) respectively. In infection of CNS group, there was a tendency to elevate CSF cell counts and intrathecal IL-6 levels simultaneously. On the other hand, encephalopathy, inflammatory, demyelinating and autoimmune disorder and epilepsy group tend to elevate intrathecal IL-6 levels alone.

Conclusion: To measure intrathecal IL-6 levels may be beneficial to diagnose neurological disorders, including encephalopathy, epilepsy and inflammatory, demyelinating and autoimmune diseases.

Disclosure: Nothing to disclose.

PP2208

Lorenzo's oil combined with a physiotherapy program: an effective therapy in a case of X-linked adrenoleukodystrophy

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Introduction: X linked-ALD is a metabolic disorder which affects to oxidation of very long-chain fatty acids (VLCFA). The clinical manifestations include intellectual, psychological, visual, hearing, swallowing and gait disturbances. Lorenzo's oil is the usual therapy, but there are not references about its combination with an intense program of Physiotherapy. So, the aim of this study is to demonstrate the efficacy of both treatments.

Methods: A unique case of X-linked ALD (male of 24 years old), who began the treatment with Lorenzo's oil 2 months before the program of Physiotherapy (5 h per day, 5 days a week). The measures employed were Berg Scale, Barthel modified Granger Scale, Functional Ambulation Profile (FAP) for gait and Evoked Potentials (SEP) and ElectroMyography (EMG) Study of Median, Tibials and Sural Nerves, at the beginning, 3 months later (except SEP and EMG), and 6 months later (included SEP and EMG).

Results: There were changes in Barthel Scale (initial: 40; final: 55); Berg Scale (from 1 to 16); FAP (from 0 to 45, walking with a walker); and in SEP from Median (Right: from 0.2 μV to 0.3 μV; Left: from 0 to 0.5 μV) and Tibial (Right: from 0 to 0.4 μV; Left without changes); and in EMG: Motor Conduction (Peroneal begins activity, and tibial increase its amplitude) and Sensory Conduction (Sural presents first activity).

Conclusions: The combination of Lorenzo's oil therapy with Physiotherapy could be effective in a X-linked ALD patient. A longer follow-up is necessary in order to demonstrate these changes are permanent.

Disclosure: Nothing to disclose.

PP2209

Multiple sclerosis: updated prevalence and incidence in Salerno (southern Italy) and its province

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Introduction: Many Multiple Sclerosis (MS) prevalence studies since 1980 put Italy in a high risk zone. There are very few studies in southern Italy as compared to northern areas (the more recent: Salerno, 2006, 71.50/100000, southern Lazio, 2010 90/100000, Molise, 2009, 91.02/100000). This paper updates MS prevalence of Salerno and province to 2010.

Methods: Data were collected from the registry of Salerno district MS center. Included Salerno city and 35 towns in the district. Diagnosis was made by McDonald's criteria. Population screened: 366,025 (Salerno = 139,704; province = 226,321). ISTAT 2010 Italian data were used for age standardization. Prevalence day was December 31, 2010. Confidence intervals were calculated according to Kurtzke.

Results: 312 pts were collected. From Salerno, 116 (29M, 87F), age 41.44 (17–76); Female/male = 3.0; from province, they were 196 (59M, 137F); age onset 30.2 (11–54); mean disease duration 15.47 years (0–51), disease relapsing-remitting in 221 (70.83 %); secondary progressive in 79 (25.32 %); primary progressive in 12(3.84 %). Of the RR, 57(45F, 12M) were clinically isolated syndromes. Crude prevalence in Salerno is 83.03 (68.41–99.30); in province it ranges from 70.44 (Montecorvino Pugliano) to 443.46 (Controne). Province cumulative prevalence is 86.60 (74.99–99.50). Salerno and province prevalence = 85.24 (77.05–94.01). Standardized = 84.87. Cumulative 2006–2010 incidence 2006–1010 is 3.25 (m 1.95, f 4.45), in 2001–2005 it was 5.15 (m 2.32, f 7.83).

Conclusions: Our data are still underestimated for some patients skip the local center for northern hospitals. This enhances the significance of the prevalence and its increasing trend, which, except for Sardinia, is comparable to Italian literature data, and indirectly stands against a latitude gradient for MS.

Disclosure: dr. Iuliano had travel/accommodations/meeting expenses funded by Bayer Schering, Biogen Idec, Merck Serono, Novartis, Sanofi Aventis, and Teva; served on advisory board for Bayer and Teva. Dr. Napoletano and Dr. Cianfrani did not declare conflicts of interest.

PP2210

Inpatient physiotherapy management for Stiff Person syndrome

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Introduction: Stiff Person Syndrome (SPS) is a rare autoimmune neurological disorder characterized by progressive stiffness and painful spasms in the trunk and lower extremities. Little information about physiotherapy management of SPS is found in the literature. The aim of this case report was to show the effects of inpatient physiotherapy management for a patient with SPS.

Methods: The patient was a 65-year-old female with SPS diagnosed 1 year before. She spent 31 days in hospital. Plasmapheresis sessions were performed 5 times for cerebellar symptoms. Initial assessments were range of motion, muscle strength, pain, balance, coordination, ambulation and function. She got pain in shoulders; visual analogue scale (VAS) was 5. Muscle strength was affected. She had sitting balance, however could not stand up and walk. Her Functional Mobility Profile (FMP) score was 35/63. She received physiotherapy for 14 sessions. It included mainly balance, coordination, posture, strengthening, stretching exercises, and repetitive task training. After gaining standing balance, walking exercises were applied.

Results: Her coordination and muscle strength was increased. Her pain disappeared (VAS-0). Her static and dynamic balance improved dramatically and she started to walk with a walker at the 9th session. Her walking speed, distance and independence improved. The last FMP score was 49/63 and she could walk 20 m with a walker without rest.

Conclusions: Considering plasmapheresis was performed for cerebellar symptoms, it seems that the resulting improvements are caused by physiotherapy. Inpatient physiotherapy management for SPS can be effective to improve function and the impairments associated with SPS.

Disclosure: Nothing to disclose.

PP2211

Polymorphism in the methylenetetrahydrofolate reductase (C677T) gene and homocysteine levels: a comparison in Albanian patients with acute first-ever ischemic stroke

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Introduction: In the methylenetetrahydrofolate reductase (MTHFR) gene, homozygosity for MTHFR C677T polymorphism is associated with plasma elevated total homocysteine (tHcy) levels (hyperhomocysteinaemia). Hyperhomocysteinaemia is known as risk factor for first-ever ischemic stroke (FIS). We investigated whether hyperhomocysteinaemia and/or MTHFR C677T polymorphism are associated with acute clinical episode of FIS.

Methods: In a prospective case–control study, thirty-nine acute FIS patients (aged 49–82) with confirmed FIS from the neurology department, Clinical Hospital Tetovo and 103 controls (aged 27–71) without any history of stroke was performed. Fasting tHcy levels were measured by enzyme cycling method. MTHFR mutation was done with CVD StripAssay (ViennaLab Labordiagnostica, GmbH, Austria). The population genetics analysis package PyPop was used for analysis of the MTHFR data. The analysis of significance of results was done with using SPSS software package. A p value < 0.05 was taken as significant.

Results: All patients had high homocysteine levels ($\geq$15 μmol/L). Homocysteine levels was significantly high in patients compared to controls, but no significantly higher in CT (heterozygous) genotype compared to CC (normal) and TT (homozygous) genotypes. MTHFR homozygous was seen in three patients (7.69 %), but twenty (19.42 %) of controls ($p = 0.141$). MTHFR heterozygous genotype was seen in twelve of 39 cases (30.77 %), but fifty-six (54.37 %) in controls ($p = 0.121$). MTHFR CC genotype was seen in fifteen cases (38.46 %) and 27/103 (26.21 %) in controls ($p = 0.302$).

Conclusions: Our findings suggest that hyperhomocysteinaemia, but not MTHFR C677T polymorphisms represent risk factors for acute first clinical ischemic stroke in Albanian subjects.

Disclosure: Nothing to disclose.

PP2212

Safety and immune response of influenza vaccine in patients with Duchenne muscular dystrophy

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Introduction: Patients with Duchenne muscular dystrophy (DMD) are at high-risk of complications from influenza infection, however, little is known regarding response of influenza vaccine for these patients. The objective of the study was to examine safety and immune response of influenza vaccine in patients with DMD.

Methods: Forty-four patients with DMD and 41 healthy healthcare workers received one dose of 2009 pandemic influenza vaccine. We asked to report all symptoms of solicited local and systemic reactions after vaccination. Hemagglutinin inhibition antibody titers were measured in serum before (S0) and 4 weeks after vaccination (S1). The primary endpoints were geometric mean titer (GMT), seroresponse ($S1/S0 \geq 4$) and seroprotection ($S1 \geq 1{:}40$) proportion. We calculated Odds Ratio (OR) and its 95 % confidence interval (95 %CI) using logistic regression models to examine the association between immunogenicity and disease-related factors such as cardiopulmonary function or nutritional status.

Results: The patients experienced less frequent reactions than healthcare workers (local reactions 32 vs. 51 %, $p = 0.071$, systemic reactions 7 vs. 29 %, $p = 0.007$). The GMT of patients increased from 1:7 to 1:75 after the vaccination, for a mean rise of 10.5 fold. The proportions of the patients who achieved seroresponse and seroprotection were 84 and 70 %, respectively. These results were comparable to those of healthcare workers. A significantly increased OR was observed in relation between age and seroresonse ($OR = 1.14$, 95 %CI 0.99–1.22), and total protein and seroprotection ($OR = 1.45$, 95 %CI 1.04–2.01).

Conclusions: A single dose of the 2009 pandemic influenza A H1N1 vaccine was safe and sufficiently immunogenic for patients with DMD.

Disclosure: Nothing to disclose.

PP2213

The epidemiology of Myasthenia Gravis in Greater Manchester, UK

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Background: Several European studies of the epidemiology of Myasthenia Gravis (MG) have estimated prevalence rates of between 8 and 15 per 100,000 of the population. There has been recent evidence to suggest that the prevalence of MG may be increasing in the UK, especially in the elderly. We performed a large population based survey of MG in the Greater Manchester area of the country.

Methods: Multiple overlapping sources of case ascertainment were used to identify all patients with MG within a tightly defined geographical area. Patients were invited to interview either in their own home or in the hospital setting. Information was recorded by a structured questionnaire complemented by review of case records. A 'Capture-Recapture' analysis was used to estimate numbers of missed cases.

Results: A total of 378 patients with confirmed MG were identified, giving a prevalence rate of 15.1/100,000. Capture-recapture analysis suggested that the true prevalence may be as high as 16.4/100,000. The sex ratio was 1:1.17 M:F. Mean age of diagnosis was 57.6 years, with 46 % aged 60 or above at the time of diagnosis. 15.6 % of the patients had restricted ocular MG.

Conclusion: This study constitutes the largest epidemiological survey of MG ever performed in the UK. The results demonstrate a high prevalence compared to many other European studies, including results from a previous survey in Cambridgeshire, UK in 1998. The results are in keeping with recent observations that MG is being increasingly commonly diagnosed in the older population.

Disclosure: Nothing to disclose.

PP2214

Epidemiology of cerebral stroke in Tashkent

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Introduction: Cerebral strokes are considered to be one of the main problems in modern neurology. In Uzbekistan the incidences of cerebral strokes vary between 0.9 and 1.4 cases per 1000 people. The mortality rate during the acute phase of stroke goes up to 35–40 % (Asadullaev M.M., 2011).

The objective is to study the structure and risk factors for stroke among the Uzbek population.

Methods: The scientific basis for the evaluation of the epidemiological situation in the regions is the register approach. The study was conducted in Tashkent, with the population of over 3 million people.

Results: The results have shown that between 2011 and 2012 there were 4,782 cases of stroke, 52.6 % of which were among male,and 47.4 %—female. Within the structure of stroke, ischemic stroke occurs in 71.9 % cases, while hemorrhagic stroke in 28.1 % cases. The mortality rate among men is higher-53 %, than among women. The highest mortality rate, up to 34.1 %, is registered among 60–69-year-old men, and over 70-year-old woman −62.2 %.

According to the register, the major risk factors for ischemic stroke were: hypertension −26.5 %, brain arteriosclerosis – 20.8 %, and the combination of hypertensive disease with atherosclerosis − 42.9 %. The causes of hemorrhagic stroke were: hypertension—62 %, cerebral atherosclerosis—5.1 %, the combination of hypertension with atherosclerosis—13.9 %.

Conclusions: The studies have concluded that the rate of stroke among the Uzbek population is still high. Some further developments in this sphere are required to prevent this disease.

Disclosure: Nothing to disclose.

PP2215

The use of telemonitoring and illustrated handbook to assess Parkinson's disease patients' adherence to home-prescribed physiotherapy treatment

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Parkinson's Disease (PD) is a progressive neurodegenerative condition characterized by motor impairment. Although, pharmacological treatments are useful in controlling the motor symptoms, intensive long-term motor rehabilitation may provide an adjunctive improvement of the motor performance. We hypothesized that the implementation of telemonitoring and the instructive help of an illustrated handbook, may be useful in reinforcing the PD patients' adherence to physiotherapy and finalized motor training.

We enrolled 45 patients who underwent 2 cycles of motor rehabilitation in our center. They were administered questionnaires on adherence to home-prescribed rehabilitation exercises, questionnaires on depression and on the use of communication tools, either prior to the home-based rehabilitation or afterwards. The patients were divided into 4 groups according to severity of disease and gender and they were all provided home-prescribed rehabilitation indications. Group 1 had been provided only with the rehabilitative indications, group 2 received the illustrated handbook, group 3 a weekly phone-call from the center, and group 4 was followed with both handbook and phone-call.

Patients demonstrated a statistically significant increase of adherence to the home-performed exercises in the telemonitoring group compared to controls. Male patients, who were provided the handbook were more adherent to the exercise program compared to males of the control group.

The telemonitoring and the illustrated handbook have proved some efficacy in increasing the adherence to home-prescribed rehabilitation. Further studies are needed to explore implementation of these tools in order to have a better understanding of the key factors influencing the patients' response and maximizing their potential.

Disclosure: Nothing to disclose.

PP2216

Burden of pseudobulbar affect (PBA) symptoms in veterans with traumatic brain injury (TBI)

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Introduction: PBA, characterized by exaggerated or inappropriate, uncontrollable involuntary episodes of crying and/or laughing can occur in persons with neurological conditions affecting the brain. This survey was designed to estimate PBA symptom presence and impact in Veterans with TBI.

Methods: Cross-sectional survey with patient-level linkage to VA clinical data.OEF/OIF Veterans screening positive for TBI were mailed a questionnaire consisting of the seven-item Center for Neurologic Study-Lability Scale (CNS-LS) with an initial question asking if the Veteran had "involuntary episodes of crying and/or laughing that were exaggerated or even contrary to how they felt at the time". The EQ-5D questionnaire, a standardized measure of health-related quality of life (HRQOL) was included. Presence of PBA symptoms is defined as a CNS-LS score $\geq$13.

Results: Surveys were returned by 728 Veterans (22 % of traceable subjects). Survey respondents were older and had higher rates of depression and depression-related prescriptions than non-respondents. Among respondents, 60 % answered "yes" to the "involuntary episodes" question and 70 % had CNS-LS $\geq$ 13. Depression, PTSD, and anxiety disorders were significantly higher in those with PBA symptoms (CNS-LS $\geq$ 13). Mean CNS-LS involuntary crying scores were higher than involuntary laughing scores. Respondents with PBA symptoms reported significantly poorer HRQOL in all five EQ-5D functional domains. More than 85 % reported at least moderate problems with pain or anxiety/depression; 50 % reported at least moderate problems with usual activities.

Conclusions: Results suggest a high presence of PBA symptoms among Veterans with TBI. PBA symptoms were associated with significantly greater physical and mental health burden and poorer HRQOL.

Disclosure: One author (CY) is employed by Avanir Pharmaceuticals and three authors (JRF, PRH, and MWR) received financial support from Avanir Pharmaceuticals to carry out this work.

PP2217

The effect of innovative technique of postural synergies activation on balance and gait functions for patients with atactic disorders during recovery stroke period

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PP2218

Ulzibat myofasciotomy—a new method to treat muscle shortening in CP children

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PP2219

Abstract withdrawn

PP2220

Abstract withdrawn

PP2221

Physical activity and walking differences between working and unemployed women with multiple sclerosis

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PP2222

Physiotherapy referral rates and trend about the inpatient physiotherapy referral in Turkey

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PP2223

Focused low-energy extracorporeal shock waves with distally symmetric polyneuropathy (DSPNP). A pilot study

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PP2224

Symptomatic treatment of unresponsive wakefulness syndrome with transcranially focused extracorporeal shock waves

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PP2225

Focused extracorporeal shock waves improve pareses in 8 cases of spinal cord injury and 3 cases of myelomeningocele

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PP2226

The prevalence of chronic pain with neuropathic characteristics in Lithuania: a cross-sectional door-to-door survey

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PP2227

The influence of proprioceptive neuromuscular facilitation (PNF) on camptocormia in Parkinson's disease—case presentation and literature overview

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PP2228

Method of constraint induced therapy for intact limb in patients with central hemiparesis syndrome

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PP2229 Prevalence of multiple sclerosis in Volyn Region, Ukraine

O. Shulga

PP2230

Capabilities of the neurorehabilitation are under evaluated. A world wide stigma

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PP2231

Investigation of brain activity with functional magnetic resonance imaging after passive moving in post stroke patients

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Peripheral nerve disorders 2

PP2232

Prophylactic anticoagulation in Guillain-Barré syndrome: too much of a good thing?

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Objectives: Venous thromboembolic complications are common during recovery from Guillain-Barré Syndrome (GBS). The use of prophylactic anticoagulation to reduce this risk is accepted as good practice although can be associated with a risk of haemorrhagic complications.

We examined the current practice of prophylactic anticoagulation in patients with GBS admitted to a tertiary neurosciences centre. The frequency of venous thromboembolism and haemorrhagic complications were also recorded.

Methods: A retrospective notes review of 50 consecutive patients admitted with GBS to the Greater Manchester Neurosciences Centre between 2008 and 2013 was performed. Disease severity, prophylactic anticoagulation type, dose and duration, and the frequency and timing of haemorrhagic and thromboembolic complications were recorded and analysed.

Results: Details of prophylactic anticoagulation prescription were obtained for 42 of 50 patients. All non-ambulant patients (95 %, 40/42) received low molecular weight heparin (LMWH) at any dose at some point during a mean inpatient stay of 64 days.

14 haemorrhagic complications occurred in 10 patients. 7 of these coincided with the use of 'treatment (high) dose' LMWH. A bleeding tracheostomy site contributed to the death of 1 patient.

1 thrombotic event was observed: a portal vein thrombosis. No deep vein thrombosis or pulmonary emboli occurred.

Conclusions: Thromboembolic complications were infrequent in this population. However, a relatively high frequency of

haemorrhagic complications were observed and these appeared to correlate with the use of 'treatment (high) dose' LMWH.

Systematic work is required to define the optimal prophylactic anticoagulation strategy in patients with GBS to ensure that the benefits outweigh risks.

Disclosure: Nothing to disclose.

PP2233

Sensitivities of the different electrodiagnostic criteria in chronic inflammatory demyelinating polyneuropathy

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Introduction: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an autoimmune disease characterized by progressive or relapsing course lasting more than 8 weeks. Because of its highly variable clinical features and nonspecific laboratory findings, several diagnostic criteria have been proposed. In this study, I reviewed the nerve conduction study (NCS) findings of patients with CIDP in order to examine the sensitivity of various electrodiagnostic criteria.

Methods: In this study, 31 cases were recruited from seven tertiary referral centers in Southeast Korea. The distribution of four types of abnormalities suggesting demyelination of peripheral nerve was examined, and six different sets of electrodiagnostic criteria for the CIDP were applied to the individual cases.

Results: The four types of abnormalities suggesting demyelination showed relatively even distribution among four motor nerves tested. Among them, the F-wave abnormality was most frequent and the conduction blocks were least common. Each set of criteria showed sensitivity ranging from 74.2 to 96.8 %. The INCAT criteria and Nicholas' criteria showed highest sensitivity (96.8 %), while the Albers & Kelly's criteria were least sensitive (74.2 %).

Conclusion: In comparison to the previous reports, this study showed relatively higher frequency of abnormalities including conduction blocks, and thus, each diagnostic criterion showed higher sensitivity than other studies. Such discrepancies likely came from differences in the ethnic background, clinical subtypes of the patients groups, and normal limits used. Since I have chosen only the classic cases of CIDP, the selection bias cannot be excluded.

Disclosure: Nothing to disclose.

PP2234

Unusual and disabling neurological presentation of ANCA-positive small vessel vasculitis

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Introduction: PNS symptoms are usual on the course of ANCA-positive small vessel vasculitis. The commonest type of neuropathy is multiple mononeuropathy. A purely sensory axonal distal symmetric polyneuropathy is very rarely described.

Methods: We observed and followed a patient whose clinical case is described below. Furthermore, we reviewed the current scientific evidence and similar published clinical cases.

Results: Male, 54yo, who begins with paroxysms of dysesthesias on both legs and constitutional symptoms—anorexia, asthenia, weight loss, nocturnal sweeting and fever. He progressively deteriorated along $\sim$ 3mo. When observed on the ED by a Neurologist, his general status was visibly deteriorated; he was unable to stand up because of the excruciating pain on both soles. He was admitted and an extensive study excluded tumoral and infectious causes and revealed N/N anemia, elevated ESR, nephritic syndrome and positive ANA, ANCA anti-MPO, anti-SSa and anti-SSb. A skin biopsy demonstrated necrotizing angiitis and a kidney biopsy showed necrotizing and crescentic glomerulonephritis. An EMG confirmed a purely sensory axonal distal symmetric polyneuropathy.

He started immunosuppressive therapy with methylprednisolone 1 g/day for 3 days and afterward switched to oral prednisolone 1 mg/kg/day, with marked improvement of the neurological symptoms. Later on, cyclophosphamide was associated with good tolerance and additional relief of all symptoms.

Conclusions: The type of neuropathy observed on this case is rare among cases of systemic vasculitis. As described on the literature, neurological symptoms resolved promptly with the beginning of immunosuppressive therapy. An early onset of therapy is essential in order to prevent possible sequelae.

Disclosure: Nothing to disclose.

PP2235

Characteristics of polyradiculoneuropathy patients—single center 10 years retrospective analysis

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Introduction: Polyradiculoneuropathy is a post infectious or immune mediated peripheral nerve disorder. It is a clinically heterogeneous group with either acute or chronic course, axonal or demyelinating, motor or sensory nerve damage. Acute forms are known under eponym Guillain-Barré syndrome (GBS). Relapsing or slowly progressive course is a feature of chronic inflammatory demyelinating polyneuropathy (CIDP). The aim of our study was to analyze clinical features, laboratory characteristics (cerebrospinal fluid, antiganglioside antibodies), electrophysiological findings and patients' outcome.

Methods: Our hospital database was searched from 2002 to 2012 for patients with GBS and CIDP and was analyzed according to our aim.

Results: Ninety-eight patients were included in our study, 76 (78 %) with GBS and 22 (22 %) with CIDP. Major characteristics are shown in Table 1. Sensory symptoms and pain were equally present in both groups; weakness and disability were more prominent in GBS patients. Six (6 %) patients had Miller-Fischer syndrome; 5 were tested for anti GQ1b and 4 were positive. Presence of antiganglioside antibodies was not related to bad outcome after 18 months (Modified Rankin Scale 4–6). Age $\geq$ 65 years and axonal damage were predictors of worse outcome after 18 months ($p = 0.026$ and $p = 0.04$, respectively). A need for ventilatory support was not related to bad outcome.

	GBS (n=76)	CIDP (n=22)
Mean age (range)	59 (20-85)	55 (23-83)
Male: female (ratio)	50/27 (1,85:1)	12/10 (1,2:1)
Preceding infection reported	59%	13%
Albuminocytologic dissociation present	60%	85%
Abnormal nerve conduction study	80%	100%
Areflexia or hyporeflexia	91%	88%
Anti ganglioside testing done	59%	59%
positive	33%	27%
Ventilatory support	11%	0%
Died	6 (8%)	1(4%)

Table 1. Major characteristics of GBS and CIDP patients.

Conclusions: Higher age and signs of axonal damage are bad prognostic factors in GBS. Antiganglioside antibodies screening might have some diagnostic but no prognostic value in GBS patients. Proper intensive care is needed to prevent additional mortality from complications of severe initial disability.

Disclosure: Nothing to disclose.

PP2236 Capillary tolerance test in diabetic neuropathy diagnosis

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Introduction: In Belarus diabetes affects 3,900 of every 100,000 people. Diabetic Distal Sensory Polyneuropathy (DDSPN) is a common diabetes complication. In 5 years after diabetes manifests, 12.5–14.5 % of patients are diagnosed with DDSPN (FIELD Study, 2012). Electroneuromyography (ENMG) is the gold standard for the clinical stage of DDSPN.

Methods: In 2010–2012, 249 patients were examined (male 179, female 70, average age 38 ± 13) with diabetes 2 (82 %) and 1 (18 %). Vibrational, tactile, temperature, and pain legs sensitivity were defined using ENMG. There was picked a group of patients (116 people) without clinical manifestations and without ENMG criteria of DDSPN (M-response n.Suralis 21 mV (±3). Capillary tolerance test (CTT) was performed before using ENMG. The test involved M-response registration in 30 min after 2.0 ml of Xanthinol Nicotinate injected intramuscularly.

Results: After the CTT performed, 73 patients had M-response drop to 13 mV (±3)—($p < 0.03$) which is typical for DDSPN (San Antonio single ENMG program, 1988). 12 months later, ENMG was repeated. 56 patients showed typical DDSPN signs without using CTT. 24 months later, 36 patients were diagnosed with DDSPN, which proves high sensitivity and specificity of CTT (95 and 75 % correspondingly ($p < 0.05$)).

Conclusions: CTT improves the ENMG diagnosing on the preclinical stage of DDSPN.

Disclosure: Capillary tolerance test improves the ENMG diagnosing on the preclinical stage of DDSPN.

PP2237

Abstract withdrawn

PP2238
The importance of early diagnosis and therapy with intravenous immunoglobulins in patients with multifocal motor neuropathy

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Introduction: The aim of the study was to evaluate the effect of intravenous immunoglobulins (IVIG) treatment on disease progression and quality of life in multifocal motor neuropathy (MMN) patients.

Methods: This study included patients with MMN who were diagnosed and treated in the period from 2000 to 2010. Initially IVIG therapy is administered at a dose of 0.4 g/kg for five consecutive days and then at 6–8 weeks in dose of 0.5–1 g/kg. After a period of at least 2 years, check-ups were carried out including: the assessment of muscle strength (MRCscor), electromiography (EMG) and assessment of quality of life (QoL) using the SF36 and INQoL questionnaire.

Results: Twenty patients with MMN were included, 14 men and 6 women. The mean age at onset was 39.5 ± 11.9 years and the mean duration of disease 9.3 ± 5.7 years. The delay of diagnosis was 2.9 ± 2.7 years. The mean duration of IVIG therapy was 5.0 ± 4.8 years. All patients had a significant reduction in MRC score at the control neurological examination in relation to the period of diagnosis but without statistical significance (70.54 ± 4.87 vs. 63.38 ± 13.94, $p > 0.05$). In EMG examination, higher axonal degeneration was observed as a sign of progression of the disease ($p>0.05$). QoL was not in association with disease duration, clinical and EMG parameters ($p > 0.05$).

Conclusion: The basic preconditions for a favorable outcome of the clinical course of MMN are early diagnosis and initiation of IVIG therapy immediately after making a diagnosis.

Disclosure: Nothing to disclose.

PP2239
Tafamidis treatment in a patient with transthyretin amyloidosis due to domino liver transplantation

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Domino liver transplantation (DLT) increase the number of grafts available to treat patients with liver disease. But, this procedure has a risk of transmission of systemic transthyretin (TTR) amyloidosis.

A 69-year old FAP male patient whose complaints started 8 years after DLT was evaluated because of numbness and burning sensation of feet and hands, walking difficulty, dizziness, diarrhea, dry mouth, urinary retention. His neurological examination showed distal weakness of all limbs with bilateral steppage gait, stocking and glove type hypoesthesia and hypoalgesia, diminished vibration sensation and absent tendon reflexes. According to these findings his clinical disease stage was classified as I and his neurological disability score (NDS)

68. EMG showed findings consistent with distal sensory motor axonal polyneuropathy accompanied by autonomic involvement. His sural nerve biopsy disclosed severe axon loss with amyloid deposition. He did not have any cardiac, renal or eye involvement due to amyloidosis. He refused to undergo a new liver transplantation and was put under treatment with Tafamidis Meglumine (Vyndaqel). He is still receiving the treatment that started 7 months ago. He became stable and his sensory symptoms showed slight improvement.

Although estimated time of de novo amyloidosis transfer risk is expected to be minimum 20 years, according to the literature patients can become symptomatic earlier than expected. Our patient's signs and symptoms started 7 years after transplantation. We do not yet know the effects of the Tafamidis treatment in these patients.

Disclosure: Nothing to disclose.

PP2240

Acute bilateral non-traumatic radial nerve palsy—rare presentation, uncertain etiology

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Introduction: Acute transient radial nerve palsies usually have a traumatic/compressive etiology. Occasionally, no such mechanism of lesion is verified and a bilateral presentation is even rarer.

Methods: We present a case of a 63-year-old female patient, observed at emergency department. Three days before, she had noticed left hand extension weakness, followed, in the next day, by right hand extension weakness. The establishment time in each side was brief (h). She had no other motor or sensory complaint. She had controlled hypertension and hypothyroidism, and used to have frequent artistic hobbies using lead-containing dyes and ceramics.

Results: Apart from bilateral wrist and fingers extension paresis (MRC 1–2/5), her neurological examination was unremarkable. Blood analysis, immunological studies, serologies, C-reactive protein and sedimentation-rate were normal or negative. The serum-lead levels were within normal limits; however urinary-lead levels were 91.73 μmol/day (normal 0.00–0.39). She performed neurophysiological tests, 15 days after palsy-onset: (i)nerve conduction studies were normal, including motor and sensory radial potentials; (ii)needle EMG revealed fibrillations and positive-sharp waves, at rest, and reduced number of motor unit potentials, during voluntary activity, in common extensor digitorum, braquioradialis and triceps muscles, bilaterally. She has avoided contact with lead-containing substances. Five months later, without any specific treatment, she was fully recovered.

Conclusions: This presentation is rarely described in the literature. Although serum-lead level was negative, the high urinary-lead level could suggest some pathophysiologic involvement of this metal, in this case. Additionally, an underlying genetic susceptibility or immunological condition cannot be excluded.

Disclosure: Nothing to disclose.

PP2241

Mona Lisa syndrome, or peripheral facial palsy occurring during pregnancy. Report of six cases and review of the literature

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Introduction: Mona Lisa syndrome is referring to the famous work of Da Vinci. The woman's enigmatic smile has been attributed to a sequel of peripheral facial palsy (FP), having occurred during pregnancy. The higher prevalence of FP in pregnant women is acknowledged since the first description of Charles Bell in 1830, however the mechanisms underlying this association are not fully understood. We present a series of 6 cases of FP occurring during pregnancy, their specific features, and a review of the literature.

Methods: case report, retrospective study and review of the literature.

Results: Of six patients presenting FP during pregnancy, two had diabetes, two were suspected of having a demyelinating disease, and two idiopathic FP. Although an increased risk of preeclampsia has been suggested in women with FP, no case was observed in our series. Recovery was good for all but one, but it is said that prognosis is worse in pregnant patients than in the general population. As usually described, FP occurred during the third trimester of pregnancy in all cases. At that moment, corticosteroids are generally not contraindicated, for the foetus. Fast diagnosis and subsequent treatment with corticosteroids are thus mandatory. The risk of recurrence of FP in a subsequent pregnancy is not known, but probably low.

Conclusions: During pregnancy, risk of FP increases, secondary causes are more frequent and recovery is poorer. Careful maternal and foetal surveillance and specifically blood pressure measurements is recommended for pregnant women who develop FP.

Disclosure: Nothing to disclose.

PP2242

Subcutaneous is better tolerate than intravenous immunoglobulin treatment: the experience with two CIDP patients

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Introduction: Treatment with intravenous immunoglobulin (IVIg) is commonly used in patients with autoimmune neuropathy with good results but may show adverse effects partially limiting its use. Here we report our experience with two patients showing chronic inflammatory demyelinating polyneuropathy (CIDP) treated with IVIg who needed to shift to subcutaneous immunoglobulin (SCIg) because of considerable adverse events.

Methods: The first patient was a 48-year-old man who started after CIDP diagnosis a 5 days of high dosage IVIg (0.4 mg/kg/die) and a maintenance IVIg cycle (3 days) every 4–5 months.The second patient was a 70-year-old man affected by CIDP starting IVIg at high dosage (0.4 mg/kg/die for 5 days). After the treatment neurological examination showed a motor and sensory improvement in both patients.

Results: IVIg although producing a significant improvement of neurological symptoms was stopped in both patients because of a disabling symptoms such as a "tension-type headache" limiting work activities in the first patients or a lower limb venous thrombosis with subsequent pulmonary embolism after the first IVIg cycle in the second patient. The shift to SCIG (Hizentra: 8 g/week) produced no change at the neurological examination compared to IVIg without any side effects after 8–12 months. Importantly after SCIG they reported an improvement of quality of life as evaluated by a short Form Health Survey scale (SF-36).

Conclusions: SGIG treatment was effective as such as IVIg but it was better tolerate without any relevant side effects and with higher quality of life.

Disclosure: Nothing to disclose.

PP2243

Posterior interosseous neuropathy—a diagnostic challenge

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Introduction: Posterior interosseous neuropathy (PIN) is most commonly caused by posterior interosseous nerve compression (by space-occupying lesions/Frohse's arcade tendinous hypertrophy) or trauma. Neuralgic amyotrophy (NA), multifocal motor neuropathy (MMN) and inflammatory/idiopathic etiologies are considered rare.

Case report: 63-year-old male, retired banker, right-handed, complained of sudden-onset weakness of right thumb extension/abduction. He denied trauma history, repetitive supination-pronation movements, local/cervical pain and previous vaccination/infection.

Medical history of Bell paralysis.

Objectively: Without wrist radial deviation or pain on elbow/forearm palpation.

Neurologic examination: paresis of right pollicis abduction/extension and index finger extension at metacarpophalangeal-joint (grade 3 and 4, respectively). Normal osteotendinous reflexes. Without atrophy/sensitive abnormalities.

Laboratory screening: normal. EMG: right radial compound-motor action potential (CMAP) amplitude (recorded in extensor indicis proprius (EIP)) was reduced. Without conduction blocks. Positive sharp-waves/fibrillations in extensor pollicis brevis (EPB), longus (EPL) and EIP, and incomplete recruitment-pattern on voluntary activation. Extensor digitorum communis was normal. Right-forearm MRI: Abductor pollicis longus (APL) and EPL hiperintensity, without nerve compression signs.

He received analgesic/anti-inflammatory medication and physical therapy, recovering in 3 months.

Discussion: We present a rare case of PIN involving the lateral branch that innervates EPB/EPL/EIP/APL muscles. A compressive/traumatic etiology was excluded. NA seems unlikely (painless, without atrophy or previous vaccination/infection), as well as MMN (without clinical/neurophysiological evidence of other conduction blocks, spontaneous remission). So, inflammatory/idiopathic appears as the most probable etiology. Hashizume et al. found 3 similiar simple nerve paralysis in 31 non-traumatic PIN cases. Peripheral mononeuropathies might be challenging, considering the complex clinical evaluation and diversity of differential diagnosis.

Disclosure: Nothing to disclose.

PP2244

Search for autoantibodies targeting the nodes of Ranvier in chronic inflammatory demyelinating polyradiculoneuropathy (CIDP)

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Introduction: Nodal, paranodal and juxtaparanodal proteins have been the focus of ongoing research as potential antigens in both central and peripheral demyelinating disorders. Antibodies against contactin-2, which assists in the formation of axonal connections, have been detected in multiple sclerosis patients (Derfuss, *PNAS* 2009; 106, 8302) and polymorphisms in the gene encoding contactin-2 may influence treatment response in CIDP (Iijima, *Neurology* 2009; 73, 1348). Cx32, which comprises gap junctions of the paranode, is also a potential target antigen in PNS demyelination as mutations in Cx32 cause Charcot-Marie-Tooth disease. Our objective was to examine whether CIDP patients harbour antibodies against antigens expressed at the nodes of Ranvier such as contactin-2/TAG1 and Cx32.

Methods: Sera from 45 patients with CIDP (with paired CSF samples from two), 5 with multifocal motor neuropathy (MMN), and 4 with combined CIDP and central demyelination (with paired CSF from one) were examined. We established a cell-based assay (CBA), in which human embryonic kidney cells were transfected with cDNA clones encoding either the FNIII or the IgC2 domains of TAG-1 or CX32, all tagged with eGFP. Antibodies against IgC2 and Cx32 were used as positive controls. Antibody binding was visualized using an anti-human fluorescent secondary antibody.

Results: No positive staining was detected in any of the patients with autoimmune peripheral neuropathies for both antigens.

Conclusions: Contactin-2 and Cx32, which is responsible for a genetic demyelinating neuropathy, are not autoantibody targets in aquired autoimmune demyelinating neuropathies. Reactivity to other nodal, paranodal or juxtaparanodal antigens is currently explored.

Disclosure: Nothing to disclose.

PP2245

Sensory mononeuritis: differences between pure neural leprosy and non systemic vasculitic neuropathy

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Introduction: Our aim was to determine the distinguishing features of two cases of sensory mononeuritis who presented with similar clinical, electrophysiological and past medical history features.

Methods: We systematically reviewed the clinical features, laboratory studies, neurophysiologic findings, and histopathological changes of two patients with sensory mononeuritis. In one, the final diagnosis was pure neural leprosy (PNL) and the other non-systemic vasculitic neuropathy (NSVN).

Results: Our patients were females who had resided in areas endemic for leprosy (Brazil). They both developed a progressive, purely sensory, painful mononeuritis distally in the lower limbs followed, in patient 1, by asymmetric ankle edema and nodular induration without skin changes. In both cases, sensory nerve potentials were asymmetrically reduced in amplitude, and sural nerve biopsy revealed nonspecific inflammatory infiltration of the vasa nervosum in the epi- and perineurium. An axonal neuropathy, granulomas with epithelioid cells and caseous necrosis were observed in patient 1 confirming paucibacillary PNL; a skin punch biopsy revealed similar changes. Multifocal axono-demyelinating changes in patient 2 were compatible with NSVN. Both patients improved following targeted treatment (rifampicin and dapsone in case 1 and rituximab in case 2).

Conclusions: Both patients were surprisingly homogeneous in their clinical and electrophysiological manifestations. Late appearance of edema and nodular induration in the vicinity of affected nerves, as well as, distinct pathological features with granulomas and caseous necrosis in skin or nerve biopsies appeared to be the cardinal features distinguishing PNL from NSVN.

Disclosure: Nothing to disclose.

PP2246

Guillain-Barré syndrome with acute psychotic disorder during therapy with PEG-IFN and Ribavirin for chronic hepatitis C—case report

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Introduction: The first line treatment for chronic hepatitis C is the combination of PEG-IFN and Ribavirin. There are a few reports of acute inflammatory demyelinating polyneuropathy (AIDP) as a neurological side effect of this therapy. Psychiatric side effects such as depressive disorders, panic attacks and mental status abnormalities are likely to appear during immunomodulating therapy but also in the course of AIDP.

Results: We report the case of a 59 years old woman treated with PEG-IFN and ribavirin for 21 weeks for a chronic HCV infection that developed Guillain-Barré Syndrome (GBS) and acute psychosis. The patient was admitted in our department with distal rapid progressive paresthesias in her arms and feet, associating weakness, numbness, as well as intense pain in her low thoracic spine region. The normal MRI scan of the spine, the modified conduction studies and the albuminocytological dissociation of the CSF were consistent for AIDP. The Pegasis and Ribavirin treatment was interrupted and the patient received intravenous Immunoglobulin G. In the first days of the treatment the neurological status aggravated to tetraparesis with bilateral Bell's palsy. More to that point she became agitated and experienced vivid dream and visual hallucinations. The neurological symptomatology improved in the following days and the mental status abnormalities resolved after neuroleptic treatment. She recovered partially, after 6 weeks of intense neurological rehabilitation.

Conclusions: We should acknowledge that the course of Guillain-Barré Syndrome could be atypical, especially during immunomodulating therapy for chronic HCV infection.

Disclosure: Nothing to disclose.

PP2247

Bi-brachial palsy (man-in-a-barrel syndrome) from acute demyelinating polyneuropathy associated with sarcoidosis

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Introduction: 5 % of sarcoidosis has neurosarcoidosis. Peripheral nerves are involved in 20 % of neurosarcoidosis. We present a case of acute demyelinating polyneuropathy associated with neurosarcoidosis resulting in bi-brachial weakness.

Case report: A 26-year-old man developed rapid onset of bi-brachial pain and weakness over 4 days. He could barely move his upper arms, forearms, and wrists, with minimal strength in the fingers (man-in-a-barrel). He had no other neurologic findings. The following were normal: CBC, serum chemistry, CK, viral hepatitis screen, heavy metals, ANA, RPR, HIV, lyme titer, and ACE. CSF showed glucose = 68 mg/dl, protein = 77 mg/dl, 1 WBC, 81 RBC; Albumin, IgG, and IgG index were marginally high, and no oligoclonal bands. NCV studies showed conduction slowing (26–42 m/s) and blocks in the upper-limb motor nerves with relative sparing of sensory nerves. He was treated with 5 days of IVIG with no improvement. Chest CT scans showed lymphadenopathies and biopsy revealed non-caseating granulomas and negative AFB consistent with sarcoidosis. He improved on high-dose prednisone and was able to raise both arms in 1 week, and in 3 months had 4/5 strength in the proximal muscles and 5/5 in the distal ones. Repeat NCV studies showed reversal of conduction blocks, although CVs remained slow.

Discussion and conclusions: This is an unusual case of neurosarcoidosis presenting like Guillain–Barre syndrome (acute demyelinating polyneuropathy) based on the clinical, electrophysiological, and CSF features. Except that it did not respond with IVIG treatment and improved dramatically with high-dose corticosteroids.

Disclosure: Nothing to disclose.

PP2248

A rare Guillain–Barre syndrome variant: facial diplegia paresthesia

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PP2249 Delayed diagnosis of neurogenic thoracic outlet syndrome: a case report

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PP2250

Melkersson-Rosenthal syndrome—case report

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PP2251

Clinical and nerve conduction studies of paraneoplastic polyneuropathies

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PP2252

Bickerstaff's encephalitis—case report of rare clinical variant

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PP2253

Guillain–Barre syndrome without compatible electromyography findings, presenting with bilateral facial paralysis

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PP2254 Demyelinating polyneuropathy with axonal loss and spastic paraparesis as a neurological manifestation of ovarian cancer—case report

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PP2255

Heterogeneity of peripheral neuropathy in chronic lymphocytic leukemia

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Spinal cord and root disorders

PP2256

A case of Sjogren's disease presenting with transverse myelitis

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Objective: Transverse Myelitis (TM) is a clinical syndrome in which an immune-mediated process causes neural injury to the spinal cord. We here reported a case of Sjogren's disease presenting with transverse myelitis.

Case report: 63-year-old female patient had a history of back pain, difficulty in walking, joint pain and dryness of the eye and the mouth for more than 9 months. In her MR imaging, transverse myelitis was detected between the right paramedian T6-T7 level.High dose steroid (1,000 mg/day) treatment was started and the patient was referred to our clinic. In her examination, she had paraparesia and hipoestesia at the legs dominantly at the right side. Schirmer test was 5 mm, tear break-up time was 5 s. Sjogren's disease was diagnosed by: RF and Anti La positivity, thoracic transverse myelitis, history of dry eye and mouth along with a positive Schirmer test, artralgias in small joints, morning tenderness and sicca sypmtoms. After three sessions of 1 g cyclophosphamide therapy, weakness and sensorial complaints had decreased in her follow up.

Discussion: TM may occur in patients with Sjogren's syndrome. CNS Sjogren's syndrome may present as acute transverse myelitis, regressive myelitis, Brown-Sequard syndrome, neurogenic bladder or lower motor neuron disease. TM appears to be the most frequent form of spinal cord involvement in CNS Sjogren's syndrome occurring in about 1 % of all patients with Sjogren's syndrome. Retrospective analysis has to be made to determine the real incidence or prevalence of TM in Sjogren's disease.

Disclosure: Nothing to disclose.

PP2257

Lumbar spinal cord fMRI during electrical stimulation of anterolateral leg

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Introduction: To determine the feasibility and reproducibility of lumbar spinal cord fMRI by electrical stimulation of anterolateral leg and to detect the possible characteristics of lumbar spinal cord fMRI activated areas and signal intensity changes.

Methods: All studies were performed at GE1.5T Signa MR, using an eight-channel abdomen coil for RF pulse transmitting and receiving. The skin on the anterolateral leg (L5 sensory dermatome) of twelve volunteers, which have no neurological disease, were stimulated by a electrical stimulator (intermittent pulse, frequency 20HZ) in this study using a single-shot fast spin echo sequence to detect fMRI activation based on SEEP effect. Block design was used as activation patterns, such as R_1–S_1–R_2–S_2–R_3–S_3–R_4. The imaging data were analyzed with SPM8.

Results: Spinal fMRI activation was found in the lumbar spinal cord in all volunteers (12/12). In the sagittal, activations were mainly located in L1 (10/12), T12 (12/12), T11 (10/12) vertebral level. In the axial, activations were mainly located in the simulative ipsilateral dorsal horn and slight activation were also been found in ventral horn and the contralateral dorsal area. The activation signal intensity changes varied widely ranging from 0.3 to 2.0 %, among subjects.

Conclusions: It is feasible to study the lumbar spinal cord fMRI based on SEEP effect using the 1.5T MR and a repetitive activation distribution ranged from L1 to T11 was detected in this study. However, further research is needed to prove the accuracy of activation and eliminate the false activations surround the spinal cord causing by CSF pulsation.

Disclosure: Nothing to disclose.

PP2258 Necrotizing granulomatous polyradiculitis—an unusual presentation of neurosarcoidosis?

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Introduction: The approach to non-structural polyradiculitis represents a diagnostic challenge. It demands an extensive workup for infectious, inflammatory and neoplastic disorders, occasionally requiring a nerve-biopsy. Necrotizing granulomatosis (NG) is a histopathological pattern found in micobacterial/fungal infections, some forms of vasculitis and rarely in sarcoidosis.

Case report: 50-year-old man presented a 5-month progressive bilateral (left-predominant) inferior limb weakness, obstipation, erectile dysfunction and urinary retention. Neurologic examination: areflexic flaccid paraparesis, unable to walk without bilateral-assistance. Spinal-MRI: lumbosacral-root with contrast-enhancing areas of aglommeration and thickening. Laboratory screening: normal (including angiotensin-converting enzyme/serum calcium/immunological study/HIV). CSF: lymphocytic pleocytosis (27cells), hyperproteinorrachia (298 mg/dL), negative bacterial/micobacterial/fungal cultures and negative Borrelia burgdorferi/herpes virus-1,2/cytomegalovirus/Epstein–Barr/Micobacterium tuberculosis PCR. Repeated cytometry analysis: few small lymphocytes. EMG: asymmetric lumbar polyradiculopathy. Thorax/abdomen/pelvis CT-scan: normal (including high-resolution thorax CT-scan). He started corticosteroids with progressive recover. Spinal-MRI was repeated revealing normal features. After a 6-month tapering, treatment was suspended. However, symptoms/MRI abnormalities relapsed after 6 months and a lumbosacral-root biopsy was proposed, disclosing a NG. Corticosteroids were again effective and azathioprine was started as corticosteroid-sparing agent.

Discussion: We present a recurrent corticosteroid-responsive lumbar polyradiculitis.

The diagnosis remains uncertain. An infectious etiology was excluded and vasculitis seems extremely unlikely (without systemic involvement/negative immunologic study).

Neurologic involvement in sarcoidosis is well-known. Our patient hasn't symptoms/signs of systemic sarcoidosis, nonetheless neurosarcoidosis may precede this diagnosis in up to 74 % and persists an isolated manifestation in 10–17 % patients. Literature review found few neurosarcoidosis cases with NG histopathology. So, according to Zajicek criteria, this case may represent a possible neurosarcoidosis.

Disclosure: Nothing to disclose.

PP2259
Endovascular treatment of cervical intramedullary arteriovenous malformation—case report

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PP2260
Subarachnoid hemorrhage secondary to spinal arteriovenous fistula. Case report

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PP2261
A Bickerstaff's brainstem encephalitis case report: rapid responsive to IVIg and corticosteroid therapy

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PP2262

Abstract withdrawn

PP2263
Spinal cord compression revealing AL amyloidosis: a case report

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PP2264
Relationship between the Sit-to-Stand Test and lower extremity muscle strength in ambulatory patients with incomplete spinal cord injury

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PP2265
Subacute combined degeneration in a patient with anti-gastric parietal cell antibody

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PP2266
Chronic pain and blood serum glycosaminoglycan levels in patients with syringomyelia treated with combination of ceruloplasmin, oxymethyluracil and "Alflutop"

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PP2267
Electrophysiological and histological changes of paraspinal muscles in idiopathic scoliosis

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PP2268
Idiopathic acute longitudinally extensive transverse myelitis and peripheral axonal motor neuropathy in 37-year old woman

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Cerebrovascular diseases 3

PP3001
Early discirculatory manifestations in patients with internal carotid artery stenosis

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PP3002
Lacunar infarcts—clinical and imaging correlations

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PP3003
Wallenberg syndrome caused by brainstem cavernoma

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PP3004
Disorders of arterial and venous circulation of the brain in the patients with antiphospholipid syndrome (APS)

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PP3005
Factors predicting progression of malignant brain edema in middle cerebral artery infarction using computed tomography angiography images

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PP3006
Life style and delayed hospital arrival in Korean stroke patients

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PP3007
Occlusion of artery of Percheron presenting as acute alteration of level of consciousness

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PP3008
Features of epileptic seizures in a hemorrhagic stroke

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PP3009
Combined intravenous and intraarterial thrombolysis for acute basilar artery occlusion: the Cypriot experience

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PP3010
Clinical and radiological characteristics of insular involvement in acute middle cerebral artery infarction

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PP3011
Long-term survival rate for ischemic stroke with hemorrhagic transformation according to the type of hemorrhage

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PP3012
Cerebrovascular impairment in hematological patients

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PP3013

Abstract withdrawn

PP3014
A case of incidental dolichoectasic vertebrobasillar artery

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PP3015
Association of genes ACE and NOS3 in pathological brain vascular deformations

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PP3016
Polymorphism D/D of gene ACE as the risk factor of the stroke in the cerebral vascular anomalies

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PP3017
Development of new prognostic model for predicting early lethal outcome after acute ischemic supratentorial stroke using clinical parameters and parameters of quantitative electroencephalography

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PP3018
Severe acute hypertensive response is associated with poor functional outcome 3 months after ischemic stroke

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PP3019

The effect of ouhyul herbal acupuncture point injection on central post-stroke pain: a case series

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PP3020

Occlusion of the Percheron artery; acute bilateral paramedian thalamic and mesencephalic infarcts

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PP3021

The role of preexisting migraine in the acute stroke presentation

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PP3022

The role metalloproteinase gene (MMP-3, MMP-9) in the development of pathological strains cerebrovascular patients with cephalgic syndrome

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PP3023

Glycosylated hemoglobin—a modifiable risk factor for stroke

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PP3024

Correlation of cerebral hemodynamic changes and neurological symptoms in patients with high grade internal carotid stenosis

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PP3025

The incidence of hyperglycemia in stroke patients—stroke unit Banjaluka

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PP3026

Stroke in young adults

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PP3027

Proinflammatory cytokine markers for prediction of ischemic stroke

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PP3028 Functional outcome after deep spontaneous intracerebral hemorrhage

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PP3029

Prehospital stroke scale including atrial fibrillation (TOPSPIN) can be useful to distinguish ischemic stroke from cerebral hemorrhage in Japanese severe stroke patients

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PP3030

An atypical case of deep cerebral venous thrombosis

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PP3031

The content of biogenic amines in the blood serum and the content 2,3-diphosphogliceratis in erythrocytes in young patients with spondylogenic vertebrobasilar insufficiency

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PP3032

Abstract withdrawn

PP3033

Abstract withdrawn

PP3034

Analysis of the 63 patients with cerebral venosus thrombosis in a Territory center in Istanbul

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Child neurology 2

PP3035

Rare presentation of subacute sclerosing panencephalitis: an acute fulminant course

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Introduction: Subacute sclerosing panencephalitis (SSPE) is a progressive disease characterized by mental–neurological deterioration and myoclonus, occurring after years of measles infection. We present an atypical SSPE case, started with acute confusion and showed unusual radiological features.

Case: A 10-year-old previously healthy girl addmitted with headache and constant sleepiness for a week. She has a history of measles infection by the age of 9 months. She was lethargic and plantar reflexes were bilaterally indifferent. Systemic examination and biochemical evaluation were not remarkable. Brain magnetic resonance imaging (MRI) showed hyperintense lesions extending from brain stem into the cerebellar white matter. Cerebrospinal fluid examination showed 41 mg/dl of protein, 57 mg/dl of glucose (plasma glucose: 117 mg/dl), positive oligoclonal bands and IgG index >0.7. Her electroencephalography revealed disorganized background and generalized slow waves. CSF measles antibody titers were strongly positive. Intravenous (IV) metilprednizolone was given for 5 days. Because of no significant clinical response the treatment was switched to IV immunoglobuline. Following MRI showed extention of previous lesions. On the 4th week of presentation myoclonus began, the patient developed sudden cardiac arrest and died.

Conclusion: Acute fulminant course and involvement of brainstem and cerebellum is rare in SSPE. Differential diagnosis may be difficult from acute confusional states. Measles serology may be useful in the management.

Disclosure: Nothing to disclose.

PP3036 Risc factors for children's epilepsy in the Republic of Moldova

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Introduction: The goal of this study was to identify the major risk factors for epilepsy in children with epilepsy in the Republic of Moldova.

Methods: A total of 108 cases, in children aged 1–36 months were followed for epilepsy at the Pediatric Neurology Department during 2009–2012 and a control group of 108 children were included in the study. The most important examined risk factors examined were perinatal encephalopathy, febrile seizures, family history of epilepsy, arterial hypertension during pregnancy, head trauma, central nervous system infections. Data were obtained through a questionnaire, via personal interviews and the medical records and were assessed using univariate and multivariate analysis.

Results: We observed an increased risk for epilepsy in children with severe neonatal encephalopathy (OR 28.95, 95 % CI 3.8319–218.7607), CNS infection (OR 22.84, 95 %CI 2.9986–174.0101), severe head injury (OR 20.36, 95 % CI 2.1254–163.0101), presence of maternal hypertension during pregnancy (OR 13.56, 95 %CI 3.1011–9.2773), with a history of atypical febrile seizure (OR 11.31, 95 % CI 2.5652–49.9060), history of epilepsy in first, second or third-degree relatives (OR 6.54, 95 %CI 1.9930–265436).

Conclusions: The most important risk factors for epilepsy identified in this study were perinatal encephalopathy, history of atypical febrile seizures, severe head injury, CNS infection. Other identified important risk factors were a history of epilepsy in the family and maternal hypertension during pregnancy.

Disclosure: Nothing to disclose.

PP3037

Cavernoma-related epilepsy in children—questions regarding its approach and follow-up

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Introduction: The estimated incidence of cerebral cavernomas in children is 0.37–0.53, slightly inferior to adults. Epileptic seizures are the most frequent presentation and recurrence risk is high.

Results: Three previously healthy male children, aged 4–9 years-old, without family history of epilepsy or cerebral cavernomas. Admitted for a first focal epileptic seizure, single in two cases, recurrent in the other. Neurological examination was normal. Brain MRI showed a large isolated supratentorial cerebral cavernoma, with the following locations: right medial frontal-basal, left cortical parietal–occipital and right cortical-subcortical precentral, two with recent haemorrhage. They were started on antiepileptic drugs (AED) and underwent surgical resection 1–3 months after diagnosis. Afterwards, there were no deficits in the neurological or cognitive evaluations and maintained seizure freedom. In all cases, subsequent brain MRIs didn't show lesion regrowth or new lesions. The children with right frontal-basal cavernoma and left parietal-occipital cavernoma have a seizure-free follow-up of 7.5 years, the first currently without AED for 2 years and the second under discontinuation. The child with right precentral cavernoma has a seizure-free follow-up of 3.3 years, maintaining AED.

Conclusions: In the published series, the proportion of patients with cavernoma-related epilepsy who remain seizure-free after surgery is high. However, cavernomas are not static lesions. The three aforementioned children had a favourable outcome, without new lesions or seizure reoccurrence. In children, for whom long-term cognitive effects of AED are particularly significant, the fundamental question is identifying predictors of good clinical

outcome in these lesions, to support decisions regarding AED discontinuation.

Disclosure: Nothing to disclose.

PP3038

An adult Joubert syndrome case orginated from Western Anatolia

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Introduction: Joubert syndrome (JS) is a rare autosomal resessive disorder charactarized with cerebellar vermis a/hypogenesis with molar tooth malformation. Discussion of poorly known features of cerebellum is aimed with this presentation related with an adult JS case.

Case: A 54 years old woman was admitted to our outpatient clinic with forgetfulness complaint. She was cooperated and oriented but she had puerile behaviour pattern and she was answering the questions "peripherally". The left handed case had self mutilation scars on both forearms and had a replacement eye on right. Pes cavus was observed, more prominent at the right side. She had retinitis pigmentosa in left eye and had a oculomotor dysmetry. No pathologic reflex was obtained and locomotor system evaluation was normal exept a moderate dysdiadokinesia in cerebellar tests. Cranial MRI revealed cerebellar cortex dysgenesis and cerebellar vermis agenesia with molar tooth malformation and were considered as consistent of an adult JS.

Conclusions: Identification and recognization of defective cerebellar developmental pathology may enlighten the poorly known functions of this 'mysterious structure' as its reflections to the human behaviour.

Disclosure: Nothing to disclose.

PP3039

The role of ciliary neurotrophic factor (CNTF) in the treatment of specific developmental motor disorders in infants

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Introduction: In light of current research data we assessed the role of CNTF in the treatment of specific developmental motor disorders in infants.

Methods: Forty-nine infants aged between 1 and 12 months presenting specific developmental motor disorders of different degree of severity (study group) and 15 healthy children were investigated. The study group patients were administered CNTF medication (Italian company—Guna). We assessed serum levels of CNTF before and after treatment using the immunoenzymatic method.

Results: Our results are in line with research data and suggest a relationship between the serum concentration of CNTF and motor disorders in infants. We observed significantly lower serum levels of CNTF in patients with severe motility abnormalities in comparison to the control group ($p < 0.05$), but the difference between control group and infants with mild disorders hasn't reached the significance level. Moreover, we observed a significant increase of the serum concentration of CNTF in the study group after the treatment, but it remained lower in comparison to the control group.

Conclusions: Our results suggest a relationship between the serum level of CNTF and the severity of the motor disorders in infants. Furthermore, our results show an augmentation of serum levels of CNTF after the administration of the CNTF medication. We suggest that CNTF has an important role in the survival of the motor neurons and the maintenance of the muscle fibers trophicity in infants with neurological problems. Further studies should investigate clinical aspects and prevention effects of neurotrophic factors in cerebral palsy.

Disclosure: Nothing to disclose.

PP3040

Structure and clinical features of 56 children with developmental and benign movement disorders

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Introduction: Developmental and Benign Movement Disorders (DBMD) are characterized by the absence of associated neurological manifestations and by their favorable outcome. We analyzed structure and clinical features of DBMD cases among children evaluated in Tashkent Children Medical Consulting Diagnostic Centre.

Methods: Children up to 10 years with normal neurologic and psychomotor development were recruited from our center. Neurological examination, detailed history taking, video monitoring were performed. We excluded children with abnormal interictal or ictal EEG, abnormal MRI findings.

Results: 56 patients (32 male) were diagnosed with DBMD. The median age of admission was 16 months. 32 cases (57 %) started within the first year of age. The diagnosis showed a wide spectrum of DBMD including stereotypic movements 12/56 (21.4 %); benign myoclonus of early infancy 7/56 (12.5 %); sleep-related rhythmic movement disorders 6/56 (10.7 %); benign neonatal sleep myoclonus 6/56 (10.7 %); benign jitteriness of newborns 5/56 (9 %); gratification behavior in early childhood 5/56 (9 %); Sandifer's syndrome 4/56 (7.1 %), transient dystonia of infancy 3/56 (5.4 %); benign paroxysmal torticollis 3/56 (5.3 %); mirror movements 1/56 (1.8 %), shuddering attacks 2/56 (3.6 %); spasmus nutans 1/56 (1.8 %); paroxysmal tonic upgaze 1/56 (1.8 %).

Conclusions: Predominance of stereotypies (21.4 %) and benign myoclonus of early infancy (12.5 %) were revealed in structure of DBMD. Recognition of DBMD depends from careful neurological examination, detailed history taking, and video EEG recordings. The differential diagnosis of DBMD from epileptic seizures is crucial for correct management of DBMD, to avoid unnecessary concern and costly investigations.

Disclosure: Nothing to disclose.

PP3041

Early postoperative neurological complications in patients with congenital heart disease

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Introduction: Identify a variety of neurological complications in patients with CHD in the early postoperative period.

Methods: We studied 53 (100 %) children operated in the research center in the department of surgery for congenital heart defects. Children surveyed were between the ages of 3 to 5 years. Of these, 23

(43 %) of girls and 30 (57 %) boys. In the early postoperative period, all children underwent a thorough neurological examination.

Results: The most significant group consisted of patients with cerebral hypoxia, due to the long artificial circulation (AC)—15 (28 %) cases. In 2 (3.7 %) patients with fatal intraoperative brain damage (after the accident during AC) had complete areflexia, quadriplegia, no pupil reaction to light, EEG straight line. All the patients died during the period from 16 h to 2 days. Paresis (no movements in the limbs of varying severity)—4 (7.5 %) cases. Violations by the peripheral nervous system was observed in 12 (22.6 %) patients: Horner's syndrome—7 cases, the peroneal nerve neuropathy—3 cases; hypoglossal nerve damage—2 cases. Expressed vegetative symptoms (tachycardia, sweating, hypertension) 12 (22.6 %) cases. Long term awakening after anesthesia—8 15 %) cases.

Conclusions: The frequency of CNS complications give rise to social and economic consequences, which if severe can negate the success of operations.

Disclosure: Nothing to disclose.

PP3042

Transcranial direct current stimulation in the treatment of the attention deficit hyperactivity disorder (ADHD) in children aged 7–12 years old

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Introduction: ADHD is a prevalent neurodevelopmental disorder. Pharmacological treatment of ADHD may be associated with a range of serious adverse effects (seizures, psychotic symptoms, cardioiovascular events), so non-pharmacological treatment without adverse effects is needed to develop. Transcranial direct current stimulation (tDCS) is a non-invasive technique for brain stimulation and it increasingly being used in the treatments of some neurological disorders.

Methods: With tDCS, cortical neurons excitability increases in the vicinity of the anodal electrode and suppressed near the cathodal electrode. There is EEG and neuropsychological evidence that ADHD is associated with hyperactivity in right and left dorsolateral prefrontal cortex (DLPFC), in right and left frontal cortex (FC), in left anterior temporal region (ATR). tDCS has a potential in facilitating inter- and intra-hemispheric balance.

Results: We investigated the efficacy of the method tDCS by proof assay and by EEG processed by method of transitional probabilities one EEG wave by another on the symptoms of ADHD comparing the data before and after the treatment. 70 children with ADHD were included in this study. All subjects completed the tDCS for 25–30 min/day 2–3 times a week for 2.5 weeks. A tDCS protocol is proposed applying anode electrodes over the most problem zones of the brain (right FC,right DLPFC, left ATR).

Conclusions: By treated of such tDCS protocol alleviated the symptoms of ADHD and improved executive functions and general condition in children with ADHD for a long period of time (6–18 month) without any adverse effects (in catamnesis data).

Disclosure: Nothing to disclose.

PP3043

Seizures in hemorrhagic stroke of the young children

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Introduction: One of the features of childhood stroke in general, is manifest vascular accident as seizures. According to some authors, in patients with hemorrhagic stroke is dominated by boys, although no explanation for this fact.

Methods: We analyzed 150 children 89 (59.3 %) boys and 61 (40.7 %) girls who had a stroke at an early age. Hemorrhagic stroke was 90 (60 %), which 65 of them (72 %) children experienced seizures.

Results: Age when there was a hemorrhagic stroke: 0–29 days—40 %, 30 days–3 months to 45 %, from 3 to 6 months—4.6 %, from 6 to 12 months—7.5 %, from 12 months to 3 years—2.9 %. The main causes of hemorrhagic stroke: DIC 44 %, a combination of viral infection with DIC 20 %, viral infection, 12 %, CNS malformation 9 %, traumatic birth 9 %, blood diseases 6 %. When analyzing children convulsions were observed during the acute period of hemorrhagic stroke was 39 (60 %), which have led to 45 % of symptomatic epilepsy. Earlier onset of seizures peaks within 24 h after stroke 30 (46 %), late onset of seizures peaks in the 6–7 years-14 (21.5 %).

Conclusions: Can conclude that the severity of the neurological deficit, seizure type, localization of epileptic focus affect the overall outcome of stroke. Development of symptomatic epilepsy creates additional complexity and reduces stroke rehabilitation potential patient that affects the timing of treatment.

Disclosure: Nothing to disclose.

PP3044

Headache in Russian adolescents: frequency, structure according international classification of headache disorders-2nd edition (ICHD-II) criteria, and age-gender differences

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Introduction: Data regarding the headache frequency and structure according to ICHD-II in Russian adolescents are very limited and have been never published in international medical journals as reported by PubMed searching.

Methods: 1012 urban Siberian (Krasnoyarsk, Russia) adolescents aged 12–18 years were asked about headache frequency and 267 randomly selected adolescents were examined by specially trained neurologist to diagnose the headache subtypes (12 month prevalence). Based on ICHD-II criteria, a classification of migraine and tension-type headache (TTH, including the subtypes "infrequent episodic TTH, frequent episodic TTH, chronic TTH") were given. Yates-corrected Chi square test was used.

Results: Headache frequency was higher in girls, than in boys (Table 1).

Table 1. Headache frequency and gender related differences in Russian adolescents (in %, n=1012)

QUESTION	ANSWER					
How many times did you experience a headache in the past year?	Never		< 10 times		> 10 times	
	Male	Female	Male	Female	Male	Female
	26.5	14.1*	56.6	56.0	16.9	30.0*
Over the past 3 months, how many days per month did you experience a headache?	1 day or Never		2-15 days		> 15 days	
	Male	Female	Male	Female	Male	Female
	77.1	63.4*	21.2	33.6*	1.8	3.0

* – male-female $p<0.05$

According ICHD-II criteria one or more types of headache were diagnosed in 75.3 % (201/267) adolescents: TTH in 43.8 % (infrequent episodic TTH—36 %, frequent episodic TTH—5.2 %, chronic TTH—2.6 %), migraine in 13.5 % (without aura—8.6 %, with aura—4.9 %). Mixed type of headache (in subjects fulfilling the diagnostic criteria for both probable migraine and probable TTH) was diagnosed in 16.1 %, secondary headaches (mainly post-traumatic)—in 1.9 %. The age related differences have been found for migraine only (9.3 % in 12–14 age vs. 22.0 % in 15–18 age, $p = 0.009$). No gender related differences have been found in the ICHD-II diagnosed headache prevalence (including migraine), probably, because of low statistical power.

Conclusions: Headache is high in Russian adolescents and its structure has no principal differences between previously reported worldwide data.

Disclosure: Nothing to disclose.

PP3045
Intermittent diazepam versus continuous phenobarbital to prevent recurrence of febrile seizures: a randomized controlled trial

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PP3046
Neurobehavioral performance in novel object recognition test in mice which were exposed during whole gestation to different doses of valproic acid

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PP3047
Role of oral myorelaxants in complex therapy of children with cerebral palsy

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PP3048
Pseudotumor cerebri revealing aldosterone-producing adrenal adenoma

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PP3049 New diagnostic technology in the prediction and evaluation of effective treatment of newborns with hypoxic brain lesions

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Cognitive neurology/neuropsychology

PP3050
A double dissociation in virtual reality based episodic memory abilities: case studies of two adolescents with medial temporal and frontal brain lesions

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Introduction: Episodic memory (EM) has both retrospective (RM, recalling past specific actions in their context) and prospective (PM, remembering to accomplish specific future actions) components that undergo a gradual development. Standard EM tests usually do not evaluate all its aspects, potentially lacking sensitivity. Also, no study seems to compare RM and PM with the same material. Our aim was to explore RM and PM abilities in a pathological developmental perspective using the same ecological but controlled and detailed experimental environment in virtual reality (VR).

Methods: Two patients (aged 12 and 15) with focal brain lesions in EM neural areas (medial temporal and frontal) underwent RM and PM VR tasks and a standard neuropsychological battery. Their scores were compared to 15 controls' results on the experimental tasks and to normative data on standard tests.

Results: While the patients' performance was normal on standard tests, a double dissociation appeared on the experimental tasks: the temporal patient had mostly normal RM but below the mean PM results whereas the frontal patient presented the inverse pattern.

Conclusions: It thus seems that EM development can be disrupted in case of a medial temporal (RM) and a frontal lesion (PM), suggesting differential implications of these brain regions. More patient studies with different ages but similar lesions are required to better understand pathological EM development patterns. Nevertheless, VR seems to be more sensitive than standard tools for revealing subtle EM deficits, potentially guiding decisions about the patients' medical treatment and cognitive rehabilitation.

Disclosure: Nothing to disclose.

PP3051

EEG markers in a sample of children with attention deficit hyper activity disorder

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Introduction: Recent studies demonstrated that children with Attention Deficit Hyper Activity Disorder (ADHD) have different Electroencephalographic activity compared to non ADHD children. In this study we aimed to find possible EEG markers for ADHD patients.

Methods: Sleeping Electroencephalography (EEG) was recorded for 39 children with ADHD and 17 children without ADHD of 5–8 years old. They were recruited from the outpatient child clinic in Ain Shams university institute of psychiatry, Cairo, Egypt. Subjects had no history of medical, neurological or IQ abnormalities that might cause EEG changes. Analysis of the quantitative EEG data was done by 2 different methods. The first method aimed at finding and comparing the different rhythm in both ADHD and non ADHD groups using True Scan Deymed version 6.42software. The negative wave amplitude analysis was done using BESA EEG software version 11. Data was analyzed statistically with two-sided student *t* test for non-equal variance. Differences expressing $P < 0.05$ were considered significant.

Results: Results showed increase in the EEG theta activity in ADHD group compared to the control group. Moreover, we found statistically significant difference in the negative wave amplitudes at several frontal electrodes especially F10 ($P = 0.01$), F3, F8 and F9 ($P = 0.03$). However, negative wave amplitudes at other frontal electrodes showed no statistically significant difference.

Conclusions: Children with ADHD have prominently increased theta activity, more in the frontal areas and high negative wave amplitudes in many frontal EEG electrodes which may be used as markers for ADHD patients.

Disclosure: Nothing to disclose.

PP3052

Normative data for the Arabic version of the Mattis dementia rating scale

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The Mattis Dementia Rating Scale (MDRS) (Mattis, 1976; 1988), used in the assessment of general cognitive status, is considered as a very useful instrument for rating patients with dementia. The total score is 144. Our study aims to adapt and standardize the MDRS in the Moroccan population.

We translated and adapted the MDRS in colloquial Arabic, with 36 tasks grouped in 5 subscales (Attention, Initiation, Construction, Conceptualization and Memory) as in the original version and in the same order. 192 Moroccan subjects were included, in equal parity between genders, classified into 4 age groups (18–39, 40–59, 60–69, and 70 years and older) and three educational levels (3–6, 7–10 and 11 years and over). We excluded those having hearing and visual disorders, depression, psychiatric or neurological history, drug or alcohol abuse, hypertension or diabetes.

The average total score was 124.6 (SD 4.3) for all subjects. There were no significant differences between male and female. The average score was 126.8 (SD 4.3) in the first age group, 126.5 (SD 4.01) in the second, 124.3 (SD 4.2) in the third and 122.5(SD 3.7) in the fourth. Regarding the educational level, the average total score was, respectively, 119.3 (SD 4.9), 124.3 (SD 4.4) and 130.2 (SD 3.9). The subtests most affected by educational level were Initiation and Conceptualization.

Our study shows a negative influence of age and positive influence of educational level on MDRS performance. These normative data will be very helpful for neuropsychologists who test patients in Arabic language.

Disclosure: Nothing to disclose.

PP3053

Moroccan Arabic adaptation and standardization of the Free and Cued Selective Reminding Test

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The Free and Cued Selective Reminding Test (FCSRT; Grober and Buschke, 1987) remains the most relevant neuropsychological assessment for episodic memory impairment and its nature. To our knowledge, there is no Arabic adaptation of this test. Our purpose is to describe its adaptation and standardization in Moroccan population.

The sample of our study is composed of 170 normal subjects (88 men and 82 women). All the participants can read Arabic, have no neurological, neuropsychological, psychiatric or toxic history, and have a preserved cognitive functioning, as assessed by the Moroccan version of the Mini Mental State Examination (El Alaoui Faris et al., 2003). Subjects were equally divided between genders, and into 4 age groups (18–39, 40–59, 60–69, 70 years and older), with 3 education levels (3–6, 7–10, 11 years and over).

The global memory performance of subjects was 14.9 (SD 1.4) for the first total recall (TR) and 15.7 (SD 0.5) for the third. The total of the 3 TR was 47.1 (SD 1.1) in the first age group; 46.2 (SD 2.3) in the second; 45.7 (SD 2.1) in the third; 45.1 (SD 2.7) in the latter. This score was 44.9 (SD 2.6) in the first education level; 46.3 (SD 1.7) in the second; 47.2 (SD 1.2) in the third. There were no significant differences between men and women.

This study provides normative data of the FCSRT in Arabic. Our results show that memory performances decrease with advancing of age and increase with educational levels, with no significant influence of gender.

Disclosure: Nothing to disclose.

PP3054

Prediction of driving performance in patients with Parkinson's disease: preliminary findings on the role of the Comprehensive Trail Making Test

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Introduction: The Trail Making test (TMT) has been identified in several studies as predictor of driving skills in patients with Parkinson's disease (PD). Objective of the present work is to assess the capacity of an alternative version of the TMT, namely of the

Comprehensive Trail Making test (CTMT; Reynolds, 2002) to serve as predictor of driving fitness in patients with PD.

Methods: Inclusion criteria were the presence of a valid driver's license, regular car driving, a score equal to or less than 0.5 on the CDR, and a score between 1 and 3 in the scale of Hoehn & Yahr. A total of 11 patients with PD were introduced in the study. The collection of the data included: (a) a clinical, medical and neurological assessment, (b) extensive neuropsychological assessment, and (c) a driving simulation experiment.

Results: Very high correlations of certain subtests of the CTMT were observed with the average speed and speed variation that surpassed the correlations obtained with the classical TMT. Indicatively, CTMT-4 explained 82.3 % of the variance in average speed [$R^2 = .823$, $F(1,9) = 37.29$, $p < .001$] and 82.8 % of the variance in speed variation [$R^2 = .828$, $F(1,9) = 38.38$, $p < .001$]. Additionally, two subtests of the CTMT were significantly correlated with reaction time of the driver in unexpected incidents, while the classical TMT subtests did not.

Conclusions: Preliminary findings underscore the role of executive abilities in various measures of driving performance and support the usefulness of CTMT in the investigation of driving capacity in drivers with PD.

Disclosure: Nothing to disclose.

PP3055

Blood flow velocity changes in anterior cerebral arteries during cognitive tasks performance in left-handed subjects

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Introduction: Blood flow velocity (BFV) changes during cognitive activity can be recorded by transcranial Doppler ultrasonography (TCD) with great temporal resolution. BFV changes during mental activity were monitored primarily in middle cerebral arteries (MCAs) and mostly in right-handed subjects and little is known about these changes in anterior cerebral arteries (ACAs; Boban M, Crnac P, Junaković A, Garami Z, Malojčić B. Blood flow velocity changes in anterior cerebral arteries during cognitive tasks performance. Brain Cogn 2014;84:26–33.) and left-handed subjects.

Aim: To determine the effect of different cognitive tasks performance on mean BFV (MBFV) changes with hemispheric dominance assessment and to define the most suitable activation test for monitoring of MBFVs in ACAs in left-handed subjects.

Methods: Left-handed healthy subjects aged 20–26 were included in the study. Simultaneous recording of both ACAs were preformed during performance of cognitive tasks designed to activate frontal lobes: phonemic Verbal Fluency test (pVFT), Stroop test with incongruent stimulus and Trail Making tests (TMTA and TMTB) that were presented on a computer screen.

Results: During performance of all cognitive tasks, a statistically significant MBFV increase was recorded in both ACAs. Statistically significant left-sided dominance was found during TMTA. Additionally, the most significant MBFV changes was obtained during performance of TMTA.

Conclusion: Our results imply TMTA as the potential candidate for monitoring of ACAs in left-handed subjects.

Disclosure: Nothing to disclose.

PP3056

Correction cognitive impairment in patients with vascular brain damage

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Dementia develops within 6 months in patients with stroke in 4–6 % of cases.

Purpose: To study the efficiency of memantine hydrochloride in patients with cognitive impairment, which were developed for 2–3 months after acute cerebrovascular accident.

Methods: Cognitive impairment revealed by using a scale MMSE and the test of 10 words.

Results: Included 60 people, aged 47–78 years, which divided into 2 groups:

1 group (30 patients) received memantine hydrochloride by the scheme with basic therapy,

2 group (30 patients)—a control that received basic therapy.

In 1group prior therapy MMSE was 24.95 ± 0.66 points, after 1-month of treatment—28.14 ± 0.45 points, after 3-months—29.45 ± 0.19 points. In the control group before treatment score was 25.56 ± 0.52 points, after 1-month—26.32 ± 0.53 points, after 3-months—27.44 ± 0.27 points. In 1 group according to the test of 10 words before treatment—could play immediately 5.68 ± 0.35 words, and after 1-h—3.91 ± 0.48 words, after 1-month of treatment indicators were: 7.14 ± 0.35 words, deferred—6.36 ± 0.37 words, after 3-months—8.56 ± 0.33 words and 7.89 ± 0.37 words accordingly.

In 2group before starting treatment with this method, once able to reproduce 5.98 ± 0.46 words and deferred- 4.59 ± 0.24 words, after 1-month of treatment indicators were: 6.24 ± 0.15 words, deferred—5.06 ± 0.27 words, after 3-months—.05 ± 0.33 words and 5.78 ± 0.73 words accordingly.

Conclusion: The results show the efficiency of memantine hydrochloride in complex treatment of cognitive impairment in patients with acute (2–3 month after stroke), cerebral vascular events.

Disclosure: Nothing to disclose.

PP3057

Fear recognition impairment in autoimmune limbic encephalitis: a case study

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Introduction: Limbic encephalitis onset is characterized by memory deficits, disorientation, confusion and agitation. Temporal cortex and limbic structures, which are usually affected by the inflammatory process, have a prominent role in social abilities. Nevertheless, social cognition abilities are poorly explored in such patients. In particular, while negative emotion recognition deficit have been reported, cognitive and affective empathy are still unexplored.

Objective: To explore social cognition impairments and to underline possible neural correlates in a case of limbic encephalitis.

Methods: D.M., a 57-year-old male patient, underwent an in-depth standard neuropsychological battery exploring basic cognitive functions and social cognition abilities (i.e., emotion recognition, mental states attribution and empathy). Moreover, we analysed grey-matter (GM) volume using voxel-based morphometry (VBM) comparing D.M. with 20 healthy controls, matched for age and education.

Results: Neuropsychological evaluation highlighted a selective impairment of long-term verbal-auditory memory and a specific deficit in fear recognition measured with the Ekman 60-Faces Task. Other social abilities resulted unaffected. VBM analysis highlighted a GM volume reduction restricted to left temporal cortex (i.e., hippocampus and amygdala).

Conclusion: Our findings confirm previous data showing a selective impairment of fear recognition in limbic encephalitis patients, which seems to be crucially related to the left amygdala damage. We also provide novel evidence of a well preservation of empathy and cognitive/affective mental states attribution. Our study extends knowledge on cognitive disorders in limbic encephalitis, suggesting impaired fear recognition as neuropsychological signature of limbic encephalitis, together with the well-known mnestic deficits.

Disclosure: Nothing to disclose.

PP3058

A multimodal BCI for communication and assessment of consciousness in non-responsive patients

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In this publication we present a tool that uses three different Brain-Computer Interface (BCI) approaches: An auditory P300 approach, a vibrotactile P300 approach and a Motor Imagery (MI) based approach. The vibrotactile P300 and the MI based approaches can be used for both, the assessment of consciousness and communication with patients. The auditory P300 approach can be used only for assessment of consciousness. Figure 1 shows an overview of the system. The user wears an EEG cap with 16 electrodes, distributed to fit for all three BCI approaches. The laptop controls the paradigms, performs the signal processing and displays the results to the user. Three vibrotactile stimulators are used for the tactile P300 approach, earphones are used for the auditory P300. The cues that are needed for the MI approach are also played via the earphones. The vibrotactile approach was tested on a group of ten healthy users showing a grand average accuracy of 80 %. The MI based BCI was evaluated on a group of twenty healthy patients with an average accuracy level of 80.7 %. A recent study proved the feasibility of this approach for detection of awareness in vegetative state [1]. The feasibility of auditory P300 for cognitive assessment was also proved in previous studies [2, 3]. In future studies, all approaches of the device system will be validated on both: healthy users and patients.

Disclosure: Nothing to disclose.

PP3059

Visual memory binding in young versus older adults

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Introduction: Older age is associated with mild uneven decline of cognitive functions. Especially memory domain is vulnerable to aging due to functional and structural changes in the hippocampus. The aim of this study was to examine whether the hippocampus-specific memory binging test based on associative learning paradigm would be sensitive to visual memory binding impairment in older age.

Methods: 42 older adults (60–84 years old) without cognitive deficit on standard neuropsychological testing and without pronounced hippocampal atrophy on MRI brain scan and 24 young particicpants (20–24 years old) were tested with experimental computer test of visual memory binding, which required subjects to remember spatial positions and temporal orders of series of pictures in three successive levels of difficulty (with 3, 5 and 7 items). The Mann–Whitney *U* Test and ROC analyses where used.

Results: Older adults performed poorer on visual memory binding test compared to young participants. Specifically, older adults had lower scores in 3-item ($p = .020$), 5-item ($p = .049$) and 7-item ($p = .001$) subtasks than younger participants.The best discriminating power was found for the 7-item subtask ($AUC = 0.72 \pm 0.06$, $p = .002$), where the sensitivity was 80 %.

Conclusions: We found a visual memory binding deficit in adults 60 years of age and older. The visual memory binding test is a sensitive tool for detection of hippocampus-related cognitive decline in older age.

Disclosure: Nothing to disclose.

PP3060

Vascular risk factors and associated diseases, not focal brain lesions, determine deficits of reward-based reversal learning in acute basal ganglia stroke

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Introduction: Besides their motor function, the basal ganglia have been implicated in feedback learning. In patients with chronic basal ganglia infarcts, deficits in reward-based reversal learning have previously been described.

Methods: In a probabilistic feedback task, we examined reward-based learning in eleven patients with acute basal ganglia stroke (8 men, 3 women), aged 57.8 ± 13.3 years, which were compared with eleven healthy subjects of the same age, sex and education, which were recruited outside the hospital, and eleven hospitalized control patients of the same age, sex and education with similar vascular risk profile as stroke patients without stroke history.

Results: In a neuropsychological assessment 7 ± 3 days post-stroke, verbal and spatial short-term and working memory and inhibition control did not differ between groups. Compared with healthy subjects, control patients with vascular risk factors exhibited a significantly worse performance in the reward-based reversal task ($F[2,30] = 3.47$; $p = 0.044$; post hoc comparison between risk factor controls and healthy controls: $p = 0.030$), but not the acquisition ($F[2,30] = 1.01$; $p = 0.376$) and acquired equivalence ($F[2,30] = 1.04$; $p = 0.367$) tasks. In all three tasks, the performance of vascular risk factor patients closely resembled that of basal ganglia stroke patients. Correlation studies revealed a significant association of the number of vascular risk factors with reversal learning ($r = -0.33$, $p = 0.012$), but not acquisition learning ($r = -0.20$, $p = 0.121$) or acquired equivalence ($r = -0.22$, $p = 0.096$).

Discussion: The previously reported impairment of reward-based learning may be attributed to vascular risk factors and associated diseases, and not to focal brain lesions. This study emphasizes the necessity of appropriate control subjects in cognition studies.

Disclosure: Nothing to disclose.

PP3061

Physical, cognitive and emotional factors contributing to quality of life, functional health and participation in community dwelling in chronic kidney disease

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Background: Quality of life (QoL) impairment is a well-known consequence of chronic kidney disease (CKD). Factors influencing QoL and late life functional health are poorly examined.

Methods: Using questionnaires combined with neuropsychological examinations, we prospectively evaluated physical, cognitive and emotional factors influencing QoL, functional health and participation in community dwelling in 119 patients with CKD stages 3–5 including hemodialysis (61.5 ± 15.7 years; 63 % men) and 54 control patients of the same age without CKD but similar cardiovascular risk profile.

Results: Compared with control patients, CKD patients showed impairment of the physical component of QoL and overall function, assessed by the SF-36 and LLFDI, whereas disability, assessed by LLFDI, was selectively impaired in CKD patients on hemodialysis. Multivariable linear regressions (forced entry) confirmed earlier findings that CKD stage ($\beta = -0.24$; $p = 0.012$) and depression ($\beta = -0.30$; $p = 0.009$) predicted the QoL physical component. Hitherto unknown, CKD stage ($\beta = -0.23$; $p = 0.007$), cognition ($\beta = 0.20$; $p = 0.018$) and depression ($\beta = -0.51$; < 0.001) predicted disability assessed by the LLFDI, while age ($\beta = -0.20$; $p = 0.023$), male gender ($B = 5.01$; $p = 0.004$), CKD stage ($\beta = -0.23$; $p = 0.005$), stroke history ($B = -9.00$; $p = 0.034$) and depression ($\beta = -0.41$; $p < 0.001$) predicted overall function. Interestingly, functional health deficits, cognitive disturbances, depression and anxiety were evident almost only in CKD patients with coronary heart disease (found in 34.2 % of CKD patients). The physical component of QoL and functional health decreased with age and depressive symptoms, and increased with cognitive abilities.

Conclusions: In CKD, QoL, functional health and community participation are influenced by physical, cognitive and emotional factors, most prominently in coronary heart disease patients.

Disclosure: Nothing to disclose.

PP3062

The association between the Expanded Disability Status Scale (EDSS) and cognitive function in patients with relapse remitting multiple sclerosis

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Introduction: The Expanded Disability Status Scale (EDSS) is a widely used method of quantifying disability in people with multiple sclerosis (MS). Cognitive impairment occurs in about half of patients with MS but it is not known if the EDSS score is associated with cognitive function. We investigated the relationship between the EDSS score and neuropsychological tests in patients with relapse remitting MS who were about to start therapy with natalizumab.

Methods: Forty-eight patients with relapse remitting MS were enrolled in the study. Of them 31 (64.6 %) were women; mean age was 41.3 ± 10.0 years; mean disease duration was 11.0 ± 9.9 years; mean EDSS score was 4.0 ± 1.9. Two neurologists assessed neurological function and assigned the EDSS score. A clinical neuropsychologist administered a neuropsychological battery measuring attention, information processing speed, verbal and visuospatial learning and memory, word retrieval, visual perception and executive function.

Results: A higher EDSS score was significantly ($p < 0.05$) associated with lower performance on neuropsychological tests measuring information processing speed and executive function. There was no relationship between the EDSS score and tests measuring attention, verbal and visuospatial learning and memory, word retrieval or visual perception. All tests that were significantly related to the EDSS score required speeded use of hand except the Stroop Color-Word test which measures cognitive flexibility and response inhibition.

Conclusions: Our findings show significant associations between the EDSS score and measures of information processing speed and executive function but no association with measures of attention, memory or visual perception.

Disclosure: Nothing to disclose.

PP3063

Relationship between side of onset and number of spatial errors measured by Rey-Osterrieth complex figure test in Parkinson' disease

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Background: Asymmetry is one of the unique and mysterious features of Parkinson's disease (PD). Motor symptoms develop unilaterally either on the left (left dominant PD, LPD) or the right (right dominant PD, RPD). Incongruent data is available whether the side of onset has an impact on the cognition in PD.

Methods: Seventy-one non-demented, non-depressive and right-handed patients were categorized into RBD ($n = 36$) and LPD ($n = 35$) groups in a way that age, disease-duration, education-years, Unified PD Rating Scale scores and levodopa-equivalent dosages were balanced. Besides Addenbrooke Cognitive Examination, Montgomery-Asberg Depression and Mattis Dementia Rating Scales, and Rey-Osterrieth Complex Figure Test (ROCF) was obtained. For evaluation of ROCF, we applied both the Taylor's and Loring's scoring systems. Subsequently, we also performed subgroup analyses on patients having short disease-duration (≤5 years, 15–15 patients in RBS and LPD groups).

Results: The standard analysis of ROCF (Taylor's system) did not reveal any differences; however, the utilization of the Loring's system demonstrated that LPD patients made significantly more spatial errors than the RPD subjects (3,229 ± 1,646 vs. 2,229 ± 1,285 points, $p = 0.006$). Correlation between the number of spatial errors and the degree of asymmetry was highly significant ($r = -0.435$, $p = 0.001$). However, on PD patients having the maximum disease-duration of 5 years, we could not demonstrate any differences.

Conclusions: LPD patients make more visuospatial errors than the RPD subjects and the number of errors tightly correlates with the degree of asymmetry. However, this difference could not be demonstrated on PD patients having short disease-duration.

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PP3064
−2518 A/G polymorphism of the monocyte chememoattractant protein-1 (MCP-1) gene in Tunisian Alzheimer patients in relation to β-amyloid (1–42)

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Introduction: Inflammation of the central nervous system (CNS) (neuroinflammation) is now recognized to be a feature of all neurological disorders. It is characterized by the production of various molecules that initiate the recruitment of immune cells to the lesion sites, including in the brain. Monocyte chemoattractant proteins (MCPs) might play an important role in AD pathology through participating to the maturation of senile plaques or APP endocytosis.

Methods: In this study, we evaluated whether the MCP-1 (2518) polymorphism might be responsible for susceptibility to AD, utilizing a clinically well-defined group of 173 sporadic AD patients and 150 control subjects.

Results: The distribution of genotype and allele frequencies of the MCP-1 (−2518G/A) polymorphism did not differ significantly between AD and control groups ($p > 0.05$). Stratifying by ApoE genotype, gender or age at onset, no differences in both allele frequencies were observed.

Conclusions: Our results suggest that the A-2518G polymorphism in MCP-1 gene may not play a major role in the development of AD in the Tunisian population, but its presence correlates with lower levels of CSF Aβ42, which can contribute to increase the inflammatory process occurring in AD.

Keywords: Alzheimer's disease, MCP-1, Single nucleotide polymorphism, Aβ42

Disclosure: Nothing to disclose.

PP3065
Value of immunological factors in the forecast of consequences of acute period of pediatric stroke in children of early age

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Introduction: To study value of immunological factors in the forecast of consequences of a children's stroke.

Methods: Definition of the maintenance of pro-inflammatory cytokine (IL6) in blood serum at 18 children under 3 years in the acute period of pediatric stroke and control group of 10 healthy children of similar age was carried out. Method of determination of concentration of pro-inflammatory cytokina (IL6) in blood serum on the test to system of OChB SPb developed by State Research and Development Institute and based on "sandwich"—a method of three-phase IFA of the analysis.

Results: We examined 28 children, and 18 from them are children of general group and 10 are healthy children from control group. The age structure of the surveyed children were 39 % up to 1 month life, 17 % from 1 to 6 month, 33 % from 6 month to one year old, 11 % up to 3 years old.

Conclusions:

1. Extensiveness of the focus of lesions depending on level of proinflammatory cytoikines. The baby is infirm when he has a high level pro-inflammatory cytokines.
2. In children of early age during the acute period of stroke all-brain symptoms are prevailing over the focal.
3. The acute brain violations of brain blood circulation are more often observed at prematurely born children.

Disclosure: Nothing to disclose.

PP3066
Impairment of subtle language in patients with traumatic brain injury

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Introduction: Subtle language is in relationship with higher level knowledge and usage of language. It comprises of elements of semantics, metalanguage and pragmatics. Patients with traumatic brain injury (TBI) classically show fair recovery of basic lexical and syntactic disorders. However, subtle language has never been analyzed. Our aim was therefore to evaluate this language in TBI patients.

Methods: We included 44 patients having suffered a TBI, most often severe (GCS < 8). The mean time post-injury was 8.1 months. The subtle language was analyzed by 15 tests: definitions, evocation of names from definitions, sentence construction, synonyms, antonyms, polysemy, intruders, differences, figurative expression, proverbs, verbal logic, absurd sentences, procedural discourse, declarative discourse and argumentative discourse. There were three levels of difficulty in each subtest. Patient performance was compared to that of an equivalent (age, education level) group of normal control subjects.

Results: Multivariate analysis showed a significant ($p < 0.05$) overall deficit of patients, with preferential impairment of synonyms, antonyms, differences, proverbs, figurative expressions and verbal logic. But definitions and discourses were relatively preserved. The difficulty level had a definite effect in most subtests. These disorders correlated with the severity of deficits in conventional aphasia tests (verbal fluency, naming) and dysexecutive syndrome assessment (Trail Making Test), but not with episodic memory disorders.

Conclusions: TBI patients can present with subtle language difficulties, when basic language abilities are relatively preserved. These disorders could be promoted by the dysexecutive syndrome and require specific assessment and adapted care.

Disclosure: Nothing to disclose.

PP3067 Retest reliability of event-related potentials in unresponsive patients

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Introduction: Patients with unresponsive wakefulness syndrome (UWS) or in minimally conscious state (MCS) after severe brain injury show significant fluctuations in their behavioural abilities over time. Imaging techniques and event-related potentials (ERPs) are used to detect traces of consciousness even if clinical ratings imply UWS. In this study, we probed the retest-reliability (rr) of ERPs with repeated tests at 4 different time points.

Methods: 12 healthy controls and 12 inpatients (8 UWS, 4 MCS; 6 traumatic, 6 non-traumatic) were tested with an auditory oddball task (2 times per day [morning vs. afternoon)] for 2 days). This was

correlated with behavioural testing using the Coma Recovery Scale-revised (CRS-R). ERPs were recorded using a 256 channel EEG-system.

Results: 33 % of the controls and 12.5 % of the UWS patients showed a P300 four times; 16 % of the controls and 37.5 % of the UWS patients showed no P300. The rest showed detectable P300 responses between one and three times. Rrs amount to Krippendorff's $\alpha = .425$ for morning vs. afternoon and $\alpha = .245$ for day one vs. two in the patient group. Rr was strong for the CRS-R scores for all comparisons ($\alpha = .833$–.945).

Conclusions: The relatively low ERP rr implies that it is necessary to perform repeated tests when probing for consciousness. We suggest testing on two different days, once in the morning and once in the afternoon. Otherwise, a single negative test result may be mistaken for proof that a UWS patient truly is unresponsive.

Disclosure: Nothing to disclose.

PP3068

SHANK3 gene polymorphisms and schizophrenic patients in Tunisia patients

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Introduction: Schizophrenia (SCZ) is a severe and polygenic inherited disease. Recently, several studies Have Shown the involvement of the SHANK3 (SH3 and multiple ankyrin repeat domains protein) gene in the pathophysiology of schizophrenia, recent evidence indicates that the SHANK3 gene polymorphism may increase the risk of schizophrenia. This study was under taken to evaluate the association between single nucleotide polymorphism (SNP rs9616915, rs6010065) of the SHANK3 gene and genetic susceptibility to schizophrenia in the Tunisian population.

Methods: 147 schizophrenia patients and 149 control subjects were enrolled in this study. Two SNPs of SHANK3 were successfully genotyped by using PCR–RFLP.

Results: The distribution of genotypes and frequencies of rs9616915 and rs6010065 of SHANK3 exhibited no significant differences between patients and controls ($p < 0.05$).

Conclusions: Our results suggest that SHANK3 polymorphism may not play a major role in the development of schizophrenia in the Tunisian population.

Keywords: Schizophrenia; SHANK3; polymorphism; rs96169145; rs6010065

Disclosure: Nothing to disclose.

PP3069

Correlation of the Epworth scale with impaired memory evocation

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PP3070

Piracetam effectiveness in post stroke aphasia

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PP3071

Cognitive differences in minimal hepatic encephalopathy between alcoholic and viral compensated liver cirrhosis

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PP3072

Self-assessment of performance in cognitive testing: preliminary evidence of differences between healthy elderly and MCI patients

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PP3073

Anton syndrome due to a giant hypophysial adenoma

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PP3074

Cliniko-neurophysiologic features of cognitive disturbances in patients with hypertensive encephalopathy

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PP3075

Case study presentation of Marchiafava-Bignami syndrome—surprise final diagnosis discovery of seemingly clear and cut case

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PP3076

Charles Bonnet syndrome: a report of two cases

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PP3077

The neurocognitive effect of metformin treatment and diabetic diet on newly diagnosed type 2 diabetes mellitus patients

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PP3078
The relation between intentional and incidental memory in healthy young versus older individuals

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PP3079

Abstract withdrawn

PP3080
Does event-related potential P300 component predict memory recall?

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PP3081
QEEG based nonlinear analysis of physiological conditions for alcoholics: a preliminary study

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PP3082
The influence of poor sleep quality on the development of acute cognitive disorders in acute cardiac care unit patients

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PP3083
The effect of Cavinton on cognitive-mnestic function in patients with encephalopathy of different genesis

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PP3084
Predictors of progression in mild cognitive impairment: focused on comorbidity and medication use

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PP3085
Unawereness for cognitive and motor abilities in the left and right hemisphere stroke patients

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PP3086
Does stroke affect diabetes mellitus induced cognitive impairment?

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PP3087

Abstract withdrawn

PP3088
The effect of carotid artery stenting on cognitive function in patients with carotid artery stenosis: a prospective, 3 months follow-up study

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Critical care; neurotraumatology

PP3089
Delayed neurological complications after lightning injuries: results from a case series

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Introduction: Lightning injuries are a worldwide cause of disability and death. In Germany alone, every year about 30–70 people are struck by lightning. The lethality of lightning injuries is about 10 % and survivors often suffer from acute or delayed complications. While immediate effects of lightning injuries like cardiac arrest, impaired consciousness, and skin burns are frequent complications, less knowledge exists about delayed and long-term symptoms, in particular regarding the peripheral and central nervous system. On this background, our study presents neurological and neuropsychological long-term effects and complications occurring after lightning injuries.

Methods: We examined eight patients (5 male, 3 female) to 20 years at a point of time up to 20 years ago after their lightning strike in a cross-sectional study. Neurological examination, electrodiagnostic testing and a neuropsychological test battery were done.

Results: We found a consistent pattern of neurological and psychiatric disorders after lightning strike injuries. Affection of the central and peripheral nervous system and chronic pain syndrome were found frequently. In the long term, sequelae of lightning injuries often have a substantial effect on the quality of life, resulting in severe medical and social health problems.

Conclusion: In the long term, survivors of lightning injuries suffer from various neurological, psychiatric and social problems. Early diagnosis, classification and a long-term treatment of neurological symptoms are essential for these patients. Counseling and education can help to minimize negative impact with regard to the social dimension like social isolation or disability.

Disclosure: Nothing to disclose.

PP3090

Respiratory failure in the Neurology Intensive Care Unit (NICU)—diference between central (CNL) and peripheral motor neuron lesion (PMNL)

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Introduction: Respiratory failure, a severe complication in NICU, influences disease course, complications occurrence and ultimately leads to death. The aim was to compare mechanical ventilation (MV) duration, complications frequencies and survival rates between NICU patients who had a lesion of either CNL or PMNL.

Methods: A 1 year, single-center, retrospective observational study in NICU compared all the patients with respiratory failure treated by MV assigned in groups: 1-patients with PMNL and 2-patients with a CNL. We compared age, frequency of co-morbidities, Glasgow Coma Score (GCS) at the hospital and NICU admission, time until MV and MV length, complications frequency, length of NICU stay and survival rates.

Results: Group 1 had 17 patients (6 females), and group 2–15 patients (7 females). Group 2 had significantly lower mean GCS at the hospital and NICU admission (4.67 ± 2.3 vs. 14.6 ± 1.06, $p < 0.0001$), shorter length of time until MV initiation (1.1 ± 0.1 vs. 3.06 ± 3.54, $p = 0.03$). Group 1 had longer MV (20.0 ± 22.9 vs. 3.53 ± 5.33, $p = 0.01$), more frequent pneumonia ($p < 0.0001$), sepsis ($p = 0.016$) and hospital length (35.4 ± 26.6 vs. 4.1 ± 5.5, $p = 0.0001$). Worsening of neurological disease as an indication for MV was more frequent in group 1 ($\chi^2 = 12.7$, $p < 0.0001$). Neurological, somatic complications and co-morbidities at the time of the NICU admission were similar ($p > 0.05$). Mortality was significantly greater in group 2 ($p = 0.048$).

Conclusions: Patients in NICU with respiratory failure and CNL had lower GCS, but shorter MV and had greater mortality. Patients with PMNL had more infective complications, longer MV duration and both NICU and hospital length of stay.

Disclosure: Nothing to disclose.

PP3091

Pacemaker-induced pseudo-myoclonic status epilepticus following cardiac surgery for infective endocarditis in a young patient with rheumatoid arthritis and embolic cerebellar stroke

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Introduction: Neurological complications occur in about 5 % of all cardiac surgeries. Status epilepticus is even less likely to occur. We report the case of abnormal cardiac pacemaker-induced movements that were misdiagnosed as refractory status epilepticus following surgical treatment of infective endocarditis.

Methods: We report the case of a 38 y/o patient with infective endocarditis who developed abnormal cardiac pacemaker-induced movements that were misinterpreted as refractory status epilepticus.

Results: A 38 year-old male patient, with a previous history of rheumatoid arthritis, was admitted due to multiple peripheral emboli and a cerebellar stroke secondary to infective endocarditis with a moveable vegetation on the aortic valve. He underwent surgical removal of the vegetation and reconstruction of the valve, but had severe compromise of the conductive atrio-ventricular system, which prompted the use of a temporary cardiac pacemaker. In the immediate post-operative night, he presented with abnormal generalised movements that were interpreted as convulsive myoclonus. As Phenitoyn and Phenobarbital did not stop the 'seizures', the Neurology Service was called on the next day. On close examination, the abnormal generalised movements were rhythmic, including a side-to-side head jerk and abdominal contractions. As the rhythmicity was similar to the heart-rate, adjustments to the pacemaker programming were made and the 'seizures' subsided immediately (video segment). Further EEG had no clear epileptogenic activity. A few days later he died of multiple clinical complications.

Conclusions: We presented the case of pseudo-status epilepticus due to abnormal movements secondary to the use of a temporary cardiac pacemaker.

Disclosure: Nothing to disclose.

PP3092

Socioeconomic status doesn't influence the mortality rates in stroke patients—a nationwide population based research in Taiwan

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Introduction: Low socioeconomic status may be associated with higher mortality rate in the stroke patients. However, the mechanism behind the association and the influence with insurance plan are uncertain. Our study determined whether the patients with very low income were associated with higher mortality rates after stroke.

Methods: All the admitted stroke patients in one million beneficiaries data during 2005–2008 were identified from the NHI database. All patients were assigned to three groups based on mean income of Taiwan ($13529 in 2004 and $15276 in 2009) and categorized as the very poor, lower income (lower than mean income) or higher income (higher than mean income). The very poor patients were recognized by the special codes issued by our social welfare system with zero copayment for hospital admission. Multivariable analyses were performed to compare the in-hospital mortality rates for stroke patients.

Results: Overall 862 hemorrhagic stroke and 2133 ischemic stroke patients were included in the analysis. There was no significant difference in mortality rates in the two groups. Compared with the higher income group, the odds ratios of in-hospital mortality for the very poor patients in hemorrhagic stroke was 1.92 (OR = 1.92, 95 % CI 0.18–21.38). And the odds ratios of in-hospital mortality for the very poor patients in ischemic stroke was 1.45 (OR = 1.45, 95 % CI 0.15–14.13).

Conclusions: Compared with the others, the mortality rates in the very poor stroke patients have insignificant higher mortality rates under our insurance plan.

Disclosure: Nothing to disclose.

PP3093

Post-partum posterior reversible encefalopathy syndrome in a pre-eclamptic woman with twin pregnancy

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Introduction: Posterior reversible encefalopathy syndrome (PRES) is a serious neurological condition with various clinical manifestation. It is rare during pregnancy. We present a case of PRES in a 35-years-old female immediately after delivery two neonates with caesarean section. Patient was fully recovered.

Case report: A 35-years old primigravida with twin pregnancy underwent a cesarean section at 35 weeks gestation because of pregnancy-induced preeclampsia (hypertension, proteinuria, bilateral pedal oedema). Approximately 20 h after cesarean section occured a rapid decline of visual acuity. We clinically diagnosed cortical blindness. A computed tomography (CT) of the brain showed bilateral occipital hypodensity, CT angiography was without pathological findings. The patient was immediately shifted to neurological Intensive Care Unit (ICU). Magnetic resonance demonstrated hyperintensity (T2W2) in the occipital lobes and cerebral trunk. After delivery was patient normotensive. Subsequently after development of neurological symptoms increased BP of the patient to 200/110 mm Hg. With respect to clinical presentation and radiological reports, PRES was diagnosed and the patient was prompt treated with intravenous antihypertensive and magnesium sulphate. Visual acuity disappeared until 24 h, clinical symptoms didn't repeat, the clinical neurological examination was normal. The patient was discharged after 1 week with normal blood pressure due to oral antihypertensive medication.

Conclusion: Pre-eclampsia is predisposing factor for PRES in pregnancy. We report a case of uncommon post-partum PRES and focus the importance of early diagnosis and optimal critical care management.

Disclosure: Nothing to disclose.

PP3094

EEG patterns in patients with minimally conscious state and vegetative state

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Methods: 23 comatose patients investigated. Vegetative state (VS) and minimally conscious state (MCS) diagnosed. Patients evaluated by Glasgow Coma Scale (GCS). Coma recovered patients accessed by Disability Rating Scale (DRS). Etiologically coma was divided in 5 groups. EEG activity patterns detected by 16 channel EEG. Statistical analysis performed by SPSS 11.0.

Result: Among 23 VS-patients 9 evaluated as MCS. In 1st group From 6 VS-patients (GCS = 5) with theta EEG pattern 2 were defined as MCS, at 1 year one recovered (DRS = 14), one died. 4 patients defined at 1 year as PVS. Second group: 3 VS-patients (GCS = 5–7) with beta EEG pattern. 2 developed PVS, 1 patient defined as MCS and recovered (DRS = 18). 3rd group: 2 VS-patients with alpha EEG pattern (GCS = 6) died. 4th group: from 4 VS-patients (GCS = 5–7) with delta EEG pattern 2 defined as MCS. At 1 year 1 died and 3 developed PVS. 5th group: from 8 VS-patients (GCS = 5–8) 4 diagnosed as MCS, 4 with delta EEG patterns and 4 with theta EEG patterns. 4 VS-patients remained with delta EEG pattern. At 1 year 1 patient with MCS recovered (DRS = 11), 2 with MCS and 3 with VS died, 2 patients developed PVS. Correspondence analysis revealed that sound localization (Chi-sqr. = 31.10493; $p = 0.000001$) is significantly associated with EEG theta rhythm and with outcome. The high amplitude frontal and temporal lobe theta frequencies in MCS patients were strongly correlated with auditory long latency evoked potentials (p300) arising by binaural stimulation ($r = +0.47$; $p < 0.01$).

Conclusion: High amplitude theta frequencies in VS-patients where significant for favorable outcome.

Disclosure: Nothing to disclose.

PP3095

Abstract withdrawn

PP3096

Effects of low molecular weight hydroxyethyl starch on blood brain permeability and brain edema following traumatic brain injury in rats

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Introduction: Severe traumatic brain injury is one of the leading causes of death and disability in the United States. The urgent resuscitation administrated immediately after the primary injury could attenuate the mortality and morbidity. However, the optimal resuscitation approach is unclear; in particular, treatment of TBI patients with colloids remains controversial due to the side effects of these solutions. Our objective was to examine what molecular range is the optimal choice for the resuscitation after traumatic brain injury.

Methods: The Marmarou weight drop model induced severe traumatic brain injury was used in this study. And the rats were administrated with drugs after injury. The motor function was evaluated with Rota rod test and TruScan machine, which evolves the open field test and nose poking tests. The blood brain permeability was tested by Evans blue extravasations, and brain swelling was tested by the wet/dry weight method.

Results: In brain water content, the low molecular weight group showed less brain edema and Evans blue extravasation then other groups. And the low molecular weight BPZ improved the motor

function then other groups; in addition, the low molecular weight BPZ improved the cognitive function too.

Conclusions: Our findings indicate that the low molecular weight hydroxyethyl starch attenuate brain edema and blood brain permeability as well as improve the motor and cognitive deficits in clinical related traumatic brain injury model in rats.

Disclosure: Nothing to disclose.

PP3097

Cerebral imaging findings and neurologic outcome of methanol poisoning

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Introduction: Methanol is an extremely toxic alcohol, with organoleptic properties similar to those of ethanol. Intoxication with methanol can lead to severe metabolic acidosis, blindness, neurologic deficits and death. Though rare, basal ganglia necrosis, with or without hemorrhage, is the most common radiologic finding.

Case report: A 60 year-old male, with a history of diabetes mellitus, chronic kidney disease and alcohol abuse, presented with abdominal pain, vomiting and, shortly thereafter, a respiratory arrest. He was admitted in the Intensive Care Unit with severe metabolic acidosis, hyperglycemia and a Glasgow Coma score of 6 (E1V1M4). The neurologic examination later revealed a non-reactive bilateral mydriasis and a bilateral Babinski sign. The CT scan showed bilateral putaminal hemorrhagic necrosis. The patient's family later confirmed the suspicion of methanol intoxication (initially overlooked because of the presumed diabetic etiology of the acidosis), admitting consumption of windshield washer fluid. The evolution was slowly favourable, the patient being discharged however with complete blindness and mild bradykinesia.

Conclusions: The classic radiological finding in methanol intoxication is bilateral putaminal necrosis. Many theories have tried to explain this selectivity, among which a higher metabolic demand of the basal ganglia, a deficient venous drainage leading to a higher concentration of toxic metabolites and a predisposition to watershed infarcts due to their lying in arterial junction territories. The hypoxemic episode may have as well contributed in our case to these lesions. Methanol intoxication is a rare cause of parkinsonism and must always be considered in patients with metabolic acidosis and neurologic deficits.

Disclosure: Nothing to disclose.

PP3098

Abstract withdrawn

PP3099

Limited efficacy of engrafted neural stem and progenitor cells for severe spinal cord injury

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Introduction: There have been so many reports about the effectiveness of engrafted neural stem/progenitor cells (NSPCs) for injured spinal cord. Most evaluations of the efficacy, however, are applied to mild or moderate injured model. The efficacy of NSPCs administration to the severe injured spinal cord is still unknown. The purpose of this study is to investigate the efficacy of NSPCs administered to the severe injured spinal cord.

Methods: Contusive spinal cord injury of three types strength (mild: 50kdyn, moderate: 70kdyn, severe: 90kdyn) was performed in adult mice at the thoracic 10th level. NSPCs (5×10^5 cells per mouse) were grafted into the center of the injured site immediately after injury. Control mice only received conditioned medium.

Results: Motor function recovery was better in the mild and moderate injured models than in each of the control groups. No function recovery was detected in the severe injured model. The engrafted NSPCs of all three groups became differentiated into neural and glial cells. Both of the survival rate and the differentiation of engrafted NSPCs revealed no significant difference in all groups. The quantitative PCR analysis revealed that the neurohumoral expressions of engrafted NSPCs were significantly higher than in the mild and moderate injured models than in the severed injured model.

Conclusions: In this study, we clarified that the efficacy of NSPCs is dramatically suppressed only applied to the severe injured model. These results highlight the importance of considering therapeutic protocols individually of spinal cord injury patients in accordance with the degree of severity.

Disclosure: Nothing to disclose.

PP3100

The value of APACHE II, NIH and FOUR scores for determInatIon of early prognosIs in acute ischemIc stroke

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Introduction: In order to determine the prognosis of stroke patients in Neurology Intensive Care Unit, APACHE II, NIH and FOUR scales are used. In this study, the role of mortality prediction of these scoring systems were investigated.

Methods: In this retrospective study, 105 stroke patients admitted to Neurology Intensive Care Unit within the first 48 h from symptom onset were included. Fourty-seven patients were female and 58 patients were male. The mean age was 71.6. The stroke risk factors and lesion characteristics were analysed in relation with mortality. The APACHE II, NIH and FOUR scores on admission 1, 2, 3 and 10 days were also calculated and the relationship between these scores and mortality were investigated.

Results: A total 49 (46.7 %) of patients were died in the hospital. The age, sex, duration of hospitalization, lesion size and localization was not found associated with the mortality. The state of consciousness at the presentation, infection, brain edema and the need for mechanical ventilation were found significantly associated mortality. APACHE II, NIH, and FOUR scores are found to be effective in predicting mortality. According to ROC analysis, the first day the sensitivity ranking in descending order; FOUR > NIH > APACHE

II, descending sequence specificity of APACHE II > NIH > FOUR formed.

Conclusions: All of the scale were found effective predicting of prognosis in acute stroke. Ranking first in the NIH score, second FOUR and third APACHE II score took place.

Disclosure: Nothing to disclose.

PP3101
Changes of blood supply in patients who have suffered head injuries of varying degrees of severity

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PP3102
A systemic review and meta-analysis of the impact of perioperative antiplatelets and anticoagulants on the clinical course of chronic subdural haematoma

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PP3103
Adult case with isolated complex III deficiency of the mitochondrial respiratory chain presenting acute encephalopathy

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PP3104
A case of non-convulsive status epilepticus in acute ischemic stroke

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PP3105
Establishment of new focal weight drop model of traumatic brain injury

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PP3106
Therapeutic plasma exchange for neurologic disorders: single center experiences

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PP3107
Acute hyperglycemia exacerbates functional outcomes in human and mouse spinal cord injury via NF-κB pathway

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Epilepsy 2

PP3108
Epilepsy and its investigation in a GIS environment

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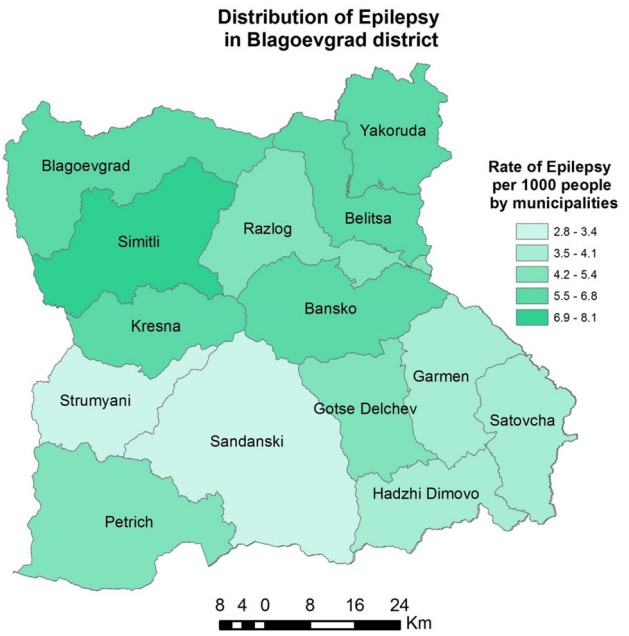
Introduction: The relation between cartography and medicine seems at first sight impossible. As early as 1854 the first thematic map in the field of medical mapping created by John Snow allowed him identify the cholera cause in London. The maps and Geographic Information System (GIS) are becoming important tools in planning, managing and monitoring of public health. Their application is mandatory for the program INSPIRE (INfrastructure for SPatial InfoRmation in Europe) that contains the theme Human health and safety as well.

Methods: The spatial location of data and spatial analysis methods are suitable for the health investigations. GIS is a technology for collecting, processing and visualization of spatial and temporal data. It has spatial analysis functions and is used for monitoring of the spread of a disease and its prevention. Spatial analysis always depends on the accurate location information. The purpose of this study is the geographic distribution of epilepsy for 2013 in Blagoevgrad district.

Results: Based on data from the Regional Health Fund and National Statistical Institute several maps were created. The total number of patients diagnosed with epilepsy is shown by age, gender and distribution by municipalities.

Conclusions: The prevalence in Blagoevgrad district is comparable to the world standards (Fig. 1).



GIS allows the identification of any relationship and factors' influence for the presence and distribution of diseases for a certain territory and population.

Disclosure: Nothing to disclose.

PP3109

Clinical features of seizures in patients with human immunodeficiency virus infection: a retrospective single-center study

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Objectives: The patients with human immunodeficiency virus (HIV) infection have a higher burden of neurologic disease including seizures. Various studies about seizures and HIV have been performed, but there are limited data in the Far East. We attempt to a retrospective analysis for clinical aspects of seizures among HIV-infected patients in South Korea.

Methods: We reviewed medical records of consecutive patients with HIV infection between 2008 and 2012 in a single clinic of infectious disease. We analyzed various clinical features; prevalence of seizure, immunological status, etiologies, EEG, imaging study and treatment. We identified predictors for seizure recurrence by using of univariate analysis.

Results: Among a total of 1141 patients, 34 (3 %) had seizures or epilepsy. Three of 34 patients had epilepsy before HIV infection, others had new onset seizures. Most patients revealed moderate (200–500, n = 13) and low (below 200, n = 16) CD4 count. The most common etiology was progressive multifocal leukoencephalopathy (n = 14), subsequently metabolic abnormalities (n = 6) and CNS infections (n = 5). The imaging study showed visible brain lesions in 21 patients. Nine patients had only single seizure and 24 patients had multiple seizures or status epilepticus (n = 2). Multiple seizures were more common in patients with brain etiology (P = 0.091) or epileptiform discharges in EEG (P = 0.074), but not statistically significant. Seizures were well controlled without anticonvulsants (n = 12) or by single anticonvulsant (n = 12).

Conclusions: Seizures are less frequent in patients with HIV infection than expected. Progressive multifocal leukoencephalopathy is most common etiology of seizure in our study. Seizure recurrence or development of epilepsy is associated with etiology and EEG abnormality.

Disclosure: Nothing to disclose.

PP3110

Should we consider intravenous levetiracetam an option in the management of status epilepticus and acute exacerbation of seizures in children?

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Intravenous Levetiracetam was approved in United States in August 2006 for patients aged 16 years and above. We retrospectively analyzed data at our institution of children who received intravenous levetiracetam for acute seizure management since not much information is available.

Methods: A retrospective chart review was conducted on all children less than 18 years who received intravenous levetiracetam at Scott and White Hospital/Texas A & M HSC College of Medicine, Temple, TX. Subject data were acquired from electronic medical records. Approval of this retrospective analysis was given by our hospital's institutional review board.

Results: We retrospectively analyzed 80 patients who met our inclusion criteria for neonatal seizures, status epilepticus and acute repetitive seizures and received intravenous levetiracetam from January 2008 to August 2013. The loading dose of intravenous levetiracetam was 50 mg/kg in most patients followed by a maintenance dose of 25 mg/kg every 12 h. The variables analyzed included clinical data, electrographic documentation, indication of initiation of this medicine, adverse events and seizure control at 6-month well child visits. Response to levetiracetam was favorable. 63 out of 80 patients reached seizure freedom within 24 h and 14 within 48–72 h. Seizures continued in one patient and two patients died because of continued seizure activity on three anticonvulsants. No serious side-effects were apparent. Patients were discharged on oral levetiracetam and did well at 6-month clinic visit..

Conclusions: Intravenous Levetiracetam seems to be efficacious in acute seizure management in children.

Disclosure: Nothing to disclose.

PP3111

Prevalence of intellectual impairment in idiopathic and symptomatic epilepsy

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Introduction: Most authors indicate that the development of cognitive impairment in epilepsy affects a large number of factors. It would be interesting to study epilepsy patients similar in age and duration of the disease, but having a different cause to clarify the state of intelligence.

Methods: We examined 45 patients with epilepsy, including 23 patients with idiopathic epilepsy (IE) and 22 patients with symptomatic epilepsy (SE). The average age of the IE group was 30.6 years (95 % CI 25.3–36.0) in the SE group was 34 years (95 % CI 30.4–37.6). Duration of the disease in the group of IE was 16 years (95 % CI 9.9–22.0) in the SE group was 13.2 years (95 % CI

7.53–19.0). We use Raven test for IQ assessment and describe in terms of Wechsler IQ Classifications.

Results: Mean IQ the IE group was 100.8 (95 % CI 94.1–107.5) in the SE group was 104.6 (95 % CI 98.5–109.6).In our study patients of both groups dominated the average IQ, but in the IE group 47.8 % (11/23) patients had a lower average IQ, in the SE group 18.2 % (4/22) patients had a lower average IQ. There were no differences in the reliability of IQ between idiopathic and symptomatic epilepsy ($p = 0.09$).

Conclusions: According to our sources in different forms of epilepsy, no statistically significant differences in intelligence.

Disclosure: Nothing to disclose.

PP3112

Localizing value of ictal electroencephalography in sleep in patients with mesial temporal lobe epilepsy

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Introduction: Localizing value of interictal electroencephalography (EEG) patterns in wakefulness and sleep in patients with mesial temporal lobe epilepsy (MTLE) are well known, but research on localization value of ictal electroencephalography (iEEG) in wakefulness ($iEEG_W$) and sleep ($iEEG_S$) is scarce. Our objective was to test the localizing value of $iEEG_S$ compared to $iEEG_W$ in patients with the MTLE.

Methods: We retrospectively analyzed 196 $iEEG_W$ and 76 $iEEG_S$ in 40 patients with intractable MTLE in Center for epilepsy and sleep disorders, Clinical Center of Serbia from 2006 to 2013. All patients included in the analysis are seizure-free after temporal lobectomy. Ictal EEG was analyzed for presence of muscle artifacts at ictal onset, regional onset, colocalisation of ictal onset and epileptogenic zone, presence of a fast rhythmic-theta pattern, contralateral propagation and generalization. Statistical significance was determined using the Chi square test.

Results: Our analysis shows that iEEGw were more likely to be obscured with artifacts ($p < 0.01$), while iEEGs were more likely to have regional onset which was more likely to be colocalised with the epileptogenic zone and more likely to have a fast rhythmic-theta pattern ($p < 0.01$, $p < 0.01$ and $p < 0.05$). iEEGs were more likely to propagate contralaterally ($p < 0.01$) and had a tendency to generalize more often but the difference was not statistically significant.

Conclusions: The localizing value of iEEGs may be greater than that of iEEGw in surgical candidates with MTLE.

Keywords: mesial temporal lobe epilepsy, sleep seizures, ictal EEG

Disclosure: Nothing to disclose.

PP3113

Epilepsy and depression

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Introduction: Patients with epilepsy are at increased risk for comorbidities that can complicate epilepsy treatment and increase the health-care costs. In our study, we aimed to investigate the presence of depression in epilepsy.

Methods: A total of 143 epileptic patients who admitted the epilepsy outpatient clinic from 2013 January to December and 53 healthy subjects were included to the study. Beck Depression Inventory (BDI) was evaluated in both of the groups. Patients with a BDI score greater than 11 were interpreted as the presence of symptoms of depression. The relationships between demographic data, duration of epilepsy, seizure type (partial/generalized) antiepileptic (AEDs) therapy (monotherapy/polytherapy) and BDI scores were investigated.

Results: Mean age was 33.24 ± 14.12 in the partial epilepsy (PE) group ($n = 75$) and 38.25 ± 13.45 in the generalized epilepsy (GE) group ($n = 70$). BDI scores were significantly higher in both epileptic groups compared with the control group ($p = 0.011$ and $p = 0.000$) A significant correlation was found between epilepsy and depression and BDI scores were found to be significantly higher in the PE group ($p = 0.026$). BDI scores of female patients were also higher but there was no relationship between the type of the treatment, the duration of epilepsy and the BDI score.

Conclusions: Our results suggest that patients with epilepsy, especially in the partial epilepsy group, have an increased possibility to develop depression.

Disclosure: Nothing to disclose.

PP3114

Frequency and risk factors for seizures in Alzheimer's disease and vascular dementia

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Introduction: Little information is available about seizures in dementias. Our goal is to evaluate the frequency of seizures in a population of dementia patients and to determine the features associated with its development.

Methods: A retrospective study of seizures in 147 consecutive patients with Alzheimer's disease (AD) and 150 with vascular dementia (VaD) followed-up in neurologic consultations in Salamanca and Ávila, Spain. The mean age at onset of dementia was 74.8 ± 7.1 years (mean duration 4.3 ± 2.6 years). Seizures were defined as any report of new-onset unprovoked seizures after diagnosis of dementia. The relationship between potentially related variables (demographics, duration and severity of dementia, physical and diagnostic test findings, and comorbid medical and psychiatric conditions) and the probability of seizures was assessed using statistical analysis.

Results: We identified 7 (4.8 %) AD and 25 (16.7 %) VaD patients with an incident diagnosis of seizures. AD patients with a longer disease duration had a higher risk of developing seizures, whereas in patients with VaD that relation was not observed. Other predictors of seizures were a lower MMSE score in AD and a younger age at dementia onset, chronic obstructive pulmonary disease, antipsychotic use, a higher NPI score and euphoria in VaD patients. In postroke dementia, patients with a higher NIH stroke scale score and atherotrombotic infarctions were significantly more frequent in the seizure group.

Conclusions: Seizures were substantially more common in patients with VaD than in AD patients. Risk factors for seizures seem to differ between AD and VaD.

Disclosure: Nothing to disclose.

PP3115

Epilepsy and sleep quality

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Introduction: Sleep complaints may accompany epileptic seizures. In clinical practice, daytime sleepiness is a well-known and frequent complaint of patients with epilepsy. In our study, we have investigated the sleep quality and daytime sleepiness in epileptic patients.

Methods: A total of 143 epileptic patients who admitted the epilepsy outpatient clinic from 2013 January to December and 53 healthy subjects were included to the study. Beck Depression Inventory (BDI), Epworth Sleepiness Scale (ESS) and Pittsburgh Sleep Quality PSQ) were evaluated in both of the groups. Patients with a BDI score greater than 11 were interpreted as the presence of symptoms of depression. The relationships between demographic data, duration of epilepsy, seizure type (partial/generalized) anti-epileptic (AEDs) therapy (monotherapy/polytherapy) with ESS and PSQ scores were investigated.

Results: A significant correlation was found between sleep quality and excessive daytime sleepiness and depression ($p = 0.000$). In the depressive group PSQ scores seemed to be higher than the nondepressive group. ($p = 0.032$). ESS scores were found to be significantly higher in the partial epilepsy group ($p = 0.042$). There was no relationship between the type of the treatment, the duration of epilepsy and the PSQ and ESS scores.

Conclusions: Our results suggest that epileptic patients with depression have worse sleep quality than the ones without depression.

Disclosure: Nothing to disclose.

PP3116 Clinical experience with perampanel in a regional epilepsy clinic

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Introduction: Perampanel is a novel antiepileptic drug that inhibits the AMPA class of glutamate receptors. Data from open label post marketing studies can complement those from regulatory trials. We undertook a retrospective analysis of efficacy and tolerability of perampanel in patients with refractory epilepsy attending a regional epilepsy service in the UK.

Methods: Demographic and clinical data of patients with refractory epilepsy prescribed perampanel were collected by review of records. Responder rate (> 50 % reduction in seizure frequency), retention and adverse effects were analysed.

Results: 30 patients were prescribed perampanel, 16(53 %) female. Median age was 30.5 years (range 19–59). 26 (87 %) had focal epilepsy, 3 (10 %) had generalised. 26 patients had simple and complex partial seizures, 15 had generalised tonic–clonic seizures, 3 had myoclonic jerks and 1 patient each had absence and atonic seizures. Median dose of perampanel was 8 mg (range 2–12 mg).

19/30 patients continued perampanel until the end of follow up (retention rate 63.33 %). Of these 5 (26 %) patients were classed as responders (>50 % reduction). 3 (15 %) had <50 % improvement in seizure frequency, and 11 (58 %) had no change or deterioration of seizure frequency. 11 withdrew, 9 (82 %) due to adverse effects, and 2 (18 %) due to lack of efficacy. Dizziness, sedation, unsteadiness, behavioural disturbance, confusion and abnormal thoughts were the most commonly reported side effects.

Conclusions: Responder and retention rates of perampanel mirror regulatory studies in our study. Neurocognitive and behavioural adverse effects appear the most common reason for treatment withdrawal.

Disclosure: This study was supported by an unrestricted grant from Eisai.

PP3117

Oro-facial automatisms in temporal lobe epilepsy

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Introduction: The semiological value of orofacial automatisms (OA) in temporal lobe epilepsy (TLE) is not well established. Our aim was to characterize OA in TLE and to evaluate their lateralization and localization value.

Methods: We performed a retrospective study with patients presenting the following criteria: age $\geq$ 18; TLE diagnosis operated between 2009 and 2012; Engel Ia class after surgery; pre-surgery Video EEG monitoring test with a visible face. TLE was classified in mesial (MTLE), mesiolateral (MLTLE) and lateral (LTLE) according to the localization of the lesion by imaging. OA were classified in oroalimentary (OAA) and mimic-facial (MFA) whether masticatory muscles were involved or not.

Results: Twenty of the thirty-one patients with TLE operated met our inclusion criteria. The majority were women (70 %), with a TLE localized in the left hemisphere (55 %) and in a mesial region (60 %). Eighty-one seizures were analyzed. OA were found in the majority of the seizures (70.4 %) within which OAA alone were the most frequent (75.4 %). OAA were significantly longer in duration when compared to MFA ($p = 0.03$). TLE lateralized to the left hemisphere had more OA than the right one ($p = 0.02$). When comparing MLTLE to MTLE, the first one presented more MFA ($p = 0.02$). There was only one patient with LTLE who didn't have automatisms in the recorded seizures.

Conclusions: OA were frequently visualized in patients with TLE and seemed to be more frequent in TLE lateralized to the left hemisphere. MFA appeared more in patients with a TLE involving the mesial and neocortical cortex.

Disclosure: Nothing to disclose.

PP3118

Newly developed nocturnal 2′ generalized seizure as a cause of intractability after anterior temporal lobectomy

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Introduction: Some patients after anterior temporal lobectomy (ATL), who could not achieved complete seizure control, showed new ictal semiology. The clinical factors related to newly developed ictal semiology after ATL were analyzed, which might be a possible cause of intractability.

Methods: Prognosis of 66 patients after ATL with AH was analyzed with mean follow up 9.2 years (5–20 years). Thirty nine patients achieved complete seizure remission and 27 patients could not reached complete seizure control. Patients with incomplete seizure remission divided into group with habitual seizure and with newly developed semiology. The clinical characteristics of seizure were compared between two groups and also.

Results: Fourteen patients (51.8 %) among 27 patients with incomplete seizure control had newly developed 2′ generalized nocturnal seizure, which was the only semiology in 10 of them. Ten of them actually recurred after prolonged seizure remission. Statistical analysis showed significant differences in sex and laterality of HA, respectively, female and left HA, and also low prevalence of clustering tendency.

Conclusions: These results showed nocturnal 2′ generalized seizure could be newly developed after ATL with AH. Sex and laterality of HA in addition to the clustering tendency were related to development of 2′ nocturnal seizure. Newly developed ictal semiology might be explainable as one of cause of intractability after ATL with

HA in patients with MTLE with HA. Encephalomalacia due to epilepsy surgery on temporal lobe could not exclude the cause of newly developed semiology after removal of the epileptogenic foci, which need much more data and discussion.

Disclosure: Nothing to disclose.

PP3119

Long-term prognosis of Juvenile myoclonic epilepsy

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Introduction: The purpose of this study was to evaluate long-term prognosis and the related risk factors of patients affected by Juvenile Myoclonic Epilepsy (JME).

Methods: This is an observational, open-label, long-term study. Patients affected by JME regularly followed by our Centers were recruited. Statistical analysis were performed using discriminant analysis as multivariate analysis.

Results: 53 patients affected by JME were recruited [29 F, mean age 29.3 ± 8.2 years (range 16–53)]; in 4 cases JME was an evolution of Childhood Absence Epilepsy. 43 (81 %) patients showed generalized tonic–clonic seizures (gtcs) and 19 (36 %) absence seizures.

Mean follow-up was 95 ± 60 months (16–239). 40 (75 %) patients resulted seizure-free for at least 2 years; an higher likelihood of refractoriness of JME was associated to: family history of epilepsy and febrile convulsions, gtcs and absence seizures, focal abnormalities and photosensibility on EEG, earlier age at epilepsy onset. 21 (39 %) patients, after seizure-freedom, withdrew treatment, at a mean age of 22.9 ± 9 yy (15–49); seizures relapse was observed in 20 (95 %) cases. One patient who withdrew drug treatment after the forth decade of life (49 yy), remained seizure-free.

Conclusions: Our study confirms good prognosis of JME and its tight relation to drug therapy, which should be maintained long-term. Among the potential prognostic factors, focal abnormalities and photosensibility on EEG seem related to difficulty in achieving seizure control.

Disclosure: Nothing to disclose.

PP3120

To the issue of somatic comorbidity influence on the course of epilepsy

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Introduction: To examine the frequency of somatic comorbidity in epilepsy patients according to age, sex, possible etiology of epilepsy, to investigate the impact of physical illness on the course and prognosis of the disease.

Methods: Under the supervision of a long—for 3 years (mean 8.5 ± 3.0 years) were 124 patients (90 males and 34 females) with epilepsy aged 15–87 years (average – 43.8 ± 8.2 years). All cases of epileptic seizures were distributed by nature and the form of the disease based on the classification, signed in ILAE (ILAE Commission report, 1997).

Among all included in this study of patients with symptomatic epilepsy were 86 (69.3 %) with cryptogenic—25 (20.1 %) and idiopathic—13 (10.4 %).

Results: Comorbid somatic diseases were identified in 75.8 % of patients, among whom were 22 women and 72 men. 55.3 % patients had a single somatic disease and 31.9 %—two, in 7.4 %—three, in 4.2 %—four and one (1.06 %)—five patients 18–30 years on average 0.72 disease was noted per human, 31–45 aged—1 disease, 46–60 aged—1.83, after 60 years old—2.33 diseases. The average age of patients with somatic diseases was 40.6 years, in patients without comorbidity—29.0 years.

Conclusions: In epilepsy was observed dependent polymorbidity according to the age, 2. Often somatic comorbidity was presented with symptomatic epilepsy 3. long-term use of two AED or polytherapy leads to an increase of somatic diseases and to its development.

Disclosure: Nothing to disclose.

PP3121

Concordance rate between EEG and MRI findings in focal epilepsy in pediatrics population with pictorial review

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Objectives: MRI is able to detect epileptic lesions but the detection rate of lesions in focal epilepsy in our institution remains below 50 %, similar to international data. We reviewed children with focal epilepsy and ascertain the concordance rate between the EEG and MRI findings in such children.

Methods: We did a retrospective analysis of 55 children with focal epilepsy seen in KKH. Out of these 55 patients, unilateral localization of seizures on EEG were seen in 47 cases (21 to right and 26 to left) with generalized/bilateral seizures present in 8 cases.

All these patients had MRI scans on a 1.5T General Electric scanner using epilepsy protocol.

Results: MRI was positive in 33 of the 55 cases giving detection rate of 60 % and overall concordance of MRI with EEG is seen in (18/47) 38 %. MRI showed concordant abnormalities on the right in 9 patients (43 %), on the left in 9 patients (35 %) and bilateral lesions in 5 patients (63 %).

Positive lesions seen on MRI were congenital/developmental (schizencephaly, heterotopias) in 18 % (6/33), due to previous insult (encephalomalcia/PVL/atrophy) in 48 % (16/33) and tumors in 4 % (1/33). MRI findings were non-specific (T2 hyperintensities, subcentimeter cysts) in the remaining 30 % (10/33).

Conclusions: Structural MRI showed poor sensitivity in detecting epileptogenic areas in our patients with focal seizures. However, new MRI techniques that assess function may contribute to better detection.

Disclosure: Nothing to disclose.

PP3122

Autosomal dominant cortical tremor, myoclonus and epilepsy: pshychiatric features

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Introduction: Autosomal Dominant Cortical Tremor, Myoclonus and Epilepsy (ADCME) is an inherited condition characterized by familial occurrence of cortical tremor, myoclonus and epileptic seizures. The genetic background of this condition is heterogeneous: linkage to three different loci (8q24, 2p11.1-q12.2, 5p15.31-p15) was describe. We have recently reported a relatively high frequency (>40 % of the cases) of pshychiatric symptoms clinically defined in a large series of patients. Aim of this study is to further assess pshychiatric comorbidity in a subgroup of ADCME/BAFME patients by using reliable and valid pshycodiagnostic scales.

Methods: Sixteen patients and sixteen healthy controls underwent a pshychiatric interview and self administered tests: BDI (Beck Depression Inventory), STAI-Y (State-Trait Anxiety Inventory Y), MMPI-2 (Minnesota Multiphasic Personality Inventory-2) and QoLIE-31 (Quality-of-Life in Epilepsy Inventory).

Results: Severe to mild depression symptoms were present in almost all the patients whereas a clinically relevant anxiety disorder was evident in eleven of them. MMPI-2 results supported the coexistence of a personality disorder in nine patients. Quality of life scores were lower than previously reported in Italian epileptic patients.

Conclusions: This pilot study firstly confirms a high incidence of mood disorders, particularly depression and anxiety, in ADCME patients, often associated to pathological traits of personality if compared to healthy controls. Moreover these patients show a worse quality of life compared to other patients presenting only with seizures, probably due to the influence of tremor on daily life activities.

Disclosure: Nothing to disclose.

PP3123

The frequency of SNP A118G of the mu opioid receptor gene and the SNP C3534T of the MDR1 gene in patients with tramadol induced seizure

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Introduction: Seizures have been reported with tramadol use; however, exact mechanism is not yet proven. An individual genetic susceptibility may render some more prone to develop seizures.

Objective: To find out the frequency of mutant allele of the OPRM A 118G and MDR1 C3534T in tramadol abusers with seizures.

Methods: A cross sectional study on 74 Egyptian tramadol abusers, with and without seizures. Subjects with true epileptic seizures were assessed clinically, radiologically and by electroencephalogram. When other causes for seizures were excluded, seizures were nominated as tramadol induced. Genotyping of the μ opiod receptor gene (OPRM) and the multidrug resistant (MDR1) genes was carried out for all subjects.

Results: Thirty seven subjects had seizures. A history of head trauma and more opioid antitussives abuse were reported by the group with seizures. Family history of epilepsy was present in 2 subjects with seizures. There was no significant difference between the 2 groups regarding the frequency of occurrence of the SNP A118G of the mu opiod receptor gene or the SNP C3534T of the MDR1 gene.

Conclusions: This study could not illustrate a potential genetic background in the studied point mutations that could explain the development of tramadol induced seizures.

Disclosure: Nothing to disclose.

PP3124

Impact of nootropics on convulsive readiness of the brain

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Introduction: The use of anticonvulsants in the treatment of epilepsy leads to significant side effects: substantially reduce IQ, impair cognitive processes, decrease the amount of memory and the velocity of n-gram repetition. Nootropics are used to lessen the severity of these complications during the combined anticonvulsant therapy. Therefore, we believe that current study to investigate anticonvulsant profile of some nootropics is quite relevant.

Methods: The study was conducted on 96 white nonlinear rats of both sexes weighing 180–220 g. The animals were injected with entropy, piracetam, olatropil, noofen for 20 days prior to testing. Seizures were simulated using the maximal electroshock procedure (MES).

Results: Under the influence of maximal electroshock effects, all animals of the control group developed tonic seizures. It was established that the use of entropy (600 mg/kg) completely prevented the occurrence of seizures in the treated group. Noofen (500 mg/kg)—also accomplished anticonvulsant effect, but it was weaker than with entropy. Introduction of this drug resulted in complete absence of seizures in half of the rodents, decrease of the hindlimb extension time by 41.6 % ($p < 0.05$) and decrease of total duration of seizures by 63.4 % ($p < 0.05$). Olatropil in a maximum dose (500 mg/kg) prevented the occurrence of seizures in 60 % of animals. It is noteworthy that the appointment of piracetam under these experimental conditions had practically no effect on the parameters of a convulsive attack, caused by MES application.

Conclusions: Thus, nootropic drugs, except for piracetam, have anticonvulsant effects, varied to a different extent: entropy > noofen > olatropil.

Disclosure: Nothing to disclose.

PP3125

The effects on cognitive function of topiramate compared to valproate in children with Benign Rolandic epilepsy

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Purpose: To evaluate the cognitive effects of Topiramate (TPM) compared to Valproic Acid (VPA) using minimal efficacious doses of each drug as monotherapy in children with Benign Rolandic epilepsy.

Methods: 62 children in the age of from 5 till 14 years have been surveyed. TPM was introduced at a dose of 12.5 mg/day with the minimum target dose of 50 mg/day in patients < 30 kg and 75 mg/day in patients > 30 kg over 8 weeks. VPA was started at a dose of 15 mg/kg/day with the minimum target dose of 20 mg/kg/day.

Results: Neuropsychological tests have been performed at 62 patients (30 patients for TPM and 32 patients for VPA). All tests had a larger change in the negative direction for TPM-treated patients especially, arithmetic test showed a statistically significant difference in comparisons between the treatment groups ($p = 0.037$), with poorer performance in TPM-treated children. However, integrated functions such as verbal comprehension, attention and concentration did not show statistically significant differences between the two treatments. The other integrated functions such as perceptual organization, prefrontal lobe function and memory showed improved scores for both drugs. When 30 patients on the minimum target dose for TPM were compared to 32 patients treated with minimum target VPA, there was no significant worsening of cognitive and behavioral effects in the TPM.

Conclusion: Neuropsychological changes in treatment by TPM seemed to be slightly worse overall than VPA. However, outcome with the minimum target dose did not differ significantly in comparisons between the treatment groups.

Disclosure: Nothing to disclose.

PP3126

Effects of cytidine 5′-diphosphocholine (CDP-choline) on seizure-induced neuron death

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Introduction: Citicoline serves as a choline donor in the metabolic pathways for biosynthesis of acetylcholine and neuronal membrane phospholipids, mainly phosphatidylcholine. The ability of citicoline to reverse the neuronal injury has been tested in animal models of cerebral ischemia and also has been performed clinical trial in stroke patients. However, no previous report has examined the effect of citicoline on seizure-induced neuron death. To clarify the therapeutic potency of citicoline on seizure-induced neuron death, we used an animal model of pilocarpine-induced epilepsy.

Methods: Temporal lobe epilepsy (TLE) was induced by intraperitoneal injection of pilocarpine (25 mg/kg) in male adult rats. Citicoline (100 or 300 mg/kg) was injected into the intraperitoneal space two hours after seizure onset and a second injection was performed 24 h after the seizure. Superoxide production was detected by dehydroethidium at 3 h after the seizure. Neuronal injury and microglia activation was evaluated at 1 week after the seizure.

Results: Here we found that post-treatment of citicoline showed no protection of superoxide production. Even citicoline treatment increased seizure-induced neuron death and microglia activation in the hippocampus compared to vehicle treated group.

Conclusions: These results suggest that citicoline may not have neuroprotective effects after pilocarpine-induced seizure. The present study suggests that clinical application of citicoline after seizure needs careful considerations.

Disclosure: Nothing to disclose.

PP3127

Prevalence of vascular epilepsies after sroke. Neurology department, Fann hospital in Dakar, Senegal

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Introduction: Vascular epilepsy is defined by repeated seizures on stroke effects and seems as a public health problem. Our objectives were to estimate the prevalence of epilepsy after stroke in Senegal.

Methods: We conducted a cross-sectional study from August 1st 2009 to July 31st 2010, concerning cases of epilepsy after stroke in older patients over 60 years, cared in the neurology department of FANN Hospital in Dakar.

Results: We identified 223 cases of stroke in which 27 cases of epilepsy were found, giving a prevalence of 12.10 %. Patients with epilepsy after stroke were 61–82 years old with a mean of 69.74 years (±8.05). 48.1 % presented partial motor seizures, and 22.2 % presented generalized motor seizures. This prevalence did not vary significantly with age (Chi square: 4.848, $P < 0.2$). On 27 cases, 15 were male without a statistically significant difference ($p < 0.063$). Specific prevalence of epilepsy was estimated at 3.13 % after hemorrhagic stroke and at 8.96 % after ischemic stroke. However, among patients with epilepsy, we identified 7 cases occurred in a waning hemorrhagic stroke and 20 cases in the waning of ischemic stroke.

Conclusions: Vascular epilepsy is a common complication of vascular stroke and has to be watched. Suitable treatment must be undertaken when it is confirmed.

Disclosure: Nothing to disclose.

PP3128

Kleine-Levin syndrome as a manifestation of anti-NMDAR encephalitis

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Introduction: Kleine-Levin syndrome is a rare sleep disorder characterized by hypersomnia, cognitive impairment and behavioral disturbances such as hyperphagia and hypersexuality. The underlying pathophysiology remains unknown.

Case-report: A 18-year-old girl, with no previous illness, was hospitalized with generalized tonic–clonic seizure. Brain MRI was normal and electroencephalogram (EEG) showed bilateral slow activity in the frontotemporal regions. The patient was discharged asymptomatic with antiepileptic drugs. The following days, she suffered from insomnia, decreased cognitive skills, behavioral disorder and visual hallucinations. She was readmitted. Blood tests, cerebrospinal fluid (CSF) and second brain MRI showed no relevant findings. Serum and CSF samples were sent for analysis of infectious, paraneoplastic and autoimmune etiology. Video-EEG monitoring showed slow paroxysmal activity in the left temporal region. The neurological status deteriorated with psychomotor agitation, aggressiveness, catatonic state, oromandibular dyskinesias and autonomic dysregulation.

Autoimmune encephalitis was suspected and it was prescribed sequential treatment with methylprednisolone and IV Ig, with no improvement. Clinical condition progressed with hypersexuality. Screening for occult tumor was negative. Weeks later, anti-NMDAR antibodies were received and found positive in a CSF and blood samples. She received plasma exchange with no improvement. She received rituximab, during which she exhibits hypersomnia, hyperphagia, irritability, acathisia, with gradual recovery of all symptoms.

An outpatient follow-up revealed, 6 months later, that she was back to college, taking her driver's license and with her previous personality.

Conclusions: Anti-NMDAR encephalitis has a wide range of neuropsychiatric symptoms, including Kleine-Levin symptoms. Awareness and recognition is important because outcome depend on early diagnosis and treatment.

Disclosure: Nothing to disclose.

PP3129

EEG, Hallucinatory seizures and sociocultural implications in an West African country—Senegal

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Introduction: Hallucinatory seizures are partial seizures with strong subjective connotation. They are difficultly or awkwardly reported by

the patients and their relatives. This study is one part of a research long term project comprising 4 sections (electrophysiological, socio-psychiatric, ORL and ophthalmologic). We try to understand these hallucinatory manifestations knowing origin and cultural impregnation of our patients.

Methods: We did a prospective study during 5 months in our Neurophysiological unit in 2010 concerning all patients refer for hallucinatory seizures. Patients were interviewed by neurologist and after psychiatry, ORL and ophthalmologist for eliminating organic troubles explaining hallucinations.

Results: We recense 31 patients, including 76.9 % old (20–50 years), and a sex-ratio of 1.38 in favor to men. 25 % had done their first seizure before 5 years old and 39 % after 18 years. We found 19 cases of visual hallucinations, isolated or associated with convulsive seizures, 14 cases of auditive hallucinations and 5 cases for gustative and psychosensorial hallucinations. In 17 cases EEG was normal; focal abnormalities was in 90 % cases in pariéto-temporal areas.

Conclusion: Hallucinatory seizures have a large share of subjectivity and critical polymorphism. Their dissociation from a particular psychological state and cultural influences make more difficult their interpretation, because of variable origin and different interpretations of hallucinations toward ethnics. Correlations anatomo-electroclinic are also difficult because they are in the borders between lobes frontal, parietal, temporal, and occipital. EEG helps to specify the localization of the discharge and its propagation. Our study shows 42 % of parieto-temporal discharges with posterior propagation.

Disclosure: Nothing to disclose.

PP3130

Cortical reflex focal motor seizures in an adult with chronic hemispheric autoimmune encephalitis

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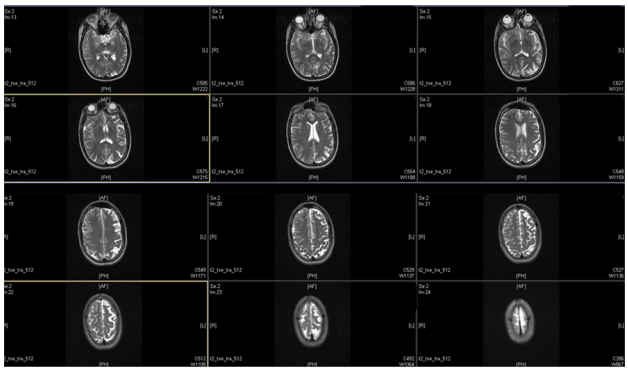
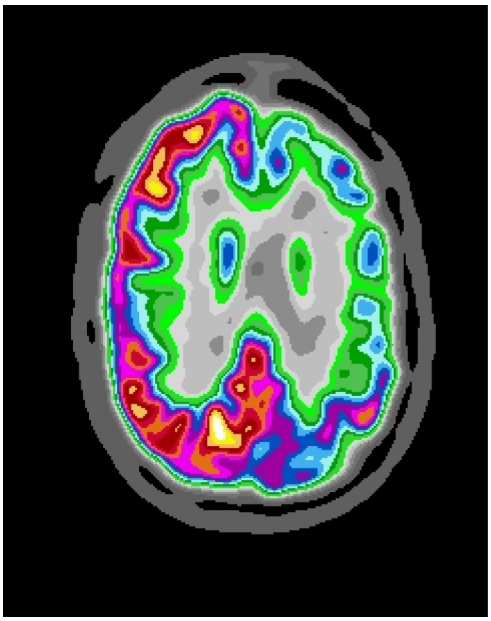
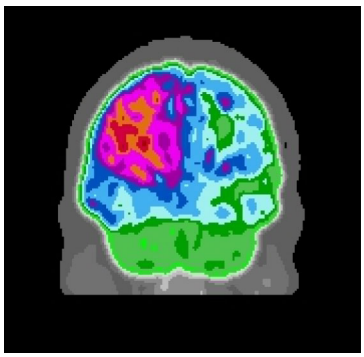
Introduction: We present a 36-year-old woman diagnosed with possible Rasmussen syndrome at the age of 18.

Methods: She first presented with sudden right leg weakness, and her right leg motor seizures started few weeks later. Subsequently within a year, she developed progressive right sided weakness and generalized nocturnal seizures. Since the age of 20 her mild hemiparesis has remained stable with multiple focal motor seizures daily. These remained restricted to the right foot, occurring spontaneously and also induced by sudden movements. Generalized convulsions have been monthly.

Results: The patient was referred to us at age 32. Physical examination revealed mild right hemiparesis (4+), the brain MRI showed diffuse left hemispheric volume loss and the FDG-PET scan extensive left hypometabolism; CSF showed increased IgG index, but was negative for voltage gated antibodies. Video-EEG studies showed frequent focal motor seizures associated with midline and left central fast epileptic activity, but also cortical activation on command aiming to provoke a seizure ("move your foot up and down") and also upon stimulation of the right foot. Three courses of IVIG resulted in complete but temporary resolution of generalized convulsions (now back on a baseline of 2/year), but had no effect on the focal motor seizures.







Conclusions: This patient with chronic hemispheric encephalitis is remarkable for the partly reflexive epileptogenic mechanism in the context of the limited topography and stability of the epileptogenic area over time, and the positive (albeit temporary) response to immunotherapy.

Disclosure: supported by FP7 grant on epilepsy (287720).

PP3131

A novel intronic variant of SCN1A gene responsible for severe epileptic encephalopathy with refractory status epilepticus

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Introduction: We describe a 32 years old male with encephalopathy and drug resistant epilepsy with recurrent episodes of status epilepticus.

Methods: The patient was born at term by normal pregnancy after prolonged labour. A significant global developmental delay had been recognized since 6 years of age. At age 5 months he experienced the first epileptic seizure during hyperpyrexia characterized by a left hemiclonic seizure during sleep followed, a few hours later, by a tonic–clonic seizure. Since then he has had monthly febrile and afebrile tonic–clonic seizures, mainly arising from sleep. Despite trials of several antiepileptic drugs, seizures increased on frequency, becoming weekly. Recurrent episodes of intractable status epilepticus worsened by phenilidanthoyn were also reported. At our first assessment (32 years of age) the patient underwent a comprehensive clinical, neurophysiological and neuroradiological study.

Results: Neurological examination showed craniofacial dysmorphism and severe delay in language and motor acquisition. Interictal EEG showed diffuse background slowing and independent epileptiform discharges over both the temporal regions. During prolonged video-EEG monitoring we recorded one of his typical status epilepticus clinically characterized by left arm clonic seizures and secondarily generalized seizures. Brain MRI disclosed a mild cerebellar atrophy with evidence of cerebellar sulcus. Molecular analysis of SCN1A gene identified a de novo intronic mutation, causing nucleotidic substitution c.338+3A>C.

Conclusions: We describe a new de-novo mutation of SCN1A gene responsible for severe early-infantile epileptic encephalopathy with recurrent status epilepticus resistant to sodium blocker AEDs.

Disclosure: Nothing to disclose.

PP3132

New manage of epileptic status. The power of the lacosamide

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Introduction: The lacosmide (LCS) is new drug recently introduced for the epilepsy managed. It is studying the effectiveness in the epileptic status (ES) or cluster seizure treatment.

Methods: The sample was taken from Lozano Blesa Hospital patients, who had cluster or ES. They were treated with LCS in different steps of it.

Results: 330 patients were included, the age average was 60.85 years old (18–91), 63.3 % (N = 19) were male. The 53.3 % (N = 18) had epilepsy history, from them 43.8 % (N = 7) generalized seizure and 37.5 % (N = 6) complex focal. The 56.7 % (N = 17) were in ES, and the most frequent was non convulsive with 30 % (N = 9). The EEG was generalized in the 34.5 % (N = 10) and pathological neuroimage was in 70 % (N = 21). The LCS intravenous was used because the others antiepileptic drugs (phenytoin, valproic acid, levetiracetam) weren't effective in 53.3 % (N = 16), and in second line of the treatment in 56.7 % (N = 17). The initial intravenous doses was 200 mg in the 80 % (N = 25), and the main doses during the hospitalization was 406.67 mg/day. The LCS was effective in 83.3 % (N = 25). Only 3 patients got mild side effects (dizziness, nausea, headache), but we didn't need to stop the treatment neither to reduce the doses. The LCS was effective with statistic significance (p = 0.035). The 20 % (N = 6) were taken to the intensive care unit, 10 % (N = 3) of them was generalized seizure, but only 6.7 % (N = 2) were sedated. The 44.7 % (N = 14) were discharged in less than 10 days.

Conclusions: The LCS is a new drug that has showed effectiveness for the ES treatment, low incidence of side effects, rapid control and reducing the cost of the management.

Disclosure: Nothing to disclose.

PP3133

Epileptic seizures at patients with low cerebral contusion foci

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Introduction: Time of occurrence and incidence of epileptic seizures (ES) in traumatic brain injury (TBI) depends on type, location and volume of cerebral contusion focus, premorbid state of the patient (cerebrovascular diseases, a history of repeated head trauma, genetic predisposition, chronic alcoholism, etc.).

Methods: We conducted the prospective analysis of data of clinical and instrumental examinations and surgical treatment outcomes at 181 patients with moderate and severe HI (consciousness level is from 4 till 13 scores according to Glasgow Coma Scale). Among 181 patients the cerebral contusion of moderate severity was seen at 136 (75.1 %) patients and severe cerebral contusion—at 45 (24.9 %) patients. We operated 60 (33 %) patients and 121 (67 %) patients were treated conservatively.

Results: On the brain computer tomography (CT) in 181 patients low cerebral contusion foci (1–15 ml) were found in 31 cases (17 %). Low cerebral contusion foci predominantly localized in the frontal—15 (49 %), in the temporal—7 (23 %) in fronto-temporal lobes—4 (13 %). ES were detected in 4 patients (12 %). In patients with ES foci were located in the frontal (50 %) and temporal lobes (50 %). In 3 (75 %) cases were immediate ES and in 1 case (25 %) early ES.

Conclusions: ES developed in 12 % patients with low cerebral contusion foci. 75 % of the patients were recorded immediate ES, 25 %—early ES. Risk factor for ES at patients with low cerebral contusion foci is cerebral contusion localized in frontal and temporal lobes.

Disclosure: Nothing to disclose.

PP3134

Fixation loss sensitivity in child patient with symptomatic occipital epilepsy: case presentation

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Introduction: Fixation-off sensitivity (FOS) defines epileptiform discharges that appear in electroencephalography (EEG) by closing eyes and continue as the eyes are closed; it is an electrophysiological phenomenon that is known as bilateral with elimination of fixation. FOS is thought to occur with occipital hyperexcitability which is

frequently seen in idiopathic epilepsy in childhood accompanied by occipital paroxysms.

Case: 15 years old male at was evaluated in our child neurology polyclinic with a seizure story since two years. During the seizure which continued for 5 min tonic–clonic motor phenomena was seen. He was operated for intracranial hematoma after a car accident at the age of 7 and he stayed in intensive care unit for fifteen days. His examination revealed only mild mental retardation. Cranial MR imaging showed encephalomalacia at the posterior temporal and occipital lobe of his left cerebral hemisphere. EEG revealed organization disorder in the left occipital area and existence of epileptiform discharges, which showed continuity while eyes were closed. It drew attention that the discharges disappeared when the eyes were opened. Then EEG was performed again in full darkness and under opaque rift swim mask with opened and closed eyes and similar patterns were observed. It was accepted as FOS with these EEG changes. Carbamazepin 200 mg/day was started and he became seizure free.

Conclusions: Although, cerebral mechanisms that cause FOS development are not known well, we think that FKD encounter not only in idiopathic epilepsies but also in symptomatic epilepsies like our case and that it is not a syndromic phenomenon.

Disclosure: Nothing to disclose.

PP3135

Improving seizure risk management for patients with acute neurological insults: a re-audit following local evidence based guideline introduction

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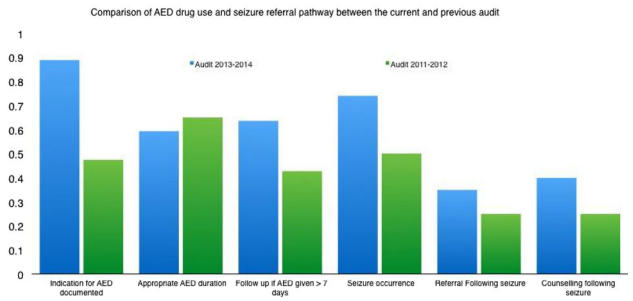
Introduction: Deficiencies in care for patients with/at risk of new onset seizures presenting to non-neurologists within a tertiary neuroscience centre compared to published guidelines[1–3] were identified in a previous audit. Following the introduction of local guidelines we undertook a re-audit to evaluate potential improvements and guide future practice.

Methods: Patients initiated on anti-epileptic drugs (AEDs) by neurosurgical or stroke teams were prospectively identified between June and November 2013. Clinical and demographic data was then retrospectively collected from electronic and paper based medical records. Statistical analysis was carried out using Fisher's exact test.

Results: Of the 36 initially identified patients, 3 were lost to follow up, 2 passed away before data collection, 2 were under the care of neurologists and 2 had their first seizure and AED initiation in previous hospitals. 24/27 patients (88.9 %) had indication for AED documented, in comparison to 19/40 patients (47.5 %) in 2012($p < 0.05$). There was also a trend towards improvement in other parameters, Graph 1.



Conclusions: There has been significant improvement in the documentation of indication for AED use since following the introduction of guidelines, and trends towards improvement in almost all other assessed areas. That fewer patients had been started on AEDs suggests there may also have been a reduction in inappropriate prophylaxis. Local guidelines and education can improve patient care.

1. Bederson, E. et al., *Stroke,* 40 (2009), 994–1025.
2. Chang, BS et al., *Neurology,* 60 (2003), 10–16.
3. NICE, CG0137 (London, 2012), pp. 1–635.

Disclosure: Nothing to disclose.

PP3136

Epilepsia partialis continua associated with non-ketotic hyperglycemia: a case report

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Introduction: Epilepsia partialis continua (EPC) is a rare neurologic condition associated with cortical cerebral lesions and metabolic disorders. Here, we report a case of patient with EPC and hyperglycaemic hyperosmolar state (HHS).

Case report: A 67 year old female patient attended our emergency department with continuous rhythmic clonic jerks of his right arm and paresis for the past two days. He was a known hypertensive and no diabetes mellitus (DM). Head CT scans appeared normal, and an MRI scan with diffusion-weighted imaging (DWI) was reported as showing no acute abnormality, with evidence of mild bilateral microangiopathic disease. Laboratory tests were normal apart from an elevated serum glucose level of 1000 mg/dL and a serum osmolality of 320 mmol/kg. Urinalysis revealed glucosuria (3+) and ketonuria (−). Blood gas parameters were normal (pH 7.42; pCO_2 43 mmHg), consistent with a (HHS). Electroencephalography 24 h after admission showed rhythmic sharp waves over the frontoparietal regions. Administration of lorazepam and phenytoin on admission to the medical ward had no effect. Addition of levetiracetam to phenytoin 3 days later was similarly without benefit. Because of continued seizures, the patient's hyperglycemia was managed with insulin and fluid replacement; the clonic jerks decreased about 15 days after the glucose level returned to normal. The patient remained free of seizures and taking antiepileptic after a month later.

Conclusions: EPC may be the first manifestation of DM and response to antiepileptic drugs is poor. This condition should be kept in mind for early diagnosis and treatment.

Disclosure: Nothing to disclose.

PP3137

Epileptic seizures in multiple sclerosis patients

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Introduction: The presence of epileptic seizures in patients with multiple sclerosis (MS) is a well-known phenomenon. The aims of our study was to determine mean age/gender and age of MS patients with the onset of seizures, to identify the types of epileptic seizures in MS patients by sex/age, to identify the correlation between relapses and seizures, and to identify the main electrophysiological/imaging changes.

Methods: The medical records of 300 MS patients observed between January 2000 and December 2009 in the Neurological Clinic of University Clinical Centre of Kosova were reviewed. All patients fulfilled the McDonald MS criteria Epilepsy diagnosis was based on the ILAE (1983) criteria while epileptic seizures were classified based on the ILAE classification (1981).

Results: Out of 300 MS patients enrolled in this study, 49 (16.33 %) were identified with seizures or epilepsy. In 23 (47 %) patients out of 49, seizures or epilepsy appeared after the MS diagnosis. In 6 patients (12.2 %), epileptic attacks preceded the MS diagnosis, while in 20 patients (40.8 %), epilepsy was diagnosed before multiple sclerosis. These patients were treated with antiepileptics. Out of 23 patients (47 %) in whom the epileptic seizures appeared after the MS diagnosis, 17 (74 %) had simple partial seizures, and 6 (26 %) had complex partial seizures. Based to our study, the epileptic seizures in MS patients appeared about 2.2 years after the MS diagnosis.

Conclusions: Simple partial seizures were 2.8 times more frequent compared to complex partial seizures. Females were more affected than males.

Disclosure: Nothing to disclose.

PP3138

Clinical features of adult onset neuronal ceroid lipofuscinosis: a long term follow-up of two siblings

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Introduction: Neuronal ceroid lipofuscinoses (NCL) are rare neurodegenerative lysosomal storage disorders, and one of the causes of progressive myoclonic epilepsy (PME). They present as progressive psychomotor destruction, visual failure, ataxia, epilepsy and are classified according to the age at onset and the defective gene. We present two siblings diagnosed as NCL-type-6 with a novel mutation who had photosensitive myoclonus, stimulus-sensitive seizures, cerebellar signs and excellent response to piracetam (PRC).

Methods and results: A 32 year-old female whose seizures started at age 18 was presented with photosensitive myoclonus, stimulus-sensitive myoclonic, absence and generalised tonic–clonic seizures (GTCS). She had slow progressive cerebellar signs with psychological problems. EEG revealed generalised spike/polyspike and wave, prominent on awakening and photic stimulation. Cystatin-B protein gene for Unverricht-Lundborg disease (ULD), muscle biopsy for myoclonic-epilepsy and ragged-red fibers (MERRF) and sweat gland biopsy for Lafora disease were negative. Ataxia dramatically ameliorated and seizures were under control with high dose of PRC, topiramate (TPM), valproate (VA). Seizures of the 28-year-old brother started at age 26, and were rare and composed of GTCS and myoclonia. He had ataxia and dysarthria. EEG revealed photosensitivity. Same treatment regimen was started, clinic response was dramatic. Genetic analysis revealed that both siblings had a homozygous, previously unreported mutation, c.509A > G, p.Tyr170Cys in the *CLN6* gene. Parents who had consanguineous marriage were heterozygous carriers, compatible with autosomal recessive inheritance.

Conclusions: Adult-onset NCL with PME, dementia and ataxia was recently associated with mutations in *CLN6*. In epilepsy with myoclonus, photosensitivity and cerebellar signs, NCL should be in the differential diagnosis.

Disclosure: Nothing to disclose.

PP3139

Determinants of depression among patients with epilepsy in Athens, Greece

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Objective: Depression is common among patients with epilepsy. The aim of our study was to estimate the prevalence of a major depressive episode and to identify its determinants among patients with epilepsy treated in the largest Greek hospital, in Athens.

Methods: All consecutive patients with epilepsy that visited the epilepsy outpatient's clinic of Evangelismos General Hospital were invited to participate to the study. Ninety-four patients met our inclusion criteria.

Results: A diagnosis of a current major depressive episode was established in 21 out of 94 eligible to participate (22.3 %) patients. Being a female was associated with a 17.87-fold increase in the odds of having a major depressive episode (95 % CI 3.18–100.57, $p = 0.001$); being unemployed was associated with a 5.78-fold increase in the odds of having a major depressive episode (95 % CI 1.13–29.52, $p = 0.035$) and each extra seizure experiencing per month was associated with a 1.36-fold increase in the odds of having a major depressive episode (95 % CI 1.06–1.76, $p = 0.018$).

Conclusion: Female gender, seizure control and unemployment are important determinants of a major depression episode among patient with epilepsy.

Disclosure: Nothing to disclose.

PP3140

Electroencephalographic patterns recorded by continuous video-EEG monitoring in the critically ill patients with altered mental status

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PP3141

The comprehensive diagnostic approach to epileptic encephalopathy in children

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PP3142

Abstract withdrawn

PP3143

Effect of oxcarbazepine (Oxapine) on cognitive functions in epilepsy

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PP3144

Abstract withdrawn

PP3145

Valproic acid induced non-epileptic negative myoclonus

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PP3146

Autoimmune epilepsy—diagnosis, therapeutic remarks and outcome

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PP3147

Efficacy and safety of Zonisamide as 1st add on therapy in Indian adults with partial, generalized or combined seizures: a sub-analysis

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PP3148

Efficacy and tolerability of zonisamide in partial onset seizures in Indian adults: a sub-analysis

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PP3149

Hypothalamic hamartoma associated epilepsy—not always gelastic, not always refractory

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PP3150

Online epilepsy counseling in Croatia: what do the users want to know?

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PP3151

Comparison of the psychiatric features between conversion disorder and epilepsy patients with non- intractable seizures

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PP3152

Congenital bilateral perisylvian syndrome: a case report

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PP3153

Epilepsy: a rare manifestation of Fahr's syndrome

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PP3154

Clinical outcomes of non-convulsive status epilepticus

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PP3155

Cardiac asystole presenting as epileptic seizure

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PP3156

Dyke-Davidoff-Masson syndrome: a case report

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PP3157

Modern aspects of therapy symptomatic epilepsy: efficiency and safety

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PP3158

Objective background of the refractory epilepsy development founded on structural-metabolic alterations of brain

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PP3159
Dyke-Davidoff-Masson syndrome: case report

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[Figure 1a,b)hemiatrophy of the left side of body]

PP3160
Progressive encephalopathy with edema, hypsarrhythmia, and optic atrophy (PEHO) syndrome

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PP3161
Oxidative stress in epilepsy and experience of using the recombinant human superoxide dismutase in epileptic patients

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PP3162
Embolization with particles and coils for intracranial dural fistula—a good choice for reducing the frequency of recanalization and seizure control

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PP3163
Antiepileptic drug withdrawal in adult epilepsy and the risk factors associated with seizure relapse

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PP3164
For a better life: clinical and therapeutic correlations in epilepsy

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PP3165
Epilepsy in phenylketonuria—case presentation

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PP3166
Single seizure in children: EEG recurrence criteria

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PP3167
Assessing *p*-glycoprotein expression in patients with drug resistant epilepsy by noninvasive quantitative analysis through dynamic (R)-[(11)C]-Verapamil PET

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PP3168
Juvenile myoclonic epilepsy combined with systemic lupus erythematosus

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Headache and pain 2

PP3169
Hypertrophic cranial pachymeningitis: diagnostic and therapeutic challenges

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Introduction: Hypertrophic cranial Pachymeningitis (HCP) is an inflammatory process that thickens the dura mater. This disease has various etiologies. The aim of this study was to describe the clinical presentation of HCP and therapeutic options.

Case report: The clinical features, neuroimaging findings, and treatment outcomes for four patients with different causes of HCP are reported here. Inaugural clinical presentations were: subacute intracranial hypertension syndrome (n = 1), visual disturbances (n = 1), orthostatic headache (n = 2). In all patients, brain MRI revealed a thickened dura mater. Investigations lead to three different diagnosis: tuberculosis of the central nervous system, sarcoidosis and spontaneous intracranial hypotension. Treatment included anti-tubercular therapy, corticosteroid and immunosuppressive drugs and epidural blood patch.

Discussion: Hypertrophic cranial pachymeningitis is an uncommon disorder with few studies correlating clinical, imaging and histopathological features. Clinical manifestations depend on the location of lesions. Headache is the most common sign, and can reach 100 % in cases of idiopathic HCP. Involvement of cranial nerves is also frequent especially the VI's pair, none of our patients had cranial nerves involvement. MRI is the gold standard, it confirms the diagnosis of HCP, assesses its intensity and the lesions distribution, and also detects possible complications. The biopsy of meninges is of great interest especially for idiopathic HCP but it remains an invasive procedure which must be left for last intention.

Conclusion: This report highlights the challenges of the diagnosis and management of hypertrophic pachymeningitis. Despite frequently posing diagnostic challenges, HCP has favorable outcome when treated appropriately.

Disclosure: Nothing to disclose.

PP3170

Patient's perspectives on a minimal-contact self-help intervention for migraine

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Introduction: Migraine affects 10 million people in the UK, with total costs estimated at £5 billion a year. We aimed to test a self-help behavioural intervention for migraine-related symptoms and disability.

Methods: We undertook a nested qualitative study within a Self-management migraine Headache Education pilot trial. The intervention consists of relaxation techniques with aspects of CBT, delivered in 5 sessions by a nurse CBT therapist. Participants were recruited by headache specialists. The first participants to complete the intervention and follow-up were invited to a semi-structured interview. The aim was to explore the aspects of the intervention which participants liked or found difficult, and their beliefs and anxieties about migraines. Interviews were transcribed verbatim and analysed for themes.

Results: Half the intended group (9/10) of participants have been so far interviewed. The majority had well-established migraines and the impact on their work and social lives was important. Nearly all participants identified stress as a triggering or exacerbating factor to their migraines. Anxiety over the lack of control or underlying cause of the migraine was common. Participants found the CBT-like aspects of the intervention challenging. The relaxation techniques were popular, and easier to maintain. Participants reported that the benefits included reduction in headache frequency, anxiety and increased ability to relax.

Conclusions: Participants learnt some CBT and relaxation techniques. Some participants continued to practice them, more frequently relaxation. Preliminary findings suggest this intervention is acceptable to patients, and it may reduce a vicious cycle of migraine symptoms.

Disclosure: Nothing to disclose.

PP3171

Atypical nummular headache or circumscribed migraine? Pressure algometry data in 3 cases

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Nummular headache (NH) is characterized by head pain circumscribed to an area of 1–6 cm diameter. Migraine features including photophobia, phonophobia, nausea, or triggering by physical activity have been occasionally described. We present 3 cases in whom pressure algometry facilitated differential diagnosis between NH and migraine.

Three patients fulfilling diagnosis criteria for NH. Pressure pain thresholds (PPT) assessed on 21 points distributed over the scalp according to normalized positions for electroencephalogram recordings, as well as symptomatic area and non-symptomatic symmetrical point. Pain sensitivity maps constructed for the whole scalp.

Patient 1: 21 year-old woman with episodic pain confined to a circular area of 5 cm diameter over left frontal scalp, accompanied by photophobia and phonophobia, and triggered by physical activity.

Patient 2: 48 year-old man with continuous pain in a rounded area of 2 cm diameter on right parietal scalp, with superimposed exacerbations accompanied by nausea.

Patient 3: 78 year-old man with episodic pain in a circular area of 4 cm diameter with right frontal location, triggered by physical activity. PPT maps in first two cases showed anterior to posterior gradient as previously described in migraineurs; none of them responded to gabapentin but in both significant improvement with beta-blockers. PPT map in third patient typical of NH, with hypersensitivity restricted to symptomatic area; complete relief was achieved with amitriptyline.

NH concomitant with symptoms suggesting central sensitization might correspond to a circumscribed migraine. Pressure sensitivity maps may allow to answer this question and to guide treatment.

Disclosure: Nothing to disclose.

PP3172

Multifocal nummular headache: a cartographic study

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Introduction: Nummular headache (NH) was defined as a pain felt in a small circumscribed area of the scalp. This confinement of pain suggests a peripheral mechanism. Infrequently NH is multifocal, each symptomatic area retaining all typical characteristics of NH. Here we present a case report of multifocal NH studied with pressure algometry.

Methods: 14-year-old-woman with a 3-year history of continuous pain in four rounded areas 4 cm in diameter, all of them with the same size and shape. Pain lasted about 3 h in each area. They were located in symmetrical areas of the parietal and occipital regions. Pain intensity was 5 out of 10 in a visual analog scale. Pressure pain thresholds (PPT) were measured with a mechanical algometer on 21 points distributed over the scalp. Locations of these points were based on normalized positions for electroencephalogram recordings. Symptomatic points were also assessed. A pain sensitivity map was constructed. Neurological exam was normal, without sensory symptoms with palpation in painful areas or local trophic changes. Brain magnetic resonance imaging and blood tests were obtained with no abnormalities.

Results: As previously shown in NH, symptomatic points had lower PTT values than the surrounding areas, so the map showed four patches of hyperalgesia at the painful zones. Preventive treatment with gabapentin achieved complete pain remission.

Conclusions: As far as we know, this is the first multifocal NH assessed with pressure algometry. According to our results, peripheral mechanisms are maintained in multifocal NH.

Disclosure: Nothing to disclose.

PP3173

Idiopathic intracranial hypertension: clinical characterization and prognosis of a group of patients

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Introduction: Idiopathic intracranial hypertension (IIH) is characterized by signs of intracranial hypertension, in the absence of meningeal inflammation and structural lesions.

Methods: Identification of patients with IIH, based on criteria by Friedman 2002, observed between 1990 and 2013. Clinical files review.

Results: Twenty patients were identified, seven excluded for not meeting criteria. From thirteen patients, nine were female with mean age at presentation 31.3 ± 14.2 years. Eight had obesity I-II, five were overweighed/normal. Headache was the presenting symptom in ten patients, visual loss in two, ocular pain in one. Six patients had diffuse headache, four hemicrania. Six experienced a tightening headache and four pulsatile. It was paroxysmal in three patients and continuous in seven (three with morning worsening). All experienced visual disturbances: seven diplopia, three blurred vision, three photophobia. Twelve had papilledema, eleven bilateral. Blind spot enlargement was the commonest visual defect (nine). Mean CSF opening pressure was 393 ± 98.6 mmHg. All were treated with acetazolamide, mean dose 1,000 mg, plus furosemide in five. Median follow up was 4.0 years (0.5–10.0). Seven stopped medication after median time 1.2 years (0.1–9.3). Two were submitted to ventriculoperitoneal shunt, seven months and nine years after first symptoms.

Conclusions: Headache is a key symptom in IIH, as recognized by International Headache Society. It was the commonest presenting symptom in our series; however a significant proportion of patients did not have the classical intracranial hypertension headache. There should be a high level of suspicion for IIH, even when headache lacks the typical clinical features.

Disclosure: Nothing to disclose.

PP3174
Somatoform dissociative experiences in migraine without aura

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Introduction: The comorbidity of headache and psychiatric symptoms is frequently found in clinical practice. Most papers on psychiatric and headache comorbidity are focused on depressive and anxiety disorders. Less known comorbidity of other somatic symptoms with headache, especially migraine. The aim of this study was to assess somatoform dissociative experiences among patients with migraine without aura.

Methods: 110 patients suffering from migraine without aura according to ICH-III criteria who applied to the outpatient unit of Neurology Department of Erzurum Regional Training and Research Hospital in Erzurum, Turkey, and 33 subjects without migraine were recruited for the study. The participants were asked to complete sociodemographic form, the Somatoform Dissociation Questionnaire (SDQ), Beck Depression Scale (BDS), Beck Anxiety Scale (BAS), Migraine Impairment Disability Assessment Scale (MIDAS) and Visual Analog Scale (VAS).

Results: In patients group; SDQ scores showed that 47.2 % were normal 29.1 % had Somatoform Dissociation, 18.2 % Dissociative disorder not otherwise specified (DDNOS), 10 % Dissociative identity disorder (DID). In DID group 63.6 % had 10 point VAS score. The test values were correlated with MIDAS scores. 17.3 % had severe, 21.8 % moderate, 23.6 % mild, 37.3 % minimum depression. 40.9 % had severe, 32.7 % moderate, 16.4 % mild, 10 % minimal anxiety levels. MIDAS were found severe disability in 43.6 % of patients.

Conclusions: This findings imply that migraine patients have high risk of somatoform dissociative experience. A significant positive correlation was found between SDQ scores and MIDAS and VAS scores. Future studies with psychiatric evaluation are needed to investigate further the influence of somatoform and dissociative disorders in migraine related disability.

Disclosure: Nothing to disclose.

PP3175
Intramuscular stimulation of pericranial myofascial trigger points in the treatment of frequent episodic tension-type headache

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Introduction: The present study aimed to evaluate the efficacy of intramuscular stimulation (IMS, also known as Trigger Point Dry Needling) at the pericranial muscles in patients with frequent episodic tension-type headache (ETTH).

Methods: The study included 48 patients with frequent ETTH that were randomized into two groups. IMS was administered to group 1 ($n = 24$), massage therapy was administered to group 2 ($n = 24$); IMS was applied to the trigger points of the frontal, temporal, masseter, sternocleidomastoid, semispinalis capitis, trapezius and splenius capitis muscles bilaterally. The frequency of painful days and the patients' visual analogue scales (VAS) were evaluated before treatment, and 1, 2, 4 weeks and 3 months after treatment.

Results: Mean age of the patients was 34.28 ± 9.41 years (range 21–57 years). In both groups, the number of painful days in a month, visual analogue scale values, amount of analgesic use in a month after the treatment. As a result, all of the parameters were found to have improved in both groups ($p < 0.05$), the results were statistically significant, and the IMS group's response to the treatment was better than the Massage group ($p < 0.001$).

Conclusions: IMS into the myofascial Trigger points located in the pericranial muscles could be considered as an effective alternative treatment for ETTH.

Disclosure: Nothing to disclose.

PP3176
Ocular and cervical rectified vestibular evoked myogenic potentials in patients with migraine and tension type headache

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Introduction: Numerous studies have identified an association between primary headache disorders and several vestibular syndromes. Cervical VEMP (cVEMP) reflect saccular function, whereas ocular VEMP (oVEMP) reflect probably predominantly utricular function. Therefore, to determine if oVEMP and cVEMPs differ in patients with migraine without aura (MO), tension type headache (TTH) and controls.

Methods: 15 female patients with MO, 18 female patients with episodic TTH were included in the study. 34 healthy volunteers for comparable age were taken as the control group. The participants underwent a Korean dizziness handicap inventory (DHI) questionnaire. oVEMP and cVEMP using a blood pressure manometer were recorded. From the VEMP graphs, latency, amplitude parameters and asymmetry ratio were analyzed after EMG rectification.

Results: The mean DHI scales of patients were significant higher in patients with MO compared with TTH groups ($p < 0.05$). But, P13, n23 latencies and amplitudes of rectified cVEMP in MO and TTH patients were not significantly different from the results of the healthy controls ($p > 0.05$). Rectified oVEMP mean n1, P1 latencies and amplitude asymmetry ratio among groups were not significant

($p > 0.05$). Also, no significant correlation were noted between scores of DHI and VEMP parameters.

Conclusions: This preliminary study suggested that MO and TTH seem to be associated with a normal interictal ocular and cervical VEMP profile. Therefore, a larger study including migraine subtypes such as vestibular migraine necessary for improved understanding of the clinical usefulness of the VEMP test.

Disclosure: Nothing to disclose.

PP3177

Carotid stenting headache

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Introduction: The carotid stenting can cause secondary headache. But it is unclear who could develop neither its features.

Methods: We used a prospective observational study. We registered patients who went to carotid stenting and were hospitalised in the Lozano Blesa Hospital. We studied sociodemographic, cardiovascular risk factors, carotid affectation and primary headache history. We made a structured interview, before, after technique and twenty-four hours later, to know if the headache appears.

Results: 36 patients were included. The average age was 67 years. The 83 % ($N = 30$) were males. The 22.9 % ($N = 8$) had primary headache history, 37.5 % ($N = 3$) migraine with aura and 62.5 % ($N = 5$) of headache tensional. The secondary headache appeared in 8 patients (22.2 %), in 50 % ($N = 4$) during the technique, 37.5 % ($N = 3$) during the first six hours and in one case after 24 h. In the 50 % ($N = 4$) the headache lasted less than ten minutes, in 25 % ($N = 2$) between 2–120 min and 25 % ($N = 2$) 2–24 h. The principal localization was in the fronto-temporal region (50 %, $N = 4$), facial (25 %, $N = 2$) and occipital and hemicraneal 12.5 % ($N = 1$) each one. The 75 % ($N = 6$) was unilateral and 37.5 % ($N = 3$) bilateral. It was described as oppressively in 75 % ($N = 6$) with mild intensity in 62.5 % ($N = 5$) and moderate 37.5 % ($N = 3$) and 75 % ($N = 6$) didn't need analgesia. It had seen a power significance associated to developed who were younger ($p = 0.02$), primary headache history ($p = 0.033$) and left carotid affectation ($p = 0.05$).

Conclusions: The carotid stenting headache appears in 20 % of the patients, and there is higher risk to develop the younger people, the primary headache history and left internal carotid artery affected.

Disclosure: Nothing to disclose.

PP3178

Iatrogenic intracranial hypotension associated with cerebral venous thrombosis

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Introduction: Intracranial hypotension (IH) may be a complication of dural puncture during epidural anesthesia (EA). The association between IH and cerebral venous thrombosis (CVT) is rare; the mechanism is probably related to venous enlargement that leads to stasis, increasing the risk of thrombosis. A change in the character of the headache should prompt a possible diagnosis of CVT.

Case report: Female, 20 years old, healthy. She gave birth under EA. 24 h later she complained of a headache related to orthostatism that ceased when supine. Neurological examination, performed 8 days after symptoms onset, was normal. She had been treated with endovenous caffeine, analgesics and bed rest with no improvement. A brain venous MRI was performed three days later, which showed bilateral subdural hematomas (SH) as well as venous thrombosis of a parietal cortical vein and superior longitudinal sinus (SLS). At the same day, an epidural blood patch (BP) was performed, with immediate relief of the headache. Follow-up MRI (6 days after BP) showed complete reabsorption of the SH and complete patency of the cortical vein with partial recanalization of the SLS. Patient was discharged, asymptomatic.

Conclusions: We report the occurrence of CVT as an uncommon consequence of severe IH secondary to EA. Due to the association between both disorders the usual clinical presentation of CVT was not observed. BP is an efficacious therapy for IH and its complications.

Disclosure: Nothing to disclose.

PP3179

Evaluation of anti-neuronal autoimmunity in migraine patients with white matter lesions

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Introduction: Immunological mechanisms have been proposed for the pathogenesis of migraine with white matter lesions (MWML). However, specific antigenic targets have never been investigated in MWML patients.

Methods: To investigate potential neuronal target autoantigens, sera of 13 MWML (10 women, 3 men; mean age 37.2 ± 3.1), 50 migraine patients without MRI lesions (39 women, 11 men; mean age 35.1 ± 4.7), 23 relapsing remitting multiple sclerosis (RRMS) patients with multiple periventricular plaques (18 women, 5 men; mean age 34.8 ± 5.2) and 23 hypertension-related cerebral small vessel disease (SVD) patients (17 women, 6 men; mean age 58.2 ± 6.4) were screened with protein macroarray and ELISA. Antibody levels were compared with ANOVA.

Results: Protein macroarray analysis produced 75 reactive clones. Four clones (ENSA, SRI, LPPR3, ATP1B2) with the highest signal intensity and number of duplicates were selected for further investigation. ELISA studies showed high-titer serum antibodies to one or more of these proteins in 7/13 of MWML, 13/23 of SVD, 8/23 of RRMS and 1/50 of migraine patients with no MRI lesions. A common reactivity against four examined antigens could not be found in any group. As assessed by ANOVA, serum levels of antibodies to ENSA, SRI and LPPR3 were significantly higher in MWML, RRMS and SVD groups than control migraine patients.

Conclusion: Our study failed to find an autoantibody response unique to MWML. Nevertheless, demonstration of antibodies in neurological diseases with cerebral white matter destruction but not in migraine patients without brain lesions suggests that migraine associated lesions might not have a benign nature.

Disclosure: Nothing to disclose.

PP3180

Evaluation of sensory and pain perception and its central modulation in chronic low back pain

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Introduction: Chronic low back pain (LBP) is one of the most common painful conditions, but the exact mechanisms of chronic pain development are still not fully understood in these patients. The objective of this study was to evaluate the sensory profiles and function of central modulation of pain perception in LPB patients in order to reveal possible underlying mechanisms of chronic pain.

Methods: A detailed evaluation of sensory and pain perception according to DFNS QST protocol was performed in 42 chronic LBP patients (24 men, median age 36 years) and 47 age-matched healthy volunteers (17 men). Furthermore, magnitude of conditioned pain modulation (CPM) and temporal summation (TS) using thermal stimuli were assessed.

Results: LBP patients showed significantly increased detection thresholds for most of the non-painful sensory modalities examined (warm, cold, vibration, mechanical detection), more frequent paradoxical heat sensation phenomenon and decreased thermal and pressure pain thresholds in comparison to controls, particularly in feet. The differences in CPM and TS effect between the groups were not significant, but NRS scoring of all the painful stimuli applied during these tests was higher in LPB patients comparing to controls. Similarly, higher mechanical pain sensitivity in LBP group was found.

Conclusions: Clearly decreased sensory perception and increased pain perception and pain sensitivity were found in LBP patients compared to healthy controls, particularly in feet. Normal function of CPM and TS shows that abnormity of these central modulatory mechanisms doesn't play a key role in the LBP development.

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PP3181

Face recognition in patients with migraine

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Introduction: Prosopagnosia is a rare dysfunction seen during the aura phase of migraine. We aimed to evaluate the face recognition which has not previously been investigated in migraineurs during the interictal period and its relationships with clinical features.

Methods: Seventy-four migraineurs with or without aura diagnosed according to the International Headache Society criteria and 37 healthy control subjects were included. Benton Face Recognition Test (BFRT) and Judgment of Line Orientation Test (LOT) for complex visual perception were applied to all participants.

Results: Migraineurs showed significantly lower performance in both of the BFRT and LOT scores (p:0.027; p:0.014, respectively); indicating impaired visuospatial perception. In the subgroup analysis, these impairments were more pronounced in the group with migraine without aura, interestingly.

Conclusion: Migraineurs had poorer performance in both face recognition and visual-spatial perception. We think that our findings could be based on functional differences in the migraineurs' brain or genetic changes.

Disclosure: Nothing to disclose.

PP3182

Headache characteristics in the geriatric age group

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Introduction: We analyzed geriatric people presenting with headache, aged over 65 years, admitted to our outpatient clinic between the years 2011–2013. The cases were selected according to the International Headache Classification 3rd Edition.

Methods: We scanned 175 patients (126 female, 49 male), mean age was 74 years. The cases were classified as primary, and secondary headache groups, then were scanned according to any accompanying comorbidities, along with imaging (MRI) characteristics.

Results: In the primary headache group (142 patients) 21 % of the patients were subclassified as migraine type headache, 56 % as tension type headache, and 45 % as trigeminal neuralgia. In secondary headache group (30 patient) 27 % were associated with hypertension, 17 % with temporal arteritis, and 20 % with cervical pathology, 14 % with intracranial mass. MRI characteristics were as 75 % nonspecific differences, 25 % normal findings.

Conclusions: This study was designed to determine the type of headache most frequently encountered in the geriatric population, along with accompanying chronic diseases, and imaging characteristics. These preliminary data of our ongoing study, will be presented with detailed statistical analysis.

Disclosure: Nothing to disclose.

PP3183

Decreased antioxidative status in migraine patients with brain white matter hyperintensities

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Introduction: Migraine patients have an increased risk to develop deep white matter hyperintensities (WMH) than the general population, and the prevalence of these lesions is higher in migraine with aura (MWA) than in migraine without aura (MWoA).Oxidative stress is believed to play a role in the pathogenesis of migraine. The present study was undertaken to assess oxidant-antioxidant balance of migraineurs with and without WMH. We hypothesized that increased oxidative stress and decreased antioxidant response may play a role in the pathophysiology of WMH in migraineurs.

Methods: We evaluated oxidative status with MDA as its major indicator and to determine the activities of antioxidant enzymes: SOD, GSH-Px and catalase in serum of migraineurs with and without WMH. The study included 18 migraine patients with WMH at the age

of 33.28 ± 9.94 years and 14 migraine patients without WMH, aged 34.71 ± 9.09 years.

Results: The MDA, SOD and GSH-Px levels in serum were not statistically different between patients with WMH and without WMH. In the migraine group with WMH, serum catalase activity was significantly lower than in migraine group without WMH ($p < 0.013$).

Conclusions: We demonstrated that the levels of catalase were decreased in migraine patients with WMH. These finding suggest that decreased antioxidant response may play a role in the pathophysiology of WMH in migraineurs. Further studies are necessary.

Disclosure: Nothing to disclose.

Neuroimaging

PP3184

A comparative value of T1 and T2-weighted magnetic resonance imaging (MRI) and transcranial sonography (TCS) in Parkinson's disease: a prospective pilot study of 16 cases

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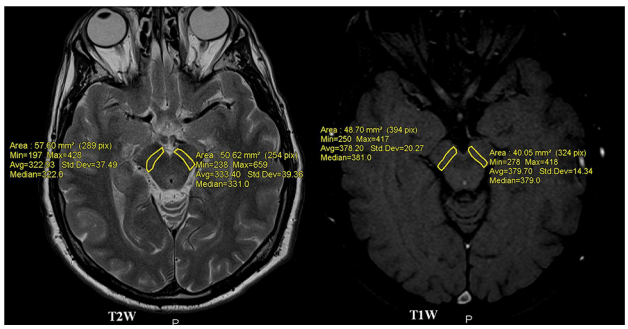
Introduction: The aim of the study was to: (1) evaluate quantitatively the diameter and plot of the substantia nigra (SN) on T1 W and T2 W MRI sequences for the patients with idiopathic Parkinson's disease (IPD) and healthy controls; (2) to compare MRI and TCS parameters.

Methods: A prospective case–control study of 11 IPD patients and matched-to-IPD group 5 healthy subjects was performed at Kaunas Clinics in 2011–2013 according to an established imaging protocol. TCS was performed by one neurosonologist (2–5 MHz PA transducer, Voluson 730 Expert, GE, Austria), followed by brain MRI (1.5 T Magnetom Avanto, Siemens, Germany). The latter imaging was performed and measured by two radiologists at different time intervals (Fig. 1).

Results: The majority in IPD group were male (n = 8, 72.7 %), the mean (±SD) age was 59.6 ± 7.0 years (min. 48–max. 69), symptom duration 5 ± 3.6 years (min. 2–max. 12), and stage according to Hoehn-Yahr 2 ± 0.8 (min. 1–max. 3). The main MRI findings are presented in Table 1. Bland–Altman plots revealed sufficient diagnostic agreement among MRI-SN and TCS-SN measurements, with more narrow limits for T1 W than T2 W (right $x = 0.088$, left $x = 0.042$, bilateral $x = 0.065$). A significant correlation was found between T2W-SN proximal diameter and TCS-SN plot on the right side ($r = -0.7$, $p = 0.01$).



Subjects n=16	T2W/TSE/448 ax			T1W/SE/fs/3mm ax			T2W/TSE/448 ax			T1W/SE/fs/3mm ax		
	Right side (mean+/-SD, mm or mm^2)						Left side (mean+/-SD, mm or mm^2)					
	Prox	Dist	Plot	Prox	Dist	Plot	Prox	Dist	Plot	Prox	Dist	Plot
IPD (n=11)	2.5±0.8	2.8±0.8	38.4±12.7	2.5±0.7	2.5±0.6	34.3±15.2	2.5±0.7	2.8±0.9	40±10.8	2.5±0.7	2.4±0.9	31.8±9.7
Control (n=5)	3.3±0.8	3.1±0.7	53.6±11.5	3.3±0,8	3.2±0.5	45±8.9	3.2±0.6	3.4±0.5	51.7±12.7	3.3±0.6	3.2±0.7	43.3±11
P value	0.05	NS	0.04	0.03	NS	NS	NS	NS	NS	0.04	NS	0.05

Conclusions: When performing diagnostic MRI for the patients with IPD, the measurements of the SN diameter (mm) on T1W, but plot (mm^2) on T2W sequences can be more informative. A sufficient diagnostic agreement was established between MRI-SN and TCS-SN, however the only significant negative correlation was found between T2W-SN diameter and TCS-SN plot on the right side.

Disclosure: Nothing to disclose.

PP3185

Morphological brain changes in men and women with poststroke cognitive impairment

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Introduction: The association between ischemic stroke and cognitive impairment (CI) is well documented. The aim of the study was to find sex differences of neuroimaging brain changes in ischemic stroke patients with CI.

Methods: Fifty two women at the acute phase of ischemic stroke (mean age 64.3) and 36 matched by age and education men (mean age 65.0) without other severe medical conditions, psychiatric disorders or aphasia underwent neurological examination and magnetic resonance imaging (MRI); additional measurements included the Frontal Assessment Battery (FAB), Clinical Dementia Rating Scale, Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). Types of CI were defined according to currently established criteria.

Results: The following spectrum of CI was revealed: subtle CI (15.3 % in women vs. 13.9 % in men), mild CI (38.5 vs. 16.7 %), dementia (46.2 % vs. 69.4) ($p < 0.05$). According to the IQCODE prestroke CI occurred in 41.9 % men and 29.1 % women ($p < 0.05$). The MRI has shown that prestroke CI group and men were characterized by more severe degree of internal cerebral atrophy whereas women surpassed men by the average rate of periventricular leucoaraiosis ($p < 0.05$–0.01). In men, unlike women, positive correlations are revealed between the index of lateral ventricle bodies and the summary FAB score ($r = 0.39$, $p < 0.05$). Men had more often than women ischemic lesions in strategic areas like frontal lobe (48.7 vs. 33.1 %), basal ganglia (23.3 vs. 13.3 %), thalamus (27.7 vs. 17.8 %).

Conclusions: The received data expand information about neuroimaging brain changes of men and women with poststroke CI.

Disclosure: Nothing to disclose.

PP3186

Atypical language networks in epilepsy: the interaction with the epileptic network

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Introduction: Atypical language network location and/or lateralization have been reported in a relevant proportion of patients with epilepsy. The presence of structural lesion, early age of epilepsy onset and epilepsy severity have been associated with atypical language; however the underlying mechanisms of this phenomenon are still unknown. In this study we used fMRI to map both the epileptic network and the language network and analyse the correlation of these two as well as the effect of interictal epileptiform discharges (IED) on language activation.

Methods: An 8-year-old left handed girl with left frontal lobe epilepsy secondary to a left middle cerebral artery perinatal stroke underwent simultaneous EEG-fMRI and language fMRI. Maps of the epileptogenic network related to the IED and language maps for verb generation, picture naming and describing were generated using statistic parametric mapping.

Results: EEG-fMRI analysis showed bilateral frontal cortical areas and basal ganglia involvement during the generation and spread of IED. In particular, it revealed involvement of language relevant areas (inferior and middle frontal gyrus right > left). Crucially, these regions were not significantly activated during language fMRI. Instead, language activation in the structurally-intact (right) hemisphere was located more posteriorly and superiorly.

Conclusions: Lack of activation in this patient's expected language areas (right inferior and middle frontal gyrus) may be explained by the overlap between the epileptic network and the language network. Interaction between epileptic and cognitive networks provides some insight to understand atypical organization on cognitive networks in patients with epilepsy.

Disclosure: Nothing to disclose.

PP3187

White matter microstructural investigation of coherent motion perception with diffusion MRI

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Introduction: Brain function and the underlying structure are in the highlight of neuroscience. Grey matter structures involved in motion detection in a noisy environment are well known from human functional imaging studies (Buchel et al. 1998). The functional connectivity between these nodes is a highly investigated property of the motion detection and attention networks (Buchel and Friston 1997; Friston et al. 1997; Penny et al. 2004). However, the structural connectivity and its relation to the brain function is not well known yet (Johansen-Berg 2010). In order to resolve this issue, we investigated the white matter microstructural background of motion discrimination with random dot kinetogram.

Methods: Parameters describing the white matter microstructure were estimated from high-angular resolution diffusion MRI data. Voxelwise fractional anisotropy in the white matter skeleton (Smith et al. 2007) was correlated with motion discrimination threshold in random dot kinetogram paradigm. Probabilistic tractography was used to reveal the connectivity of identified regions.

Results: Significant positive correlation was found between the motion discrimination threshold and the local fractional anisotropy in the posterior part of the right superior frontal gyrus, right juxta-cortical superior parietal lobule, left parietal white matter, left superior temporal gyrus and the left optic radiation. Pathways initiated from these seed regions passed over the segregated branches of the superior longitudinal fascicle, which are probably related to the dorsal and ventral attention networks (Corbetta and Shulman 2002).

Conclusions: Our study calls attention to the tightly linked visual and attention systems and the correlation between brain structure and function.

Disclosure: Nothing to disclose.

PP3188

Clinical correlations of microstructural changes in progressive supranuclear palsy

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Introduction: In patients with progressive supranuclear palsy (PSP), previous reports have shown a severe white matter (WM) damage involving supra and infratentorial regions including cerebellum. In the present study, we investigated potential correlations between WM integrity loss and clinical-cognitive features of patients with PSP.

Methods: By using magnetic resonance imaging and diffusion tensor imaging (DTI) with Tract Based Spatial Statistic (TBSS) analysis, we analyzed WM volume in 18 patients with PSP and 18 healthy controls (HCs). All patients underwent a detailed clinical and neuropsychological evaluation.

Results: Relative to HCs, patients with PSP showed WM changes encompassing supra and infratentorial areas such as corpus callosum, inferior fronto-occipital fasciculus, midbrain, anterior thalamic radiation, fornix, superior cerebellar peduncle and superior longitudinal fasciculus. Among different correlations between motor-cognitive features and WM structural abnormalities, we detected a significant association between fronto-cerebellar WM loss and executive cognitive impairment in patients with PSP.

Conclusions: Our findings, therefore, corroborate the hypothesis that cognitive impairment in PSP may result from both "intrinsic" and "estrinsic" frontal lobe dysfunction, likely related to cerebellar disconnection.

Disclosure: Nothing to disclose.

PP3189

Regional metabolic change in superior temporal gyrus in children with congenital sensorineural hearing loss: study by magnetic resonance spectroscopy (MRS)

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Introduction: To study the changes of regional metabolic in Superior temporal gyrus (STG) in children with congenital sensorineural hearing loss (SNHL) by magnetic resonance spectroscopy (MRS).

Method: In 54 individuals (1–5 years old) with congenital sensorineural hearing loss (SNHL) and 20 healthy controls (1–3 year old, n = 10) and (3–5 years old, n = 10), two regions of interest (ROIs) positioned in the Superior temporal gyrus (STG) were investigated

bilaterally using MRS. SNHL patients were divided into two groups: group A (1–3 years old, n = 28)and group B (3–5 years old, n = 26). N aceytl aspartate (NAA), N aceytl aspartate (NAA)/creatine (Cr), choline (Cho), choline (Cho)/creatine (Cr) in both side of Superior temporal gyrus were calculated by MRS and analysed by LC model in all subjects.

Results: Compared with healthy control group (age-matched), MRS showed regional metabolic of NAA were decreased in group A, and Cho were increased in group B in superior temporal gyrus in children with congenital sensorineural hearing loss. There is statistically difference of NAA in STG between control group and patient group A ($P < 0.05$), and statistically difference of Cho in STG between control group and patient group B ($P < 0.01$).

Conclusions: Regional metabolic change in superior temporal gyrus in children with congenital sensorineural hearing loss may be corresponding to the lack of auditory input since birth, after 3 years old, increased of CHO might suggest that a loss of myelin and axonal fibers in SNHL patients. To gain optimal benefits, early implantation in prelingually deaf children is necessary.

Disclosure: This work was supported by the Natural Science Foundation of Guangdong Province, China (Grant No.S2012010008974), and was sponsored by Shantou University Medical College Clinical Research Enhancement Initiative.

PP3190

Micro and macrostructural alteration of the subcortical structures in cluster headache: a neuroimaging study

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Objectives: Previous studies showed that basal ganglia involved in pain processing. Neuroimaging studies detected activation in basal ganglia in acute and chronic pain. Limited data is available in cluster headache; therefore, in the current study we examined deep brain structures in cluster headache patients.

Methods: High resolution T1-weighted and diffusion weighted MRI images with 60 directions were acquired from eleven patients with cluster headache and eleven age-matched healthy controls. Images were mirrored to make sure that all patients had the pain on the right side. VBM and FIRST analysis were used to measure the cortical thickness and the volume of the basal ganglia, respectively. Group differences were evaluated with independent sample t-test. Intra-subject inter-structure correlations of basal ganglia volumes were investigated. Mean of the diffusion parameters of the basal ganglia were defined in each group. Correlation between basal ganglia volumes, mean diffusion parameters and cumulative number of headache days was examined.

Results: There were no differences in the volume of basal ganglia between the healthy and patients' group. Volume of subcortical structures in cluster headache showed strong intra-subject inter-structure correlation. Diffusion parameters showed alteration (amygdala, pallidum, putamen) in patients compared to controls and correlation with attack/life was detected. No cortical changes were found in patients.

Discussion: Strong inter-structure volume correlation might mean the same rate of changes. The laterality specific diffusion alterations point to pain specific changes. Analysis of basal ganglia in cluster headache might offer a deeper insight into the pathomechanism of the pain processing in the disease.

Disclosure: Nothing to disclose.

PP3191

Diffusion tensor imaging and plaque volume quantitation of normal-appearing white and grey matter of the brain in clinically isolated syndrome: a longitudinal study

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Introduction: To investigate whether diffusion tensor imaging (DTI) measurements and brain lesion volume on conventional MRI of patients with clinically isolated syndrome (CIS) are associated with conversion to multiple sclerosis (MS) over a 4-year follow-up period.

Methods: Twenty patients with CIS and 10 healthy controls were included in the study. The mean diffusivity (MD) and fractional anisotropy (FA) measures in 9 brain regions of normal-appearing white (NAWM) and grey matter (NAGM), together with volumes of brain T1 and FLAIR lesions, were assessed for up to 4 years.

Results: Over the follow-up period, MS was diagnosed in 11 of the 20 patients (55 %). The baseline T1 and FLAIR lesion volumes but none of the DTI indices were associated with conversion to MS (T1: $p = 0.021$; FLAIR: $p = 0.015$). At baseline, both converting and nonconverting patients had lower FA in one NAWM region (the cerebral peduncle) and higher MD in three NAWM regions (the internal capsule, corona radiata anterior, and centrum semiovale) than controls. However, only converting patients had a lower FA in the caudate nucleus. Over the follow-up period, the worsening of DTI measurements was primarily observed in converting patients.

Conclusions: DTI abnormalities in NAWM and NAGM were already present in patients with CIS, but over the follow-up period, these changes worsened, especially in patients developing MS. A higher volume of T1 and FLAIR lesions but not the severity of DTI changes in NAWM or NAGM are predictive for conversion to MS.

Disclosure: Nothing to disclose.

PP3192

Early left atrial diastolic dysfunction measured by transthoracic echocardiography is a risk factor of atherosclerosis in cerebral infarction patients

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Introduction: Last year we indicated that early cardiac diastolic dysfunction is related to development of atherosclerosis in acute cerebral infarction patients, using transthoracic echocardiography (TTE). In addition to our previous findings, this year we evaluated the actual left atrial volume as a parameter to assess developed left atrial dysfunction using 3D TTE.

Methods: We evaluated 320 patients hospitalized for acute atherosclerotic cerebral infarction from April 2012 to December 2013.

Blood examination, TTE, and carotid ultrasonography were performed in the acute phase. Parameters representing systolic and diastolic cardiac function were assessed: left ventricular ejection fraction (EF), early inflow atrial wave (E), atrial contraction wave (A), and mitral annulus velocity (e′). We also evaluated left atrial volume of 43 patients using 3D TTE at the same time. Carotid atherosclerosis was measured as plaque score (PS). These parameters and fibrinolysis marker D-dimer were statistically analyzed.

Results: E′ and E/A negatively correlated with PS. On the contrary, correlation of left atrial volume and PS were not statistically significant.

Other parameters shown no significant correlation with PS or D-dimer.

Conclusions: E′ and E/A reflecting early cardiac diastolic dysfunction. Decrease of left atrial diastolic function leads to elevation of left ventricular end diastolic pressure and activation of sympathetic nervous system leading to damage of endothelial cells. Left atrial diastolic dysfunction are also observed as increased left atrial volume, but in the late phase. Our results suggests that decreased left atrial diastolic function in the early stage is associated with development and worsening of carotid atherosclerosis.

Disclosure: Nothing to disclose.

PP3193

Subcortical atrophy and it's relation to the white matter microstructural alterations in multiple sclerosis

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Introduction: MRI is a key approach for the diagnosis and the monitor of multiple sclerosis (MS). According to recent studies the subcortical atrophy is a sensitive MRI-marker of the disablement. The aim of our investigation is to reveal the connection between the white matter (WM) microstructural disintegration and the subcortical atrophy.

Methods: T1-weighted and FLAIR images and diffusion MRI data, with 60 directions were acquired in 31 RRMS patients and 31 age-matched controls on a 1.5 T MRI scanner. Subcortical atrophy was evaluated with a surface based segmentation approach (FIRST). WM microstructure was evaluated with track based spatial statistics (TBSS). Whole WM diffusion parameter changes as compared to the mean of the healthy were related to the subcortical atrophy.

Results: The statistical analysis revealed significant atrophy in case of the left ($p < 0.048$) and right ($p < 0.024$) caudate nucleus, the left ($p < 0.024$) hippocampus, left ($p < 0.024$) and right ($p < 0.036$) putamen and the left ($p < 0.007$) and right ($p < 0.048$) thalamus.

Stepwise linear regression confirmed the FA in the area of the normal appearing white matter (NAWM) was the main predictor of the atrophy in case of the right and left caudate nucleus ($p < 0.004$; $p < 0.011$;), the right and left hippocampus ($p < 0.007$; $p < 0.010$) the left pallidum ($p < 0.004$); the right and left putamen ($p < 0.006$; $p < 0.000308$); the right thalamus ($p < 0.010$; $p < 0.008$).

Conclusions: According to our results the subcortical atrophy was primarily driven by the disintegration of the NAWM.

Disclosure: Nothing to disclose.

PP3194

Cortical activity modulation by botulinum toxin type A in patients with post-stroke arm spasticity: real and imagined hand movement

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Introduction: In post-stroke spasticity functional imaging may uncover modulation in central sensorimotor networks associated with botulinum toxin A (BoNT) therapy. Investigations were performed to localize brain activation changes in stroke patients treated by BoNT for arm spasticity using functional MRI (fMRI).

Methods: 14 ischemic stroke patients with hand weakness and spasticity were studied. Spasticity was scored by modified Ashworth scale (MAS). FMRI was performed 3 times: before (W0) and 4 (W4) and 11 weeks (W11) after BoNT. Group A: 7 patients with hand plegia, who imagined moving fingers. Group B: 7 age-matched patients able to perform sequential finger movement. Statistic analysis (FSL) yielded group session-wise statistic maps and paired between-session contrasts.

Results: BoNT transiently lowered MAS in W4 in both groups. In group A, activation of frontal premotor cortex dominated. At W4, ipsilateral cerebellum engaged and persisted at W11. Paired contrasts showed activation decrease in bilateral occipital cortex $W0 > W4$ and left occipitoparietal increase $W4 < W11$, resulting from occipital deactivation (also precuneus and medial orbitofrontal cortex) at W4. Group B additionally activated contralateral motor and parietal cortex and bilateral cerebellum. From W0 to W4, activation was markedly reduced, which persisted at W11. Paired contrasts confirmed differences $W0 > W4$ (ipsilateral parietal, occipital and premotor) and $W0 > W11$ (occipitoparietal). The effect of deactivation was limited.

Conclusion: Study of 2 age-matched groups with mild and severe weakness demonstrated different effect of BoNT-lowered spasticity on motor system engagement.

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Disclosure: Nothing to disclose.

PP3195

Accelerated reconstruct MRI T2 map from sub-sampled K-space Data using compressed sensing at 7.0 Tesla

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Introduction: We aim to use less k-space data to obtain high quality reconstructed MRI T2 map based Compressed sensing (CS) by optimized DWT-based nonlinear conjugate gradient (DWT-NCG) algorithm.

Methods: The phantom and in vivo SD mice brain experiments were conducted under an Agilent 7.0 T animal MRI system. The T2 map was obtained by FSE pulse sequence. The frequency code of all the images was fixed to 256, and the based phase encoding was 256. We sub-sampled the k space data by altering phase encoding, namely 32, 64, 96, 128 and 192. We speedily reconstructed by optimized NCG algorithm using MATLAB software and closely analyzed the peak signal to noise ratio (PSNR) by comparing with the original

image. Then corrected the gradient and update the number of iterations to modify the gradient image.

Results: After being compressed, the retained energy is 99.29 %, and the number of zeros is 93.73 %. By wavelet transformation, most coefficients are small. T2 map obtained from a reduced data set can be reconstructed precisely by optimized DWT- NCG algorithm when the accelerated factor is 4.

Conclusions: In this work, the optimized DWT-NCG algorithm of compressed sensing could accelerate MRI T2 map by reducing the number of acquired kspace data which can significantly achieve rapid high quality imaging in MRI at 7.0 Tesla. The performance of the proposed algorithm would especially meaningful to clinical application.

Disclosure: Nothing to disclose.

PP3196

A potential method for imaging GABA in vivo using chemical exchange saturation transfer

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Introduction: To develop a novel MRI technique to measure gamma-aminobutyric acid (GABA) based on its chemical exchange saturation transfer (CEST) effect and to investigate the concentration dependent CEST effect of GABA in rat brain tumor model with blood brain barrier (BBB) disruption.

Methods: CEST Z-spectra of GABA with different peak B1 amplitude and other metabolites (glutamine, myo-inositol, creatine and choline) were acquired at 7 T, 37° and pH 7.0, respectively. CEST images of phantom consisting of test tubes with different concentrations of GABA solutions (pH 7.0) and solutions of other metabolites were collected to investigate the concentration dependent CEST effect and the potential contributions from other.

Results: CEST and 1HMRS data of rat brain with tumor were gathered at baseline and 0.5, 1.0, 1.5 and 2.0 h following the injection of GABA solution and then analyzed using LCModel.

CEST asymmetry of GABA was observed at $\sim$2.75 parts per million downfield from bulk water. The CEST effect of GABA increased with the peak B1 amplitude but kept steady when peak B1 reached 255 Hz (6.0 μT). The CEST effect of GABA was proportional to the GABA concentration at pH 7.0 in vitro. CEST maps of GABA from a rat brain with tumor whose BBB was compromised showed a significant gradual increase in CEST effect after GABA injection, which was consistent with the 1HMRS data.

Conclusions: These findings demonstrate the feasibility and potential to map changes in GABA concentration using CEST. It is likely that this method provides noninvasive images of GABA with excellent spatial and temporal resolution.

Disclosure: Nothing to disclose.

PP3197

Motion aftereffect by means of circular vection depicts role of MST and OP2 in visual-vestibular interaction

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Objectives: Several works have revealed a visual-vestibular interaction at the cortical level (1).

Aim of this fMRI and videooculography (VOG) study was to induce egomotion and differentiate the phenomenons of torsional afternystagmus (tOKAN) and motion aftereffect (MAE) during circular vection (CV).

Methods: The effects of CV were studied in 21 volunteers in a clinical 3 T scanner. Data was analysed with SPM8. Eye movements were also recorded and analyzed offline by VOG to quantify tOKAN.

Results: There was no significant correlation for the MAE with the duration and gain of tOKAN. FMRI analysis gave bilateral activations in the dorsal visual stream as well as deactivations in the posterior insular cortex (cytoarchitectonic area Ig2). T-contrast results for the MAE in comparison to the visual stimulation showed bilateral activations in the medial superior temporal area (MST) and a deactivation of the right cytoarchitectonic area OP2.

Conclusions: MAE due to CV is independent of tOKAN and may be based in area MST which has been reported to receive vestibular information (2). Visual motion deactivated multisensory structures in the posterior insula; during periods of MAE on the other hand we found a deactivation of the parietal operculum. The concurrent deactivation of the main cortical vestibular area OP2 during the MAE suggests that MST and OP2 could be the gateways for conflicting visual-vestibular information.

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Disclosure: Nothing to disclose.

PP3198

Abstract withdrawn

PP3199

Reversible splenial lesions of the corpus callosum in association with symptomatic epilepsy—two cases with different pathogenesis

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PP3200

Neuro-imaging in Behçet disease: a report of 5 cases

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PP3201

Neuroimaging findings in an adult patient with Hunter disease

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PP3202
Sonographic findings of the ulnar nerve in patients with carpal tunnel syndrome

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PP3203

Abstract withdrawn

PP3204
Diagnosis of carotid body paragangliomas by various imaging techniques and treatment

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PP3205
Quantitative EEG (Q-EEG) in posterior reversible encephalopathy syndrome (PRES) due to post-vaccination encephalopathy

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PP3206
Tracking of brain activation using EEG signals: a preliminary study

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PP3207
Usefulness of susceptibility-weighted imaging for the detection of thrombus in acute cardioembolic stroke

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PP3208
Activity in object manipulation network is sustained afters acute tactile deafferentation: an fMRI study

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PP3209
White matter atrophy in Parkinson disease

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PP3210
Kings cardiac MIBG PD grading (KCMP) in clinically uncertain Parkinsonism: reproducible and an easily characterized imaging tool

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PP3211
Cerebral perfusion changes in patients with carotid artery stenosis after surgical revascularization

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PP3212
Detection of acute ischemia with chemical exchange saturation transfer imaging based on gradient echo sequence

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PP3213
Blooming artifact on 3T T2*-weigted MRI as a potential detector of multiple occlusions of cerebral arteries in acute stroke

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PP3214
Wernicke encephalopathy mimicking vasculitis and neoplasia

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PP3215
Auditory neural pathway evaluation on sensorineural hearing loss using diffusion tensor imaging

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PP3216
An analysis of factors related to the accuracy of quantification of GABA levels in brain using LCModel software: a 7T 1H-MRS study in rats

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PP3217
Spatiotemporal evolution of blood brain barrier damage and associated changes of brain metabolites within the first 3 h after ischemia onset

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PP3218
Study of whole brain MRI before cochlear implant assessment

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PP3219
Prognosis for cochlear implantation in children with myelin development delay

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Neuro-oncology

PP3220
Disseminated cystic lesions: a case of disseminated oligodendroglial-like leptomeningeal tumor

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Introduction: Disseminated oligodendroglial-like leptomeningeal neoplasms are unusual presentation of oligodendroglial tumors and mostly seen in pediatric patients. Disseminated cystic lesions are mostly seen along the surface of the posterior fossa especially cerebellum. Brain stem, medial and inferior of temporal and frontal lobes are also affected. Spinal cord involvement is common in most of the cases. We present an atypical case of disseminated oligodendroglial-like leptomeningeal tumor with an older onset and preserved spinal cord parenchyma.

Methods: EEG, brain and spinal MRI, brain biopsy were performed for diagnosis.

Results: A 22-year-old female referred to our hospital after having two generalized tonic–clonic seizures and auras of smell and nausea. Seizures that started 2 months before admission, lasted 2 min with tonic posture on her right hand and deviation of head and eyes. Brain MRI showed multiple hyperintense cystic and nodular lesions on T2 weighted images. Some of them had contrast enhancement on T1 weighted images. Spinal MRI was normal. CSF evaluation was normal, except for the elevated opening pressure. Pathological evaluation showed a nodular lesion consisting of oligodendroglial-like cells which were negative with NeuN, synaptophysin, pNF, GFAP, CD34, Ki-67, IDH-1, p53 staining and mostly resembled disseminated oligodendroglial-like leptomeningeal tumor morphologically. The patient is stable with antiepileptic treatment.

Conclusions: Disseminated oligodendroglioma-like tumors are a rare form of low-grade glial tumors. Differential diagnosis includes parasitic infections and other glial and sarcomatous neoplasms with leptomeningeal involvement. Radiological and pathological evaluations are essential. Diagnosis is difficult because of the imprecise pathological characteristics of the neoplasm.

Disclosure: Nothing to disclose.

PP3221
Paraparesis and sciatic pain caused by bilateral sacral solitary fibrous tumors: when the least plausible cause is the diagnosis

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Introduction: Solitary Fibrous Tumors (SFT) are rare soft-tissue tumors of pleural or, less often, extrapleural location. Although sciatic pain is very common, extraspinal compression of the nerve is extremely rare.

Results: A 44-year-old man, healthy apart from a totally resected left pelvic SFT in 2010, presents at the emergency department with bilateral sciatic pain and gait disorder. He had progressive sciatic pain at the right for 11 months, and left for 1 month, that aggravated walking and sitting. Numbing and tingling of the right foot for 6 months. One month before, he developed constipation and effortful micturition, after a week, paresis of the right foot and leg, and later also his left foot. Neurological examination disclosed an asymmetric paraparesis (Right leg grade 2, left leg grade 4 MRC), normal deep tendon reflexes apart from abolished right aquilian reflex and indifferent right plantar response. He also showed reduced tactile and algic

sensation distally in both legs. At this point cauda equina syndrome due to compressive lesion was suspected and spinal MRI was performed. With a normal MRI, an extraspinal cause was pursued, pelvic CT showed bilateral sacroiliac lytic mass lesions. Histology was compatible with bilateral SFT recurrence and the patient was oriented to chemotherapy and radiotherapy.

Conclusions: To our knowledge this is the first report of sciatic pain as manifestation of SFT. Progressive compression of the sacral plexus and sciatic nerve in the thigh was responsible for the symptoms and its appropriate investigation allowed the diagnosis.

Disclosure: Nothing to disclose.

PP3222

Primary central nervous system lymphoma with diffuse lesions in an immunocompetent patient

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Introduction: In immunocompetent patients, lesions of primary central nervous system lymphoma (PCNSL) are usually solitary, located in a cerebral hemisphere, thalamus/basal ganglia, corpus callosum, periventricular region and cerebellum. Authors report the case of an immunocompetent patient with an unusual aspect of lesions.

Methods: A 61 years old woman presented a vestibular syndrome. Two weeks later behavioral changes appeared, apathy, Millard Gubler syndrome, then tetraparesis, right ataxia, aphasia, urinary incontinence. Brain MRI showed: multiple lesions with hyperintensity on T2/FLAIR, isointensity on T1, with moderate water restriction in diffusion sequences, some of them with moderate contrast enhancement, imprecisely delimited, located in bilateral fronto-insular periventricular white matter, corpus callosum, bilateral capsulo-lenticular, right caudat nucleus, with nodular appearance in the anterior pole of frontal lobe, left midbrain, right pons, left superior cerebellar peduncle. The differential diagnosis was made between: acute disseminated encephalomyelitis, lymphoma, gliomatosis cerebri, viral encephalitis and prion disease.

Results: CSF examination showed: 7 monocytes/mm^3, normal glucose and protein, protein 14-3-3 and oligoclonal bands were negative. Blood biochemistry and CBC were normal. HIV, cytomegalovirus, Epstein Barr virus and herpes simplex virus serology were normal. Bone marrow aspirate was normal. Corticosteroids produced temporary clinical remission. The brain stereotactic biopsy established the diagnosis: non Hodgkin lymphoma with large B cells, CD20 positive. Spinal cord MRI, contrast enhanced CT of chest, abdomen and pelvis, and dilated eye examination were normal. Methotrexate, idarubicin and cytarabine produced partial remission.

Conclusions: This case showed that diffuse lesions may be also found in immunocompetent patients with PCNSL.

Disclosure: Nothing to disclose.

PP3223

Multiple myeloma relapse presenting as meningeal myelomatosis

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Introduction: Leptomeningeal infiltration by monoclonal plasma cells is a rare clinical presentation in patients with multiple myeloma (MM), ocurring in around 1 % of such patients.

Case report: We report the case of a 70-year-old male patient, diagnosed in early 2012 with Durie-Salmon Stage III A non secretory MM that presented as a sacral plasmacytoma. He underwent radiotherapy, four chemotherapy cycles with cyclophosphamide, bortezomib and dexametasone, followed by autologous bone marrow transplant, with very good response. He relapsed 2 months later, needing another 6 chemotherapy cycles, with adriamicine, carmustine, cyclophosphamide and melfalane, having good response with disease control (marrow samples with 1.2 % plasmocyte count). One week after the last cycle, the patient presented with a progressive encephalopathy, gait abnormalities and a right third cranial nerve palsy. The head CT scan was normal, excluding space occupying or lytic lesions. A lumbar puncture revealed mild pleocytosis (227 leucocytes/μL) with predominantly aberrant plasmocytes (around 96 %, CD38+). He was diagnosed with meningeal myelomatosis and started intrathecal chemotherapy.

Conclusions: MM presenting as meningeal myelomatosis is a rare neurological entity. It is usually associated with multifocal (and variable) neurological deficits and should be suspected in patients with MM even without evidence of intracranial masses or cranial intraparenchymal infiltration. The treatment options include intrathecal chemotherapy but the prognosis is generally very poor.

Disclosure: Nothing to disclose.

PP3224

Two cases of chronic polyradiculoneuritis revealing asymptomatic multiple myeloma

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Introduction: The spectrum of multiple myeloma's (MM) neurological manifestations is diverse including mainly the spinal cord compression. The involvement of the peripheral nervous system (PNS) is rare. We report two cases with MM revealed by isolated chronic polyradiculoneuritis (CPRN).

Case reports: A 34-year-old woman (1) and a diabetic 66-year-old man (2), were admitted for progressive weakness and numbness of four limbs. Neurological examination showed quadriplegia with areflexia predominantly in the lower limbs. Electromyography and neuromuscular biopsy findings were consistent with demyelinating CPRN. Laboratory tests revealed a monoclonal IgG-lambda antibody. Cerebral spinal fluid examination showed increased protein level with normal cell count. Spinal MRI disclosed an osteolytic lesion the right iliac crest for both patients, associated with multiple locations on the vertebrae, and hepato and splenomegaly in one case 1. The diagnosis of MM was confirmed by the presence of a bone marrow plasma cell infiltration. Search for Bence jones proteinuria and amyloidosis was negative in case 1. The treatment started with systemic chemotherapy.

Discussion: Involvement of the PNS is rare in MM. Axonal sensorimotor polyneuropathies are the most common, and usually associated to the osteosclerotic form. CPRN are exceedingly rare, but frequent with solitary plasmacytoma. The pathophysiology of these neuropathies remains obscure with numerous theories including amyloidosis, ischemia, toxic metabolic factors (circulating abnormal protein) and myelin antibodies. The management of the neuropathy consists in treatment of the tumor.

Conclusions: These observations emphasize the need for systematic testing for plasma cell proliferation in patients with unexplained lasting CPRN.

Disclosure: Nothing to disclose.

PP3225

CNS disorders induced by radiation therapy of the brain

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Introduction: CNS radiation therapy is commonly used to treat a variety of CNS tumors including primary and metastatic tumors of the brain or in an attempt to prevent the development of metastases like in small cell lung cancer. The treatment dose and volume depend on the histology, location and size of the tumor. Radiation administered to treat CNS neoplasms can result in acute, subacute, and delayed neurologic syndromes. Most important in clinical practice is radionecrosis which occurs 1 to 3 years after radiation. Symptoms depend on the location and size of necrotic lesion. Their presentation can mimic tumor recurrence. Cerebral radionecrosis often occurs after focal EBRT or brachytherapy.

Methods: This is a case study about 60 years old man with initially squamous cell carcinoma of the lung in IIIA stage with complete pathologic response on the treatment of primary tumor and disease free survival of 2 years when he developed headaches accompanied by ataxia, right homonymous hemianopia and hemiparesis. Brain MRI revealed brain metastases in cerebellum, left occipital and temporal lobe. The whole brain RT (30 Gy: 3 Gy/10fr) was delivered with sequentially chemotherapy.

Results: The patient had 12 months disease free interval, then the same symptoms in more aggressive form occurred and brain MRI showed focal radionecrosis.

Conclusions: RT of the brain can lead to necrosis and the dose which gives a 5 % probability of a given late effect 5 year after treatment for whole brain RT is 45 Gy. Sometimes necrosis can occur with even lower doses which depends of endogenic factor.

Disclosure: Nothing to disclose.

PP3226

Bing Neel syndrome mimicking Lyme neuroborreliosis

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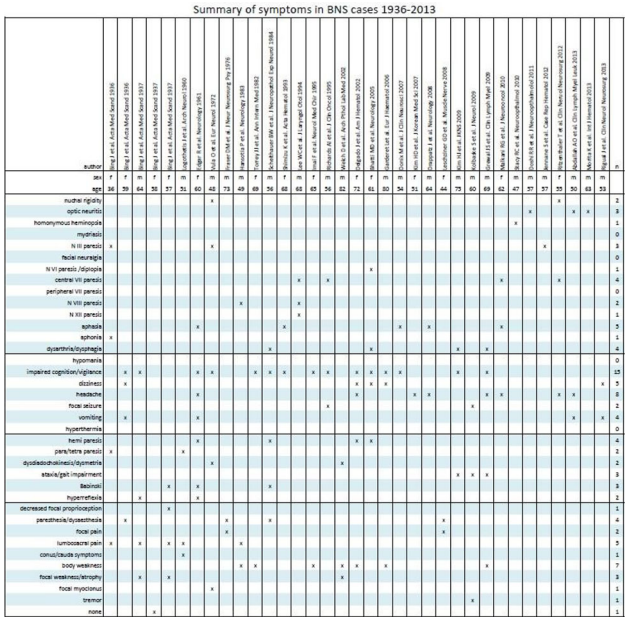
Introduction: Central nervous system (CNS) affection in Waldenstrom Macroglobulinemia (WM) is called Bing Neel Syndrome (BNS).

Methods: We report on a patient with peripheral paresis of the VIIth cranial nerve.

Results: An 82-year-old man with ongoing WM was referred to our hospital due to intractable nocturnal pain in his legs.

Clinical manifestation was a mild hemi paresis on the right and a painful sensory and motor polyneuropathy of both legs. CCT detected a small old left middle cerebral artery infarction. Cerebrospinal fluid (CSF) showed 400 cells/μL. Penicillin G 20 MegaIE per day was given due to the assumption of CNS affection in Lyme disease (LD). Nocturnal pain improved but motor function of both legs worsened. Peripheral paresis of the VIIth cranial nerve on the right, impairment of cognition and urinary retention developed within days.EMG displayed the active axonal demyelinisation mostly of motor fibers and MRI confirmed affection of the equine cauda. CSF FACS analysis showed 98 % clonal CD 19+, CD20+ and CD79+B-cells. CSF was negative for LD IgM, confirming BNS. The patient refused chemo or radiotherapy and died within 2 months.

Conclusions: Among the 35 BNS cases in English literature, impairment of cognition or vigilance, headache, body weakness and aphasia are frequent symptoms but mimicking of Neuroborreliosis was not reported before. Only FACS analysis of CSF confirmed the diagnosis of BNS in this case. Due to the pure prognosis of BNS, hematologists need to be alert to neurological symptoms in their patients.



Disclosure: Nothing to disclose.

PP3227

Progressive bilateral ptosis in a patient with midbrain metastasis and chronic inflammatory demyelinating polyneuropathy

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Introduction: A midbrain lesion is a rare but recognised cause of bilateral ptosis. This presentation in isolation, without vertical gaze involvement, is exceptionally rare, but may herald a sinister aetiology that should not be missed.

Methods: Case report of a 68-year-old woman.

Results: A 68-year-old lady with a history of chronic inflammatory demyelinating polyneuropathy presented with progressive asymmetrical bilateral ptosis, but no change in her limb function. Brain MRI showed a midline midbrain lesion displacing the cerebral aqueduct. Chest CT scan revealed a left upper lobe mass, confirmed histopathologically as a poorly differentiated adenocarcinoma.

Conclusions: The clinical presentation of isolated bilateral ptosis resulting from a midline midbrain metastasis is rare but important. In this patient's case, it was essential to seek a central cause, even in the context of a plausible peripheral explanation.

Disclosure: Nothing to disclose.

PP3228

Abstract withdrawn

PP3229

Breast carcinoma presenting as paraneoplastic brainstem syndrome associated with anti-Ri antibodies

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Introduction: Anti-Ri antibodies are onconeural antibodies mainly associated with breast and gynecological cancers and small cell lung carcinoma, being mostly associated with cerebellar degeneration and opsoclonus-myoclonus. Symptom onset often begins prior to the diagnosis of systemic cancer, such that identification of antineuronal antibodies may facilitate diagnosis.

Clinical case: Female, 49 years old, with a 2-month history of diplopia and gait instability. On examination there was a right convergent squint, horizonto-rotatory nystagmus in lateral gaze and an unstable normal-based gait. Brain MRI was normal except for two small arterial aneurisms. Demyelinating, infective causes, vitamin deficiency, toxic exposure and celiac disease were excluded. CSF flow-cytometry was negative for malignant cells. Autoimmune screening showed positive anti-Ri antibodies, leading to the assumption of paraneoplastic syndrome. Steroid treatment was unsuccessful, and monthly intravenous immunoglobulin was then commenced, with slight improvement.

All investigations in search for malignancy were unremarkable, except for breast echography which showed a small nodule in the superior-external quadrant of left breast. Breast MRI was subsequently performed, showing two small nodules in the same location. Core biopsy showed invasive ductal carcinoma grade II. The patient was submitted to conservative surgery followed by radiotherapy and chemotherapy, with progressive improvement since surgery and only slight residual gait imbalance.

Conclusions: This case illustrates that the diagnosis of paraneoplastic syndromes requires a high level of suspicion. Given the onset of symptoms can pre-date the diagnosis of systemic cancer, a thorough investigation is warranted, as treatment of underlying malignancy is the most effective step in controlling the neurological disorder.

Disclosure: Nothing to disclose.

PP3230

Choroid plexus papilloma (4th ventricle) with spread leptomeningeal

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Introduction: Choroid plexus papilloma (CPP) is a rare, histologically benign intracranial tumor, but may present local recurrence or leptomeningeal dissemination. In adults it's usually located in the fourth ventricle. Clinical manifestations result from increased intracranial pressure or hydrocephalus caused by obstruction of cerebrospinal fluid flow or increased production.

We report a case of choroid plexus papilloma of the fourth ventricle with diffuse leptomeningeal seeding.

Methods: A 35-year-old woman, with a history of chronic migraine, presented with oppressive headache beginning two months before, and characteristics significantly different from their usual migraine crisis. Physical examination revealed a papilledema. Neuroimaging findings are described, treatment performed and histopathology.

Results: Neuroimaging studies showed a space-occupying lesion in the fourth ventricle and cystic lesions scattered throughout the subarachnoid space, affecting supratentorial, infratentorial and spinal regions. Completed resection and histopathology of the tumor, confirmed the origin: CPP, with disseminated metastases. After surgery, the patient is asymptomatic. Radiotherapy will be considered in the future.

Conclusions: The CPP dissemination is a rare event. An appropriate differential diagnosis and histological study are very important, to get a definitive diagnosis. Treatment with complete resection of the tumor is the best procedure and derivation of hidrocephalus, when present, must be considered. Adjuvant chemotherapy and radiotherapy have been demonstrated to increase survival in the treatment of choroid plexus carcinoma and may be indicated for aggressive disease.

Disclosure: Nothing to disclose.

PP3231

Immunological findings in patient with Surgical granuloma (case report)

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Objectives: The immune status of the patient with postoperative intra-cerebral aseptic granuloma 7 months after the removal of fibrillar-protoplasmic astrocytoma of the right frontal lobe was observed.

Methods: We have studied immune status of the patient with the determination of the content of CD4+/8+, CD16+, CD25+, CD38+, CD54+, CD95+, CD150+, antibodies to neuroantigen. Cell counts were measured using immunoenzymometric PAP method. Antibodies to neuroantigen studied by Dechtyarenko T.V. described method.

Results: We demonstrated a reduction in the immunoregulatory index CD4+/CD8+ to 1.72, significant increase in the absolute content of CD25+ to 719 cell/mcl, a reduction of the content of phagocytizing neutrophils to 1,500 cell/mcl, a substantial increase in the absolute content of CD38+ to 754 cell/mcl, a significant increase in the level of antibodies to neuroantigen to 22. The amount of lymphocytes expressing molecule of the adhesion ICAM-1 CD54+ (565 cell/mcl) exceeded the normative indices significantly. We found an increase in the content of oncomarker level such as CD150+ to 712 cell/mcl. Furthermore, a quantity of CD95+ (502 cell/mcl) exceeded the normative indices twofold.

Conclusions: For the first time we carried out a study to investigate the immune status of the patient with postoperative intra-cerebral aseptic granuloma formed 7 months after the removal of low grade astrocytoma of the right frontal lobe. The revealed changes describe the presence of the significant immunosuppressive effects, deep disturbances of the processes of intercellular interaction of immunocompetent cells, increased proapoptotic readiness of cells together with the presence of the expressed autoimmune aggression.

Disclosure: Nothing to disclose.

PP3232

Malignant optic pathway glioma in adults with clinicopathologic and molecular features

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Introduction: Malignant gliomas of the optic pathway are rare, and their genetic alterations are poorly known.

Methods: We report a 64-year-old woman with an anaplastic astrocytoma arising from optic pathway together with the molecular features.

Results: She presented with a progressive visual field loss and underwent a biopsy of mass lesion in optic chiasm. After receiving radiosurgery plus concomitant chemotherapy with Temozolomide, she remained stable without aggravation of her visual field defects for 10 months after her initial presentation. Histopathology revealed a hypercellular tumor composed of predominantly pleomorphic astrocytes displaying indecisive biphasic pattern. Molecular analysis by immunohistochemistry showed focal expression of MGMT and p53, whereas no expression was detected in EGFR or mutant IDH1. Sequence analysis revealed wild type *IDH1*, *IDH2*, and *BRAF*. *BRAF-KIAA1549* fusion was not detected.

Conclusions: The presented molecular analysis did not show conclusive molecular changes that specifies glioma type, and which indicated that malignant optic gliomas in adults may share common molecular genetic features with conventional primary glioblastoma.

Disclosure: Nothing to disclose.

PP3233

Ganglioglioma centered in the superior medullary velum

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PP3234

A case of cerebral metastasis mimicking acute inflammatory demyelinating polyradiculoneuritis (Guillain-Barré syndrome)

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PP3235

A hard to diagnose gliomatosis cerebri case

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PP3236

Consecutive occurrence of two primary central nervous system tumors in the same localization

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PP3237

Metastatic brain neuroendocrine tumor originated from liver misdiagnosed glioblastoma multiform. A first case report

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PP3238

Cystic falx meningioma: a case report

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PP3239

First case described of brain metastases heralding a squamous cell carcinoma of the supraglottic larynx

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PP3240

A case of patient with radiation anaplastic meningioma after X-ray therapy of anaplastic oligodendroglioma

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PP3241
Brain tumor- is it so obvious diagnosis?

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PP3242
Paraneoplastic autoimmune brainstem encephalitis; case report

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Neuro-ophthalmology/-otology

PP3243
Superficial siderosis: important consideration in differential diagnosis of syringomyelia

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Introduction: Superficial siderosis is a rare condition secondary to recurrent haemorrhage in the subarachnoid space leading to haemosiderin deposition in the subpial layers of the brain and spinal cord. Patients typically present with a combination of sensorineural hearing loss, pyramidal signs and ataxia with a proportion developing bilateral vestibular failure. Syringomyelia can also present with hearing loss, ataxia and spasticity.

Methods: A 46-year-old gentleman presented aged 14 with a few months history of muscle wasting, weakness of his left hand and loss of pain sensation affecting his left forearm. MRI confirmed syringomyelia (C1–T7) and subsequently underwent urgent foramen magnum decompression. Six years later he developed progressive bilateral hearing impairment, tinnitus and imbalance, presumed to be secondary to the syrinx. On examination, he was dysarthric with saccadic hypermetria and positive head impulse to the left. He had left claw hand deformity, dissociated sensory loss affecting upper limbs, absent reflexes left upper limb, pyramidal signs in left lower limb with bilateral limb dysmetria, intention tremor and broad based, ataxic gait.

Results: Audiometry confirmed bilateral sensorineural hearing loss and calorics showed left vestibular hypofunction. MRI showed residual syrinx cavity and, additionally, revealed marked siderosis with extensive leptomeningeal deposition outlining the bilateral frontal lobes, cerebellum, brainstem and cervicomedullary junction.

Conclusions: We describe a case of syringomyelia with likely post-surgical complication of siderosis, then likely responsible for the audio-vestibular and neurological progression. This case highlights the importance of considering superficial siderosis in the differential diagnosis of syringomyelia.

Disclosure: Nothing to disclose.

PP3244
Dizziness in out-patients and efficient otoneurological examination brief scale

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Introduction: 80 patients with dizziness complaints, treated in out-patients department of clinic of Nervous Diseases at I.M. Sechenov First Moscow State Medical University.

Methods: The survey was conducted according to the otoneurological examination brief scale. It included otoneurological tests, collecting of complaints & medical histories. We assessed spontaneous nystagmus, end-position nystagmus, visual saccades, pure tracking eye movements, position of the sample Dix-Hallpike & McClure-Pagnini; Unterberger&Romberg trials; performed orthostatic hypotension, hyperventilation, coordination tests; evaluated emotional status according to the hospital anxiety & depression scale.

Results: Only 11 out-patients had correct diagnosis before addressing to our clinic. None of them underwent any specific treatment. Benign paroxysmal positional vertigo (BPPV) is the most common cause of dizziness (40 patients); anxiety-depressive disorder without agoraphobia is the second (17 patients); the third is cerebrovascular disease (8 patients). The other diagnoses are:

Ménière's disease (4 patients); vestibular neuritis (4); depression (3); migraine-associated vertigo (2); orthostatic hypotension (2). A brief otoneurological examination allowed to diagnose correctly (82 % of cases). Applied therapy helped significantly (63 patients; 79 %); reduced the frequency of dizziness attacks (23; 29 %) and cured completely (40; 50 %). Only 18 % required additional methods of inspection or hospitalization.

BPPV, being the most common cause of dizziness in out-patients, was exclusively clinical and had an effective treatment. Conducting otoneurological examination allowed to diagnose (82 %), to cure (50 %), to achieve significant results (28 %).

Conclusions: We recommend to perform such surveys in every patient with dizziness complaints. It improves the quality of treatment and reduce the costs.

Disclosure: Nothing to disclose.

PP3245
Recurrent attacks of unilateral fully reversible monocular visual loss: two cases of retinal migraine

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Introduction: Transient monocular visual loss (TMVL) reflects a heterogeneous group of ophthalmologic or neurologic disorders. Among the most important causes to rule out are emboli and anterior ischemic optic neuropathy. However, it could also be due to a rare and poorly understood migraine variant. We report two cases of TMLV.

Methods: A 23-year-old man with history of 2 attacks of migraine with conventional visual aura (hemianopic scotomata) presented with ten fully reversible attacks of left TMLV which were preceded by scintillating scotomata spreading gradually over few minutes lasting 10–15 min over 3 years. A 30-year-old woman with no medical history experienced 11 attacks of TMLV, lasting from 2 to 6 min over 2 years. Neither had headache during or following attacks and had normal neurological and ophthalmologic examination. All investigations particularly brain MRI and arterial investigations were normal. The woman was treated by Metoprolol 200 mg daily, which reduced the attacks by 50 %.

Results: These two patients meet the International Headache Society's criteria for retinal migraine except for the lack of headaches. However in our cases no other diagnosis was consistent. Clinical presentation of retinal migraine is variable and can associate negative and positive symptoms such as TMLV or monocular scintillating scotomatas. The pathophysiology is thought to be a spreading depression in the retina. A preventive treatment like Beta-blockers can be used to reduce the frequency of the attacks, although data is very limited.

Conclusions: Retinal migraine remains a diagnosis of exclusion but must be considered in case of transient monocular visual disturbances.

Disclosure: Nothing to disclose.

PP3246

The correlation of nitric oxide synthesis and visual evoked potential in ophthalmic migraine patients

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Introduction: A migraine attack has a complex pathophysiological mechanism associated with changing of blood flow and function in several brain regions. Some chemical mediators, as is nitric oxide (NO), may play an important role in blood flow changes due to vasodilatation effect. The objective of this paper is to study the correlation between visual evoked potential (VEP) and plasma nitric oxide concentration due to migraine attack in ophthalmic migraine patients.

Methods: We compared 35 healthy volunteers with 56 patients with ophthalmic migraine. Other cerebral diseases were excluded by clinical neurological examination and MRI examination. Other ophthalmologic pathology was excluded by ophthalmological examination. The clinical evaluation of migraine severity was performed by migraine disability assessment scale (MIDAS). The assessment of NO plasma concentration (by Griess reaction) and VEP (by monocular and binocular pattern reversal stimulation using a checkerboard) was made in 2 h from the onset of ophthalmic migraine attack.

Results: The plasma NO concentration was higher in ophthalmic migraine patients. The latency of P100 was significantly longer, and the amplitude diminished. The plasma level of NO was significantly correlated with VEP changes, and with migraine severity.

Conclusions: NO may play an important role in triggering the ophthalmic migraine attack and is correlated with visual pathways dysfunction. The inhibition of NO production may contribute to ophthalmic migraine prophylaxis.

Disclosure: Nothing to disclose.

PP3247

Ocular ischemic syndrom-ultrasonographic characteristics

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Introduction: The internal carotid artery (ICA) is the main route by which the blood is supplied from the heart to the brain and eye. The ocular and orbital circulation is assured by the ophthalmic artery, which is the main collateral branch of the ICA. Occlusion or severe stenosis of the ICA (which is more than 70 % of the arterial lumen's diameter) may lead to transient or permanent symptoms of retinal ischemia and to an increased risk of ischemic stroke. Our purpose was to define orbital circulation abnormalities identified by color Doppler imaging (CDI) of retrobulbar vessels in patients with ICA occlusive/severe stenosis disease.

Methods: We used a Loqic 500 sonographer with 9 MHz linear probe for Doppler investigation of retrobulbar vessels, and an ultrasound equipment (My Lab 50 Esaote) with a 7.5–10 MHZ linear array transducer for extracranial Duplex sonography.

Results: We presented 12 patients with severe ICA stenosis/occlusion that developed or not an ocular ischemic syndrome. We discussed the hemodynamic status (orbital and cerebral) in order to elucidate the contribution to the ischemic symptoms. Cerebral and retinal perfusion is dependent not only on the degree of stenosis, and embolic risk, but also on the presence of unilateral or bilateral lesions and on the patency of collateral pathways.

Conclusions: The presentation of ocular ischemic symptoms may be the initial sign of carotid artery stenosis/occlusion and can also be used to predict the severity of ICA's disease.

Disclosure: Nothing to disclose.

PP3248

Saccade dynamics in adult Pompe disease

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Introduction: Glycogen storage disease type II (Pompe disease) affects mainly proximal skeletal muscles. Despite older histological evidence of extraocular muscle involvement, ocular motor palsies or other eye movement abnormalities are not considered part of the clinical picture.

Methods: In this pilot study, we studied the dynamics of saccadic eye movements of three patients suffering from Pompe disease and compared their performance to that of age matched healthy controls. Horizontal rightward and leftward saccades were recorded binocularly with an infrared photoelectric device (IRIS, Skalar Delft) at 500 Hz sampling rate with 12-bit resolution, while subjects looked at LED targets placed at $\pm 5°$, 10° and 15° eccentricities.

Results: No differences in saccade amplitudes, peak velocities or durations were observed between controls and patients. More specifically, for 5° saccades, patients had a mean peak velocity of 142.1°/s with a duration of 82.4 ms. For 10° and 15° saccades these values were 245.7°/s, 91.2 ms and 331.9°/s, 101.6 ms, respectively, thereby lying well within one standard deviation of the mean of normal data.

Conclusions: Patients with late onset Pompe disease perform fast and accurate horizontal saccades without evidence of muscle paresis or other ocular motor abnormalities. Reported histological abnormalities of extraocular muscles do not appear to have a phenotypic impact.

Disclosure: Nothing to disclose.

PP3249

Gait characteristics of patients with phobic postural vertigo: effects of fear of falling, attention, and visual input

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Introduction: Phobic postural vertigo (PPV) is the most common cause of chronic dizziness in middle-aged patients. Many patients report symptoms during gait. We investigated the gait performance and its relationship to the fear of falling and attention of PPV patients.

Methods: Prospective study of 24 patients with PPV and 24 healthy subjects (HS) using a pressure-sensitive mat (GAITRite®). Subject walked at three different speeds (slow, preferred, fast), during cognitive dual task (DTc), and with eyes closed (EC). Fall efficacy and balance confidence were rated by the Falls-Efficacy Scale-

International (FES-I) and the Activities-specific Balance Confidence Scale (ABC).

Results: PPV patients walked slower with reduced cadence (all $p < .01$), stride length ($p < .05$), and increased double support ($p < .01$) compared to HS. These changes correlated with FES-I ($R = -.528$, $p < .001$) and ABC ($R = .481$, $p < .01$). Walking deterioration under DTc did not differ between PPV and HS, but patients showed a reduced processing speed ($p < .05$). When walking with EC, gait speed decreased more in PPV compared to HS ($p < .05$).

Conclusions: Patients with PPV show gait changes which correlate with the fear of falling and balance confidence. Absent visual feedback led to more pronounced gait deteriorations in PPV than in HS, indicating a higher reliance of the patients on visual information during gait.

Conclusion: These findings support the view that the gait characteristics of PPV can be attributed to an inadequate, cautious gait control.

Disclosure: Nothing to disclose.

PP3250

Incidence, seasonality and comorbidity in vestibular neuritis

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PP3251

Visual perseveration precipitating clomiphene citrate

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PP3252

Prevalence, demographics, and clinical characteristics of vertigo disorders in a specialized multidisciplinary outpatient clinic

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PP3253

Gradenigo syndrome mimicked by nasopharyngeal carcinoma: beyond the classical triad of diplopia, facial pain and otorrhea

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PP3254

Abstract withdrawn

PP3255

RNFL thickness changes in coexistence of optic disc drusen and idiopathic intracranial hypertension

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PP3256

A case report of Vogt-Koyanagi-Harada disease

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PP3257

Neurologic etiologies of visual loss in the young adult

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PP3258

Cavernous sinus syndrome associated with herpes zoster ophthalmicus

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PP3259

Evaluation of retinal nerve fiber layer thickness in a patient with bilateral optic disc drusen

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PP3260

Unilateral papilledema without headache in the pseudotumor cerebri

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PP3261

Abstract withdrawn

PP3264

Bilateral optic neuritis in an immunocompetent adult with herpes zoster

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PP3265

About a rare case of Webino (Wall-eyed bilateral internuclear ophthalmoplegia) syndrome

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PP3266

Dizziness and vertigo in outpatient practice: main causes and algorithm for the clinical assessment

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Sleep disorders

PP3267

The evaluation of cognitive deficits in obstructive sleep apnea syndrome patients through event related potentials

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Introduction: Obstructive Sleep Apnea Syndrome (OSAS) is characterized by desaturation in blood oxygen level and sleep fragmentation because of repeated upper airway obstruction. OSAS related neurocognitive deficits are the result of a combination of both hypoxemia and decreased vigilance. Event related potentials (ERPs) are scalp recorded voltage fluctuations, which reflects several cognitive processes generated within specific brain regions during stimulus processing. In this study, we aimed to investigate cognitive dysfunctions in OSAS patients with ERP.

Methods: 34 OSAS patients and 36 healthy control subjects participated in the study.

Results: Statistical analyses indicate that the P300 amplitudes were significantly lower, and P300 latencies were significantly longer in OSAS patients group. There were no significant differences in latency and amplitude values of N100 and P200 responses between the two groups.

Conclusions: Our results suggest that event related potentials are useful methods for evaluating cognitive functions of OSAS patients. Negative effects of OSAS on cognitive functions could be observed with event related brain responses.

Disclosure: Nothing to disclose.

PP3268

Sleep-related rhythmic movement disorder: case presentation

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Introduction: Sleep-related rhythmic movement disorder (SRRMD) is characterized by repetitive, stereotyped and rhythmic motor behaviors involving large muscle groups often arising at sleep onset or during superficial non-REM sleep. Pathophysiology is yet to be clarified. However, the differential diagnosis of this disease more frequently encountered in mentally retarded children should be carefully performed.

Case: A 34-year-old man presented with uncontrollable head banging and daytime sleepiness of 10 years duration occurring mostly when he was sleepy or at sleep onset. The patient was evaluated with activation polysomnography in our electrophysiology laboratory. Head banging was observed three times during non-REM 1 phase for 25, 27 and 22 s and an average frequency of 8 Hz, thus fulfilling the ICSD-2 criteria for "Sleep-related rhythmic movement disorders". No epileptiform activity was observed on the simultaneous video recording or the 6-chanel EEG recording.

Conclusion: Sleep-related rhythmic movement disorder is more frequently described in mentally retarded children and is relatively uncommon in normal intelligence adults. The present case is remarkable with its onset at a relatively late age and long symptom duration. Being a rhythmic pathology, SRRMD is mostly misdiagnosed as epilepsy and our case helps emphasizing the importance of activation polysomnography in the differential diagnosis.

Disclosure: Nothing to disclose.

PP3269

Microhemorheological effects of sleep apnea/hypopnea syndrome in patients with cerebral ischemia

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Introduction: The newest data prove a high incidence of cerebral ischemic stroke (IS) among patients with obstructive sleep apnea/hypopnea syndrome (OSAHS). The aim of the present study was to investigate the possible microhemorheological effects of OSAHS on cardiovascular and hemostasis system in patients with IS.

Methods: 80 male patients (mean age 61.0 years) with IS were investigated. The following haemorheological parameters was evaluated: erythrocyte aggregability index (EAI), hematocrit (Hct) and plasma viscosity (PV). All of them were underwent a polysomnography (PSG).

Results: It was especially increased EAI by 16 % ($p < 0.001$), Hct by 11 % ($p < 0.001$) and PV by 9 % ($p < 0.1$). Increased EAI was correlated with low hemoglobin saturation and increased left ventricular transmural pressure, as well as increased Hct and PV, with high body mass and Sleep apnea indexes. Almost in all cases defragmentation of the sleep II stage and high percentage of Rapid eye movement (REM) sleep was revealed.

Conclusions: OSAHS is an independent risk-factor of IS. Microhemorheological effects of OSAHS on cardiovascular and hemostasis system, may play an important role in development of IS, besides of well known mechanical, hemodynamic, metabolic and neurohumoral effects.

Disclosure: Nothing to disclose.

PP3270

Sleep-related problems in children with epilepsy: a questionnaire-based study

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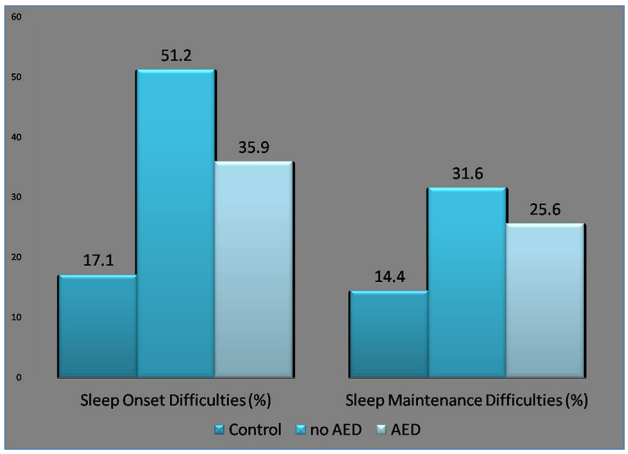
Introduction: Sleep abnormalities are very common in chronic medical disorders. However, less attention has been devoted to sleep difficulties in children with epilepsy. This study was aimed to

evaluate sleep initiate and sleep maintenance in the children having diagnosis of epilepsy.

Methods: A structured sleep-wake questionnaire was specially developed and designed on the basis of Child Sleep Questionnaire for Parents and the Pediatric Sleep Questionnaire. The child sleep problems were assessed according to the identification of difficulty for: sleep onset (a) and sleep maintenance (b) 99 children with idiopathic epilepsies (60 without treatment; 39 treated), 1–16-year-old were selected.

Healthy subjects (n = 1180; 0–16-year-old) from the database of Institute of Neurology and Neuropsychology (Tbilisi. Georgia), were used as control group.

Results: In overall, different sleep problems were identified in 37.4 % (n = 37) of children with epilepsy vs. 32.5 % (n = 384) in healthy children. 45.4 % of children with epilepsy (n = 45) has had sleep onset difficulty. In the control group, difficulties with falling asleep were found in 17.1 % only. Sleep onset difficulties were higher among the patients not receiving the antiepileptic drugs (AEDs) (Fig. 1). In overall, the outpatients having epilepsy have had more nocturnal awakenings (29.3 %) than control subjects (14.4 %). The frequency of sleep restrictions was a little higher in patients without AED (Fig. 1).



Conclusions: The findings of the present study support the opinion that inadequate/poor sleep is common among the children with epilepsy. More medical attention should be focused on the understanding the relationship between childhood sleep problems and the epilepsy management processing.

Disclosure: Nothing to disclose.

PP3271

Excessive daytime sleepiness in restless legs syndrome mimicking narcolepsy

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Introduction: Restless legs syndrome is a frequent sleep-related movement disorder and typically associated with insomnia. Daytime symptoms include fatigue and occasionally excessive daytime sleepiness (EDS). A deficient iron/dopamine transport and/or metabolism may underlie RLS. Narcolepsy-cataplexy is suggested to be an autoimmune-mediated disorder with pathology within the hypocretin system.

Case report: We report the case of a 38-year-old women who was referred to our centre for a second opinion with the diagnosis of narcolepsy.

She described her symptoms as follows: EDS since her adolescents and deterioration within the last 3 years (Epworth sleepiness scale (ESS) was 14). Further, when becoming angry or laughing, her knees became weak. Sleep was fragmented and disturbed. In the evening she felt unpleased feelings in the legs and sometimes the urge to move (IRLS: 17). No other sleep or medical disorders were reported.

Polysomnography showed a sleep efficiency of 65 % with a severe fragmentation of sleep. PLMS was 25/h, no SOREM occurred. On MSLT the following day, she had a mean sleep latency of 2.5 min and one SOREM period.

We diagnosed RLS-PLMS and started treatment with pramipexole (PPX) 0.18 mg and added PPX retard 0.26 mg later on.

Therapy was well tolerated and a severe improvement of symptoms was seen: nocturnal sleep and daytime wakefulness was described as normal (ESS was 7, IRLS was 10).

This case illustrates, that in some cases EDS in even mild-moderate RLS-PLMS can be severe. This differential diagnosis should be taken into account when it comes to excessive daytime sleepiness.

Disclosure: Nothing to disclose.

PP3272

Sodium oxybate for refractory REM-sleep behavior disorder

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Introduction: REM-sleep behavior disorder (RBD) is characterized by the loss physiological REM sleep muscle atonia and dream-enactments. It can be a potentially a harmful condition, as patients can display complex and violent behaviors in sleep. Conventional treatment for the disease is based mainly on benzodiazepines and dopaminergic drugs, however a little percentage of patients can be non-responder.

Methods: The efficacy of sodium oxybate treatment on two male patients with refractory idiopathic RBD was assessed by polysomnography and clinical follow-up.

Results: Two male patients, aged 67 and 49 years old, presented nightly complex dream enactment episodes, sometimes characterized by getting out of the bed. Both experienced violent spells leading to repeated traumas or to the attempt of choking the bed partner. They had normal neurological examination and 123I-FP CIT SPECT. The diagnosis of idiopathic RBD was confirmed by overnight sleep video-polysomnography. Conventional drugs for RBD (i.e. clonazepam, pramipexole, melatonin) and anti-epileptic drugs (carbamazepine, lamotrigine) in various combinations were ineffective. Both patients, after informed consent, were off-label treated with sodium oxybate in add-on. Both patients reported a significantly reduced frequency and intensity of RBD episodes, as confirmed also by bed partners. The beneficial effect persisted at 2 years follow-up of the older patient.

Conclusion: Sodium oxybate can be an effective treatment for idiopathic RBD refractory to conventional drugs, as reported in a previous case report [1].

References

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Disclosure: Nothing to disclose.

PP3273

Influence of sleep disorders on the impulsive behavioral disorders among cognitively-intact Parkinson's disease patients living in the Tomsk region, Russia

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Introduction: Non-motor symptoms of Parkinson's disease (PD) such as Impulsive behavioral disorders (IBDs) and poor sleep are increasingly recognized as important factors in determining the life quality of people living with these conditions. The previous research suggests a higher level of sleep complaints in PD patients who demonstrate IBDs, but the nature of sleep disturbances has to be comprehensively tested yet.

Objectives: To determine a link between sleep disorders and IBDs in PD patients.

Methods: 164 of 834 PD patients were screened for reveal of IBDs (Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale-QUIP-RS) and sleep disorders (Epworth Sleepiness Scale-ESS). Three groups were studied (homogeneous by sex, age, stage): I-50 without IBDs, II-64 with 1 IBDs, III-50 with 2 or more IBDs. Patients were given a Unified Parkinson's Disease Rating Scale motor examination. Patients with cognitive impairment based on a score < 26 by the Montreal Cognitive Assessment (MoCA) were excluded. The 39-Item Parkinson's Disease Questionnaire (PDQ-39) was used to evaluate life quality, the Hospital Anxiety and Depression Scale (HADS)-to evaluate anxiety and depression.

Results: Impulsive PD patients endorsed more sleep complaints than non-impulsive PD patients. The group difference was primarily attributable to greater daytime sleepiness, $p < .01$, in the impulsive PD patients (the II and III groups). But particular attention should pay to the fact that there were no statistically significant differences between groups I and II. The results can't be explained by medications or disease severity.

Conclusions: Poor sleep efficiency increased daytime sleepiness and associated with IBDs in PD. Further research in this area are needed.

Disclosure: Nothing to disclose.

PP3274

Abstract withdrawn

PP3275

Prevalence of rapid eye movement sleep behavior disorder and excessive daytime sleepiness among adult Egyptians: population-based study

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PP3276

Daytime sleepiness and sleep-disordered breathing in patients with acute stroke

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PP3277

Sleep habits and complaints in a 9-year-old boy with restless legs syndrome: a case report

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PP3278

The impact of CPAP treatment on white matter changes and clinical status in patients with obstructive sleep apnea

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PP3279

Obstructive sleep apnea and hearing

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PP3280

Reduced serum orexin levels in antibody positive autoimmune encephalitis and neuromyelitis optica patients

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Ageing and dementia 2

PP4001

A hierarchy of temporal receptive windows in human auditory cortex: evidence in older adults and patients with mild cognitive impairment (MCI)

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Introduction: The capacity to accumulate information over time is crucial to our functioning in an ever-changing world. As individuals age, the ability to store and manipulate information drops. Recently, in young subjects, we showed that brain uses a distributed and hierarchical network of areas to process information over time. Here we study information processing under deficient cognitive state—amnestic MCI (a-MCI), using an ecologically-relevant auditory stimulus—a real-life story. In addition, we assumed that studying healthy elders, who are at high-risk for cognitive dysfunctions, will enable to determine functional neuromarkers of predisposition to disorder.

Methods: MCI and healthy participants were invited for behavioural and fMRI sessions. During behavioural session, cognitive functions were evaluated. The fMRI session mirrored Lerner et al.'s (2011) procedure, which used a spoken story and its scrambled versions as stimuli. The data were analyzed using inter-subject

correlation approach, which measures the reliability of the responses to stimuli by comparing the BOLD signals across participants.

Results: Among healthy elders, we observed widespread sensitivity to stimulus content extended from the primary auditory regions to higher perceptual and cognitive areas. Among a-MCI patients, similar reliable responses were found at the earliest stages of processing (along STG up to Wernicke's area) only. In higher-order parietal and frontal areas, reliability of responses dramatically disrupted.

Conclusions: MCI may impact higher-order cortical regions, while regions involved in early processing remain unaffected. We suggest that differences in reliable responses could serve as functional diagnostic markers differentiating between healthy adults and patients with MCI.

Disclosure: Nothing to disclose.

PP4002

Impact of vascular factors on neuropsychiatric symptoms in Alzheimer's disease

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Introduction: Our goal is to determine the association between vascular conditions and the occurrence of neuropsychiatric symptoms (NPS) in a population of Alzheimer's disease (AD).

Methods: We screened 147 consecutive patients with AD (54 men/93 women) in outpatient consultations in Salamanca and Ávila, Spain. The mean age of participants was 79.7 ± 6.9 years (mean duration of dementia 4.3 ± 2.3 years). NPS were assessed using the Neuropsychiatric Inventory. Prior to the onset of AD, data regarding a history of hypertension, diabetes, hyperlipidemia, obesity, smoking, alcoholism and coronary disease were recorded. The relationship of each vascular factor to individual neuropsychiatric symptoms was analyzed using longitudinal regression modeling, adjusted for age, sex, education and dementia severity.

Results: One or more NPS were observed in 92.5 % of participants. Night-time behaviour disturbances were the most common (65.3 %), followed by depression (51.7 %), and irritability (48.3 %). Hypertension prior to the onset of AD was associated with increased risk of agitation (OR = 2.68, p = 0.03). Both obesity (OR = 2.39, p = 0.03) and coronary disease (OR = 2.85, p = 0.03) were related to sleep changes. Other conditions such as smoking and alcoholism were associated with disinhibition (OR = 7.14, p < 0.01) and irritability (OR = 5.56, p = 0.01). Interestingly, diabetics experienced anxiety less frequently than those non-diabetics (29.4 vs 47.7 %, OR = 0.10, p < 0.01). No association was found between NPS and hyperlipidemia.

Conclusions: These results suggest that patients with AD under certain vascular conditions are at a higher risk of developing specific NPS. Therefore, the treatment or prevention of vascular risk factors could reduce the occurrence of NPS in AD.

Disclosure: Nothing to disclose.

PP4003

Usefulness of fist-edge-palm test in dementia clinic

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Introduction: The fist-edge-palm task (FEP) has shown that more extensive areas beyond contralateral frontal lobe are activated during the task. In this study we aimed to evaluate whether FEP is able to differentiate mild cognitive impairment (MCI) or Alzheimer's disease (AD) from normal controls.

Methods: We enrolled 24 AD, 27 MCI, 19 normal controls. In the FEP, the subjects were requested to place their hand in three different positions sequentially and videotaped during the performing. We compared the score and speed of their performance among patients or controls. In addition, we analyzed common error patterns among patients.

Results: The mean age of the patients was 79.13 in AD, 71.74 in MCI, and 69.89 in normal controls. The proportion of man was 25 % in AD, 29.6 % in MCI, and 57.9 % in normal controls. The mean education years were 4.54 in AD, 7.37 in MCI, and 7.79 in normal controls. The distribution of scores in each group was as follows: 3/2/1/0: 3(12.5 %)/0(0 %)/0(0 %)/27(87.5 %) in AD, 11(40.7 %)/1(3.7 %)/9(33.3 %)/6(22.2 %) in MCI, 11(57.9 %)/1(5.3 %)/7(36.8 %)/0(0 %)) in normal controls. A total of 25 patients were scored 3. The mean duration of their performance was 17.66 s in AD, 13.70 s in MCI, 14.70 s in normal controls. The most common error was omission of task, especially "edge" in AD whereas sequential error and addition of wrong motion were commonly observed in MCI.

Conclusions: Most of AD patients were not able to do FEP. Our study suggests that FEP can be used in bed-side screening tool in the dementia clinic.

Disclosure: Nothing to disclose.

PP4004

Dementia: when caregivers do not sleep

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Introduction: Caregivers of dementia patients frequently have sleep complaints, which can be partly attributed to behavior changes of the patients, with increase burden. This work intends to characterize sleep disturbances in caregivers (SDC) and the factors that influence their sleep.

Methods: Caregivers of demented patients were enrolled and information concerning caregiver and patient demographics, clinical data and sleep patterns was collected. SDC was quantified using a questionnaire created for this purpose (QSDC). Caregivers completed the Epworth Sleepiness Scale (ESS) and the following tests: Geriatric Depression Scale (GDS), Frontal Behavior Inventory (FBI) and Zarit Burden Interview (ZBI). Patients were tested for the MMSE and Addenbrooke's Cognitive Evaluation (ACE).

Results: We recruited 25 caregivers (mean age 68 years; 16 women). The QSDC correlated positively with ZBI and FBI, negatively with the quantity of sleep of the caregiver and was not associated with ESS of the caregiver or with MMSE, ACE and GDS of the patient. The caregivers that reported disrupted sleep of the patient had higher ZBI and QSDC, and the caregivers who described a negative impact of care on their sleep had higher QDSC and less sleep.

Conclusion: These results show that disruption of sleep and altered behaviour of the patient may cause secondary sleep disturbances in caregivers and subsequently predict less hours of sleep and higher burden. In this study the severity of the dementia and depression of the patients were not associated to SDC and ESS was not sensitive to detect sleep disturbances in caregivers.

Disclosure: Nothing to disclose.

PP4005

Facilitation of word retrieval in primary progressive aphasia

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Introduction: Primary Progressive Aphasia (PPA) is a neurodegenerative syndrome with impaired language as its most prominent symptom. Impaired word retrieval is a core symptom and thus communication is restricted, yet no standardized behavioral treatments for PPA available. The aim of the naming therapy presented here is improved word retrieval in order to facilitate communication in PPA. Treated items should be retrieved more easily after therapy and should occur more often in the patients' spontaneous speech in comparison to untreated words.

Methods: Three patients with PPA (two with semantic variant, one logopenic variant) were recruited through the German FTLD consortium. 120 items to be named upon visual presentation were selected for each patient individually. Two different, but matched sets of 30 words each, were to be learned in succession with errorless learning during 12 weeks whereas the remaining 60 items served for control purposes. The patients undertook home training with a computer program for two and consequentially for 4 weeks. Spontaneous speech was measured with a semi-structured interview.

Results: In one out of three patients significant improvement in naming performance was recorded for treated items ($t_{120} = 2{,}132$, $p < .05$). Overall no change was measured in spontaneous speech. In one patient comprehension deteriorated, but her and the third patient's naming had remained stable after therapy.

Conclusions: Even if improvement in naming was not generally found, our results are encouraging. Treatment aims are different in neurodegeneration (as opposed to stroke aphasia) and stable results must be regarded as a positive outcome in PPA.

Disclosure: Nothing to disclose.

PP4006

Demographic characteristics and classification of dementia types in a cohort of patients attending a Memory Clinic in Athens

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Introduction: The objective of the study was to describe the demographic characteristics and explore the relation between them and different types of dementia in a Memory Clinic cohort of patients.

Methods: A retrospective review was undertaken on 2934 medical files of people with memory complaints who attended the Memory Clinic of the Hygeia General Hospital in Athens, during a period of 5 years.

Results: Participants' mean age was 65.8 years (range 38–96). 62 % were women. According to standardized criteria for dementia, 239 had normal cognition, 241 met the criteria for mild cognitive impairment and 310 for depression. 2144 patients were diagnosed with dementia, of whom 61.8 % had Alzheimer's Disease, 16 % had vascular dementia, 11 % had dementia with Lewy bodies or Parkinson's disease, 3 % had frontotemporal dementia and 8.2 % had other forms of dementia. Neurological examination, neuropsychological assessment and paraclinical dementia work up identified most of these conditions. The mean duration from symptoms onset to medical consultation was 1.5 year. 58 % of dementia patients had initial Mini Mental State Examination score < 20 (moderate and advanced stages). On their first visit, 95 % of participants lived in the community.

Conclusions:

1. Demographic data of patients and prevalence of different forms of dementia in our study are in agreement with the existing epidemiological data.

2. No statistically significant correlations between the demographic characteristics and the types of dementia were found.

3. In Greece, almost 6 out of 10 patients seek consultation only when being in moderate or advanced disease stages.

Disclosure: Nothing to disclose.

PP4007

Effect of arthrophytum scoparium extract on cognitive performance of mice and acetylcholinesterase activity

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Introduction: the herbal medicines represent valuable resource in prevention of the therapy of some degenerative diseases such as Alzheimer's disease, which is accompanied by an accumulation of oxidative damage. Arthrophytum scoparium grows in the desert in the North African region, and know in Tunisia by the name of "El remeth".

Methods: Aqueous extracts of A. Scoparium were screened for their antioxidant and acetylcholinesterase activities. In addition to the evaluation of these activities, the contents of flavonoids and total phenolic compounds were determined. Evaluation of rodent learning and memory was assessed by a step-through active test after a double training and an initial acquisition trial. The antioxidant activity was evaluated using the DPPH assay. Acetylcholinesterase (AChE) activity was determined by Ellman's colorimetric method.

Results: The aqueous extract had high total phenolic contents (65 mg gallic E/g extract) and flavonoids (8.3 mg Catechin E/g extract). It exhibited a significantly ($p < 0.05$) great hydroxyl radical-scavenging activity ($IC50 = 3.5$ μg/ml). Results showed also that the mice treated with 60 mg/kg body weight for 7 days exhibited a significant decrease in avoidance and discrimination errors during retention trial compared to control group ($p < 0.05$). AChE activity significantly decreased in treated mice.

Conclusions: the significant cognitive enhancement observed in adult mice after short-term supplementation with the A. scoparium extract concentrated in polyphenols, is closely related to higher brain antioxidant properties and inhibition of AChE activity.

Disclosure: Nothing to disclose.

PP4008

Analysis of stereopsis of Alzheimer disease with dementia patients using 3-Dimensional TV

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Introduction: Recently, 3-Dimensional Television (3D TV) for personal use is common. The disparity of both eyes (binocular disparity) is essential to perception of stereopsis. And this phenomenon is used to watch 3D display. However stereopsis is related to many brain functions, therefor some neurodegenerative disease patients may have problem to perceive 3D TV display. We analyze 3D perception to use the 3D TV in Alzheimer dementia patients and controls.

Methods: We enrolled 32 dementia patients and 18 controls. Before watching TV, we examined visual acuity, strabismus test and Titmus fly test (stereopsis test). We used the movie of 3D version (during 18 min), and carried out questionnaire about 3D perception, dizziness, nausea, headache, eye fatigue and so on. We controlled the same volume, brightness, and other unnecessary movements.

Results: There were no differentiation between controls and dementia patients in visual acuity, strabismus test and stereopsis test, statistically. However 3D perception was significantly decreased in dementia patients and the patients felt more fatigue of eyes during watching 3D TV.

Conclusions: 3D perception is more decreased in dementia patients than in controls although they do not have any differentiation of structural problem in eyes. 3D perception is affected by brain functions, therefor it is difficult for Alzheimer disease patients with dementia to watch 3D TV. Furthermore, we can suggest that other neurodegenerative disease patients may have problem to watch 3D TV.

Disclosure: Nothing to disclose.

PP4009

Functional ability and health status of community-dwelling late age elderly with and without history of multiple falls

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Introduction: Multiple falls have been suggested to relate to intrinsic impairments, and thus they are clinically important. However, the data were mostly reported using subjective data in the early age elderly. Thus this study explored information relating to falls and compared functional abilities in late age elderly ($\geq$75 years old) with and without history of falls during 6 months prior to participation in the study.

Methods: Ninety late age elderly were divided into 3 groups according to their fall history including non-faller, single-faller (1 fall) and multiple-faller ($\geq$2 falls) groups (30 subjects/group). All of them were cross-sectionally assessed functional ability using the 10-Meter Walk Test (10MWT), Berg Balance Scale (BBS), Five Times Sit-to-Stand Test (FTSST), and 6-Minute Walk Test (6MinWT). In addition, subjects were interviewed for their health status and information relating to the falls.

Results: The findings showed that multiple-faller subjects reported the greatest number of underlying diseases, medication required and walking device used. The functional abilities of these subjects were also significantly lower than the non-faller subjects for every test ($p < 0.01$).

Conclusions: The findings clearly confirm the intrinsic impairments in late age elderly with a history of multiple falls. Thus the improvements of physical abilities relating to the outcomes of these functional tests may help to decrease the risk of falls and subsequent injuries of these individuals.

Disclosure: The Improvement of Physical Performance and Quality of Life (IPQ) Research Group, Khon Kaen University, Thailand.

PP4010

Heterogeneity of dementia associated with Parkinson's disease

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Introduction: According to longitudinal studies, 83 % patients with Parkinson's Disease (PD) suffer from dementia. There is no common opinion of the reasons of dementia development in PD.

Methods: We have examined 34 patients with PD and dementia. We used UK Brain Bank and Huges criteria to diagnose PD; DSM IV and Clinical diagnostic criteria to diagnose dementia associated with PD. All the patients were conducted clinical neurological examination, were tested by cognitive rating scales, neuropsychological tests, the Neuropsychiatric Inventory (NPI), and MRI of the brain was done. The type of the research is comparative longitudinal (the duration of patients' examination is 2 years).

Results: The examination allowed to divide the patients into 4 groups with different cliniconeuropsychological types of dementia associated wih PD: subcortical-frontal cognitive disorders with evident behavioral disorders without somatic diseases; subcortical-frontal cognitive disorders with large amount of vascular risk factors; cognitive disorders approximate to dementia with Lewy Bodies (DLB); patients with Alzheimer's memory and language disorders.

After 2 years of observation, neuropsychological profile changed in 14 % cases due to addition of Alzheimer's disorders.

Conclusions: Dementia in Parkinson's disease is heterogenic. Dementia with typical for PD neuropsychological profile develops only in 40 % cases. Probably, the development of dementia is potentiated by the age and vascular risk factors. In 30 % cases dementia in PD is clinically indistinguishable from DLB. In some cases dementia in PD is a consequence of Alzheimer Disease (AD). Cognitive impairment which is typical for AD may appear as the pathology process develops.

Disclosure: Nothing to disclose.

PP4011

The DEMNET-D-study: dementia care networks providing multiprofessional care and support in German communities

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Introduction: Great efforts are directed to support people with dementia (PwD) and their relatives in their own living arrangements. In Germany, local associations of different professional as well as honorary stakeholders are engaged in providing multiprofessional care and support for PwD in the community. However, these dementia care networks (DCN) are not implemented systematically and differ regionally. Empirical findings on DCN are lacking yet. The aim of the DemNet-D-study is to survey characteristics of DCN and relate them to outcomes of PwD.

Methods: Structures and processes of DCN are evaluated by structured interviews. Health-related outcomes of PwD and family caregivers like quality of life, depression, social participation, use and costs of health care supply, burden of care are surveyed in a longitudinal design (2012–2015) by standardized face-to-face interviews.

Results: We included 13 DCN all-over Germany and 563 dyads of PwD and family caregivers First results of the interviews show the heterogeneity of the DCN as well as the meaning of governance in such

network structures. Preliminary results of the baseline survey on outcomes of PwD and family caregivers show that users are on average 80 years old, have a severe dementia but still a moderate quality of life. The also stated a moderate to high participation in social life. Further results will be presented at the conference.

Conclusions: Our results will shed some light on the question which structural aspects describe successful DCN in order to improve care and social participation of PwD and reduce burden of caregivers.

Disclosure: Nothing to disclose.

PP4012

Burden of vascular risk factors for cognitive function in patients with Alzheimer's disease

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Introduction: Apathy and depression are included in the major psychiatric symptoms of Alzheimer's disease (AD). To clarify the influence of vascular risk factors, we investigated the relationship between the cognitive function and vascular risk factors in AD patients from the view point of apathy and depression.

Methods: The present study was based on 124 patients (43 men and 81 women). All patients underwent laboratory testings including brain natriuretic peptide (BNP), MRI, MMSE and Apathetic state was evaluated by Starkstein's Apathy Scale (SAS). The Zung's Self-rating Depression Scale (SDS) was used for the evaluation of depressive state. According to the SAS scores, the subjects were classified into two groups; those with and without apathy. Based on the SDS scores, the subjects were also classified two groups: those with and without depression. The relationship between MMSE and those risk factors was analyzed statistically.

Results: The mean MMSE score was significantly greater in those without apathy than in those with apathy ($p < 0.05$). The MMSE score correlated negatively with SAS score ($p < 0.05$), and positively with the years of education ($p < 0.01$). There was no significant correlation between the MMSE and SDS score. The BNP correlated negatively with the MMSE score in those with apathy ($p < 0.05$).

Conclusions: Apathy was strongly associated with the cognitive function in elderly AD patients. The vascular risk factors such as congestive heart failure influenced on the cognitive function in AD patients with apathy.

Disclosure: Nothing to disclose.

PP4013

Abstract withdrawn

PP4014

FOur sporadic Creutzfeldt-Jakop cases presenting in one year

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PP4015

Effects of balance-cognitive dual—task training on postural stability and cognitive function in the patients with vascular mild cognitive impairment

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PP4016

Neurodegeneration and vascular damage in mixed dementia (clinical, CSF and PET study)

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PP4017 Complex assessment of cerebral metabolism in early diagnostics of cognitive impairment

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PP4018

Early brain metabolic changes in patients with prodromal stage of Alzheimer's disease

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PP4019

Fibrinogen and the risk of vascular dementia

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PP4020

Cerebral amyloid angiopathy-related inflammation presented as steroid-responsive rapidly progressive dementia

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PP4021

Molecular pathogenesis of Alzheimer's disease

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PP4022

Abstract withdrawn

PP4023

Public opinions toward dementia: awareness, knowledge and attitudes

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PP4024

Abstract withdrawn

PP4025

Use of walking devices in elderly

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PP4026

Cerebrovascular lesions affect Alzheimer's disease clinical manifestation

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PP4027

The relation of circulating levels of leptin with cognition in patients with Alzheimer's disease

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PP4028

Assessing legal capacity in dementia

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Cerebrovascular diseases 4

PP4029

Prognostic factors for successful short term outcome (The Modified Rankin Score ≤ 2; mRS) after thrombolysis

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Introduction: Thrombolysis may be a successful treatment in acute stroke. However, it is not clear which factors have influence on outcome. With our study we wanted to identify prognostic factors for successful thrombolysis (mRS $\leq$ 2 after 3 months) in Slovenian population.

Methods: We divided 171 patients (80 women) in four groups according to mRS 3 months after thrombolysis. Means of age, onset to treatment time (OTT), baseline NIH Stroke Scale score (NIHSS), blood pressure (BP), glucose, creatinine, urea, cholesterol, triglycerides, low density and high density lipoproteins were compared using ANOVA.

Results: Three months after thrombolysis 50 patients had 1 or less on mRS (group 1), 30 had 2, 37 had 3 (group 3) and 54 had 4 or more. Means and standard deviations for prognostic factors were: age 65.4 $\pm$ 11.1 years, OTT 152.7 $\pm$ 44.9 min, NIHSS 16.2 $\pm$ 5.8 points, systolic BP 152.6 $\pm$ 19.6 mmHg, diastolic BP 87.6 $\pm$ 14.1 mmHg, creatinine 88.7 $\pm$ 29.2 μmol/l, glucose 7.3 $\pm$ 2.7 low density 3.1 $\pm$ 0.9 and high density lipoproteins 1.3 $\pm$ 0.4 (all mmol/l). Haemorrhage occurred in 12 patients.

Significantly predictive factors were age and NIHSS. Patients in group 1 and 2 were significantly younger (59.6 $\pm$ 14.2 vs. 69.2 $\pm$ 9.6 or 67.6 $\pm$ 9.1 years) and less impaired before thrombolysis (13.55 $\pm$ 5.8 vs. 17.2 $\pm$ 4.8 or 18.6 $\pm$ 5.4 points) than patients in group 3 and 4.

Conclusion: Thrombolysis was successful (mRS $\leq$ 2) in 80 patients (47 %). The only significant predictive factors were age and baseline NIHSS. Although it is surprising to some extent that other risk factors didn't show any predictive values, our results are similar to previous studies.

Disclosure: Nothing to disclose.

PP4030

Bilateral carotid artery occlusion

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Introduction: The bilateral occlusion of the carotid arteries is a rare entity, there are only a few data in the literature regarding its epidemiology. The aim of the study was to analyse the prevalence of this rare vascular pathology and the clinical and diagnostical characteristics.

Methods: We analysed 5,000 cerebrovascular ultrasound records performed over a 7-year period (2006–2013). The examinations were carried out in the Ultrasound Laboratory of Neurology Clinic I, Târgu Mureş, Romania. The indication for ultrasound examination in the majority of cases was acute stroke (3,000/5,000 cases).

Results: 171 patients were diagnosed with carotid artery occlusion, 12 of them with bilateral carotid artery occlusion. 7 cases had bilateral ICA occlusion, 4 cases ICA occlusion + CCA or CCA + ICA occlusion controlaterally and only one case bilateral common carotid artery occlusion with patent distal vessels. 8 cases were symptomatic, from this 3 had major stroke, 5 minor stroke. 4 patients were asymptomatic (no stroke) and were examined for nonspecific symptomatology. The etiology in all cases was the atherosclerosis. The mean age of the patients was 63.4 $\pm$ 10.7 years. The males were more frequently affected (75 %). The most important risk factors were: hypertension (100 %), smoking (58.3 %), dyslipidemia (50 %) and peripheral vascular disease (33 %). The diagnosis in the majority of cases was based only on ultrasound examination.

Conclusions: The prevalence of bilateral carotid occlusion is low (0.24 %), is more frequent in males, the main etiological factor is atherosclerosis, an important number of cases could be asymptomatic.

Disclosure: Nothing to disclose.

PP4031

Outcome and disability of patients with intracerebral hemorrhage

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Introduction: The aim of this study was to analysed outcome and disability of patients with intracerebral haemorrhage (ICH).

Patients and methods: This study included 75 patients with acute ICH, both sexes and all ages who were hospitalised at our Department during period from 01.06.2007 to 31.03.2008. Criterion of inclusion was ICH confirmed by computed tomography. We analysed neuroradiological characteristics (volume of hematoma, hematocephalus and brain oedema) at the onset of ICH. The outcome was evaluated as survival and disability (Rankin Scale and Barthel index), and patients were tested after first, third and sixth month from ICH.

Results: Out of total patients (75), 40 were male (53.4 %). Sixth month after the onset 36 (48 %) survived. Predictors of poor six-month outcome were brain oedema ($p = 0.002$), blood spreading in ventricles ($p = 0.004$) and Glasgow Coma Scale ≤ 8 ($p < 0.0001$). The best cumulative survival had patients with volume of hematoma up to 29 ml, 64 % have survived. The highest mortality rate had patients with hematoma greater than 60 ml, only 15 % of them survived in first 7 days. The number of patients with a lower level of disability increased from 28.5 % after first month to 61.1 % after sixth month, and consequently reduced with higher level of disability (Rankin Scale > 2) ($p = 0.03$). More than half of patients who survived (61.1 %) were functionally independent.

Conclusion: Brain oedema, intraventricular blood spreading, and large volume of hematoma adversely affect short-term outcome in patients with intracerebral hematoma. Six month after intracerebral hemorrhage more than 50 % of patients were functionally independent.

Disclosure: Nothing to disclose.

PP4032

Evaluation of inflammatory biomarkers and Ala16Val-MnSOD2 gene polymorphism in patients with chronic stroke

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Introduction: The superoxide dismutase manganese dependent (MnSOD2) catalyzes O2 into H2O2. It is encoded by a single gene with a common polymorphism which results in replacement of alanine (A) with valine (V) in codon 16. This polymorphism has been implicated in a decreased efficiency of MnSOD2 transport in targeted mitochondria in V allele carriers. Previous studies have described an association between VV genotype and neurological diseases, such as stroke. The exact mechanism of such associations is still unknown. The aim of this research is to investigate if the Ala16Val-MnSOD polymorphism could influence the inflammatory response in the patients with chronic stroke (CS).

Methods: We performed a cross-sectional study. CS patients ($n = 27$) were compared to control group ($n = 30$). Patients were evaluated by a questionnaire and blood exams—serum glucose (GLU; mg/dL), glycated hemoglobin (HBA1C; %), cholesterol (CHO; mg/dL), urea (mg/dL), phosphatase (PHO; UL/mL), acetylcholinesterase (ACHE; UL/mL), interleukin 1β (IL-1β; pg/ml) and 6 (IL-6; pg/ml), tumoral necrosis factor (TNF-α; pg/ml) and interferon gamma (INF-δ; μg/ml). Ala16Val-MnSOD results were presented in mean (%). The level of significance was set at 5 %.

Results: Patients with CS presented higher frequency of VV genotype (37 %—control 6.6 %) and higher serum levels of GLU ($t = 3.58$;), HBA1C ($t = 2.6$), CHO ($t = 3.89$), LDL ($t = 3.09$) Urea ($t = 6.37$), PHO ($t = 5.7$), ACHE ($t = 6.7$), IL-1β ($t = 12.03$), IL-6 ($t = 8.5$), TNF-α ($t = 8.8$) and INF-δ ($t = 10$) comparing to the control group.

Conclusion: Our results suggest that the Ala16Val-MnSOD polymorphism could influence the inflammatory response in patients with CS.

Disclosure: Nothing to disclose.

PP4033

Craniocerebral hypothermia in patients with malignant acute ischemic stroke

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Introduction: Therapeutic hypothermia is perspective course in management of ischemic stroke patients. Craniocerebral hypothermia (CCH) is the hypothermia variant with primary brain cooling. This method is noninvasive and doesn't require profound sedation of patients. We studied CCH effect on neurological state and cerebral blood flow.

Methods: 30 patients (mean age 69 ± 11.1, men 13, women 17) with malignant middle cerebral artery (MCA) ischemic stroke were treated by CCH and standard stroke management protocol; control group included 30 similar patients (mean age 68.8 ± 12.3, men 13, women 17). Including criteria was acute ischemic stroke National Institutes of Health Stroke Scale (NIHSS) score > 16 points. Excluding criteria was bradycardia. We used the therapeutic hypothermia helmet device for CCH and the ultrasound Doppler analyzer for recording the MCA cerebral blood flow velocity. Patients were treated with 2 CCH procedure (12 ± 3.3 h). Neurological state (NIHSS), hemodynamic parameters, and tympanic temperature were studied before and after CCH. Intracranial pressure calculation was based on MCA mean blood flow velocity and BP data (Klingelhofer method).

Results: We observed significant regress of the neurological deficit (36.4 %) in hypothermia group. MCA mean blood flow velocity increased in hypothermia group (65 %). Tympanic temperature significantly declined from 37.2 ± 0.72 to 34.7 ± 0.82 °C. Intracranial pressure decreased in patients with brain edema.

Conclusions: Craniocerebral hypothermia promotes regression of the neurological deficit, increasing of the cerebral blood flow velocity and decreasing of the intracranial hypertension.

Disclosure: Nothing to disclose.

PP4034

Cannabis: a considerable cause of ischemic strokes in young adults

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Introduction: A large part of unexplained strokes could be linked to illegal drug abuse and 10 % are estimated to be directly linked to illegal drugs in some international studies. Cannabis is the most consumed illicit drug suspected to have an important role in neurovascular diseases.

Case report: We report a case of a 42 years old man who has presented suddenly a right neurological regressive palsy without headache, nausea, vomiting or blind trouble. The patient reported cannabis consummation 6 h and a half before the onset of symptoms. Neurological exam was normal. Brain MRI objectified a left frontal ischemic stroke. There were no arguments for an infectious or inflammatory vasculitis. Cerebrospinal fluid (CSF) examination was normal. Toxic research in urine was positive for cannabis. MRI angiography cerebral revealed irregularities of vascular walls in favor of reversible vasoconstriction syndrome.

Discussion: A reversible cerebral angiopathy secondary to cannabis consummation is a frequent cause of stroke in young adults. In our case, we incriminate cannabis as a cause of stroke because of the temporal relationship between the intake of this drug and the occurrence of cerebral infarction. The combination of vasospasm and orthostatic hypotension caused by cannabis could be the cause of cerebral infarction.

Conclusion: The relationship between stroke and cannabis consummation is strongly suspected, which justifies further questioning and a precise cerebral arterial imaging.

Disclosure: Nothing to disclose.

PP4035

When we don't prescribe anti-coagulants after cardioembolic strokes due to auricular fibrillation

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Introduction: Atrial fibrillation (AF) contributes for approximately 10–20 % of all strokes, and its prevalence increases with age. The decision for anticoagulation is a challenge, especially in the group of older patients.

We purpose to estimate the prevalence of patients with cardioembolic stroke due to AF undergoing oral anticoagulation, and assess the main reasons for non-anticoagulation in the remaining patients.

Methods: We conducted a retrospective study including patients hospitalized with cardioembolic stroke due to AF from November 1st 2012 to October 31st 2013. Descriptive analysis of anticoagulated and non anticoagulated groups was performed.

Results: Among 276 patients admitted with diagnosis of ischemic stroke, 29 % (n = 80) are cardioembolic due to AF. Mean age was 80.58 ± 8.72 years and 60 % were women. The majority were previously autonomous, 40 % with newly diagnosed AF and 60 % with known AF. Of these, 77.1 % were not anticoagulated, with CHA2DS2-VASc score 5 on average. Most of anticoagulated patients before stroke, had subtherapeutic INR.

At discharge, the mean of mRS score was 3.13 ± 1.5. Anticoagulant therapy was prescribed in 55 %. Older patients, those with high risk of falls or high NIHSS and mRS scores were less likely to receive anticoagulant therapy. 15.38 % of patients with significant functional disability (mRS > 3) were anticoagulated. Only the patients functional status was independently associated with the decision of not prescribe anticoagulants (OR 19.33; IC 2.74–136.2; $p = 0.03$).

Conclusions: In our study, high prevalence of cardioembolic stroke due to AF was found. A greater functional dependence raises the probability of non-anticoagulation at discharge.

Disclosure: Nothing to disclose.

PP4036

Clinical and radiological predictors of poor outcome in patients with cerebral venous thrombosis

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Introduction: Cerebral venous thrombosis (CVT) is a rare cerebrovascular disease that usually affects young to middle aged people. Although prognosis is usually favorable and the mortality rate is relatively low, the outcome can be very unpredictable.

In this study, we aimed to determine the clinical and radiological predictors of poor outcome in patients with CVT.

Methods: This is a retrospective study conducted from January 2007 to June 2013 on patients diagnosed with CVT at Neurology Clinic in Belgrade. We analyzed the associations of demographic factors, risk factors, and the clinical and radiological characteristics of CVT with poor outcome at discharge, which was defined as death or dependency (mRS > 3).

Results: Of the 48 patients, 17 were males and 31 were females with a mean age of 42 years (range 18 to 78 years). The poor-outcome group included 11 patients (23 %); seven of which (14.6 %) were severely handicapped (mRS = 4 or 5) and four (8.3 %) died. The univariate analysis identified factors related to poor outcome: development of coma within 72 h of the disease's onset ($p = 0.002$), NIHSS on admission (p-0.001), parenchymal lesion on initial imaging ($p = 0.043$), thrombosis of the deep cerebral venous system ($p = 0.037$) and malignancy ($p = 0.004$). In the multivariate analysis, NIHSS on admission and malignancy were significantly associated with a poor outcome.

Conclusions: These predictors of poor outcome can be used to define a subgroup of CVT patients who require close monitoring and more aggressive therapy.

Disclosure: Nothing to disclose.

PP4037

The value of juxtaluminal carotid plaque echodensity in the development of cerebrovascular manifestations

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Introduction: It has been demonstrated that symptomatic carotid plaques are echolucent on ultrasound, whereas asymptomatic ones echogenic. The aim of this study was to determine whether the juxtaluminal plaque echodensity constitutes a better discriminator of symptomatic and asymptomatic status, as compared to global plaque echodensity.

Methods: Analysis included imaging by duplex of 102 carotid plaques of more than 50 % stenosis (90 patients, 51 symptomatic and 51 asymptomatic plaques), capturing, digitisation and normalisation in a computer. The global plaque Grey Scale Median (GSM_{global}) was evaluated semi-automatically in a computer software to distinguish dark (low GSM) from bright (high GSM) plaques. Subsequently, in the same software the juxtaluminal 25 % plaque area GSM ($GSM_{jl25\ \%}$) was automatically calculated. Stenosis was evaluated on duplex.

Results: Symptomatic plaques were associated with median GSM_{global} of 7 whereas the asymptomatic ones of 26 ($p = 0.0001$). The corresponding values for median $GSM_{jl25\ \%}$ were: 0 for symptomatic plaques and 29 for asymptomatic ones ($p = 0.0001$). ROC curves demonstrated a more adequate ability of $GSM_{jl25\ \%}$ over GSM_{global} in separating symptomatic from asymptomatic plaques (difference between areas: 0.104, $p = 0.003$). Median stenosis for the symptomatic plaques was 85 % and for the asymptomatic ones 75 % ($p = 0.065$).

Conclusions: Our results suggested that juxtaluminal 25 % plaque echodensity proved to be a more adequate index, compared with global plaque echodensity, in the separation of symptomatic and asymptomatic carotid plaques. This position might be solidified in natural history studies of asymptomatic individuals with carotid plaques, with stroke as an exit point.

Disclosure: Nothing to disclose.

PP4038

Peculiarities of cerebellar motor syndrome in acute isolated infarctions of the cerebellum

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Introduction: Cerebellar motor disorders are one of the most frequent clinical manifestations that restrain functional abilities or lead to patient's disability after cerebellar infarction.

Objective: To examine specific symptoms of cerebellar motor syndrome in patients with acute isolated infarction of the cerebellum and to assess peculiarities of restoration of functions according to affected vascular territory.

Materials and methods: 31 patients (21 men and 10 women, mean age 57.1 ± 13.9) after acute isolated infarction were examined by neurological scales (ICARS,NIHSS, mRS, Barthel Index) on admission, on the 7th,14th and 21st day; brain MRI.

Results: MRI showed infarctions of SCA in 16 patients, PICA- in 12, AICA- in 3. Volume of motor deficit in patients with infarction of PICA was 74.8 ± 3.96 and manifested with vertigo, gait ataxia, nystagmus; in the territory of SCA was 46.3 ± 3.18 and characterized by dysarthria, limb ataxia, dysmetria; and in the territory AICA was 18.0 ± 3.41 and characterized by vertigo, vestibular disturbances, nystagmus. On the 7th day of treatment full recovery of motor functions was seen in 25 % of patients ($p < 0.01$), on the 14th day—in 40 % and on the 21st day—in 85 % of cases ($p < 0.001$).

Conclusion: Peculiarities of cerebellar motor syndrome after acute isolated infarction of the cerebellum depended on involved vascular territories; restoration of motor functions was seen after 2 weeks in the territory of SCA and AICA, but some patients had ataxic signs and needed rehabilitation.

Disclosure: Nothing to disclose.

PP4039

Successful 5 years of intravenous thrombolysis in University Hospital Dubrava

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Introduction: It's been 5 years since University Hospital Dubrava introduced intravenous thrombolysis for treatment of acute stroke; we now evaluate our results during that period.

Methods: All patients who received intravenous thrombolytic therapy as treatment of acute stroke from December 2008 to September 2013 were included in our evaluation; total of 134 patients, 67 men and 67 women. We gathered all medical records, time aspects, short and long-term clinical results and complications and compared the data with other SITS register data and published studies.

Results: Initial median NIHSS score of our patients was 10.0. We are proud to present our intravenous thrombolysis treatment results: 70 % of our patients had significant early improvement, in comparison to only 56 % in all SITS centers. 73 % of our patients had much better 7 day global outcome, in comparison to only 43 % in all SITS centers. 3 months after rt-PA treatment 71 % of our patients were functionally independent (mRankin 0–2), in comparison to 55 % in all SITS centers, high 57 % of our patients were with excellent recovery (mRankin 0–1), in comparison to only 40 % in all SITS centres. We also evaluate our patients with poorer outcomes: 5 % of patients treated with intravenous thrombolysis had SICH RCT. 16 patients (12 %) died, only 2 due to symptomatic intracerebral hemorrhage.

Conclusions: Intravenous thrombolysis with rt-PA in treatment of acute stroke in University hospital Dubrava has proven to be safe and highly efficacious method of treatment. Our excellent results prompt us to do even better in future.

Disclosure: Nothing to disclose.

PP4040

Intracerebral hemorrhage as the most common cause of brain death in the context of cadaveric organ transplantation

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Due to a more consistent application of the Regulation on Reporting Patients in the State of Brain Death and precise Protocol of Clinical Center Nis/which minutely describes procedures in twelve phases, as well as performance time, people in charge of performance, with checking all the steps performed/in the period of 1 year, and with the help of precise instrumental methods, brain death was confirmed in twenty patients, all of them being diagnosed with intracranial hemorrhage. Processing the patients with brain death is a standardized process conducted at the Clinic of Neurology and Clinic of Neurosurgery. Based on the insight into the electronic patient registry of the Clinic of Neurology for the year 2013, it has been confirmed that there were 948 patients with the diagnosis of brain death. Out of 948 patients, 143 were treated for ICH (67 women and

76 men, mean age 64.63 ± 11.49 years). Brain death was confirmed in twenty patients, and there were discussions held with ten relatives, seven of whom gave consent to transplantation. Thirteen cadaveric kidney transplants were performed in Clinical Center Nis in 2013.

Disclosure: Nothing to disclose.

PP4041

The usefulness of DWI/FLAIR imaging in timing of stroke

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Introduction: Patients admitted within 4.5 h from stroke onset are candidates for reperfusion. However in wake-up strokes it is impossible to determine the time of onset. It would be useful to find a radiological marker reliable in timing of stroke. One candidate is the DWI/FLAIR mismatch: the presence of hyperintensive signal in MR DWI without relevant change in FLAIR. The goal was to assess if the DWI/FLAIR can help to identify patients with acute ischemic stroke within 4.5 h from onset.

Methods: This retrospective study was performed with use of the data of 85 patients admitted with ischemic stroke of known onset. Patients were imaged with MR protocol composed of DWI and FLAIR. The presence of lesions in applied imaging modalities was assessed in light of the time, type and severity of stroke.

Results: The time from stroke onset was significantly shorter for patients with the ischemic lesion only in DWI (2.25 h (range 1.5–7 h, n = 34), when compared to patients with signs of ischemia in both modalities (range 2.2–18 h n = 51) (p = 0.005, Kruskal Wallis ANOVA) The DWI/FLAIR characterized with global sensitivity 58 %, specificity 97.5 %, PPV 94.7 % and NPV 75.4 % in identification of patients in 4.5 h time window. For lacunar strokes (n = 22) these parameters were as follows: sensitivity 50 %, specificity 90.2 %, PPV 75 % and NPV 77 %.

Conclusions: The presence of acute ischemic lesions only in DWI can identify patients with both lacunar and nonlacunar ischemic stroke, who are in 4.5-time window for intravenous thrombolysis with high specificity and PPV.

Disclosure: Nothing to disclose.

PP4042

Cardiac investigation in ischemic stroke patients

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Objective: Up to 15–30 % of ischemic strokes are caused by cardiac sources of emboli being associated with poor prognosis and high index of fatal recurrence. In recent studies, left atrial volume is increased in cardioembolic strokes. In this study, electrocardiography (ECG), transthoracic (TTE) and transesophagial echocardiography (TEE) findings were evaluated for cardioembolic risk factors.

Materials and methods: The data of 502 acute ischemic stroke patients who were admitted to our clinic in three years period, between January 2010 and January 2013, were analyzed. The causes of ischemic stroke were classified according to TOAST criteria. Demographic variables including age and gender, history or evidence of diabetes mellitus, hypertension, dyslipidemia, ischemic heart disease, atrial fibrillation, congestive cardiac failure, previous stroke, and tobacco use were recorded. ECG and TTE findings were analyzed.

Results: The mean age of 502 patients was 60.8 ± 14.9 years (18–90 years) and 42.4 % (n = 213) of them were female, 57.6 % (n = 289) male. According to TOAST classification, common subtypes were large artery atherosclerosis (%46) and cardioembolism (%40.4). Cardioembolic stroke patients had a higher proportion of left ventricular segmental or global hypokinesia (44.9 %), atrial fibrillation (34.5 %) and left ventricular ejection fraction less than 40 % (25.7 %). ECG and TTE showed 46.8 % high risk and 53.2 % intermediate risk for cardioembolic stroke. Patients with cardioembolic stroke had increased left atrial volume (43.6 %) compared to the other stroke subtypes.

Conclusion: In this study, cardioembolic risk factors were similar to the literature and left atrial volume indices may also be linked to cardioembolic stroke.

Disclosure: Nothing to disclose.

PP4043

Abstract withdrawn

PP4044

Characteristics of patients with transient global amnesia; data from Evangelismos Stroke Registry

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Introduction: Transient global amnesia (TGA) is a clinical syndrome of reversible anterograde amnesia accompanied by repetitive questioning, with an unknown etiology. We aimed to describe the characteristics of patients with TGA admitted in Evangelismos Hospital, a tertiary hospital in Athens, Greece.

Methods: We looked into data of all relevant patients, over a period of 3 years. Demographic and clinical characteristics were recorded.

Results: Between 01/2011 and 12/2013,34 (21 female,13 male)were diagnosed with TGA. Their mean age was 60.1 ± 6.2years (range 34–69, median 60, mode 60 years).

Four patients (11.8 %) had experienced another episode of TGA in the past. The mean duration of the current episode was 4.6 ± 2.7 h (range 1–12, median 4, mode 5 h). Six patients (17.6 %) reported a stressful event prior to the TGA.

Vascular risk factors included smoking (17.6 % of the patients), diabetes (2.9 %), hypertension (52.9 %), coronary disease (5.9 %), atrial fibrillation (2.9 %), dyslipidemia (73.5 %), sleep apnea (5.9 %) and alcohol abuse (8.8 %).

Interestingly, 7 patients (20.6 %) had a history of an anxiety disorder and 3 patients (8.8 %) had a history of cancer.

Electroencephalography (EEG) was performed on all patients shortly after the resolution of the TGA symptoms. Only one

EEG (2.9 % of patients) showed paroxysmal epileptiform activity. Nine patients (26.5 %) showed paroxysmal non-specific theta activity (1 diffuse, 2 in frontotemporal and 6 in temporoparietal regions).

Conclusion: Our results are concordant with most registries in which TGA occurs in middle to older aged patients, who also show various vascular risk factors. Dyslipidemia is the most common risk factor, followed by arterial hypertension. A female predominance (2:1) and a high percentage of comorbid anxiety disorders are also highlighted.

Although the majority of patients had EEG within normal limits, a fourth of them showed paroxysmal non-specific theta activity mainly in the temporoparietal regions.

Disclosure: Nothing to disclose.

PP4045
Gender differences of risk factors of the ischemic stroke

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PP4046
Bilateral septic internal jugular vein thrombosis

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PP4047
Bilateral subclavian steal syndrome—case report

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PP4048

Abstract withdrawn

PP4049 Severity and duration of hypertension and the outcome of ischemic stroke

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PP4050
Assessment of D-dimer in stroke patients at 1 year in Tehran University affiliated Hospital- Tehran-Iran

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PP4051
Capabilities of ADP and collagen-induced light-transmission aggregometry for the estimation of platelet function against the background of antiplatelet therapy at ischemic stroke

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PP4052
Cerebral venous sinus thrombosis associated with iatrogenic intracranial hypotension: presentation of 2 cases und literature review

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PP4053
Cerebrovascular disease developed on the background of pathological tortuosity of cerebral vessels in young people

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PP4054

Abstract withdrawn

PP4055
Immunomodulatory effect of brain derived low-molecular polypeptide fraction in patients with early post-stroke depression

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PP4056

Abstract withdrawn

PP4057
Atherosclerotic lesion of carotid arteries in young patients

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PP4058
Cervical dystonia as a complication after stroke—case presentation

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PP4059
Pseudoperipheral facial paresis as a rare variant of acute ischemic stroke

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PP4060
Risk of thromboembolic stroke in elderly patients with non-valvular atrial fibrillation

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PP4061
Clinical and computer tomographic comparisons in patients with stress hyperglycemia in acute period of hemispheric cerebral ischemic stroke

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PP4062
Unilateral hypoplastic vertebral arteries and stroke territories: a retrospective analysis in Italian patients

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PP4063
Encephalopathy resulting from dural arteriovenous fistula

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PP4064
Hypertrofic olivary degeneration and cerebrovascular disease: movement in a triangle

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PP4065
RIsk factors affectIng recurrent stroke after transient ischemIc attack and their importance In predIctIng stroke development

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PP4066
Peripheral blood T lymphocytes count may be associated with ischemic stroke outcome

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PP4067
Combination of statin and inosine pranobex has anti-inflammatory, immunomodulatory effect and improves functional outcome in the patients with acute ischemic stroke. The pilot study

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PP4068
Gamma-delta T lymphocytes are reduced after ischemic stroke in a Polish population

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PP4069
Paroxysmal dysphonia caused by an aortic arch aneurysm

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PP4070

Acute hemiparesis without cognitive symptoms: Creutzfeldt Jakob disease?

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PP4071

Treatmeant in the acute phase and pharmaceutical prophylaxis in a patient with an antiphospholipid syndrome associated M1-occlusion

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PP4072

Artery of Percheron: an anatomical variation as an unusual cause of coma

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PP4073

Case report: lethal progressive bilateral stroke of the posterior circulation—primary CNS angiitis or vasoconstriction syndrome?

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PP4074

Bilateral medullary syndrome: report of a challenging case

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PP4075

Basal ganglia hemorrhages and functional outcome: a proposed classification

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PP4076

Demographical, etiological, clinical and radiological evaluation of 31 cerebral venous thrombosis patients

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PP4077

A case report of a cerebrovascular disease in young person due to abused of synthetic cannabinoids called "Bonzai"

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PP4078

A shimmering touch

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PP4079

Heroin, marijuana and postpartum—a convulsive cocktail

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PP4080

Dynamic evolution of some oxidative stress markers after ischemic stroke

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PP4081

Predictors and risk-factors of postpartum stroke

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PP4082

The relation of apolipoprotein B, lipoprotein (a) and lipids in patients with first ever ischaemic stroke

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PP4083

Ischemic stroke in the course of the internal carotid artery dissection-therapeutic possibilities

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PP4084

Moya moya disease associated with elliptocytosis leading to haemodynamic cerebral infarction—a case report

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PP4085

Basilar artery occlusion and stroke in young adult associated with antiphospholipid antibody syndrome

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PP4086

Clinical evaluation of cerebral venous sinus thrombosis

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Motor neurone diseases

PP4087

***TARDBP* mutation mimics a distal motor neuropathy in a Sardinian patient**

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Introduction: *TARDBP*-related Amyotrophic Lateral Sclerosis (ALS) patients present an adult-onset, autosomal dominant clinically typical form of ALS. *TARDBP* mutations are also observed in both ALS-Fronto Temporal Dementia (FTD) and pure FTD cases. Since first *TARDBP* mutations were reported in familial ALS cases in 2008, over 40 mutations have been identified in several populations of different geographic origin. Here we report an atypical case of *TARDBP*-associated ALS patient, coming from Sardinia, an Italian island historically genetically segregated and distinct from other European populations.

Methods: A 50-year-old man came to our attention for a 10-year story of slowly progressive mild symmetrical limb distal hyposthenia and amyotrophy with cramps and fasciculation. No upper motor neuron sign either sensitive impairment was present. Electrophysiological examinations were consistent with second motor neurons damage. A psychiatric history of bipolar disorder was present without cognitive impairment. No family history of neuromuscular disorders.

Results: Genetic analysis revealed that the patient was carrying in heterozygosis the c.1144G->A (p.A382T) pathogenic missense mutation of the TARDBP gene.

Conclusions: *TARDBP* p.A382T missense mutation accounts for approximately one-third of all ALS Sardinian cases. Despite a quite heterogeneous spectrum of resulting phenotypes, the flail arm variant of ALS occur with greater than expected frequency in these patients, although clinical presentation may also include forms of parkinsonism and FTD. To our knowledge, this is the first report of a distal motor neuropathies-like syndrome associated with this mutation.

Disclosure: Nothing to disclose.

PP4088

Amyotrophic lateral sclerosis—clinical signs and epidemiology of the last 15 years in *entre Douro e Vouga*—Portugal

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Introduction: Estimated incidence of Amyotrophic Later Sclerosis (ALS) in Europe is 2/100.000hab/year, and prevalence 3–6/100.000 hab/year, with males being affected more frequently (M:F = 1.5:1). The major risk factor is age, and median survival about 3 years. Poor prognosis has been ascribed to an early diagnosis, late beginning, female gender and bulbar onset. Only 20 % of cases begin as progressive bulbar palsy (PBP).

Methods: Clinical and epidemiological characterization of ALS patients followed in our centre between January/1999 and December/2013, through retrospective analysis of their clinical registrations.

Results: 55 patients were identified, rendering an incidence of 1,1/100.000 hab/year and prevalence of 5.3/100.000 hab. Median age of onset was 65 years and median survival was 38 months. A shorter survival was associated with initial bulbar signs and shorter time to diagnosis. Males were 1.4 fold times more affected than women, with women displaying a later onset ($p = 0.01$). Initial bulbar signs were also more frequent among women, with an overall incidence of 44 % (36.4 % as PBP). Following multivariate analysis, physiotherapy, age of onset, non-invasive ventilation and gastrostomy didn't show to be associated with longer survival.

Conclusions: This study corroborates the clinicians' impression of an unusual high prevalence of premature bulbar signs in our population, what proved to be associated, as previously reported in literature, to a shorter survival. Prospective studies will be needed to prove the effect of other variables upon survival and prognosis.

Disclosure: Nothing to disclose.

PP4089

A case of amyotrophic lateral sclerosis associated with distal agenesis of an upper limb, hyperinsulinaemic hypoglycaemia, and hypocupraemia

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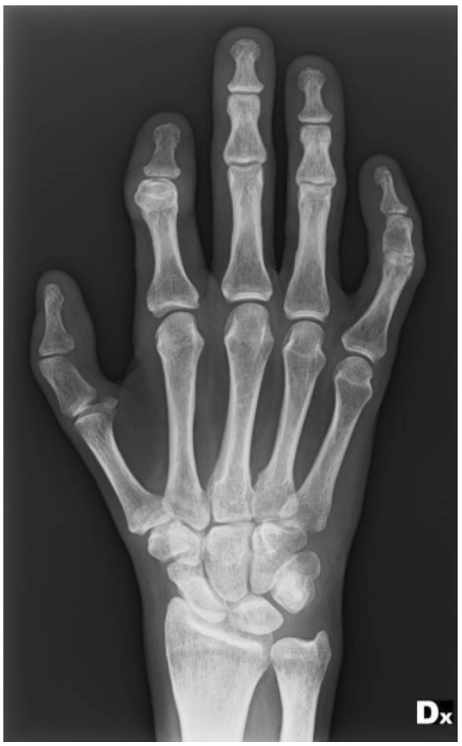
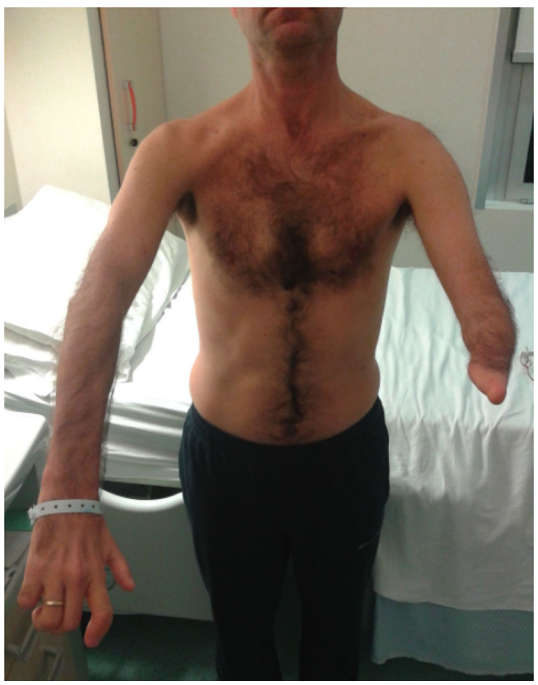
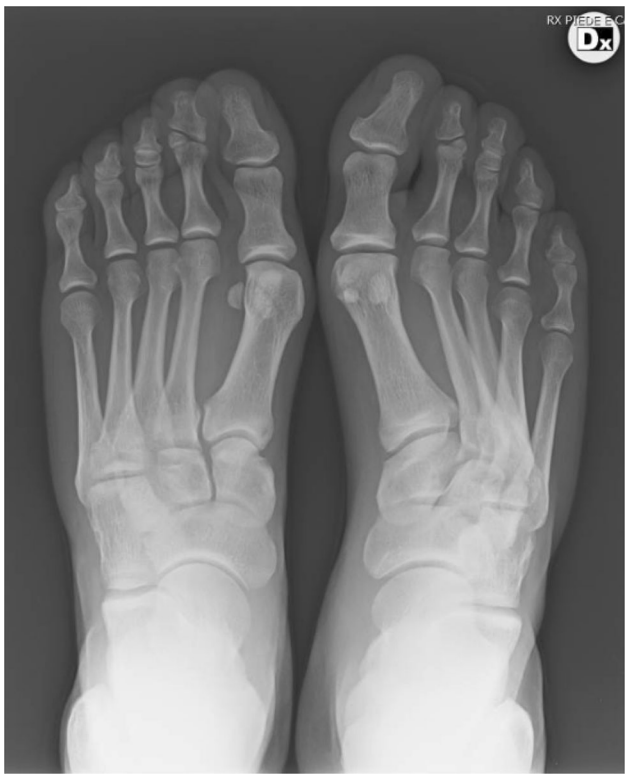
Introduction: We describe a case of motor neuron disease accompanied by congenital skeletal abnormalities, hyperinsulinaemia and hypocupraemia.

Methods: Description of the patient: A 47-year-old Caucasian man presented to our Institute with a 20-month history of progressive distal right upper limb weakness and muscular atrophy. He also had a congenital somatic defect consisting of agenesis of the left forearm and hand (Photograph of t…), and had suffered for 10 years from episodes of hypoglycaemia.

Results: On neurologic examination, distally-predominant weakness of the right upper limb was present, accompanied by fasciculations of the tongue and of the four limbs with generalized hyperreflexia. This pattern, as well as the electromyographic examination, was consistent with the diagnosis of amyotrophic lateral sclerosis (ALS). Radiographs of the skeleton showed hypogenesis of the phalanges of the right hand (Radiograph of t…) and of the feet (Radiograph of t…) in adjunct to the obvious defect of the left upper limb. Blood tests demonstrated hypoglycaemia with a high insulin level, suggesting the presence of an insulinoma which was, however, not found by computed tomography and endoscopic ultrasonography. Reduced serum levels of both copper and ceruloplasmin were also found, with a normal urinary copper excretion.







Conclusions: To our knowledge, the association of ALS with such skeletal developmental defects and endocrine-metabolic abnormalities has not been previously described. As it is statistically unlikely that such anomalies coexist by chance, we consider that they could represent a genetic syndrome or, alternatively, be consequence of a pathogenic insult occurred during embryogenesis.

Disclosure: Nothing to disclose.

PP4090

A case of bulbar-onset amyotrophic lateral sclerosis associated with Alzheimer's disease

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Introduction: We report a case of bulbar-onset amyotrophic lateral sclerosis (ALS) associated with Alzheimer's disease (AD).

Methods: Description of the patient: A 76-year-old woman insidiously developed forgetfulness and difficulty in performing activities of daily living. After 2 months, dysarthria arose, followed by dysphagia. The symptoms progressed over time, and the patient came to our attention 14 months after the onset of the cognitive problems.

Results: On neurologic examination, the patient was severely dysarthric, with tongue atrophy and fasciculations and a brisk jaw jerk. There was very mild weakness of right biceps brachii and wrist flexors. Deep tendon reflexes were normal in the upper limbs and reduced in the lower limbs. Electromyographic examination was consistent with a diagnosis of ALS. Neuropsychological testing demonstrated moderate deterioration of multiple cognitive functions. Imaging studies showed global cerebral atrophy and reduced glucose uptake in the temporal and occipital lobes. Positron emission tomography with florbetapir disclosed pathological brain deposition of amyloid, while cerebrospinal fluid analysis demonstrated reduced A-beta 1–42 and elevated tau and phospho-tau. These findings are consistent with the diagnosis of Alzheimer's disease.

Conclusions: This case illustrates that when ALS is accompanied by dementia, the cognitive impairment is not necessarily due to frontotemporal lobar degeneration as most frequently reported, but can occasionally be caused by AD. More intriguingly, the almost simultaneous onset of the two diseases leads us to consider the possibility that AD pathology may underlie not only dementia but also ALS.

Disclosure: Nothing to disclose.

PP4091

Adult-onset case of Brown-Vialetto-Van-Laere syndrome with SLC52A3 mutation

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Introduction: Brown-Vialetto-Van Laere syndrome (BVVLS) is a rare neurological disorder characterized by childhood onset motor neuron involvement, sensorineural deafness and ponto-bulbar palsy. Recently, mutations in SLC52A3, coding for riboflavin transporter 2, have been identified as the molecular basis for most of the individuals with BVVLS, providing a unique opportunity for treatment. Majority of the patients with genetically proven BVVLS in the literature manifested in childhood and adult onset disease is considered as atypical.

Methods: Case presentation with clinical, electrophysiological and whole genome sequencing data.

Results: 41-year-old female patient presented first with difficulty in gait about 10 years ago. Five years later, she developed dysphagia and dysarthria. Symptoms were slowly progressive. She was on riluzole therapy when she was first seen in our clinic. Her history revealed mild loss of hearing and prominent loss of weight at about age of 25. She is between 35 and 40 kg since then. Electromyographic studies showed mildly active, chronic, diffuse lower motor neuron involvement. BVVLS was suspected and genome wide analysis and sanger sequencing was done revealing homozygous p.P267L mutation in SLC52A3 gene. Riboflavin treatment has been started thereafter.

Conclusions: Although very rare, BVVLS may first present at adulthood. As riboflavin treatment, at least, is shown to halt progression of disease; it is important to consider BVVLS in differential diagnosis of patients with motor neuron disease.

Disclosure: Nothing to disclose.

PP4092

Bee venom effects on UPS system in ALS model

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Introduction: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease that results from a progressive loss of motor neurons. Familial ALS (fALS) is caused by missense mutations in Cu, Zn-superoxide dismutase 1 (SOD1) that frequently result in the accumulation of mutant-protein aggregates that are associated with impairments in the ubiquitin–proteasome system (UPS). UPS impairment has been implicated in many neurological disorders. Bee venom (BV) extracted from honey bees has been used as a traditional medicine for treating inflammatory diseases and has been shown to attenuate the neuroinflammatory events that occur in a symptomatic ALS animal model.

Methods: NSC34 cells were transiently transfected with a WT or G85R hSOD1-GFP construct for 24 h and then stimulated with 2.5 μg/ml BV for 24 h. To determine whether a SOD1 mutation affects UPS function in NSC34 cells, we examined proteasome activity and performed western blotting and immunofluorescence using specific antibodies, such as anti-misfolded SOD1, anti-ubiquitin, anti-GRP78, anti-LC3, and anti-ISG15 antibodies.

Results: We found that GFP-hSOD1G85R overexpression induced SOD1 inclusions and reduced proteasome activity compared with the overexpression of GFP alone in NSC34 motor neuronal cells. In addition, we also observed that BV treatment restored proteasome activity and reduced the accumulation of ubiquitinated and misfolded SOD1 in GFP-hSOD1G85R-overexpressing NSC34 motor neuronal cells. However, BV treatment did not activate the autophagic pathway in these cells.

Conclusions: Our findings suggest that BV may rescue the impairment of the UPS in ALS models.

Disclosure: Nothing to disclose.

PP4093

The effects of scolopendra subspinipes mutilans on neuroinflammation in symptomatic ALS mice

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PP4094

Tandem mass spectrometry resting and exercise-related plasma levels of C6 and C12 bi-carboxylic carnitines in ALS: a putative new disease biomarker

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PP4095

Case report of spinal muscular atrophy (autosomal dominant type of inheritance?)

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PP4096

Pattern difference of dissociated hand muscle atrophy in upper limb-onset amyotrophic lateral sclerosis, progressive muscular atrophy, brachial amyotrophic diplegia, and Hirayama disease

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PP4097

In silico analysis of the *SOD1* gene mutations

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PP4098

Inflammatory reactions in ALS: possible effects on clinical symptoms and laboratory parameters by treatment

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PP4099

Blood pro- and antioxidant system in patients with the motor neuron diseases at different progression rates

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PP4100

Disruption of deglutition and respiration interaction is caused to the dysphagia in ALS patients

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PP4101

Abstract withdrawn

Movement disorders 2

PP4102

Occipital cortex alpha activity lateralization correlates with L-dopa motor response in de novo Parkinson's disease

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Introduction: In Parkinson's disease (PD), L-dopa may modulate topographically-defined cortical-subcortical oscillatory networks detectable using quantitative electroencephalography (EEG).

Methods: We retrospectively selected N = 34 L-dopa untreated PD patients who performed a standardized EEG assessment. N = 18 subjects matched by age, sex and hand dominance with a normal EEG study and no parkinsonism and/or cognitive decline were selected as control group. For all patients, EEG signals were recorded from homologous pairs of electrodes over each hemisphere. A Welch's periodogram was applied to artefacts-free detrended signals epochs selected off-line from continuous EEG recordings during eyes-closed and eyes-open tasks. An Index of Lateralization (IL) was then obtained as the absolute value of the EEG asymmetry index, computed by subtracting left from right sided log power spectral density for each homologous site and frequency band. A standardized L-dopa acute challenge test was performed to all PD patients.

Results: In mid/lateral frontal regions of PD patients, we obtained higher IL for the beta band ($p = 0.015$) whereas lower IL for the theta band ($p = 0.036$) compared to controls. Both parameters correlated with Hoehn-Yahr stage (respectively: $r = 0.428$, $p = 0.012$; $r = -0.464$; $p = 0.006$). In occipital region of PD patients, we obtained instead lower IL for the alpha band compared to controls ($p = 0.024$). Such parameter correlated with L-dopa motor response magnitude ($r = 0.456$; $p = 0.007$).

Conclusions: Lateralization of occipital cortex alpha activity may correlate with L-dopa motor response in de novo PD.

Disclosure: Nothing to disclose.

PP4103

PANDAS in the structure of tic disorders

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Introduction: Most of hyperkinetic syndromes that occur during childhood and adolescence is an autoimmune caused by sensitization of the β-hemolytic streptococcus group A (BGSGA) and known as PANDAS ("children autoimmune neuropsychiatric disorders associated with streptococcal infection").

Methods: We examined 69 patients with tics in age from 6 to 29 years. In the history of heredity was traced in 4 patients (5.8 %), chronic source of infection in 28 people (40, 6 %).

The study's design included a comparison of clinical and laboratory findings included ASL- O, RF, C-reactive protein; swab from the nasopharynx to the BGSGA, circulating immune complexes, ANA, JgA, JgM, JgG;CD4, CD8—lymphocytes.

Results: ASL-O 42.3 % was higher than normal levels of 2–4 times in 42.3 % of patients; BGSGA was detected in 11.5 % of patients.

Significant differences of severity of tic were identified in patients with a positive BGSGA (10.33 ± 1.11 and 6.22 ± 4.19, $p < 0.01$); with reduced performance CD4—lymphocytes (13.67 ± 3.56 and 25.17 ± 6.33, $p < 0.03$); with reduced performance of JgA (9.75 ± 1, 31, u5, 33 ± 4.37, $p < 0.03$; 27.75 ± 3.38 and 22.11 ± 7.35, $p < 0.04$).

Conclusions: In 34.5 % of the patients with tics an elevated level ASL-O and identified BGSGA. BGSGA, CD4-lymphocytes, Jg A—according to our study are reliable diagnostic value in the differentiation of idiopathic tics and autoimmune nature. In 40.6 % of patients had the presence of chronic foci of infection.

These characteristics can meet PANDAS.

Disclosure: Nothing to disclose.

PP4104

Treatment of essential tremor with Pramipexole

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Introduction: To investigate the influence of Pramipexole at the dose of 1.0 mg per day in patients with essential tremor (ET) .

Methods: 28 patients with ET (12 males, 16 females) were included and observed. Mean age was 51.0 ± 19.6 years, mean age at onset was 23.6 ± 18 (range 12–66 years). Previous medication with either anticholinergics or b-blockers was continued. The core criteria for patients with ET include: bilateral action tremor of the hands and forearms (but not rest tremor) or isolated head tremor; absence of other neurologic signs, with the exception of the cowheel phenomenon; long duration (> 4 years); positive family history; beneficial response to alcohol. Standardized clinical examination were performed twice: at the first visit (before starting Pramipexole) and after 3 months. Sweet Scale was also used. The patients' life quality was estimated with the help of "The Short Form (36) Health Survey" (The SF-36).

Results: At the first visit the average severity of ET was 301.3 ± 2.4 points according to the Sweet Scale. After 3 months of regular usage of Pramipexole 1.0 mg per day severity of ET was 221 ± 2.2. There was a statistically significant difference in decreased severity of action tremor of the hands and forearms in 46 % patients among all ($n = 13$) according to the Sweet Scale, $p < .01$. At the second visit the SF-36 showed that life quality was higher by item: General Health, Vitality, Social Functioning, Role Emotional, Mental Health, $p < .01$.

Conclusions: The using of Pramipexole at the dose of 1.0 mg per day effectively reduces ET and improves quality of life.

Disclosure: Nothing to disclose.

PP4105

Impact of motor and non-motor fluctuations on quality of life in patients affected by Parkinson's disease

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Introduction: Parkinson's disease (PD) is characterized not only by motor dysfunctions, but also by non-motor symptoms (NMS), which often affect strongly the disability of parkinsonian patients and their quality of life (QoL). Moreover, the definite impact of motor and non-motor fluctuations (NMF) on QoL is not clearly definite. Our objective was to examine the presence of motor and NMF in a population of PD patients and to assess their relation with QoL.

Methods: Consecutive PD outpatients from the Movement Disorders Center of the University of Cagliari were included in the study. Motor disability was assessed with the Modified Hoehn & Yahr (HY) staging and the UPDRS part-III: Motor fluctuations and NMF were evaluated with the Wearing-Off Questionnaire a 19 items (WOQ-19). The PDQ-8 was used for the QoL assessment.

Results: One hundred and two PD (59 male and 43 female) patients were enrolled. Mean age at enrollment ± standard deviation was 67.2 ± 16.7 years, with mean PD duration of 6.2 ± 4.0 years. At UPDRS-IV evaluation, patients with motor fluctuations were 33 (32.4 %), while dyskinesias were present in 20 patients (9.8 %).The correlation study between the number of motor and NMF relieved at WOQ 19 with PDQ-8 scores showed a significant correlation for NMF and reduced QoL ($r = 0.241$; $p < 0.02$), while this correlation was lower in patients with both types of fluctuations ($r = 0.226$; $p < 0.03$).

Conclusions: Our results showed that presence of NMF significantly impairs QoL in PD patients, with a greater effect in comparison to the simple presence of motor fluctuations.

Disclosure: Nothing to disclose.

PP4106

Clinical phenotype (motor and neuropsychological presentation) and neuroimaging in Sardinian patients affected by atypical parkinsonisms, carriers of 20–22 repeats of C9ORF72 hexanucleotide expansion

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Introduction: Expansions of more than 30 hexanucleotide repetitions (long expansions) in the first intron of the C9ORF72 gene are a recognized cause of amyotrophic lateral sclerosis and motor neuron disease (ALS and MND) and frontotemporal dementia (FTD). In some studies the range of 20–22 mutation patterns also have been related to dementia cognitive deterioration. Based on our previous finding of the p.A382T of TARDBP in patients with concomitant parkinsonism in the Sardinian population, we hypothesized that also the the C9ORF72 repeat expansions gene may underlie classical atypical parkinsonism or other forms of degenerative parkinsonism on this Mediterranean island.

Methods: We screened for the C9ORF72 repeat expansions. a cohort of 67 patients with primary degenerative parkinsonism different from the classic form of Parkinson's disease. Of these 67 patients, 55 were in accordance with the criteria for a diagnosis of classical form of atypical Parkinsonism (MSA-P, MSA-C, LBD, CBD, PSP), while 12 presented a clinical picture quite different from classical atypical parkinsonism.

Results: The C9ORF72 repeat short expansions was identified in 3 patients with degenerative primary parkinsonism, anybody had the C9ORF72 repeat long expansions. Surprisingly these 3 patients were all within the 12 patients who had a peculiar clinical presentation quite different from classical atypical parkinsonism (4.5 of all parkinsonism investigated, 25 % of atypical parkinsonism).

Conclusions: Our findings suggest that the clinical presentation of The C9ORF72 repeat short expansions may include forms of parkinsonism different from the classic form of Parkinson's disease and/or of classical atypical parkinsonism, with peculiar extrapyramidal signs.

Disclosure: Nothing to disclose.

PP4107

Rotigotine-related severe reversible off-dystonia: report of two cases

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Background: Severe fluctuations induced by dopamine agonists in Parkinson's disease (PD) patients have been rarely described. We describe two PD patients who developed severe, reversible off-dystonia on rotigotine treatment, which resolved after discontinuation of rotigotine.

Methods and results:

Case 1: This 56 year-old woman developed right-sided hypokinetic-rigid syndrome at the age of 51 and was started on rasagiline. At age 53 she was started on rotigotine up to 8 mg with partial improvement and shortly thereafter levodopa up to 200 mg, which was discontinued 2 weeks later due to side effects. Rotigotine was increased to 14 mg, and amantadine 200 mg was added. One year later, she developed severe painful dystonic episodes, which improved after cessation of rotigotine and the re-introduction of levodopa.

Case 2: This 48-year old man developed PD at the age of 40 and was started on pramipexole (0.18 mg $\times 3$) and levodopa 200 mg. A year later he was switched to rotigotine (8 mg), due to side effects. Two months on 8 mg rotigotine he developed severe off-dystonia on his right side and craniocervical region. Rotigotine was discontinued and the episodes resolved.

Conclusion: This is the first report of an association between Rotigotine and reversible severe, painful, off-dystonias. Continuous D2 stimulation achieved by rotigotine may set the stage or lower the threshold for dystonia to occur. The cases were either primed or on levodopa when the dystonia started. It is important to highlight these cases, as apparent off-dystonia would have prompted to increase rather than decrease treatment in these patients.

Disclosure: Nothing to disclose.

PP4108

Reduction of thalamic tremor with deep brain stimulation performed for post stroke chronic central pain

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Introduction: Deep brain stimulation (DBS) of the sensory thalamus and the periventricular/peri-aqueductal grey area complex may be applied for treatment of intractable chronic neuropathic pain syndrome.

Methods: We present a patient who experienced ischemic stroke within the posterolateral part of left hypothalamus with subsequent severe burning pain localized in right upper limb, predominantly within the hand and thalamic tremor which occurred 4 months after stroke. After 2 years of ineffective pain treatment the patient was offered deep brain stimulation with implantation of electrodes to the periventricular grey matter (PVG)/periaqueductal grey matter (PAG) as well as implantation an electrode to ventroposterolateral thalamic nucleus (VPL). Correct target localization within the VPL was confirmed when an intraoperative 50 Hz stimulation elicited paresthesia in the contralateral limb. Once the physiologic targets have been defined with stimulation, permanent electrodes were introduced, and the leads were externalized through a stab wound in the scalp for trial stimulation.

Results: Soon after starting permanent simultaneous PAG/PVG and PVL stimulation we observed not only alleviation of the patient's pain but also significant reduction of the patient's thalamic tremor in the hand, which persisted over subsequent months. In this case study we discuss possible mechanism underlying tremor suppression in our patient, probably at the level of cerebellar outflow pathways.

Conclusions: The study highlights the fact that DBS provide more insight into the functional anatomy of the thalamus, which used to be available from animal studies only.

Disclosure: Nothing to disclose.

PP4109

An acoustic analysis of diadochokinesis in patients with Parkinson's disease

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Introduction: Parkinson disease (PD) shows not only the cardinal symptoms of tremor, rigidity, and bradykinesia, but also the features of hypokinetic dysarthria. In speech-language pathology, diadochokinesis (DDK) is used to assess the rate and regularity of repetitive movements of the oral articulators, and the acoustic analysis of DDK

has been used to evaluate dysarthria. However, there has not been an automatic method to evaluate dysarthria. The aim of this study was to introduce a new automated program to measure DDK tasks and to apply this to clinical patients with idiopathic Parkinson's disease (IPD).

Methods: Forty-seven patients with IPD and a healthy control group of twenty participants were selected with every DDK task and run three times, respectively. Twenty-five acoustic parameters in the program were developed. The relevant parameters were times of DDK, pitch related parameters, intensity parameters which were analyzed by 2-way ANOVA.

Results: Significant differences between the groups were found in the times of DDK, pitch related parameters, and intensity parameters. The findings indicated that the pitch of control group was more stable than that of the IPD.

Conclusions: Even though the patients with IPD had a higher intensity value, this phenomenon was caused by the weakness of the IPD group who could not control their speech with a breath. Autonomic acoustic analysis of DDK has the potential to evaluate the status or severity of hypokinetic dysarthria in patients with PD. Our results provide the necessity of assessment for describing and monitoring changes in acoustic characteristics following therapeutic intervention.

Disclosure: Nothing to disclose.

PP4110

Prevalence and phenomenology of psychotic symptoms in Huntington's disease

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Introduction: Neuropsychiatric features are characteristic symptoms in Huntington's disease (HD). Compelling evidence proved high prevalence of alterations on mood and affect. However, little is known about psychotic symptoms in HD.

Objective: Describe the characteristics and phenomenology of psychotic symptoms in a Spanish cohort of Huntington's disease patients.

Methods: From the Spanish Registry cohort, genetically positive patients with psychiatric, cognitive and motor assessment were included. We analyzed demographic, genetic and clinical data. Cognitive and motor functions were measured with Unified Huntington Disease Rating Scale (UHDRS), psychiatric disturbances with the Problem Behavior Assessment Scale (PBA-S) and function with the total functional capacity (TFC).

Results: 264 patients were included (46.2 % males; mean age of 45.2 ± 12.5 years; disease duration 5.5 ± 5.5 years and mean CAG 44.1 ± 4.7). Delusions were present in the 10.2 % of the patients and hallucinations in 4.5 %. Visual hallucinations were the more frequent 3.4 % followed by auditory 1.9 %. UHDRS cognitive score ($p = 0.05$) and TFC ($p = 0.01$) were more impaired in patients with psychotic symptoms. No other differences or correlations between delusions/hallucinations and cognitive, motor or functional scores were found.

Formal diagnosis of schizoaffective disorder was present in two patients, previous acute psychotic episode in one, dementia in one and young HD in one.

Conclusions: Psychotic symptoms are infrequent in HD. Delusions are more frequent than hallucinations being the visual ones the more recurrent. Despite not found correlation, patients presenting psychosis/hallucinations are significantly more impaired on cognition and functional capacity.

Disclosure: Nothing to disclose.

PP4111

Adaptive deep brain stimulation (aDBS) in Parkinson's disease: a case report

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Introduction: Because the conventional DBS (cDBS) only partially controls motor fluctuations in Parkinson's disease (PD), this treatment could be optimized by adapting the stimulation to the patient's clinical state (i.e. adaptive Deep Brain Stimulation or aDBS). An aDBS device is a closed-loop system able to record and analyze a control signal, and to adapt stimulation parameters. Local field potentials (LFPs, i.e. the sum of the pre and post-synaptic neural activity around the DBS electrode) correlate with the patient's clinical state and can be a reliable control signal for aDBS. We developed an external portable aDBS device controlled by LFPs and we present its clinical assessment in a freely moving PD patient.

Methods: The 5th and the 6th day after the DBS electrodes implant in the subthalamic nucleus, the patient, after the standard antiparkinsonian medication, underwent 2 h of cDBS and 2 h of aDBS, respectively. The patient was not aware of the DBS type. The motor state was evaluated by a blinded neurologist through the Unified Parkinson's Disease Rating Scale (UPDRS III), and the Rush Dyskinesias Rating Scale (DRS).

Results: Whereas the UPDRS III score was the same during aDBS (12/108) and cDBS (12/108), the dyskinesias were less severe during aDBS (4/28) than cDBS (14/28).

Conclusions: The aDBS device controlled better the motor fluctuations than cDBS, reducing dyskinesias. Our portable device unlocks new opportunities to study aDBS in PD patients during their daily activities providing new insights into the impact of this novel technology on their quality of life.

Disclosure: Lorenzo Rossi, Sara Marceglia, Alberto Priori, Marco Localtelli, Paolo Maria Rampini and Filippo Cogiamanian are stakeholders of the Newronika s.r.l, a spin-off company of the Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico and of the Università degli Studi di Milano.

PP4112

Hypokinetic movement disorders in childhood

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Introduction: Hypokinetic movement disorders (HMD) are uncommon and usually misdiagnosed in childhood. The aims of our study were to determine clinical and radiological characteristics and to identify etiologies and the outcome of HMD in childhood.

Methods: A retrospective study (2004–2013) included children with HMD. Clinical and radiological findings, treatment and outcome were recorded and analyzed.

Results: Twelve children (6 males, 6 females) were included. Mean age of onset was 3 years (3 months–11 years). The onset was insidious in 7/12 cases and acute in 5/12 cases. All patients had bradykinesia associated to cogwheel rigidity (8/12), rest tremor (7/12) and dystonia (8/12). Main brain MRI abnormalities corresponded to involvement of substantia nigra (6/12), striatum (1/12) or both (1/12). Etiologies were classified into inborn errors of metabolism (7/12) and acquired causes (5/12) with predominance of postencephalitic parkinsonism (4/12). Several anti-parkinsonian drugs were used: levodopa (7/12), bromocriptine (4/12) and selegiline (2/12). A good response was obtained in patients with acquired parkinsonism (5/12) with full recovery (4/12). Fluctuations and dyskinesia were noticed in one patient with chronic dopatherapy.

Conclusions: Few studies focused on HMD in childhood. Etiologies correspond to inherited degenerative and metabolic disorders and acquired causes with predominance of neuroleptic intake or cerebral infections as in our series. Brain MRI is a useful tool to detect involvement of dopaminergic pathways. Anti-parkinsonian drugs, particularly levodopa, seem to be more efficient in acquired causes of HMD and to shorten the clinical course.

Disclosure: Nothing to disclose.

PP4113

Nicotine as adjunct therapy to relieve levodopa-induced dyskinesias

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Introduction: Although levodopa is one of the best treatments for PD, its use is limited because of the development of motor fluctuations. Epidemiological studies show that smoking is associated with lower incidence of PD while studies in non-humane primate show that nicotine could reduce motor complications as dyskinesias. Objective of this study is to investigate whether nicotine as an adjunct therapy could reduce levodopa-induced dyskinesias in Parkinson's disease (PD).

Methods: Patients with a clinical diagnosis of idiopathic PD who developed levodopa-induced dyskinesias (LID) were included in open-label 12 weeks duration study after signed informed consent was obtained. Nicorette (transdermal invisipatch, 23.6 mg nicotine) was administered as transdermal patch every 12 h in each patient without any change of levodopa and/or other medication. Patients took their own diary recording time of medication, time with and/or without dyskinesias.

Results: Total of 13 PD patients were enrolled in the study (7 males, 6 females; mean age 57.4 years; mean disease duration 7.5 years, mean H&Y scale 3.5). Only 2 patients drop-out from the study (1 after first Nicorette application because of unpleasant sensation in his legs, 2 patient 5 days after Nicorette application without any change in motor complications score). Other 11 patients finished 12-week study with significant reduction of recorded dyskinesia. Only mild vomiting was observed in one patient during first day of treatment.

Conclusions: This preliminary data suggest that combined treatment with nicotine, or preferably nicotinic agonists that selectively stimulate nACh receptor subtypes, could improve LID. Prospective, controlled study is needed.

Disclosure: Nothing to disclose.

PP4114

Impulse control disorder and olfaction in Parkinson's disease

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Introduction: Impulse control disorder (ICD) and olfactory dysfunction (OD) are two non-motor symptoms of Parkinson's disease (PD) that have been linked to orbitofrontal functioning. The relationship between ICD and OD in PD is still unknown.

Methods: One hundred and thirty one consecutive patients with idiopathic PD stage 1–3 Hoehn & Yahr (52 % men; mean age = 66.8, SD = 10.9; mean education = 6.5 years, SD = 3.9; mean disease duration = 6.9 years, SD = 4.5; mean levodopa equivalent dose = 713 mg, SD = 469) were included. Unified Parkinson's Disease Rating Scale-III (UPDRS-III; mean = 29.7, SD = 9.2) was applied after 12 h without antiparkinsonian medication. The Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease (QUIP-Current-Short) and the Brief Smell Identification Test (B-SIT) were applied after the effect of the usual medication of the patient. Mann–Whitney test and multiple logistic regression analysis were used for data analyses.

Results: ICD (i.e., $\geq$1 positive answer on the QUIP-Current-Short) and OD (i.e., B-SIT $\leq$ 8) were found, respectively, in 17 and 78 % of patients. Patients with ICD had better performance on B-SIT ($p = 0.011$) than patients without ICD (mean = 8.09, SD = 1.77 vs. mean = 6.77, SD = 2.03). The odds of having ICD increased with better scores on the B-SIT, even while adjusting for covariates sex, age at onset, disease duration, and levodopa equivalent dose (ORadj = 1.486; $p = 0.009$; 95 %CI 1.104–2.001).

Conclusion: OD is more common than ICD in PD. Surprisingly; this exploratory study revealed that the risk of having ICD was higher in patients with better olfactory functioning. This result suggests that ICD and OD in PD result from distinct pathophysiological processes and raises the possibility of competitive neural circuits.

Disclosure: Nothing to disclose.

PP4115

Nonmotor features in young patients with essential tremor; sleep quality, excessive daytime sleepiness, anxiety, depression, cognitive functions: a case comparison study

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Introduction: The classical knowledge about Essential Tremor (ET) as a monosemptomatic, slowly progressing,benign, pure motor system disease has been questioned in last years. There is increasing evidence to suggest that apart from motor features, patients with ET may have significant nonmotor features such as mild cognitive deficits, neuropsychiatric symptoms (anxiety, depression, specific personality traits…), sleep disorders, fatique. The goal of this study was to evaluate the nonmotor features in young patients with ET.

Methods: 30 patients (23.83 ± 5.83 years old) with ET and 15 healthy controls were evaluated using Pittsburg Sleep Qualty İndex (PSQİ), Epworth Sleppines Scale (ESS), Beck Depression Scale (BDS), Beck Anxiety Scale (BAS), Fatique Severety Scale (FSS). We ruled out the other possible causes of tremor. Cognitive functions were evaluated using Montreal Cognitive Assessment Battery (MoCA) by a neuropsychologist. Tremor was evaluated using Fahn Tolosa Marin Tremor Rating Scale (FTM-TRS).

Results: In patients group; 63.3 % had poor sleep quality, 56.7 % fatique, 23.3 % moderate and 50 % severe anxiety levels, 23.3 % moderate and 13.3 % severe depression. PSQİ, ESS, BDS, BAS,FSS scores in ET group were significantly higher than the controls. Total MoCA scores and subscores were lower than the controls. 13.3 % had excessive day time sleepiness. But these results were not statistically significant.

Conclusions: ET has canonically been viewed as a motor disorder, there is now a growing interest in nonmotor features of ET. The aim of this study was to contribute this new concept. Further studies of these nonmotor features will go a long way in understanding and comprehensively treating ET.

Disclosure: Nothing to disclose.

PP4116

Nonmotor features in essential tremor: a comparison with Parkinson's disease

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Introduction: Essential Tremor (ET) is the most common movement disorder and the cause of functional disability. ET is increasingly thought to involve a heterogeneous group of patients with some also exhibiting ataxia, postural instability, resting tremor, and cognitive deficits. Some ET patients of motor signs also found in Parkinson's disease. The goal of this study to evaluate existence of nonmotor features in ET patients.

Methods: 22 patients with ET and 21 patients with PD (age: 61.95 ± 7.57, 66.80 ± 9.70) were evaluated by using Nonmotor Symptoms Questionnaire (NMSQ) and Montreal Cognitive Assessment (MoCA) to determine nonmotor features. To rate of illness we used Fahn Tolosa Marin Tremor Rating Scale (FTM-TRS) for patients with ET and The Unified Parkinson's Disease Rating Scale (UPDRS) and Hoehn and Yahr scale for patients with PD.

Results: In ET group; most common nonmotor features were 'feeling sad, low or blue (72.7 %), getting up regularly at night to pass urine (68.2 %), a sense of urgency to pass urine (63.6 %). NMSQ total score means were 8.59 ± 4.43 in ET patients, 14.66 ± 4.62 in PD patients (p value < 0.05). Except 7 items of NMSQ, one by one comparison of other items had no statistical difference. MoCA total scores were 18.31 ± 4.32 in ET patients, 16.85 ± 3.96 in PD patients. There was no statistical significant difference MoCA total scores (p value 0.25) and subscores.

Conclusions: The emerging view of ET is that it may be a neurological disease characterized by a number of motor and non-motor features. Future studies with large sample size are needed. This study contributes some evidence for this new concept.

Disclosure: Nothing to disclose.

PP4117

Abstract withdrawn

PP4118

The FAB fails to discriminate PSP from FTD and to capture disease progression in frontal disorders

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Introduction: The frontal assessment battery (FAB) has been suggested as a useful tool in the differential diagnosis of progressive supranuclear palsy (PSP) from Parkinson's disease (PD) and multiple system atrophy with parkinsonism (MSA-P). However, the utility of the FAB in the differential diagnosis of PSP from frontotemporal dementia (FTD) phenotypes is still under research.

Methods: We performed the FAB, in a large multi-centre cohort of probable PSP ($N = 70$), FTD ($N = 76$ behavioral variant FTD, $N = 10$ semantic dementia, $N = 9$ progressive non-fluent aphasia), as well as PD ($N = 26$) and MSA-P ($N = 11$) patients, according to established criteria. Patients were also rated with the mini mental state examination and motor scales.

Results: The FAB total score and subscores failed to discriminate PSP from bvFTD and PNFA patients. Moreover, the FAB did not correlate with disease duration and was insufficient to capture disease progression in these disorders. In contrast, we confirmed that the FAB was useful in differentiating PSP from PD and MSA-P. In fact, two FAB subscores together (verbal fluency and Luria motor series) were sufficient and better than the total score in differentiating PSP from PD and MSA-P.

Conclusions: The FAB can neither differentiate PSP from FTD related disorders, nor can capture disease progression in PSP and FTD. This

should be taken into consideration in clinical practice but also in planning clinical trials. When used to differentiate PSP from PD and MSA-P, verbal fluency and motor series are sufficient and the total score is rebundant.

Disclosure: Nothing to disclose.

PP4119

Clinical and genetic characteristics of dopa-responsive dystonia in Serbian population

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Introduction: Dopa-responsive dystonia (DRD) is neuromethabolic disorders inherited in two ways: autosomal-dominant (AD) with heterozygous mutations in GPT-cyclohydrolase 1 gene (GCH1-DYT5a) and autosomal-recessive (AR) with homozygous or compound heterozygous mutations in genes for thyrosin-hydrolase (TH) or sepiapterin-reductase (SPR) (DYT5b). AD form is characterized by reduced penetrance and excellent and permanent response to levodopa, while AR form is more severe, with developmental delay and cognitive impairment. The aim was to assess genetic and clinical characteristics of DYT5a mutations carriers in patients with dystonia-plus syndrome in Serbia.

Methods: Study comprised 66 patients with dystonia-plus syndrome and 60 healthy controls. Genetical analysis was performed by method of direct sequencing of coding exones of GCH1 gene. Clinical characteristics of patients were evaluated using standardized rating scales for assessment of dystonia and parkinsonism.

Results: We found 5 mutations of GCH1 gene (L157P, 209delA, c.C08G > A, c.558c > T, ex + 1G > C) in 10 carriers. The most frequent mutation (L157P) was demonstrated in a family with 5 affected members, all with spastic paraparesis as initial presentation and excellent levodopa responsiveness. Phenotype spectrum was wide in our group of patients, from lower extremities dystonia to hemiparkinsonim, dystonia-parkinsonism complex and spastic paraparesis. All patients were on continuous levodopa treatment. DAT was normal in all patients, while 2 of them had pathological finding on TCS.

Conclusions: Our results showed GCH1 mutations in 15 % of patients with dystonia-plus syndrome. It is important to stress phenotypic heterogeneity of the disease with wide spectrum of clinical expressions in forms of dystonia, parkinsonism and spastic paraparesis.

Disclosure: Nothing to disclose.

PP4120

Frequency of non-motor symptoms in patients of Parkinson's disease

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Introduction: In multiple studies around the globe, non-motor symptoms have been identified as a source of immense disability in patients of Parkinson's disease. However, there is scarcity of data from Asia. This is the first study from Pakistan assessing the impact of non-motor symptoms on patients with Parkinson's disease.

Objectives: To investigate the frequency of non-motor symptoms of Parkinson's disease in Pakistani population and compare it with the Western data.

Methods: In this cross-sectional survey, data was retrospectively collected from Shifa International Hospital Neurology database. This study comprised of 97 patients at different stages of Parkinson's disease who were questioned at neurology OPD or through telephonic interviews. Disease severity was assessed using 'Hoehn & Yahr's staging' while 'NMS Quest' was employed to identify the non-motor symptoms present. Medical records were reviewed for demographic data and recent treatment history.

Results: The mean age was 67.33 years (adult onset = 76.3 %, young onset = 23.7 %). No correlation was found between the disease duration and the disease stage. The most frequent non-motor symptoms were nocturia (77.3 %), urinary urgency (61.9 %), constipation (59.8 %), forgetfulness (58.8 %), insomnia (52.6 %) and orthostatic hypotension (52.6 %). The earliest manifestations of non-motor symptoms were nocturia, forgetfulness, low mood and orthostatic hypotension. Sleep abnormalities, falling episodes & hallucinations are prevalent amongst patients of advanced disease.

Conclusion: There is a direct correlation between disease progression and number of non-motor symptoms present.

Disclosure: Nothing to disclose.

PP4121

Parkinsonism, myoclonus and focal signs in nonketotic hyperglycemic chorea

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Introduction: Nonketotic hyperglycemia may be complicated by chorea. However, other movement disorders have not been reported.

Methods: We describe a patient which developed parkinsonism and myoclonus while recovering from nonketotic hyperglycemic chorea.

Results: A 68-year-old woman with complicated diabetes mellitus, treated with oral antidiabetics, associated with sensory motor polyneuropathy and with degenerative spine disease, was admitted due to generalized chorea (2 weeks of evolution).

Neurological examination revealed generalized chorea (left > right hemibody), left hemiparesis and central facial paresis, algic, tactile and proprioceptive hypoesthesia with socks-pattern distribution and gait instability due to chorea and mild ataxia.

Laboratorial analysis revealed glucose >500 mg/dL and A1cHb of 15.8 %. CT-scan showed bilateral hiperdensity of corpus striatum (right > left). Cranial MRI, performed 9 days after admission, revealed T1-hiperintensity of the right corpus striatum, associated with mild diffusion-restriction on DWI/ADC map.

A nonketotic hyperglycemic chorea was diagnosed. While chorea slowly resolved, with improvement of glicemic control, the patient developed severe myoclonus, involving trunk and limbs, in association with treatment with CBZ 600 mg/d. Myoclonus regressed after withdrawal of CBZ but recurred with amitriptyline.

In parallel, she developed parkinsonism, with generalized bradykinesia.

Conclusions: Chorea is a rare but classical complication of nonketotic hyperglycemia. We describe a patient with parkinsonism, myoclonus and hemiparesis in the setting of nonketotic hyperglycemic chorea. This suggests that nonketotic hyperglycemia brain damage is more widespread than classically thought. Myoclonus was associated to drug administration. Damage by hyperglycemia might have lowered the threshold to drug side-effects.

Disclosure: Nothing to disclose.

PP4122

Task specific spasmodic dysphonia

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Introduction: Spasmodic dysphonia is a voice disorder resulting from involuntary movements (or spasms) of the vocal muscles. These spasms interrupt normal phonation with a strained, strangled voice (adductor type), or with breathy, soundless voice (abductor type). Clinically, Spasmodic dysphonia is a type of dystonia; the cause is unknown, there is no specific tests for diagnosis and resultantly, there is no known cure; but treatment can and does improve symptoms. Botulinum toxin injections into muscles of phonation can alleviate symptoms—although relief is only temporary and treatments are usually repeated according to symptomatic exacerbations. A professional (or occupational) voice user is anyone whose voice is essential to their job. Among different professional voice users, priests (who are named as imams in Islam) are in a specific condition. During Islamic acts of worship, Turkish imams use their voices in a wide vocal range with a non vernacular language (Arabic). These special occasions which demand high intensities and high pitches may trigger stressful processes for the neuromuscular system.

Methods: Three cases are considered in this study. They are all imams and have adductor type spasmodic dysphonia. They are evaluated clinically and by laryngeal EMG and voice analysis.

Results: All three cases' voice analysis showed interruptions and elevated fundamental frequency. After botulinum toxin injection, the Fo values have decreased and jitter and shimmer are shown to be better.

Conclusions: Spasmodic dysphonia may be related to use of voice, language and psychological factors. Patients may benefit from botulinum toxin injections and rehabilitation.

Disclosure: Nothing to disclose.

PP4123

Effects of amantadine on postural instability in Parkinson's disease

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Introduction: Amantadine is a NMDA antagonist that has antiparkinson properties. Although it is widely used for treatment of l-dopa related dyskinesias some case reports also mention its effect on postural instability in Parkinson's Disease.

Methods: Parkinson's Disease patients treated with amantadine for postural instability in 2013 in our Movement Disorders Clinic were evaluated retrospectively. Patients were evaluated with UPDRS motor score. Only patients under steady dopaminergic treatment were included in the analysis. Amantadine was started as 2 × 50 per day and increased up to 500 per day when needed.

Results: There were 21 patients. Male to female ratio was 16/5. Mean age of the group was 72.5. Mean disease duration was 6.4 years. Mean Amantadine dose was 390.48/day. Mean UPDRS motor score were 34.2. All except two patients reported benefit from amantadine. The mean fall score of the UPDRS motor scale was 2.48 before amantadine and 2.00 under amantadine treatment.

Conclusions: Our study results show that amandatine might have a modest effect on postural instability in Parkinson's Disease.

Disclosure: Nothing to disclose.

PP4124

An atypical Stiff-Person syndrome associated with type 3 autoimmune polyglandular syndrome

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Introduction: Stiff-Person Syndrome (SPS) is strongly associated with other autoimmune diseases. Autoimmune Polyglandular Syndrome (APS) is characterized by the coexistence of at least two glandular autoimmune diseases.

Methods: Case report.

Results: A 74-year-old female patient with a past history of hypertension, diabetes mellitus, hypothyroidism, atrophic gastritis and depression, presented with an 18-month history of progressive stiffness and gait problems, associated with painful abdominal and lower limb spasms that caused major disability. She had a recent exploratory laparotomy for unexplained abdominal pain, and was admitted due to recurrence of severe abdominal pain and lower limb spasms. Examination revealed a "mask-like" facies, left and right gaze-evoked upbeat nystagmus and partial left gaze paresis; bradykynesia and rigidity of the four limbs, generalized hyperreflexia, a small stepped gait with freezing and retropulsion, and clusters of painful abdominal and lower limb tonic spasms, which were aggravated by tactile stimuli. Neuraxis MRI and CSF examination were unremarkable, and electromyography was normal, although it was made after clinical improvement. Serum GAD-65 antibodies were positive, along with anti-insulin, Langerhans cells, intrinsic factor and thyroid peroxidase antibodies. Investigation for an occult tumor revealed negative. Treatment with diazepam and baclofen improved the muscle spams, and Intravenous Immunoglobulin improved limb rigidity and gait.

Conclusions: We report a case of atypical SPS with prominent features of brainstem, cerebellar dysfunction and parkinsonism, and with a distinctive association with multiple autoimmune diseases, comprising APS type 3. This case alerts also for SPS to be considered in the differential diagnosis of atypical parkinsonian syndrome.

Disclosure: Nothing to disclose.

PP4125

Pain in Parkinson disease: treatment and patient satisfaction

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Introduction: Patients with Parkinson's disease (PD) frequently suffer from pain. Few studies have reported pain management in PD using pharmacologic and non-pharmacologic therapies; and patient satisfaction regarding pain management has been seldomly assessed.

Methods: One hundred and seventeen consecutive patients with idiopathic PD underwent a neurological examination and a structured interview for registration of pain characteristics. UPDRS-III and

Hoehn and Yahr Scale were applied after 12 h without antiparkinsonian medication.

Results: Pain was reported by 88 (75 %) patients [39 % men; mean age = 68.2 years, SD = 11.8; mean education = 5.3 years, SD = 3.8; mean disease duration = 8.8 years, SD = 5.7; mean levodopa equivalent dose = 893 mg, SD = 505; UPDRS-III: mean = 34.9, SD = 11.9; HY stage 1–3: 68 (77.3 %); HY stage 4–5: 20 (23 %)]. Musculoskeletal pain was reported by 54 %, musculoskeletal and dystonic pain by 14 %, central neuropathic pain by 13 %, dystonic pain by 11 %, radicular-neuropathic pain by 7 % and central neuropathic and radicular-neuropathic pain by 1 %. Fifteen percent of the patients reported two different types of pain. Fifty five percent had therapies for pain relief (69 % pharmacologic therapy, 25 % pharmacologic and non-pharmacologic therapies and 6 % only non-pharmacologic therapy). Of those, 33 patients responded to the satisfaction questionnaire and 16 (49 %) were quite or very unsatisfied with the current pain treatment.

Conclusions: Our study confirms that pain is a frequent symptom in PD patients and demonstrates that PD patients with pain are inadequately treated in many cases. Half of the patients are unsatisfied with the current pain management. Neurologists and general practitioners should be more alert to the symptoms of pain in PD patients.

Disclosure: Nothing to disclose.

PP4126

A case with autosomal recessive hypermanganesemia: clinical and MRI findings

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Introduction: Early-onset generalized dystonia with brain manganese accumulation has recently been identified. Mutations in the SLC30A10 gene, encoding a manganese transporter, cause a syndrome of hepatic cirrhosis, dystonia, polycythemia, and hypermanganesemia.

Methods: We present the clinical and MRI features of a 22-year-old girl with autosomal recessive hypermanganesemia.

Results: The case was born from a healthy first-cousin marriage. At the age of 1.5 years, she developed walking difficulty, progressing in time. Her first neurological examination revealed generalized dystonia prominent in the lower extremities when she was 3. She could not stand or walk without support. Mild hyperbilirubinemia, polycytemia, iron storage disorder and liver dysfunction were detected in the blood analysis. Metabolic screening for inborn error was negative, and copper-zinc metabolism as well as organic acids were all within normal limits. However, elevated blood manganese levels were almost 10 times as high as the normal limits. T1-sequences in MRI showed hyperintensities in the basal ganglia (caudate and lentiform nuclei) and dentate nuclei, characteristic of manganese deposition.

Conclusions: Worsening of dystonia, and hyperintensities more prominent in T1 MRI are evidence enough to search hypermanganesemia. Resulting from autosomal recessive inheritance, this condition is commonly encountered in countries where consanguineous marriage is widespread. Of note, our case is the first in Turkey who presented with this condition. It should be kept in mind that hypermanganesemia can be treated by chelation as can other treatable rare neurological disorders.

Disclosure: Nothing to disclose.

PP4127

The role of cognitive event-related potentials in detection of cognitive dysfunctions in essential tremor

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Introduction: There is growing evidence that essential tremor (ET) is a multiple-system disorder because of additional motor features (e.g., intention tremor and ataxia) and nonmotor features (mild cognitive deficits and personality changes). Cognitive event-related potential (ERP) can encompass general cognitive processing and efficiency. Among these neuroelectrical markers, P300 component of ERP is most widely studied to assess neurologic and psychiatric cognitive dysfunction. The hypothesis of this study was that cognitive dysfunction of ET may be associated with ERP changes. We compared the results of P300 values between essential tremor patients and normal controls to study the role of ERP in detection of cognitive impairment among ET patients who are seemingly normal.

Methods: Case–control comparisons of 8 patients with ET and 8 age-matched controls were performed. All subjects underwent clinical assessments, neuropsychological tests and auditory and visual cognitive ERP tests.

Results: Among 8 ET patients, 4 had mild cognitive impairment. Group with ET showed prolonged visual P300 latency than control group. Visual P300 latency was associated with frontal executive and visuospatial dysfunction, and visuospatial memory deficit.

Conclusions: This result suggested that visual evoked P300 latency serves as a potent marker in evaluating cognition among essential tremor patients. Longitudinal, prospective study is warranted to assess ERP in terms of screening cognitive deficit and quantifying the degree of impairment.

Disclosure: Nothing to disclose.

PP4128

The efficacy of three dimensional accelerometer evaluating of gait in spastic paraplegia patients with intrathecal baclofen therapy

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Introduction: It is clear that the intrathecal baclofen therapy decreases spasticity and improves gait in spastic paraplegia patients. However, it is still controversial about what is an appropriate indicator of evaluating gait in spastic paraplegia patients. We investigated whether three dimensional accelerometer is useful to evaluate gait performance of these patients.

Methods: 6 patients with spastic paraplegia were recruited. They were measured gait parameters with three dimensional accelerometer both before and after bolus intrathecal baclofen. Three patients improved by screening trial of intrathecal baclofen received continuous intrathecal baclofen therapy. They were measured gait parameters per 3 months when refilling. 25 healthy volunteers were recruited as controls from our hospital coworkers.

Results: Patients with spastic paraplegia showed significant slower walk speed ($p < 0.001$) and smaller step width ($p < 0.001$) than healthy controls. Coefficient of variation (CV) of the amplitude of the vertical ($p = 0.001$) and horizontal ($p = 0.003$) in spastic paraplegia were significant increased relative to those of controls.

Step width has increased and CV of the vertical and horizontal has decreased in all three patients after continuous intrathecal baclofen therapy. However, walk speed in patients did not show a significant difference.

Conclusions: We demonstrated that the gait of patients with spastic paraplegia was unsteady and showed highly CV with three dimensional accelerometer. Three dimensional accelerometer is quantitative and able to easily perform repeatedly. Therefore three dimensional accelerometer plays a crucial role in the assessment of gait performance in spastic paraplegia patients treated with intrathecal baclofen therapy.

Disclosure: Nothing to disclose.

PP4129

Deep neck muscles involvement in cervical dystonia: diagnostic techniques, treatment and side effects

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Introduction: Cervical dystonia (CD) is supported by different dystonic patterns, sometimes involving deep neck muscles (scalenus, longus capitis and rectus colli). Injection with Botulinum neurotoxin (BoNT) of these muscles implies more procedural risk and side effects, so usually they are treated secondly or in case of poor response. Clinical evaluation and polygraphic electromyography (poly-EMG) are sometimes insufficient to identify muscles primarily involved in dystonic patterns. Positron emission tomography (PET) could be useful to identify hyperactive muscles.

Objective: To evaluate diagnostic techniques, utility and side effects of BoNT treatment of deep neck muscles in CD.

Methods: 8 of 23 patients with CD periodically receiving EMG-guided BoNT treatment showed involvement of deep neck muscles at poly-EMG. 2 of them underwent PET after repeated poor effective treatment in order to better identify pathologic muscle activation. In one case PET results confirmed neurophysiological findings, in the other it identified muscles not evaluated at poly-EMG. Deep neck muscle were integrated in the treatment scheme of these patients.

Results: the eight patients reported clinical benefits from deep muscles treatment. PET allowed better identification of target muscles. 3 patients developed dysphagia after BoNT injection and 2 of them had to discontinuate deep muscles treatment.

Conclusions: Deep neck muscles BoNT injection is sometimes the treatment of choice in CD but dysphagia may be quite troublesome. Dysphagia may depend on many variables (site of injection, type of toxin used) so special attention must be paid in the definition of treatment. PET may improve the evaluation of dystonic patterns.

Disclosure: Nothing to disclose.

PP4130

Neuroleptic malignant syndrome in a patient with esophagus cancer: a report of a rare case

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PP4131

Postural tremor of the trunk and postural instability in patients with Parkinson's disease

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PP4132

Blepharospasm revealing lung cancer

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PP4133

Postural correlates of the empathic pain response: influence of perspective

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PP4134

Movement disorders after stroke in third level Hospital Marrakech, Morocco

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PP4135

Palilalia as early red flag in progressive supranuclear palsy

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PP4136

Abstract withdrawn

PP4137

Evaluation of impulsivity in Huntington's disease with a delay discounting paradigm

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PP4138
Is Parkinson's disease increase the risk to develop a glucose intolerance?

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PP4139
Psychometric study of the Persian short-form Parkinson's disease questionnaire (PDQ-8) to evaluate quality of life: how imprecise is it compared to the long-form version (PDQ-39)?

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PP4140
The clinical syndrome of dystonia with aphonia

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PP4141
The relationship between Parkinson's disease and mean platelet volume (MPV)

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PP4142
Influence of dopamine on cognitive functions in Parkinson's disease patients

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PP4143
Transcranial sonography is a method of early diagnosis of Parkinson's disease

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PP4144
Regional distribution of Huntington's disease in Slovenia

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PP4145
Sleep disorders in Parkinson's disease

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PP4146
Reduction of motion disability in migrainous rats with Parkinson disease

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PP4147
Decreased spreading depression susceptibility in Parkinson rat model

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Multiple sclerosis and related disorders 3

PP4148
A double-blind, randomized, versus-placebo study of palmitoylethanolamide in subjects with relapsing-remitting multiple sclerosis: preliminary results

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Introduction: Palmitoylethanolamide (PEA), the naturally occurring amide of ethanolamine and palmitic acid, is an endogenous lipid that modulates pain and inflammation. PEA has been demonstrated to have anti-inflammatory and neuroprotective effects in different experimental models, including those of MS.

Our work, a double-blind, randomized, versus-placebo study, evaluates the effect of PEA on serum levels of pro-inflammatory cytokines, such as Interferon (IFN)-gamma, Tumor Necrosis Factor (TNF)-alpha and Interleukin (IL)-17, versus placebo, over a period of 12 months.

Methods: Twenty-nine relapsing-remitting (RR)-MS patients (17 Male, 12 Female; mean age 27 ± 8 years) treated with Interferon-beta-1a 44 micrograms were enrolled and randomized to receive PEA, 600 mg daily, versus placebo. All patients performed blood samples collection at the enrollment and after 3–6–12 months to evaluate serum levels of IFN-gamma, TNF-alpha and IL-17.

Results: We observed, in 16 out of 29 patients (55.17 %), a reduction time related of IFN-gamma, TNF-alpha and IL-17 in the PEA group versus placebo, although this reduction is not statistically significative. Data have been analyzed using ANOVA for repeated measures with no hypothesis on variance.

Conclusions: Our results demonstrate the efficacy of PEA in reducing the serum levels of IFN-gamma, TNF-alpha and IL-17 over time and confirm the pharmacological properties of PEA, suggesting that PEA could be an effective tool in the control of inflammation. The therapeutic effect of PEA may prove to be a therapeutic strategy capable to affect an array of nervous system disorders as MS.

Disclosure: Nothing to disclose.

PP4149

Evaluation of sIFNAR2 as a potential diagnostic biomarker of multiple sclerosis

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Introduction: Interferon Beta (IFNβ), the most commonly treatment used for MS, acts through interaction with its receptor, IFNAR, which is composed by two subunits: IFNAR1 and IFNAR2. The soluble isoform of the subunit IFNAR2 (sIFNAR2), present in body fluids, can bind IFNβ and modulate its activity. We assessed the serum levels of sIFNAR2 in MS patients and healthy controls and then its value as a potential diagnostic biomarker was evaluated.

Methods: Recombinant sIFNAR2 was cloned, expressed and purified to be used as positive control in a non-commercial semiquantitative ELISA to detect sIFNAR2 in serum. Two independent cohorts including 377 MS patients (IFNβ-treated and untreated) and 117 healthy controls were analyzed. Moreover, 26 patients with other inflammatory neurological diseases (OIND) were included.

Results: Treated patients had higher levels of sIFNAR2 respect to untreated patients ($P < 0.001$) and healthy controls ($P < 0.001$). However, there were no differences in IFNAR2 according to response of the patients to the IFNβ treatment. Notably, untreated patients exhibited higher levels of sIFNAR2 than healthy controls ($P < 0.001$), fact that was replicated in the second cohort. Untreated patients with OIND had lower sIFNAR2 compared with untreated MS patients. The ROC analysis between controls and untreated MS patients yielded an AUC of 0.79. Finally, the proinflammatory cytokine profile was analyzed by flow cytometry and high levels of sIFNAR2 were associated with low production of TNF-alpha and IFN-gamma.

Conclusions: The results suggest that sIFNAR2 could modulate the endogenous IFNβ and it could be a potential diagnostic biomarker of MS.

Disclosure: Dr Fernández has received honoraria as consultant in advisory boards, and as chairman or lecturer in meetings, and has also participated in clinical trials and other research projects promoted by Biogen-Idec, Bayer-Schering; Merck-Serono, Teva, Novartis, Almirall and Allergan. No other disclosures were reported.

PP4150

A quantitative histopathological study of the effects of arsenic oxides on inflammation, demyelination and neurodegeneration in multiple sclerosis

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Introduction: Different preparations of arsenic-containing compounds were used for the treatment of multiple sclerosis (MS) until the mid-60s. This study aims to examine the effects of treatment with arsenic-containing compounds on MS pathology and particularly axonal survival by carrying out a quantitative histopathological study on post-mortem tissues from MS patients exposed to arsenicals and matched controls.

Methods: A total of 102 paraffin-embedded autopsy blocks from 6 secondary progressive MS (SP-MS) patients treated with arsenicals and 6 SP-MS control patients not exposed to arsenic compounds obtained from the UK MS tissue bank, were analyzed. Immunohistochemistry for a number of markers were used to assess demyelination, inflammation, axonal damage and loss and to stage demyelinating lesions. Axonal density was determined on high MW neurofilament-stained sections using a point sampling method in normal appearing white matter (NAWM).

Results: Fifteen white matter lesions (WMLs) and 6 gray matter lesions (GMLs) were identified in 50 tissue blocks from the arsenic-treated patients, whereas 34 WMLs and 13 GMLs were identified in 52 tissue blocks of the MS patients not treated with arsenicals. In both groups almost all WMLs were chronic active or inactive and all cortical lesions were subpial. A statistically significant difference was observed in median NAWM axonal densities, which were found increased by 33.7 % in tissue blocks from patients treated with arsenicals compared to control MS patients ($P < 0.01$).

Conclusions: Our data indicate that arsenicals may have exerted a protective effect on axons in MS patients.

Disclosure: The authors have nothing to disclose. This study was funded by Merck-Serono, Greece.

PP4151

Serum autoantibodies presence in patients with relapsing remitting multiple sclerosis

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Introduction: The aim of this study was to investigate the possible increased occurrence of autoantibodies in patients with newly diagnosed relapsing remitting multiple sclerosis (RRMS).

Methods: Our study group consisted of 159 RRMS patients that were studied before the initiation of any immunomodulatory treatment or steroids. These patients were serologically evaluated for an extensive panel of autoantibodies including antinuclear (ANA), thyroid microsome (anti-TPO), human thyroglobulin (anti-TG), smooth muscle (ASMA), anti-cardiolipin (aCL), anti-b-glycoprotein-1 (anti-β-GP1) and anti-neutrophilic cytoplasmic antibodies (ANCA). The control group consisted of 99 healthy individuals with similar demographic characteristics and a negative history of chronic systemic or infectious disease.

Results: A statistically significant increase in the prevalence of ANA has been demonstrated in the RRMS group, compared to healthy individuals (31.4 vs 25 %, respectively; $p < 0.01$). In the patient group there was also a significant increase in the prevalence of ASMA (8.2 % in RRMS vs. 1 % in controls; $p < 0.001$), aCL (2.5 % in RRMS vs. 0 % in controls; $p < 0.001$), antiβGP1 (1.9 % in RRMS vs. 0.5 % in controls; $p < 0.01$) and ANCA (2.5 % in RRMS vs 1 % in controls; $p < 0.01$). There was no significant difference in the frequency of anti-TPO and anti-TG between the two groups.

Conclusions: Our data indicate an increased prevalence of non-organ specific autoantibodies in the RRMS patients, further corroborating the correlation between MS and systemic auto-immune disorders.

Disclosure: Nothing to disclose.

PP4152

Validity and reliability of the Turkish version of the multiple sclerosis-related symptom scale

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Introduction: This research has been carried out to determine the validity and reliability of the Turkish version of the "Multiple Sclerosis-Related Symptom Scale" developed by Gulick et al. for the evaluation of signs and symptoms in multiple sclerosis patients.

Methods: The study has been carried out through face-to-face interviews between January and December 2013 at the Multiple Sclerosis Unit Istanbul Faculty of Medicine, Istanbul University. Sample of the study has constituted from 148 patients with a diagnosis of definite MS, age above 18, able to communicate, without any medical problems other than MS. Patients who have had attacks in the last 1 month were not included in the group.

Results: As the first step linguistic validity studies were done. Then psychometric study was done. Confirmatory Factor Analysis revealed that the scale consisted of five factors of which loads ranging from 0.39 to 0.86. Item-total score correlation coefficients have been determined between 0.39 and 0.61, and correlation coefficients of sub-scale items and total scores between 0.60 and 0.80. Cronbach's alpha reliability coefficient was determined to be 0.89 for the whole scale and between 0.60 and 0.83 for the sub-scales. The test was repeated to evaluate the invariance of the scale with respect to time, no difference between two implementations was determined ($p > 0.05$).

Conclusions: Turkish version of the "Multiple Sclerosis-Related Symptom Scale" can be used to evaluate signs and symptoms in patients with multiple sclerosis.

Disclosure: Nothing to disclose.

PP4153

Safety profile of delayed-release dimethyl fumarate in relapsing-remitting multiple sclerosis: long-term interim results from the ENDORSE extension study

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Introduction: Here we present updated safety results from ENDORSE, an ongoing, 5-year, dose-blind extension of the Phase 3 DEFINE and CONFIRM studies evaluating delayed-release dimethyl fumarate (DMF) in RRMS.

Methods: Patients randomized to delayed-release DMF 240 mg twice (BID) or three times daily (TID) in DEFINE/CONFIRM continued the same dosing regimen in ENDORSE. Placebo (PBO; DEFINE/CONFIRM) and glatiramer acetate (GA; CONFIRM) patients were randomized 1:1 to delayed-release DMF BID or TID. Safety data were analyzed according to parent/extension study treatment: BID/BID, TID/TID, PBO/BID, PBO/TID, GA/BID, GA/TID.

Results: As of 12 June 2013 data cut, the overall incidences of adverse events (AEs) were: 89 % BID/BID (n = 501), 90 % TID/TID (n = 501), 93 % PBO/BID (n = 249), 90 % PBO/TID (n = 248), 86 % GA/BID (n = 118), 84 % GA/TID (n = 119). The incidences of serious AEs were: 18 % BID/BID, 19 % TID/TID, 22 % PBO/BID, 15 % PBO/TID, 13 % GA/BID, 18 % GA/TID. The incidence of discontinuations due to AEs was 4–6 % (BID/BID, TID/TID) and 14–23 % (PBO/BID, PBO/TID, GA/BID, GA/TID). The incidence of serious infections was $\leq$3 % (all groups). There were no confirmed opportunistic infections and no new findings in hematologic outcomes compared with DEFINE/CONFIRM. Hepatic AEs occurred in $\leq$3 % of patients in any group; there was no evidence of increased risk of renal or urinary events. There were 20 malignancies in 19 patients (11 continuing and 8 new to delayed-release DMF). There were 4 deaths, none considered related to study drug.

Conclusions: The long-term safety profile of delayed-release DMF appears consistent with findings from DEFINE/CONFIRM. No new or worsening safety signals were observed.

Disclosure: Study supported by: Biogen Idec, Inc.

PP4154

An antioxidant, serum paraoxonase1 activity in multiple sclerosis

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Introduction: Paraoxonase1 (PON1), an enzyme associated with high density lipoprotein (HDL), plays an important role in the anti-oxidant and anti-inflammatory properties of HDL. Increasing evidence supports the role of oxidative stress in inflammatory processes and in the pathogenesis of multiple sclerosis.

Methods: The aim of this study was to investigate the paraoxonase and arylesterase activities and lipid profiles in controls and in patients with different types of multiple sclerosis (MS) and with different immunomodulatory treatments. Our study involved 215 MS patients and 91 age-matched control subjects. Paraoxonase and arylesterase activities of serum were measured spectrophotometrically. PON1 activities and lipid profiles were compared in subgroups of relapsing-remitting (148), benign (14), primary progressive (14), secondary progressive (22), relapsing progressive (4) and clinically isolated syndrome (13) at different stage of the disease (EDSS: group A: 0.0–1.5; group B: 2.0–4.0; group C: 4.5–6.0; group D: > 6.0).

Results: Significant differences ($p = 0.0396$) in PON1 activities were detected between patients and controls. PON1 activities did not differ in the subgroups regarding of the course or EDSS scores of MS patients. Patients with greater disability were older and had slightly lower, but statistically not significant HDL blood levels than those of

less disabled. PON1 activities were different in the groups according to the treatment type ($p = 0.0003$) and the therapeutic response ($p = 0.0458$).

Conclusions: Our results did not demonstrate association between altered lipoprotein peroxidation and different clinical types of MS, but PON1 activities were influenced by immunomodulatory treatments.

Disclosure: Nothing to disclose.

PP4155

Clinical and MRI characteristics of long-term full-responder multiple sclerosis patients treated with disease-modifying drugs

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Introduction: The objective of the study is the identification of the characteristics of clinically full-responder patients treated with first-line disease-modifying drugs (DMDs).

Methods: This is a real world, observational, single-centre, 8-year follow-up study, carried out on relapsing-remitting MS patients who had started a treatment with interferon-beta or glatiramer acetate before 2005. We defined a patient as free (FP) from clinical activity when heshe had not had any relapses and disability progression (confirmed EDSS progression $\geq$1.5 point for baseline EDSS < 2.5 and 1 point for EDSS 2.5–5.5) during an 8-year follow-up. We compared these patients and patients with at least 1 relapse or disability progression at follow-up (PR).

Results: Six hundred ninety-nine patients have been included into this study; 68 % of patients were FP in the first year, 53 % in the first 2 years and 23 % (161 pts) at 8-year follow-up. Comparing FPs with PR patients, FPs had lower disability ($p < 0.0001$) and lower number of T2 lesions at the beginning of DMD ($p = 0.024$), and fewer active lesions at brain MRI scan performed at 1-year (<2 active lesions, $p = 0.013$) and at 2-years of treatment (<4 active lesions; $p = 0.001$).

Conclusions: Our study confirms that patients with low disability and low MRI activity at DMD beginning and in the first 2 years of treatment, may remain free from clinical activity for a long time. In these patients DMD discontinuation might be considered not only to reduce the treatment burden, but also for the redistribution of health resources on more needy patients.

Disclosure: Dr Romeo, Rodegher, Messina, Moiola and Colombo report no disclosures. Prof. Comi has received personal compensation for speaking and consultancy activities from Bayer Schering Pharma, Merck Serono, Sanofi-Aventis, Biogen-Dompè, Novartis Farma, Genzyme and TEVA Pharmaceutical Ind. Ltd. Dr Martinelli has received personal compensation for activities with Biogen-Dompè, Merck Serono, Bayer Schering Pharma, Novartis Farma, TEVA Pharmaceutical Ind. Ltd and Sanofi-Aventis.

PP4156

Relevance of age in quality of life assesment in multiple sclerosis patients

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Introduction: Multiple sclerosis progression and related activity limitations are both age related and age accelerated. The objective of this study was to investigate the relation between age and quality of life in MS patients.

Methods: 100 MS patients treated at the Neurology Clinic in Sarajevo were involed in this study. Quality of life was measured by using MSQOL-54 questionaire. Mann–Whitney and Kruskal–Wallis test were used for the comparisons and the linear regression analyses for identifing significant predictors from sociodemographic and clinical characteristics in predicting MSQOL-54 physical and mental composite scores.

Results: The mean age of 100 patients (69 % female and 31 % male) was 39.88 $\pm$ 10.03 years. The majority of the patients (60 %) were 25–44 years old, 26 % of patients were 45–54 years old, 10 % were older than 55 and 4 % were 18–24 years old. Younger patients (age less than 45 years) had significantly higher physical (54.85 v. 37.90,$p = 0.002$) and mental (59.55 vs. 45.90, $p = 0.007$) health composite scores than older patients. The most significant difference was in the role limitations-physical ($p < 0.001$), physical function ($p = 0.001$) and sexual function ($p = 0.001$) items then cognitive function ($p = 0.007$), energy ($p = 0.008$) and social function ($p = 0.001$). Patient's age retained its indepent predictivity only for physical health composite score (r^2 = 0.063). Internal consistency of adapted Bosnian version was high (Cronbach's alpha range 0.78–0.95).

Conclusions: As the result of our study we want to emphasise awarness of and sensitivity to the chalenges of aging with multiple sclerosis, including wide range of health, social and wellness related issuses.

Disclosure: Nothing to disclose.

PP4157

Natalizumab beyond blood–brain barrier—cell-bound vs. free concentration in CSF vs. blood

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Background: Natalizumab (NAT) inhibits migration of leukocytes from the systemic circulation into the brain blocking VLA-4.

Objective: Whereas the pharmakinetics and -dynamics of NAT in the periphery have already been investigated, only little information is available about the central nervous system compartment.

Design and methods: For the analysis of free and cell-bound NAT as well as VLA-4 in CSF and blood, 27 paired CSF and blood samples of MS patients on continuous NAT treatment at 2 different time points were analysed in comparison to paired control CSF-blood samples of 24 untreated MS patients. Therefore, we developed a FACS-based assay to measure free and cell-bound NAT concentrations in addition to VLA-4 binding (detection limit of 14 ng/ml).

Results: CSF NAT concentrations (44.81 $\pm$ 7.98 ng/ml) were lower than serum levels before (18.52 $\pm$ 2.75 µg/ml) and after infusion (86.19 $\pm$ 6.14 µg/ml). Cell surface bound NAT and mean expression of VLA-4 were comparable in CSF (mean 3653 $\pm$ 327.3 resp. mean 756.7 $\pm$ 73.8) and blood before NAT infusion (mean 3375 $\pm$ 297.4 resp. mean 794.4 $\pm$ 82). NAT in CSF was still functional active and could block VLA-4 mediated effects. NAT levels in CSF and blood demonstrated a huge inter-individual variability.

Conclusions: Using our sensitive FACS-based assay, we could demonstrate the different pharmacokinetics and -dynamics of cell-bound and free NAT in the immunological periphery and central nervous system compartment (CSF) of NAT-treated patients. The

possibilities and procedures for implementing patient-optimized dosing have to be investigated in controlled clinical trials.

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PP4158

Peginterferon beta-1a reduces the psychological impact of multiple sclerosis relapses: results from the ADVANCE study

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Objectives: Relapses are considered a major contributor to psychological distress among patients with multiple sclerosis (MS), however; this relationship has not been quantified. We aimed to assess the impact of relapses on psychological well-being and the potential benefit of peginterferon beta-1a (PEG-IFN) on such an impact using data from the phase 3 ADVANCE study.

Methods: In ADVANCE, a randomised, double-blind, placebo-controlled study, PEG-IFN 125 μg every 2 (Q2 W) and 4 (Q4 W) weeks reduced annualised relapse rate at 1 year in patients with relapsing-remitting MS ($n = 1,512$) versus placebo. The Multiple Sclerosis Impact Scale (MSIS-29) was used to assess patients' psychological well-being at baseline, 12, 24, and 48 weeks. A mixed-effects regression model was used to assess the psychological impact of relapses by including the occurrence of relapses as a time-dependent covariate and the effect of treatment on such an impact by examining the interaction terms for treatment and relapse while controlling for other relevant covariates.

Results: The univariate analysis indicated that having a recent relapse ($\leq$ 29 days since onset) led to an 8.1-point ($p < 0.0001$) worsening of MSIS-psychological scores. After controlling for other statistically significant covariates, having a recent relapse was associated with a 10.0-point ($p < 0.0001$) worsening of MSIS-psychological scores among patients receiving placebo (Table 1) but was reduced by 6.4 ($p = 0.0309$) and 3.9 ($p = 0.1283$) points among those receiving PEG-IFN Q2 W and Q4 W, respectively.

Conclusions: Patients experiencing relapse reported a worsening of psychological well-being. This study demonstrates that in addition to the clinical benefits, PEG-IFN improves psychological sequelae associated with relapses.

Table 1. Mixed effect model for change in MSIS-psychological scores over time

Variable	Estimate (95% CI)	p-value
Treatment arm		
PEG-IFN Q2W vs. Placebo	0.91 (-0.63, 2.45)	0.2467
PEG-IFN Q4W vs. Placebo	0.92 (-0.63, 2.47)	0.2433
Cumulative number of relapses since randomisation*	1.72 (0.50, 2.94)	0.0058
Time since last relapse prior to assessment (≤29 vs. 30+ days)*	9.95 (6.46, 13.45)	<0.0001
Confirmed disability progression prior to assessment (yes vs. no)*	3.54 (1.16, 5.91)	0.0035
Treatment & time since last relapse (≤29 vs. 30+ days)#		
PEG-IFN Q2W vs. Placebo	-6.41 (-12.23, -0.59)	0.0309
PEG-IFN Q4W vs. Placebo	-3.92 (-8.97, 1.13)	0.1283

*Indicating time-dependent covariates; #Indicating interaction effects

Disclosure: Study sponsored by Biogen Idec Inc. (Cambridge, MA, USA). SG, AA, IP: employee of Evidera which receives funding from Biogen Idec Inc.; EK and BS: employees of Biogen Idec Inc.; GP: owns Biogen Idec Inc. stock.

PP4159

T-cell subpopulations changes in Peyer's patches in the model of experimental autoimmune encephalomyelitis (EAE) under the influence of immunomodulatory therapy

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Introduction: Despite of proven role of mucous associated lymphoid tissue including intestine Peyer's patches (PP) in the development of autoimmune diseases, there are no data about its condition in demyelinating processes.

Objective: To determine the PP T-cell subpopulations changes in EAE without treatment and under the influence of fingolimod.

Methods: We studied 40 mice C57B1/6 EAE (100 ug/kg MOG 35–55) of two groups: untreated and treated Fingolimod (0.3 mg/kg one time a day 11th to 25th day per os). Immunohistochemically typed CD4 and CD8a in PP on the 10th, 15th, 20th, 30th and 50th days.

Results: In the untreated group on the 10th day marked increase in the density of CD4 and thus increase in the ratio of CD4/CD8a were found. CD4 increase peaked on the 20th day, not changed on the 30th day and reduced on the 50th day. The density of CD8a didn't significantly changed. In the group treated with fingolimod CD4 as well as CD8a densities increase was observed, which resulted in decrease of the CD4/CD8a ratio, which remained at low values (compared to the group without treatment) for the entire period of therapy. After discontinuation of fingolimod, on the 50th day of the experiment the CD4/CD8a ratios were approximately equal in both groups.

Conclusions: CD4 and CD8a density phasic changes in PP were observed during the development of EAE. This indirectly suggests the involvement of intestinal lymphoid tissue in autoimmune demyelination development. Fingolimod therapy leads to the accumulation of CD4 and especially CD8a cells in PP.

Disclosure: Nothing to disclose.

PP4160

Fumarate treatment in patients with progressive forms of MS: first results of a single-center observational study

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Introduction: Therapeutic options in progressive forms of multiple sclerosis (MS) are still limited. Dimethylfumarate has immunomodulatory properties but may also exert antioxidative cytoprotective effects. Hence, it may also be a therapeutic option for progressive MS. Aim of this observational study was to evaluate safety, adherence and efficacy of fumarate in primary or secondary progressive MS.

Methods: Patients with progressive MS received the fumarate mixture Fumaderm™ licensed for psoriasis therapy in Germany or dimethyl fumarate by pharmaceutical preparation (Bochum ethics approval no. 4797-13). Typical daily dose was between 480 and

720 mg. At regular follow-up visits, tolerability and side effects were assessed. Disease course was evaluated clinically by standardized scores (EDSS, MSFC) and evoked potential studies.

Results: A total of 23 patients (age = 54 ± 7.8 years; female = 12 (52.2 %); PPMS = 10 (43.5 %); EDSS = 6.0 ± 0.5 (range 3.5–8.5); disease duration = 13 ± 6.8 years) were initiated on a treatment with Fumaderm TM (n = 15) or dimethyl fumarate (n = 8). During a mean follow-up period of 13 ± 5.5 months (range = 3–27) only four (17.4 %) patients reported minor gastric complaints. In 12 (52.2 %) of the patients the EDSS remained stable. In five (21.7 %) cases there was a decrease in EDSS and in six (26.1 %) cases an increase of EDSS of >0.5 points reflecting deterioration. Laboratory values were controlled for relative lymphopenia, without any safety problems.

Conclusions: Our pilot data indicate that fumarate therapy appears to be safe and well tolerated by patients with progressive MS. In more than 70 % no further disease progression was evident. However, controlled studies are needed to evaluate fumarate in progressive MS.

Disclosure: Nothing to disclose.

PP4161

No evidence for a cerebral signature of activation in MS-related fatigue: insight from an activation likelihood estimation analysis of available fMRI studies

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Introduction: Central fatigue in MS is yet not understood. Functional MRI (fMRI) studies have sought for relevant brain activations explaining fatigue, and have shown differences in brain activity between MS patients with (MSF) and without fatigue (MSNF).

We aimed to identify brain areas consistently activated in MSF; and to compare global patterns of activations between MSF and MSNF, by the means of coordinate-based activation likelihood estimation (ALE) analysis of available fMRI data.

Methods: Activation coordinates from 12 fMRI studies (201 MS patients and 107 controls) of motor and cognitive fatigue in MS were examined. ALE analysis was performed using an original, improved ALE method (LocalALE). Separate meta-analyses were performed for MSF and MSNF.

Results: Structures consistently activated in MSF were postcentral gyrus, anterior cingulate, thalamus and cerebellum. Fewer areas were activated in controls. Prefrontal cortex was the most frequently reported activated structure in MSF. Surprisingly, contrast analysis did not detect differences in brain activity patterns between MSF and MSNF, neither spatially or globally.

Conclusions: We identify core areas consistently activated in MSF and MSNF, respectively. Global brain activation maps in MSF and MSFN are not different.

Studying brain activation by fMRI fails to elicit a specific cerebral activation signature for fatigue in MS. Fatigue in MS may be associated with altered connectivity in MSF versus MSNF as recently suggested, but not with different localised activity. Future fMRI studies should focus on connectivity between core areas that show to be consistently activated in MSF.

Disclosure: Nothing to disclose.

PP4162

*Human Leucocyte Antigen A*02* has a protective predictive effect on multiple sclerosis disability

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Objective: To prospectively evaluate the influence of human leucocyte antigen (HLA) class II *DRB1*15* and class I *A*02*, *B*44*, and *Cw*05* alleles on the clinical measures of outcome in an Italian cohort of people with relapsing remitting multiple sclerosis (pwRR-MS).

Patients and methods: Ninety-five consecutive patients (55 with clinical isolated syndrome, and 40 pwRR-MS) were enrolled at their first visit from January 2001 to December 2003, and followed till the 30th of June 2013. Clinical outcomes were the occurrence of a second attack and the attaining of a expanded disability status score (EDSS) of 3 or 4 maintained for at least 6 months, assessed using Kaplan–Meier analysis.

Results: We genotyped 90 patients for HLA *DRB1*15*, *A*02*, *B*44*, and *Cw*05*. None of these markers influenced the occurrence of a second attack. The cumulative probabilities of attaining EDSS 3 ten years after the first attack was 10.4 % for *A*02* carriers, and 29.6 % for non carriers ($p = 0.03$). None of the *A*02* carriers reached EDSS 4, compared to a cumulative percentage of 16.7 for non carriers ($p < 0.02$). None of the other markers influenced the probability to reach EDSS 3 and 4. MS patients positive or negative for A*02 did not differ for mean age at onset, sex, presence of oligoclonal bands, type and number of Kurtzke Functional Systems involved at onset.

Conclusions: *A*02* could be associated with a more benign clinical course of MS, predicting a lower disability at 10 years of follow-up.

Disclosure: Nothing to disclose.

PP4163

Durable reduction of disability with alemtuzumab in treatment-naive relapsing-remitting multiple sclerosis patients: 3-year follow-up of the CARE-MS I study

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Introduction: Alemtuzumab is approved in over 30 countries for relapsing-remitting multiple sclerosis (RRMS) patients showing disease activity. In the 2-year, phase 3 Comparison of Alemtuzumab and Rebif Efficacy in Multiple Sclerosis (CARE-MS) I study, alemtuzumab reduced annualized relapse rate by 55 % and 6-month sustained accumulation of disability rate by 30 % (P = NS) versus subcutaneous interferon beta-1a in treatment-naive RRMS patients; the safety profile was consistent with previous studies. Eligible patients enrolled in an extension study examining durability of disability reductions.

Methods: In CARE-MS I, patients received alemtuzumab (12 mg intravenously on 5 consecutive days and 3 consecutive days 12 months later). In the extension, patients with ≥1 relapse or ≥2 unique gadolinium-enhancing or new/enlarging T2 lesions on magnetic resonance imaging could receive a third alemtuzumab course. Expanded disability status scale (EDSS) scores were assessed quarterly; worsened/improved was defined as ≥0.5-point increases/

decreases from CARE-MS 1 baseline. Sustained reduction in disability (SRD) was defined as ≥1-point EDSS decreases lasting 3, 6, or 12 months in patients with baseline EDSS ≥2.

Results: 349 alemtuzumab-treated patients enrolled in the extension; 82 % did not receive a third alemtuzumab course in Year 3. Mean EDSS scores remained below baseline at Year 2 (mean change, -0.17; n = 370) and Year 3 (−0.10; n = 333). At Year 3, 244 patients (72.4 %) had stable/improved scores; 33, 28, and 24 % of 235 patients had 3-, 6-, and 12-month SRD, respectively.

Conclusions: Treatment-naive patients given alemtuzumab had durable improvement in pre-existing disability through 3 years, with 82 % of patients not receiving a third course.

Disclosure: HW: Honoraria/travel expenses from Bayer Health Care, Biogen Idec/Elan, Lilly, Lundbeck Merck Serono, Novartis, Sanofi Aventis, & TEVA Neuroscience; consultant for Biogen Idec, Merck Serono, Novartis, Sanofi-Aventis;research support from Bayer Schering Pharma, Biogen Idec/Elan, Merck Serono, Novartis, Novo Nordisk and Sanofi-Aventis. JP and DHM are employees of Genzyme.

PP4164

CSF proteomic profile in primary progressive multiple sclerosis

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Introduction: Clinical presentation, radiologic and histopathological characteristics of primary progressive multiple sclerosis (PPMS) differ from those of relapsing-remitting MS (RRMS). Some of these issues lead to the hypothesis of axonal loss independent of inflammation as underlying pathology in PPMS. However, recent histopathologic studies revealed higher rates of B-cells and plasma cells occurring in lesions, meninges, cortical gray and normal appearing white matter in PPMS. We aimed to determine the proteomic profile reflecting various pathogenetic processes of PPMS via cerebrospinal fluid (CSF) analyses.

Methods: MS patients consisted of treatment-naive PPMS (n = 8) and RRMS (n = 20) cases, and the control group included pseudotumour cerebri cases (n = 12). Markers for intrathecal inflammation including B-cell response (Fetuin A, CXCL13, MRZ-reaction), neurodegeneration (neurofilament heavy chain [NfH]) and astrocytic activation (S100B, glial fibrillary acidic protein[GFAP]) were measured with quantitative immunoassays (ELISA) in serum and CSF.

Results: Mean disease durations of PPMS and RRMS patients were 4.57 ± 1.13 and 3.19 ± 2.23 years, and mean referral-times for clinical evaluation were 319.71 ± 413.62 and 25.76 ± 22.61 days, respectively. Abnormal albumin quotient (Qalb) and MRZ-reaction were found significantly elevated in PPMS as compared to RRMS and controls, whereas IgG-index, oligoclonal bands and CXCL13 levels were increased in both MS groups as compared to controls ($p < 0.05$). CSF Fetuin levels were decreased in RRMS vs PPMS and controls ($p < 0.05$). The mean CSF concentrations of NfH, S100B and GFAP did not reach significant differences between the groups.

Table 1. Summarized data of studied biomarkers

		Controls	PP MS	RR MS	p
	Mean±SD	0±0	0,01±0	0±0	
Q Alb	Median	0 (0-0)	0,01 (0-0,01)	0 (0-0,01)	0,002
	Mean±SD	0,78±1,1	0,86±0,34	1,28±1,2	
IgG Index	Median	0,52 (0,34-0,58)	0,78 (0,59-1,11)	0,85 (0,57-1,21)	0,008
MRZ-Reaction (AI Index)	<1,5	10 (83,33%)	2 (25,00%)	10 (50,00%)	
	>1,5	2 (16,67%)	6 (75,00%)	10 (50,00%)	0,030
	Mean±SD	265,43±145	289,75±95,49	203,51±133,71	
Fetuin A CSF	Median	213,86 (166,75-345,16)	286,81 (190,83-381,19)	170,56 (125,15-230,62)	0,038
	Mean±SD	316,42±85,96	315,04±55,01	307,13±52,46	
Fetuin A serum	Median	323,14 (239,76-365,63)	301,4 (288,56-317,83)	308,43 (289,24-338,58)	0,781
	Mean±SD	1,68±0,83	1,27±0,71	0,82±0,65	
AI Fetuin	Median	1,42 (1,07-2,28)	1,16 (0,57-1,91)	0,56 (0,43-1)	0,002
	Mean±SD	1,92±6,13	29,41±58,14	40,05±74	
CXCL-13	Median	0 (0-0)	4,13 (0-36,75)	11,59 (0,86-45,74)	0,005
	Mean±SD	0,39±0,36	1,51±2,25	0,7±1,13	
GFAP	Median	0,37 (0,04-0,63)	0,53 (0,07-3,03)	0,51 (0-0,62)	0,627
	Mean±SD	138,7±94,14	205,32±221,33	132,52±62,73	
S100B	Median	96,78 (71,74-181,49)	95,95 (79,23-256,8)	110,38 (85,66-181,38)	0,845
	Mean±SD	45,91±66,31	116,94±192,62	71,21±159,3	
NfH	Median	16,33 (0-83,63)	18,15 (0-205,41)	0 (0-41,5)	0,794

Conclusions: PPMS patients show a CSF biomarker profile consisting of bPPMS patients show a CSF biomlood-CSF-barrier dysfunction and abnormal B-cell response occurring more frequently than in RRMS.

Disclosure: Nothing to disclose.

PP4165

Real world experience across Europe: interim results from the post-approval safety program (PASSAGE) of fingolimod

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Introduction: PASSAGE is a prospective, multi-national programme consisting of two post-authorisation safety studies (one predominantly

in US [US-PASSAGE]; the other predominantly in Europe [European-PASSAGE]), evaluating the long-term safety and effectiveness of fingolimod. Baseline characteristics and interim results of the fingolimod-cohort from the European study are presented.

Design and Methods: European-PASSAGE plans to follow 3,900 multiple sclerosis (MS) patients, newly started on fingolimod (fingolimod-cohort = 2,600) or treated with another approved disease-modifying treatment (other-DMT-cohort = 1,300), until the last patient completes 5 years.

Results: As of February 2013, the fingolimod-cohort enrolled 329 patients in 8 countries, the majority (~60 %) from Italy. Most patients were on beta-interferon, glatiramer acetate or natalizumab before starting fingolimod. Mean age of patients was 39.3 years, and 65.3 % patients were females. Mean duration of MS since first symptoms was 11.9 years, the average number of relapses 1 year prior to study was 1.1, while mean baseline Expanded Disability Status Scale (EDSS) score was 3.1. Only 208/329 enrolled patients had confirmed fingolimod administration record. Of these, 15.4 % patients reported adverse events (AEs) and 3.4 % reported serious AEs (including one fatal case). Bradycardia after first dose was reported in 2 (1 %) patients. Most common AEs were fatigue (1.9 %), nasopharyngitis (1.9 %), and nausea (1.4 %). Updated results from anticipated >1,000 fingolimod patients will be presented.

Conclusions: The baseline characteristics for the fingolimod-cohort, are consistent with those of the general relapsing MS population, but differ slightly (older age, longer MS duration and higher mean EDSS score) from fingolimod phase 3 studies. No new safety concerns were observed.

Disclosure: Tjalf Ziemssen received personal compensation from Almirall, Biogen Idec, Bayer, Genzyme, GSK, MSD, Merck Serono, Novartis, Sanofi, Teva, Synthon for consulting services and received financial support for research activities from Bayer, Biogen Idec, Merck Serono, Novartis, Teva, Sanofi Aventis. Tomas Olsson received compensation for Lecture and advisory boards from Biogen Idec, Novartis, Merck, Genzyme and unrestricted MS research grants has been received from Biogen Idec, Novartis, Genzyme. Dietrich Rothenbacher received consultancy fees from Novartis, AbbVie and received research support from Novartis. Maria Trojano received honoraria for consultancy and/or speaking from Biogen Idec, Genzyme, Sanofi, Merck Serono, Novartis, Roche and received research grants from Merck Serono, Biogen Idec, Teva, Novartis. Belinda Weller has not received any personal compensation from any pharmaceutical industry. Anu Gupta, Erika Rochotte, Philipp von Rosenstiel and Malika Cremer are employees of Novartis Pharma AG.

PP4166

PANGAEA: Post-Authorization Non-interventional German sAfety study of GilEnyA in relapsing–remitting multiple sclerosis (RRMS) patients: A 24-month interim analysis of a German five-year fingolimod registry study

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Introduction: Fingolimod is a first-in-class, oral sphingosine-1-phosphate receptor modulator approved for the treatment of RRMS.

PANGAEA investigates the safety, efficacy and pharmacoeconomic data from patients treated with fingolimod over 5 years. Here, we present 24-month interim data on disease progression and therapeutic compliance from fingolimod patients, formerly treatment-naïve, on baseline therapy (IFN-β and/or glatiramer acetate (GA)) or on natalizumab.

Methods: In addition to long-term safety and efficacy data, pharmacoeconomic aspects of fingolimod in routine clinical practice were assessed using questionnaires covering quality of life, treatment satisfaction, treatment compliance and consumption of resources.

Results: At the end of 2013, more than 4,100 patients were enrolled in PANGAEA.

An analysis at month 18 (n = 406) revealed an improvement in EDSS in 16.0 % of patients (sustained for at least 6 months). 73.7 % had a stable EDSS and 10.3 % of patients experienced a sustained EDSS progression.

All patients showed a significant reduction in ARR, independent of former disease-modifying therapy (baseline ARR/ARR at month 12: all patients 1.5/0.4; former IFN-patients 1.6/0.4; former GA-patients: 1.6/0.4; former natalizumab patients: 1.1/0.4).

Within the first 12 months of fingolimod treatment (n = 2,239), 3.8 % of patients discontinued the study due to adverse events (11.5 % total discontinuation).

The ARR of former natalizumab patients, in the first year of fingolimod treatment (n = 295), correlates with duration of natalizumab washout (≤ 60 to ≤ 120 days: ARR = 0.88; >120 days: ARR = 1.19).

Conclusions: The results of the 24-month interim-analysis of PANGAEA confirm the positive benefit-to-risk profile of fingolimod shown in Phase III clinical trials, under real-world conditions.

Disclosure: This study is sponsored by Novartis Pharma GmbH, Nuremberg, Germany. The authors M. Diaz-Lorente, A. Fuchs and C. Cornelissen are employees of Novartis. T. Ziemssen has received speaker honoraria from Almirall, Biogen Idec, Genzyme, GSK, Sanofi-Aventis, Merck Serono, MSD, Novartis, Teva Pharmaceutical Industries Ltd., and Bayer Schering Pharma; serves as a consultant for Biogen Idec, Novartis, Teva Pharmaceutical Industries Ltd., and Bayer Schering Pharma; and receives research support from the Hertie Foundation and Deutsche Diabetes Stiftung and Grants from the Roland Ernst Foundation and the Robert Pfleger Foundation.

PP4167

Arterial stiffness and carotid artery changes in multiple sclerosis

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PP4168

Provide a model for assessing the impact of emotional intelligence on depressed mood MS patients (a case study of MS patients in Tehran-Iran)

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PP4169

HLA-DRB1 does not have a role in clinical response to interferon-beta among Iranian multiple sclerosis patients

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PP4170

Adverse drug reactions in Iranian multiple sclerosis outpatients (a cross-sectional study)

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PP4171

Melatonin decreases serum total oxidant status (TOS) level, improves sleep and MSIS-29-PSYCH scores in multiple sclerosis patients

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PP4172

Cognitive function in patients with multiple sclerosis

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PP4173

Addison's disease diagnosed in a patient suffering from multiple sclerosis: a rare case

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PP4174

Atypical ependymal exophytic lesion in a patient affected by multiple sclerosis: a case report

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PP4175

Association of IL7RA rs6897932 gene polymorphism with multiple sclerosis

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PP4176

Relapse rates with fingolimod versus natalizumab for the treatment of multiple sclerosis: a retrospective US administrative claims database analysis

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PP4177

Sleep disorders in patients with multiple sclerosis

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PP4178

Clinical characteristics of patients with multiple sclerosis in Tuzla-Canton, Bosnia and Herzegovina

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PP4179

Sleep disorders in patients with multiple sclerosis

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PP4180

Identification of comorbidities in multiple sclerosis patients accompanied in a reference center in Rio de Janeiro, Brazil

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PP4181

Multiple sclerosis patients' experience with natalizumab in north Algeria

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PP4182

Therapy with interferon-beta has no impact on the T cell receptor repertoire in MS patients

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PP4183

MTR characteristics in relapsing remitting multiple sclerosis

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PP4184
Hashimoto's encephalopathy: study of 7 cases and literature review

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PP4185
A cross-sectional (ACROSS), long-term follow-up of patients enrolled in the fingolimod phase II program in relapsing multiple sclerosis

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PP4186
Evaluation of serum vitamin B12 levels in multipl sclerosis patients

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PP4187
Incidence of optic neuritis in the patients with multiple sclerosis

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PP4188
Long-term remissions with use of high dose of cyclophosphamide in multiple sclerosis

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PP4189
Correlation of cognitive dysfunction and diffusion tensor diffusion tensor fiber tractography measures in patients with multiple sclerosis

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Neurogenetics 2

PP4190
Cytogenetic evaluation and identification of MeCP2 gene mutations in RETT syndrome patients in south in Indian population

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Introduction: Rett syndrome (RTT) is a postnatal neurological disorder caused by mutations in methyl-CpG binding protein 2 (MeCP2) gene. The aim of this study was to investigate this MeCP2 mutations associated with the risk of RTT in south Indian population. A total of 20 Patients (18 females/2 males) were evaluated based on the DSM IV questionnaire.

Methods: The study was approved by the Institutional ethics board. Clinical profiles of the patients were recorded. PCR amplification of MeCP2 gene coding exons was performed using primers and automated sequencing was done on the DNA sequencer. The Karyotype results of 20 subjects were carried out by Trypsin G-banding and their results were confirmed by FISH.

Results: Higher degree of chromosomal alterations were observed in X-chromosome includes 46,XX,t(X;22) (p11.22; p11), 46,XX, del(X) (Xp20.4–20.5), 46,XX,del(13)(13q12.1–q21.2)). MeCP2 mutations were observed in 10 of 20 (50 %) cases. Of these 8 of them were classical sporadic and 2 were familial. Significantly milder disease was noted in patients carrying mis-sense mutations as compared with those with truncating mutations, that mutations in MeCP2 cause RTT and other neurodevelopmental disorders has called attention to the importance of epigenetic modifications in neuronal function.

Conclusion: As MeCP2 is only one member of family genes that play a role in DNA methylation-dependent transcriptional repression, it will be interesting to find, whether mutations in other genes cause developmental disorders (like autism) which share some features with RTT. Our results support the previously described role of MeCP2 mutations and will require detailed and larger analysis.

Disclosure: Nothing to disclose.

PP4191
Fatal familial insomnia presenting with diverse age of onset in a Chinese Canadian family

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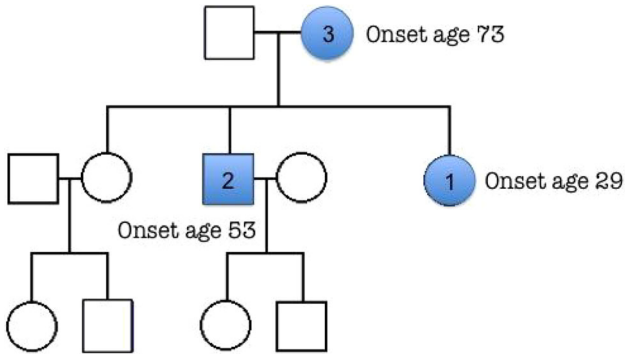
Background: Fatal Familial Insomnia (FFI) is a genetic prion disease characterized by insomnia, motor symptoms and dysautonomia due to mutation of codon 178 (D178 N) of the Prion Protein (PRNP) gene. The presence of methionine (M) or Valine (V) at codon 129 determines whether phenotype is FFI or familial Creutzfelt-Jacob disease (fCJD). A Chinese-Canadian family presenting with FFI at variable ages are described below.

Methods/case descriptions: Patient 1 presented in 1989 at age 29 with insomnia, fever and hallucinations. She developed memory

deficits, mutism and myoclonus. Extensive work-up including brain biopsy was negative. She died 14 months after onset. Autopsy showed thalamo-olivary degeneration without spongiosis.

Patient 2, brother of patient 1, presented in late 2012 at age 53 with insomnia, weight loss and hallucinations. Progressive decline continued with gait ataxia, myoclonus and mutism. Investigations were negative. Genetic testing revealed D178 N and codon 129 MM. He died 11 months after onset.

Patient 3, mother of patients 1 and 2, presented in October 2013 at age 73 with insomnia, gait ataxia and hallucinations. Genetic testing revealed D178 N and codon 129 MM.



Results/discussion: The majority of genetic prion disease in Caucasian populations are fCJD. The MM polymorphism accounts for 40 % of Caucasians but over 93 % of Han Chinese. The penetrance of PRNP mutations is 0.5–1.0 and increases with age.

Conclusion: The prevalence of codon 129 MM in Han Chinese makes FFI more likely in this population. A Chinese-Canadian family presented with FFI with variable onset highlighting the increasing penetrance of FFI with age.

Disclosure: Nothing to disclose.

PP4192

Epilepsy, optic atrophy, axonal neuropathy, sensory-neural deafness and cerebellar ataxia: extending the phenotype in argininsuccinic aciduria

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Introduction: Argininosuccinic Aciduria (AA) is a urea cycle disorder caused by defects of Argininosuccinate Lyase (ASL). A severe neonatal form is characterized by hyperammonemia, and a late-onset form is characterized by neuro-cognitive deficiencies, seizures, hepatitis, hypertension and trichorrhexis nodosa. We present two brothers with AA and a complex clinical phenotype.

Methods: Both probands, 21 and 14 years old, presented with AA due to homozygous c.532G > A mutation in the ASL gene. They were diagnosed at age 11 and 4 respectively, based on a history of cognitive deficit and epilepsy, and put on a low-protein diet and arginine supplementation. The second brother experienced also subacute vision loss, deafness and ataxia at 7, 11 and 12 years, respectively. Both underwent neurologic examination (NE), venous serum lactate assessment after standardized exercise, electroencephalogram (EEG), nerve conduction study (NCS), visual evoked potentials (VEPs), optical chorence tomography (OCT), audiometry, neuropsychologic evaluation, brain MR and complete sequencing of mitochondrial DNA (mtDNA).

Results: NE revealed signs of peripheral neuropathy and cerebellar involvement; lactate after exercise was abnormally elevated; EEG showed generalized epileptiform activity and NCV a severe axonal neuropathy. VEPs were reduced in amplitude and OCT revealed thinning of the temporal retinal nerve fiber layer. Audiometry showed severe sensorineural deafness in the second brother. Neuropsychological testing detected cognitive deficit in both. Brain MRI and complete sequencing of mtDNA were unremarkable.

Conclusions: ASL deficiency may manifest with a complex phenotype and mitochondrial dysfunction, not due to mtDNA abnormalities. The underlying mechanism is under investigation.

Disclosure: Nothing to disclose.

PP4193

Association of the PSMA3 gene polymorphisms with multiple sclerosis

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Introduction: The cause of Multiple sclerosis (MS) is still poorly understood and different metabolic pathways seem to play a role in disease development. Failure of ubiquitine proteasome system (UPS) efficiency had been recently implicated to MS pathogenesis.

Methods: The rs2348071 SNP of the PSMA3 gene (c.543 + 138G > A) has been genotyped in 281 MS patients (201 women) being diagnosed on relapsing—remitting (188 subjects) or secondary progressive (93 subjects) course of the disease, versus 191 control subjects (117 women) without inflammatory and any autoimmune disorders.

Results: In controls the rs2348071 locus showed allele and genotype presentation similar to other Europeans with minor allele frequency (MAF) about 30 % and genotype GG being most frequent (53 %). In both female and male cohorts of MS patients the minor allele A was observed slightly more frequent than in controls ($P < 0.05$), frequency of both GG and AA homozygotes was decreased (about 30 % and 5 % respectively) in favour of heterozygote GA genotypes (from 61 % to 71 % in patients of relapsing–remitting and secondary progressive course of disease respectively) that was significantly higher than in controls ($P < 0.0001$; OR = 3.539 [95 % CI 2.409–5.198] according to co-dominant model).

Conclusion: The rs2348071 heterozygous genotype appears to be the MS risk factor in Latvian population.

Disclosure: Nothing to disclose.

PP4194

The eNOS gene polymorphisms (exon 894 G/T, promoter −786T/C, and intron G10T) in migraine cases of Turkish population

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Introduction: Migraine is a neurovascular and common primary headache disorder characterised by recurrent headaches. We investigated the frequency of three endothelial nitric oxide synthases (eNOS) gene polymorphisms (894 G/T, −786T/C, and G10T) in migraine and control groups.

Methods: A total 137 individuals (84 migraine cases and 53 control) were included in this study. The eNOS gene polymorphisms

were detected using polymerase chain reaction-restriction fragment length polymorphism (PCR–RFLP) method.

Results: The intron G10T polymorphism was not significantly difference in migraine (58 GG, 26 GT) and control (38 GG, 15 GT) group (p:0.742). For exon 894 G/T polymorphism, this difference was meaningful in migraine (20 GG, 55 GT and 9 TT) and control (24 GG, 27 GT and 2 TT) group (p: 0.06). Although the promoter −786T/C gene polymorphism was not significantly higher in migraine (23 TT, 49 TC and 12 CC) than control (27 TT, 16 TC and 10 CC) group, it was nearly meaningful (p: 0.070).

Conclusions: The exon 894 G/T polymorphism is seen as related with migraine disease. Although this relation not to be meaningful for intron G10T but it was nearly meaningful for promoter −786T/C gene polymorphism. eNOS polymorphisms may be useful markers for assessment of migraine risk and clinical diagnosis. Thus an additional studies including more individuals should be performed to more exact understanding of these relations in migraine disease.

Disclosure: Nothing to disclose.

PP4195

Late-onset Huntington's disease: diagnostic and prognostic considerations

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Introduction: We sought to address diagnostic and prognostic issues in patients with late-onset Huntington's disease (HD).

Methods: We analyzed a cohort of 41 late-onset (≥60 years) HD patients and compared them to 39 late-onset patients referred for HD testing that were negative for the HD-expansion and to 290 HD patients with onset in the usual age range (usual-onset, 20–59 years). Disease severity was assessed by the Total Functional Capacity Scale.

Results: Late-onset HD comprised 11.5 % of our HD cohort. In total, 70.7 % of late-onset HD patients had positive family history compared to 15.4 % of late-onset expansion-negative patients ($p = 0.000$). Clinical features at onset or presentation could not usefully distinguish between late-onset expansion-positive and negative patients, excepting hemichorea, which was absent from the HD group ($p = 0.024$). Chorea was the first clinical feature in 53.7 % and a presenting feature in 90.2 % of late-onset HD. The mutation hit rate for late-onset patients was 51.3 %, lower than in usual-onset patients ($p = 0.04$). Frequencies of chorea, cognitive impairment and psychiatric manifestations at onset or presentation were not significantly different between late-onset and usual-onset HD patients. Gait unsteadiness however was more common at presentation in late-onset HD ($p = 0.007$). Late-onset HD patients reached a severe stage of illness on average 2.8 years earlier than usual-onset HD patients ($p = 0.046$).

Conclusions: A positive family history suggestive of HD, although absent in a third of patients, remains a helpful clue in diagnosing late-onset HD. Prognosis of late-onset HD in terms of Total Functional capacity appears somewhat less favorable than usual-onset HD.

Disclosure: Nothing to disclose.

PP4196

Coexistance of autosomal recessive spastic ataxia of charlevoix saguenay and spondyloepiphyseal dysplasia in a Turkish patient

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Introduction: Here, we present a female patient from consanguineous parents whose genetic analysis revealed the coexistance of Autosomal Recessive Spastic Ataxia of Charlevoix Saguenay (SACS) and Spondyloepiphyseal dysplasia (SED).

Methods: A 47-year-old woman with short stature presented with gait disturbance and paresthesia. She was complaining of gradually increasing ataxia since her early childhood. Neurologically, her speech was cerebellar dysarthric, she had symmetrical weakness, lower limbs were spastic, she had tenar, hypotenar, interosseal, tibialis anterior and intrinsic foot muscle atrophy. Hypoesthesia was detected in feet and hands. Deep tendon reflexes were decreased, plantar responses extensor. Patient had pronounced ataxic gait. Similar complaints were present in her two sisters.

Results: MRI revealed cerebellar atrophy, radiographically there were prominent end plate irregularities and sclerosis of the vertebral bodies, spondylosis and kyphosis. Nerve conduction study was consistent with demyelinating sensory-motor neuropathy. GAA expansion in the frataxin gene was negative. Patient was subjected to exomic sequencing due to her pronounced family history. Exome analysis revealed two homozygous novel mutations in the SACS gene (exon10:c.G8315C:p.G2772A; exon9:c.2093 + 1G>A). Additionally two homozygous novel mutations were present in the ACAN gene (exon12:c.C3635T:p.T1212I; exon12:c.C3638T:p.A1213 V). These mutations have to be validated in the affected sisters and also in the heterozygous parents.

Conclusions: One of the two mutations in the SACS gene would explain the above-described ataxic features of the patient, firmly excluding other causes of ataxia. Furthermore, either both or one of the homozygous mutations in the ACAN gene is expected to explain her skeletal deformities.

*Kurt and Kartal joint first authorship.

Disclosure: Nothing to disclose.

PP4197

RYR1 gene: three mutations c.10097G>A, c.11798A>G, c.115G>A in a patient with central core myopathy

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Introduction: Ryanodine receptor gene (RYR1) mutations have been associated with central core disease (CCD), multiminicore/minicore/multicore disease (MmD), and susceptibility to malignant hyperthermia (MH). Determining the pathogenicity and mode of inheritance of each mutation is essential for prognosis, genetic counseling and also prevention of potentially life threatening reactions to general anesthesia.

Clinical case: Woman, 35 years old, clinically diagnosed with congenital myopathy with proximal limb weakness since early childhood. She has very mild clinical impairment being able to accomplish most daily tasks. No relevant family history was known. Her CK was slightly elevated and a muscle biopsy was compatible with CCD. RYR1 gene was screened and three mutations were found: c.10097G>A (p.Arg3366His), c.11798A>G (p.Tyr3933Cys), already described with recessive trait; c.115G>A (p.Glu39Lys) not described and of unknown significance. Her asymptomatic non-consanguineous parents were screened in order to establish the allelism in the patient and mode of inheritance of these mutations. The mother carried

c.10097G>A and c.11798A>G in cis and the father carried c.115G>A.

Conclusions: Based on the literature and the findings in our case, we can conclude that these three mutations are pathogenic and all have a recessive trait. Its clinical significance is paramount for genetic counseling since the parents and all her children will be asymptomatic carriers for CCD or MmD but will be at risk for MH. Other at risk relatives may also benefit from genetic screening.

Disclosure: Nothing to disclose.

PP4198

Novel LRRK2 6165C>G mutation in a patient with Parkinson's disease-dementia: a case report

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Introduction: LRRK2-related Parkinson disease (PD) is characterized by motor and non-motor symptoms consistent with idiopathic PD. Asymmetrical, tremor-predominant parkinsonism with bradykinesia and rigidity is a core feature. Disease severity, rate of progression, occurrence of falls, dyskinesia, affection of cognition and olfaction are considered more benign than those of idiopathic PD (1). Onset is late, generally after 50 years, with an autosomal-dominant mechanism of inheritance.

Objective: We describe a novel LRRK2 heterozygous mutation 6165C>G (P2036R) in a patient with PD and dementia and a positive familial history (a sister and mother with PD).

Methods: Full clinical assessment of the patient at the age of 66 years. Genetic testing: Direct Sanger sequencing of DNA, extracted from peripheral leucocytes.

Results: The disease onset was at 60 years with asymmetrical bradykinetic-rigid parkinsonism, with bilateral involvement over the next 3 years. Mild postural tremor of the limbs appeared at age of 65, together with postural instability and on/off phenomenon. During the disease course an impaired olfaction, sialorrhea, sleep disturbances, unpleasant sensations in the legs, apathy, depression, obstipation and dementia were added. The DNA tests revealed a heterozygous nucleotide exchange cDNA.6165C>G in the exon 41(a highly conservative region) of LRRK2. The programs for prediction suggested high pathogenicity of the mutation.

Conclusions: We present a patient with the putative mutation 6165C>G in heterozygous state, affecting the kinase domain of LRRK2 and predominantly bradykinetic-rigid form of PD and dementia.

Disclosure: The work is funded by: PhD Grant 25D/2013, Science Fund, Medical University, Sofia; DUNK01-2/20009, National Science Fund, Ministry of Education and Science.

PP4199

LRRK2 mutation c.4536 + 3A>G in a patient with multiple system atrophy: a case report

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Introduction: The mutation c.4536 + 3A>G (IVS31 + 3A>G) in the *LRRK2* gene *(PARK8)* is previously described in three genetic studies of Parkinson's disease (PD), however its pathogenicity is not firmly established yet. Zabetian et al. (2005) identified it in a sporadic PD patient out of 371 tested patients and 281 controls. Shojaee et al. (2009), found this mutation in a family consisting of affected and unaffected individuals. Importantly, this variant was identified in healthy family members, but not in the affected sister of the proband. The third study, conducted by Anfossi et al. (2013) and based on 88 unrelated PD patients, identified the mutation in a patient with PD and dementia and a positive familial history.

Objective: To identify a genetic reason for parkinsonism in a cohort consisting of 137 patients with PD or atypical parkinsonism.

Methods: Full clinical assessment of the patients. Direct Sanger sequencing of LRRK2 in proband's DNA, extracted from peripheral leukocytes.

Results: The DNA tests revealed the heterozygous mutation c.4536 + 3A>G in the LRRK2 gene in a patient with clinical features consisting with the diagnosis MSA-C (probable). The disease onset was at 62 years with asymmetric bradykinetic-rigid parkinsonism. Over the next years the patient developed urinary incontinence, static and loco-motor ataxia, blurred speech and mild cognitive impairment. At age of 66, the patient is wheel-chair bound.

Conclusions: We present a MSA-C patient with the LRRK2 mutation c.4536 + 3A>G in heterozygous state and suggest its putative effect in a case of atypical parkinsonism.

Disclosure: The work is funded by: PhD Grant 25D/2013, Science Fund, Medical University—Sofia; DUNK01-2/20009, National Science Fund, Ministry of Education and Science.

PP4200

Usefulness of corpus callosum splenium versus middle cerebellar peduncle hyperintensity in FXTAS

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Introduction: FXTAS corresponds to *FMR1* premutation, ataxia, action tremor and middle cerebellar peduncles (MCP) hyperintensity, which is the only major radiological criterion for definite FXTAS. The importance of corpus callosum splenium (CCS) hyperintensity was recently reported in FXTAS, but its interest in comparison to MCP is unknown.

Methods: Twenty-two until yet unreported patients (17 men; 5 women) with suspected FXTAS, because of the combination of *FMR1* premutation and suggestive neurological signs, were included from 6 neurology centres from April 2012 to July 2013. Clinical and radiological study of these premutated patients with neurological signs has been performed.

Results: Among the 22 patients, 13 were diagnosed with definite FXTAS. Considering CSS hyperintensity as a new major radiological criterion allowed to diagnose definite FXTAS in 4 additional patients.

CCS was as frequent as MCP hyperintensity (64 % versus 64 %), 23 % of patients had CSS but not MCP hyperintensity. MCP hyperintensity was less frequent in women than in men. MCP hyperintensity was correlated to inaugural action tremor.

Conclusions: We confirm the usefulness of CCS hypersignal in FXTAS, supporting its inclusion in the diagnostic criteria as a new major radiological criterion.

Disclosure: Nothing to disclose.

PP4201

Transient central nervous system involvement as initial "stroke-like" presentation of X-linked Charcot-Marie-Tooth type 1 (CMTX1) with a novel GJB1 mutation

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Introduction: X-linked Charcot-Marie-Tooth type 1 (CMTX1) is the second most common CMT type and is associated with mutations in the GJB1 (gap-junction B1) gene, which encodes connexin-32. More than 400 GJB1 mutations have been described to date. Most hemizygous affected males have subclinical central nervous system (CNS) involvement, a few show mild CNS clinical signs, whereas only rarely overt though transient CNS dysfunction occurs.

Case report: We observed a 29-year-old man with CMTX1 who at age 16 years showed short-lived CNS symptoms with transitory white matter abnormalities on cerebral MRI as first clinical presentation of a novel GJB1 mutation (Gln99_His100 ins CAA). He had three consecutive episodes of right hemiparesis, together with sensory loss in the paretic limbs and expressive aphasia, all lasting a few hours, over a two-day period, with concurrent white matter hyperintensity on MRI. These "stroke-like" episodes occurred just after arriving at sea level, coming from home at 700 m of altitude. Only a few years later did signs and symptoms of peripheral neuropathy appear.

Discussion and Conclusion: This is another case of CMTX1 where the neuropathy is overlooked at presentation and the initial manifestations are acute transient CNS symptoms and signs with widespread white matter changes at MRI, suggesting strokes, metabolic or inflammatory disorders. Cx32 expression in the oligodendrocytes explains CNS features which appear only in particular conditions and are entirely reversible. Precipitating factors include fever, intercurrent illness or, as in this case, travels with rapid changes in altitude.

Disclosure: Nothing to disclose.

PP4202

Report of 3 unusual cases of DMD/BMD patients with very large deletion within *DMD* gene

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Introduction: Duchenne/Becker muscular dystrophy is X-linked recessive, progressive muscle-wasting disease affecting 1 in 3500 boys, caused by mutations within *DMD* gene. The prediction that Duchenne muscular dystrophy patients have out-of-frame deletions and Becker muscular dystrophy patients have in-frame deletions of the dystrophin gene hold wells in the vast majority of cases.We aimed to describe unusual cases with large deletions of the actin-binding and rod-shaped domains of the dystrophin gene associated with severe clinical phenotype.

Methods: The patients were diagnosed using standard clinical diagnostic criteria, including: EMG, serum creatine kinase (CK) levels. Screening for dystrophin gene deletion was performed on genomic DNA by using multiplex polymerase chain reaction and primer sets designed by *Ashton*.

Results: All the patients showed a raised serum CK level than normal. It has been established in-frame deletions of 3–44 exons in one patient and deletions of 1–45 exons in two patients. Due to deletion of exon 1, there is probably no mRNA and protein produced. All these mutations are not reported in Leiden Muscular Dystrophy data base.

Conclusions: We have identified 3 unusual cases: 1 case of BMD and 2 of DMD patients, with large deletions of the actin-binding and rod-shaped domains, that has not been described below. Additionaly, this observation emphasizes the uncertainty in predicting the phenotype based only on laboratory evaluation and that the clinical picture should be considered.

Disclosure: Nothing to disclose.

PP4203

SPG11 knockout in mouse mimics the phenotype observed in patients

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Introduction: Hereditary spastic paraplegias (HSPs) are inherited neurological disorders characterized by lower limbs progressive spasticity and weakness. This clinical picture can be complicated by additional neurological signs in some forms. Autosomal recessive HSP with thin corpus callosum and mental impairment is a common and clinically distinct form of familial spastic paraplegia that is associated with mutations in the *SPG11* gene on chromosome 15q in most affected families (40–80 % according to their geographical origin). *SPG11* mutations are either nonsense or indels leading to a frameshift, in agreement with a loss of function mechanism. *SPG11* encodes a 2,443 amino acid protein of unknown function named spatacsin.

Methods: To identify cellular impairments underlying SPG11 HSP form, we invalidated the causative gene in a mouse model.

Results: These mice breed normally, their offspring appear normal at birth and their survival does not differ from control littermates. Based on the complex clinical picture observed in patients with SPG11 mutations, we analyzed both cognitive and motor deficit in $Spg11^{-/-}$ mice using a series of behavioural tests at different ages. They showed a possible cognitive impairment and motor dysfunction starting from 4 months of age and worsening with time. This phenotype is associated with a progressive neurodegeneration affecting various cerebral structures.

Conclusion: This knock-out model mimics the SPG11 pathology with a relatively early onset of cognitive and motor alterations and will help decipher the physiopathology of this disabling disease.

Disclosure: Nothing to disclose.

PP4204

Role of rs333 polymorphism of the CCR5 gene in multiple sclerosis patients in Csongrád County in Hungary and the North-Bácska region in Serbia

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Introduction: Multiple sclerosis (MS) is a degenerative disease of the central nervous system characterized by the inflammatory process of demyelinization. Genetic and environmental factors have been implicated in the aetiology. Examinations of the Δ32 bp allele of the chemokine receptor V (CCR5) gene in MS have yielded conflicting results. In a few studies, the allele was confirmed as a risk factor, in others ones it was a protective factor, and some results indicated that the deletion is neither a risk nor a protective factor in MS. In the present work, the role of Δ32 bp deletion of the CCR5 gene was investigated in the MS polulation in Csongrad County and the North Bácska.

Methods: Examinations were performed on 428 unrelated patients with the relapsing/remitting or secondary progressive form of MS and on age-sex matched 831 healthy persons as controls. Fluorescent labelled Taqman probes were used for allele detection. For data evaluation, SPSS software version 20.0 was performed.

Results: No significant differences were found in the genotype (OR = 1.092 95 % CI = 0.807–1.478 p = 0.568 for wt/wt vs wt/Δ32, Δ32/Δ32) or in the allele frequency (OR = 0.914 95 % CI = 0.692–1.207 p = 0.525). Neither the deletion nor the wild allele affected the age at onset or the Expanded Disability Status Scale score.

Conclusions: These results indicate the lack of an association between the CCR5 Δ32 allele and MS, in confirmation of the literature data: the CCR5 delta 32 allele is neither a risk factor nor a protective factor of multiple sclerosis.

Disclosure: Nothing to disclose.

PP4205

HLA-DRB1* 11/15 is the predominant genotype in Iranian patients with multiple sclerosis

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PP4206

The aldehyde dehydrogenase 2 (ALDH2) and COQ2 polymorphism in Japanese patients with spinocerebellar degeneration

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PP4207

Abstract withdrawn

PP4208

Definition of expression pattern of big-H3 gene in a regeneration of zebrafish eye after cryoinjury

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PP4209

Application of whole exome sequencing to amyotrophic lateral sclerosis and schizophrenia

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PP4210

Giant angiofibroma associated with tuberous sclerosis

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PP4211

Fabry disease presenting with lymphoedema

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PP4212
Correlation of prothrombotic coagulation parameters with genetic markers of thrombosis in ischaemic stroke

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PP4213
Hereditary spastic paraplegia: clinical, laboratory, eletroneuromiographic and magnetic resonance image of eight recessive cases

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PP4214
Is inherited thrombphilia in pregnancy a risk factor for familial stroke?

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PP4215
HNPP case with CIDP like clinic

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PP4216
Polymorphisms of methylenetetrahydrofolate reductase (MTHFR-677 and MTHFR-1298) genetic in an Albanian population

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PP4217
Neonatal manipulation of sex hormones in rats and its effect on MWM performance and expression of ten memory related genes in hippocampus

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PP4218
Uncommon features in a Turkish family affected with Friedreich ataxia

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PP4219
Extrapyramidal symptoms unrelated to Huntington's disease in a member of a large family with Huntington's disease

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Neuroimmunology

PP4220
Neuromyelitis optica spectrum disorder in a patient with Myasthenia gravis

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Introduction: Neuromyelitis optica (NMO) spectrum disorders are restricted forms of NMO with either recurrent optic neuritis or relapsing transverse myelitis and positive anti-aquaporin 4 (AQP4) antibodies. Both NMO and MG are known to be associated with other autoantibodies and autoimmune disorders.

Case report: We report the case of a healthy 70-year-old woman, diagnosed in her mid twenties with generalized MG (diplopia, bilateral ptosis, dysphagia, breathing difficulties, bilateral arm weakness and positive AChR antibodies). She underwent thymectomy and remained stable with a low dose of acetylcholinesterase inhibitors. At the age of 70, she presented with an acute longitudinally extensive transverse myelitis (LETM), from C6 to T6 level, with inflammatory CSF. She was started on high-dose IV corticosteroids and a diagnosis of Idiopathic Transverse Myelitis was assumed. During the following 4 months, she had another two relapses that manifested as acute transverse myelitis. She had a normal brain MRI, normal visual evoked potentials and a positive serum anti-AQP4 antibody, so she was diagnosed as having a NMO spectrum disorder. Under oral corticosteroids and azathioprine there were no further relapses.

Conclusions: Few patients with both MG and NMOSD have been reported so far. A recent review reported that MG is more commonly associated with AQP4 antibody positive NMOSD than previously thought. It is still unclear how thymectomy contributes to the development of NMOSD in patients with MG as most of the patients reported had undergone thymectomy prior to the onset of NMOSD.

Disclosure: Nothing to disclose.

PP4221

Evaluation of neurofilament heavy chain levels in progressive multiple sclerosis patients: preliminary results

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Introduction: Primary Progressive Multiple Sclerosis (PPMS) and Progressive Relapsing MS (PRMS) are the least common forms of MS. They are mainly characterized by progression from the onset of the disease. Axonal degeneration is the likely cause of the disease progression in MS. Neurofilament proteins which are heteropolymers composed of three subunits, light (NfL), medium (NfM) and heavy (NfH) chain are scaffolding proteins of axons. Therefore, levels of neurofilament proteins can potentially be a good surrogate marker for quantifying axonal damage.

Methods: In this study, MS patients with progressive disease from onset who were followed-up in Hacettepe University, Neuroimmunology Unit were evaluated. CSF NfH measurements were evaluated as the neuroaxonal damage markers. Patients with progressive onset (PPMS and PRMS) were compared with the other subgroups of MS patients and controls. NfH levels were studied in PPMS ($n = 19$), PRMS ($n = 8$) and Relapsing Remitting MS (RRMS) ($n = 7$) patients.

Results: NfH levels in progressive MS patients (PPMS, PRMS and SPMS) were significantly higher than patients with RRMS ($p = 0.000$a). There was no significant difference between PPMS and PRMS sub-groups. "CSF NfH level" was positively correlated with the "EDSS score" ($p = 0.008$) whereas disease duration and NfH concentration were not significantly correlated ($p = 0.398$).

Conclusions: The significant higher values of "CSF NfH concentration" in progressive patients, convincingly demonstrate the presence of axonal injury in the progressive form of the disease. No significant difference was detected between PPMS and PRMS groups. CSF NfH levels may serve as appropriate candidate to distinguish clinical subtypes of MS.

Disclosure: Nothing to disclose

PP4222

Clinical and neuroradiological profile of acute disseminated encephalomyelitis in 13 children at tertiary center in Saudi Arabia

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Introduction: Acute Disseminated Encephalitis (ADEM) is usually a monophasic polysymptomatic inflammatory condition of the central nervous system with an underling autoimmune pathology that principally involves the white matter although the grey matter may also be affected.

Methods: A 10-year (2000–2010) retrospective chart review of children with the diagnosis of ADEM was conducted at King Khalid University Hospital .

Results: Thirteen patients were identifed. The age of presentation range between (10 months–11.6 years). History of preceding Upper respiratory tract infection was noted in 69 %. Polysymptomatic presentation was seen in all patients.The most often presenting signs were pyramidal signs in 92 %, cranial nerve palsies in 84.6 %,and altered sensorium in 53.8 %.

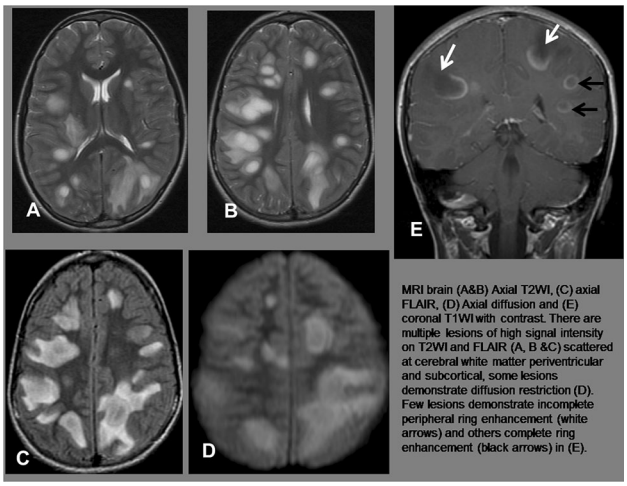
Presenting features (signs)	No. of cases(%)
- pyramidal signs	*12 (92 %)*
- cranial nerve palsy	*11 (84.6 %)*
- altered sensorium	*7 (53.8 %)*
- cerebellar signs	*5 (38.5 %)*
- meningeal signs	*5 (38.5 %)*
- spinal cord involvement	*1 (7.7 %)*
- extrapyramidal signs	*0 (0 %)*

Brain magnetic resonance imaging (MRI) identified white matter lesions in all patients. Deep grey matter involved in 23 %, and spinal cord lesions in 28.6 %.

Table-2:MRI Findings in ADEM (13 cases)

MRI Findings	*No. of cases(%)*
hemisphere/region	
frontal	*9 (69 %)*
temporal	*4 (30.7 %)*
parietal	*8 (61.5 %)*
occipital	*5 (38.5 %)*
periventricular	*6 (46 %)*
corpus callosum	*4 (30.7 %)*
basal ganglia	*3 (23 %)*
thalami	*3 (23 %)*
midbrain	*3 (23 %)*
brain stem	*8 (61.5 %)*
cerebellum	*4 (30.7 %)*
spinal cord	*2 (out of 7 pt)*

Three patients achieved spontaneous clinical remission. Favorable outcome with steroids was observed in 10 patients. Out of those 3 received additional intravenous immunoglobulin. All patients survived except for one. 41.6 % had excellent recovery, 41.6 % had mild neurologic sequel with high functional level, and 16.6 % had moderate to severe neurologic sequel.



Conclusions: The epidemiologic data was consistent with the previous reported studies. MRI remains the imaging method of choice. Prognosis for survival and outcome was favorable with the use of corticosteroids and or IV immunoglobulin in all such cases.

Disclosure: Nothing to disclose.

PP4223

Humoral response against neural precursor cells (NPCs) in central nervous system (CNS) of experimental autoimmune encephalomyelitis (EAE)

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Introduction: Multiple sclerosis (MS) is considered a T cell mediated disease, but recent data revealed that autoantibodies may contribute to its pathogenesis. In the present study we examined their potential to target CNS progenitor cells.

Methods: MOG_{35-55}-EAE was induced in C57bl/6 mice and blood-sampling was performed on day 17 (acute phase) along with naive group. The presence of autoantibodies was examined using Western blotting. We used total protein extract from NPCs and normal spinal cord (SC) as substrates stained with MOG-EAE antiserum (EAE-AS) and naive antiserum (Naive-AS) as primary antibodies. Additionally, immunohistochemistry (IHC) and double immunofluorescence (dIF) was performed on normal mouse brain sections from neonates, postnates and adults (P3, P17 and 3 months) stained with antisera. Commercially available MOG antibody (anti-MOG) was used as positive control and anti-BrdU as NPCs marker.

Results: Western blot indicated specific bands (60 KDa and 40–46 KDa) in NPCs substrate using EAE-AS, none of which corresponded to MOG. IHC exhibited EAE-AS- though not Naive-AS-positive cells in subventricular zone and periventricularly in all three ages ($p < 0.0001$). In addition, EAE-AS revealed significantly higher affinity to BrdU(+) cells, with dIF, when compared with anti-MOG: P3:45.43 ± 8.112 % versus 10.92 ± 4.225 %($p < 0.0027$); P17:50.64 ± 9.207 % versus10.13 ± 2.519 %($p < 0.0005$); 3 months: 88.54 ± 7.542 % versus 19.49 ± 11.43 % ($p < 0.0035$),respectively.

Conclusions: Activation of the immune system against MOG_{35-55} induces the production of antibodies which may recognize epitopes other than MOG on NPCs. The role of autoantibodies both in EAE and MS remains controversial and further research is required.

Disclosure: Nothing to disclose.

PP4224

P-ANCA isolated cranial pachymeningitis: a case report

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Pachymeningitis (PM) is a rare disorder, characterized by inflammatory process that thickens the dura mater. It may occur in association with a number of underlying disorders, but most cases have been considered to be idiopathic. We present a case of a patient who developed perinuclear antineutrophil cytoplasmic antibody (p-ANCA) PM. A 51-years old female patient was admitted to our department because of severe headache and multiple cranial neuropathies (IX., X., XII. nerve). Magnetic resonance imaging (MRI) showed thickening of dura mater, highly enhanced after gadolinium administration. Full blood count, biochemical profile, sedimentation rate and C reactive protein were normal. Lumbar puncture demonstrated clear watery cerebrospinal fluid (CSF) with lymphocytic pleocytosis and elevated level of protein and negative culture. The level of MPO- ANCA was elevated, 115 U/l. With extensive investigation, we excluded impairment of other organs, lung, kidney and eyes. A biopsy of dura mater showed area of ganulomatosis inflammation with no sign of vacuities. A course of methylprednisolone was initiated, followed by oral corticosteroid and intravenous injection of cyclophosphamide once a month for 6 months. There was a rapid improvement in headache and in the level MPO—ANCA, 52U/l.

In our case, diagnosis of PM was made on the basis of MRI data, clinical presentation, elevated MPO-ANCA and results of biopsy of dura mater. In conclusion, in a patient who is P-ANCA positive, complains of headache, the MRI is necessary to role out PM. Early recognition and treatment is necessary to prevent definitive neurological impairment.

Disclosure: Nothing to disclose.

PP4225

Adult post-streptococcal basal ganglia encephalitis

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Introduction: Post-streptococcal central nervous system disease comprises a wide range of clinical pictures, including extrapyramidal movement disorders. There is increasing evidence that these disorders are autoimmune, mediated by antibodies that bind and cause dysfunction specifically in the basal ganglia.

Case report: A 27-year-old female with no relevant medical history presented with headache, vomiting, right leg and perioral involuntary movements, and marked mental status deterioration progressing over hours. One week before she and her 9-month-old daughter suffered from a mild febrile syndrome. Neurological examination revealed upward gaze limitation, mild right hemiparesis, oral myoclonic movements, sialorrhoea, chorea on left abdomen and right leg. Initial analytic work-up, CSF analysis and head CT were normal. Electroencephalogram showed diffuse encephalopathy. An extensive laboratory investigation was performed revealing persistent

elevated anti-streptolysin O titer and excluding other infectious, metabolic, hormonal and autoimmune etiologies, including NMDAR encephalitis. Brain MRI showed swelling hyperintense T2-signal of lentiform and caudate nuclei and hippocampi. Despite high doses intravenous steroids, she continued worsening. Intravenous immunoglobulin G (IVIG) was initiated and progressive clinical improvement was observed. Anti-basal ganglia antibodies (ABGA), tested after steroids and IVIG treatment, were negative. After 3 months, she regained full previous cognitive and functional status. There was also significant imaging improvement.

Conclusions: We discuss a case of basal ganglia encephalitis of probable post-streptococcal origin. Although ABGA was undetectable, the elevation of anti-streptolysin O titer and the distinct neuroimaging pattern suggests that the underlying pathophysiology might involve a selective autoimmune process against the striatum triggered by streptococcus epitope cross-reactivity.

Disclosure: Nothing to disclose.

PP4226

Seronegative autoimmune encephalitis after CHOP-Rituximab in a patient with non-Hodgkin lymphoma

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Introduction: Autoimmune limbic encephalitis is a rare immune-mediated inflammatory condition of the CNS. Increasing evidence suggests that previously considered seronegative autoimmune encephalitis have in fact an undetected immune-mediated pathophysiology.

Case report: We report the case of a 63 year-old woman with a low grade mandibular non-Hodgkin lymphoma, submitted to chemotherapy with CHOP and Rituximab with progression into hematologic remission, that 6 months later insidiously developed apathy, hypersomnolence and memory impairment. On clinical examination there was severe mnestic compromise, and temporal and spatial disorientation. MRI showed bilateral temporal and diencephalic T2 hyperintensities. EEG revealed diffuse slowing and FIRDA. Cytochemical and immunologic CSF evaluation was normal, and no malignant cells were observed. PCR detection of neurotropic and JC viruses were negative. There was no evidence of lymphoma relapse or other neoplasia, including whole body PET. Systemic autoimmune disease markers, as well as cytoplasmic and membrane anti-neuronal antibodies were negative. After 5 days of IV methylprednisolone and 21 days of IV acyclovir, no clinical response occurred and MRI showed extensive bilateral temporal pole involvement. Five sessions of plasmapheresis were performed with sustained clinical and electroencephalographic improvement, without further imagiologic progression.

Discussion: Despite an infectious origin cannot be completely ruled out and no markers of an immune-mediated disorder were found, the neuroimaging pattern and response to plasmapheresis are highly suggestive of an autoimmune paraneoplastic etiology. Our case prompts consideration of plasmapheresis as a therapeutic option even without determined autoantibodies. The role of prior immunomodulation with Rituximab probably deserves to be further elucidated.

Disclosure: Nothing to disclose.

PP4227

Clinical correlation of single fibre electromyography parameters in patients with MG

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Introduction: Predicting the clinical course of myasthenia gravis (MG) at the time of diagnosis could be useful. Single fibre electromyography (SFEMG) is a routine and sensitive investigation for the diagnosis of MG. We explored the relationship between SFEMG parameters and clinical course in our MG patients. This study is to determine the correlation of baseline SFEMG parameters with the clinical course in patients with MG.

Methods: Seventy seven MG patients followed up in the Neurology clinic were retrospectively studied. All had a baseline diagnostic SFEMG done within 4–6 weeks of MG diagnosis. The severity of MG was scored from 1 to 7 depending on the extent of weakness.The clinical course in terms of severity of MG and requirement of immunosuppressants were studied and correlated with the baseline SFEMG parameters.

Results: Patients with higher clinical scores had significantly higher mean jitter (MJ) and percentage of abnormal fibres (POAF) (MJ = 90.2 μsec and POAF = 89.6 %) as compared to patients with lower clinical scores (MJ = 51.5 μs; POAF = 59.9 %) [$p < 0.0001$ for both MJ and POAF].

The MJ and POAF in patients requiring immunosuppressants (MJ = 77.0 μs; POAF = 82 %) were significantly higher as compared to patients who requiredpyridostigmineonly. (MJ = 58.5 μs; POAF = 62.7 %) [$p = 0.02$ and 0.003 for MJ and POAF respectively].

Conclusions: Baseline SFEMG parameters seem to correlate with the severity of MG. A further prospective study to explore this relationship would be useful to establish the prognostic value of SFEMG in MG patients at the time of diagnosis.

Disclosure: Nothing to disclose.

PP4228

Role of Anti GQ1b antibodies in ophthalmoplegia and optic neuropathy unrelated to Miller-Fisher syndrome spectrum

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Introduction: Antigangliosides GQ1b antibodies (GQ1bAbs) are known to be significantly elevated in Miller–Fisher syndrome spectrum (MFS).

While sensitivity of GQ1bAbs in MFS is well recognized (>90 %), data about specificity are lacking. Since GQ1b gangliosides localize on oculomotor and optic nerves sheaths, we hypothesized that other causes of acute ophthalmoplegia (AO) and optic neuritis (ON) than mere MFS could be accompanied by an increase in GQ1bAbs.

Methods: We searched for GQ1bAbs in serum and CSF of patients with AO, ON and MFS. GQ1bAbs were measured by standard assays and expressed in percentage (100 % = 12,000 U; range associated with MFS: 50–100 %). Cutoff values above 30 % were used to define a positive test result.

Results: Clinical and biological findings from 22 AO (22 serum, 9 CSF) and 13 ON (13 serum, 13 CSF) are shown in Tables 1 and 2.

5/6 MFS had elevated GQ1bAbs >140 % either in serum or in CSF (4 serum, 5 CSF). More than 95 % AO presented serum GQ1bAbs below 30 %; only one patient had a slightly elevated titer (30.1 %) in serum (CSF not available) and one had highly elevated values (>160 %) in serum but not in CSF (which was considered to be aspecific). None of the ON subjects presented elevated GQ1bAbs in serum nor in CSF. Specificity of GQ1bAbs in serum was 91 % in AO group (95 % CI: 71–98 %) and 100 % in ON group (95 % CI: 75–100 %).

Conclusions: GQ1bAbs seem not to be increased in aetiologies of AO and ON other than MFS.Disclosure: Nothing to disclose.

Pt	Sex	Age	OMN	Other clinical findings	Etiology	Serum Ig G+IGM GQ1b Ab	CSF Ig G+IgM GQ1b Ab	CSF findings	Other findings
1	F	69	III	bilateral INO	Primary CNS angeitis	8.7	7.9	OCB	MRI: Bilateral ischemic lesions, vessels irregularities
2	F	55	VI	_	Microangiopathic (diabetic)	11.2	NA	Normal	
3	F	74	III	_	Microangiopathic	7.6	_	_	
4	M	47	III	up-beat Ny	Myasthenia gravis	12.8	7.6	EP (529)	
5	M	59	III	_	Microangiopathic	7.0	7.6	EP (527)	
6	M	58	III, VI	_	Myastenia gravis	7.7	6.3	Normal	Single fiber EMG with pathological jitter
7	M	49	IV	_	Myasthenia gravis	9.2	NA	Normal	
8	F	44	IV	_	Indetermined	8.4	_	_	
9	F	75	III bilateral	dyspnea, dyshagia	Myasthenia gravis	11.4	_	_	anti Ach R positive (serum)
10	M	76	III	sensitive ataxia	Guillain-Barré sy (sensitive-ataxic)	14.7	NA	Normal	
11	M	42	III, IV	VII, multidir. Ny	Myasthenia gravis	8.2	NA	OCB	Thymoma
12	F	76	IV, III	_	Microangiopathic (vs inflammatory)	9.8	9.5	EP (499)	
13	M	75	IV	_	Mesencephalic stroke	7.7	6.9	Normal	
14	M	32	III	_	Indetermined	8.3	6.6	Normal	
15	F	86	III	Multidir. Ny, corticospinal signs	Mesencephalic stroke+MCA stroke	7.7	_	_	MRI: Acute R MCS Stroke
16	M	33	VI	Eye pain	Indetermined	12.3	7.7	Normal	
17	F	28	VI	_	Indetermined	8.2	_	_	
18	F	60	III	II , V, VII	Indetermined	**174.0**	11.9	Normal	
19	M	25	VI bilateral	V, VII, corticospinal signs	Post-infectious rhombo-encephalitis	11.7	NA	Normal	
20	M	44	IV, VI	_	Myasthenia gravis	**30.1**	_	_	
21	F	75	VI	_	Microangiopathic (diabetic)	7.3	NA	EP (503)	
22	F	65	VI bilateral	II	Microangiopathic (diabetic)	6.9	NA	EP (516)	

Table 1. Characteristics of patients with **acute ophtalmoplegia (AO):** sex, age, oculomotor nerves palsy, etiology, CSF findings and anti GQ1b ganglioside antibody titres (GQ1b Ab). GQ1bAb values are expressed in % (100% corresponds to 12000 Units), cutoff value for positive test was established at ≥30% (IgG+IgM). Positive values are in bold (patients 18 and 20).

Pt	Sex	Age	Visual Acuity	Other clinical findings	Etiology	Serum Ig G+IgM GQ1b Ab	CSF Ig G+IgM GQ1b Ab	CSF findings
1	F	33	< 0.1	papilloedema, RAPD	MS (1st poussée)	5.8	5.1	OCB
2	F	40	< 0.1		Possible MS	5.3	5.1	OCB
3	M	38	0.4		Probable MS	5.4	5.5	12 WBC, EP (572) OCB
4	M	28	0.5		Probable MS	7.2	5.2	13 WBC, EP (750) OCB
5	F	17	< 0.1		MS (1st poussée)	6.6	5.6	OCB
6	F	26	< 0.1		MS (1st poussée)	5.4	5	Normal
7	F	56	0.3	coecocentral scotoma	Isolated ON	7.7	5.2	Normal
8	F	20	<0.1		MS (1st poussée)	5.7	5.6	Normal
9	F	34	< 0.1		Post-infectious	7.9	5.5	Normal
10	M	21	< 0.1		Probable Devic	6	5.6	1300 RBC, EP (485)
11	F	39	0.5		MS (1st poussée)	5.7	5.6	7 WBC, EP (470) OCB
12	F	18	< 0.1		MS (1st poussée)	5	4.9	60 WBC, EP, OCB
13	F	34	< 0.1		MS (1st poussée)	5.6	5.4	OCB

Table 2. Characteristics of patients with **optic neuritis (ON):** sex, age, visual acuity, etiology, CSF findings and anti GQ1b ganglioside antibody titres (GQ1b Ab). GQ1bAb values are expressed in % (100% corresponds to 12000 Units), cutoff value for positive test was established at ≥30% (IgG+IgM).

Legend:
Pt= patient
OMN= oculomotor nerve palsy
INO= internuclear ophtalmoplegia
OCB= oligoclonal bands in CSF (intrathecal IgG synthesis)
EP= elevated CSF proteins (> 450 mg/L)
NA=not assessed
Ny=nystagmus
RAPD= relative afferent pupillary deficit
MS= multiples sclerosis

PP4229

Cerebral venous thrombosis as the first manifestation of isolated antiphospholipid syndrome

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PP4230

α-galactosylceramide enhanced TNF-α and decreased anxiety-like behaviors in post-weaning social Isolation

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PP4231

Atypical devic disease as first manifestation of Sjogren syndrome: a case report

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PP4232

Trigeminal neuralgia in Behçet disease

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PP4233

VGKC-complex-LGI1-antibody encephalitis: clinical course and immunotherapy influence on seizure control and long-term cognitive prognosis

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PP4234

An atypical phenotype of anti-GQ1b antibody syndrome in an 81 year-old woman

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PP4235

Abstract withdrawn

PP4236

The role of plasmaferesis when treating neurological symptoms associated with inflammatory bowel disease: a case report

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PP4237

Steroid responsive leukencephalopathy in cerebral amyloid angiopathy without bioptical evidence of vasculitis

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PP4238

Anti-NMDA receptor encephalitis (case report)

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PP4239

Late onset recurrent longitudinal myelitis with autoantibodies to Aquaporin-4 with first manifestation in an 88 year old patient

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PP4240
Limbic encephalitis, hyponatremia, faciobrachial dystonic seizure associated with voltage-gated potassium channel antibodies

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PP4241
Acute disseminated encephalomyelitis after oral therapy with herbal extracts: a case report

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PP4242
Hemorrhagic pontine stroke associated with Hashimoto encephalopathy: a case report

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PP4243

Abstract withdrawn

PP4244
Localization and viability of neural stem cells after therapeutic intrathecal transplantation in experimental autoimmune encephalomyelitis

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PP4245
Effect of pregabalin and diclofenac on tactile allodynia, mechanical hyperalgia and increase in pro inflammatory cytokines induced by chronic constriction injury of the infraorbital nerve

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PP4246
Severe reversible paraneoplastic encephalitis

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PP4247
Evidence based medicine changes the approach to the Rx of myasthenia gravis

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PP4248

Abstract withdrawn

PP4249
Interleukin-17 impedes Schwann cell-mediated myelination

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PP4250
Three case of autoimmune encephalitis

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PP4251
Diagnostic role of immunological characteristics in chronic brain ischemia

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PP4252
Biochemical markers of the chronic brain ischemia

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Neurological manifestation of systemic diseases

PP4253
Condition of cognitive functions at patients with systemic lupus erythematosus

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Introduction: Epidemiological studies in recent years have shown that SLE is more common than previously thought, according to J. Klippel and J. Decker, it is identified 50–70 new cases annually per 1 million population, approximately 500 patients per 1 million people worldwide. But along with therapeutic symptom-complex in

this disease manifests itself a number of neuropsychological syndromes. American College of Rheumatology describes about 20 such syndromes.

Methods: We observed 16 patients with clinically justified SLE (study group) and 10 healthy volunteers (control group). Age of patients was 16–49 years (mean age 29.25). SLE at all patients was sub acute or chronic and with pathology of the nervous system: a convulsive syndrome and stroke in 1 (6.25 %), intracranial hypertension, vascular encephalopathy and poly neuropathy in 2 (12.5 %), hypothalamic syndrome in 3 (18, 75 %), astenisation syndrome in 4 (25 %) cases.In both groups studied condition of the cognitive functions according MMSE, test of learning 10 words and FAB.

Results: According to the results of the MMSE in 37.5 % of patients with SLE were defined mild cognitive disorders, in 56.25 % moderate cognitive impairment and dementia in 6.25 %. For results of memorize 10 words mean point 7.3 % and FAB scale mean point was 13.8. In the comparison group cognitive functions were within normal.

Conclusions: Cognitive functions should be examined in all patients with SLE as a method of early diagnosis of CNS involvement.

Disclosure: Nothing to disclose.

PP4254

Neurologic involvement in acquired adult hemophagocytic lymphohistiocytosis: a clinico-pathological case

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Introduction: Hemophagocytic lymphohistiocyotosis (HLH) is a syndrome of severe immune activation rarely described in adults. Central nervous system is affected in up to 73 % of children with HLH; meningitis, seizures and white matter abnormalities being most frequently reported.

Case report: A 47 year-old previously healthy woman presented with a 4-month history of fever of unknown origin. Her physical examination was unremarkable. Blood tests showed anemia and high triglycerides, C-reactive protein and ferritin. Her spleen biopsy was relevant for hemophagocytosis. HLH diagnostic criteria of apparently idiopathic cause were met, after diagnostic tests have ruled out every thought hypothesis. Throughout inpatient period she developed a complex partial seizure. Brain MRI showed subcortical fuzzy lesions with hyperintensity in FLAIR, the largest one with contrast enhancement in right temporal lobe. CSF examination showed 6 normal lymphocytic cells, with negative microbiology studies. Metilprednisolone and intravenous immunoglobulin was administered before discharge. She started HLH-94 chemotherapy protocol with symptom and MRI lesions improvement. 2 months after HLH-94 induction phase she developed disorientation and visual hallucinations. Brain MRI showed a severe lesion recrudescence with diffuse brain edema causing clinical worsening by coma and death. Post mortem brain pathology was consistent with a hemophagocytosis associated with a perivascular infiltration by monoclonal lymphocytes. Intravascular lymphoma (IVL) was simultaneously identified in the kidneys and lungs.

Conclusions: We describe a rare case of proved central nervous system hemophagocytosis in an adult patient with an IVL. HLH should be considered in the differential diagnosis of white matter disease even in adults.

Disclosure: Nothing to disclose.

PP4255

Frequency of peripheral neuropathy and myogen lesion in antineutrophil cytoplasmic antibody associated (ANCA) small vessel vasculitis

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Introduction: In systemic vasculitis the peripheral nerves are affected in 60–70 %, but myogen involvement is less known.

Methods: We tested the frequency of neuropathy and muscle damage in a homogenous ANCA small vessel vasculitis patient group. Eleven patients were recruited. Time since verifying ANCA positivity in average was 4 years. Neurological and neurophysiological examination (electroneurography, electromyography) were performed. Currently we present the preliminary data and results of our long-term prospective study.

Results: The peripheral nerves were affected in the majority of the examined patients. The detailed electroneurography results were the following: 2 patients suffered from mononeuropathy multiplex affecting the lower limbs, 1 of them the sensory and motor nerves and in the other only the sensory part have been affected. Six patients had neuropathy in the lower limbs, in 2 patients only the sensory nerves were affected and the other 4 patients suffered from sensoro-motor neuropathy. Polyneuropathy was detected in 2 patients. The electroneurography was normal in 1 case, who has been diagnosed 2 weeks ago. Interestingly high percent of the patients had myogen lesion (54 %). But electromyography revealed abnormality in all patients (5 patients neurogen lesion, 1 patient both).

Conclusion: We found that in most of the ANCA positive patients not only the peripheral nerve lesion is characteristic but the myogenic lesion as well. Follow up of the patients is necessary to detect the progression of the clinical neurophysiological conditions.

Disclosure: Nothing to disclose.

PP4256

A case of autoimmune polyendocrine syndrome type 2 presenting with Hashimoto's encephalopathy and signs of lower motor neuron involvement

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Introduction: Hashimoto's encephalopathy (HE) is a steroid-responsive encephalopathy associated with elevated antithyroid antibodies, variously presenting with consciousness disturbance, psychosis, cognitive dysfunction, myoclonus, seizures and ataxia. HE can have an acute, relapsing-remitting or chronic course.

Methods: A 27-year-old man presented a progressive myoclonus epilepsy associated with ataxia and right limbs weakness and atrophy, slowly worsening over 5 years. At age 32, worsening asthenia and depression appeared and progressed to a stuporous state. Addison's disease and Hashimoto's thyroiditis were diagnosed. L-thyroxine and steroid therapy were started with clinical improvement. Brain MRI showed cerebellar atrophy. Cervical spinal cord MRI was normal. EMG showed widespread active denervation signs. Serum creatine kinase levels were increased. Anti-glutamic acid decarboxylase antibodies and high serum anti-

thyroperoxidase and anti-thyroglobulin antibodies were detected. Plasma very long chain fatty acids were normal. Anti-VGCK, anti-VGCC and anti-GluR3 antibodies were absent. CSF oligoclonal bands were detected and confirmed by two different tests, performed 6 and 11 years after the onset. No mutation was found in the *SOD1*, *SMN*, *AR*, *TBP* and *MT-ATP6* genes. The neuropsychological assessment revealed a cognitive impairment.

Results: HE in a patient with an autoimmune polyendocrine syndrome type 2 was diagnosed. An 11-year follow-up shows reduced myoclonic jerks, better control of seizures with valproate and unchanged limbs strength and atrophy.

Conclusions: This case highlights how HE, an overlooked treatable condition, can present with combined encephalopathy, lower motor neuron and adrenal insufficiency signs, mimicking an inherited metabolic or a neurodegenerative disorder, such as spinocerebellar degeneration or motor neuron disease.

Disclosure: Nothing to disclose.

PP4257

An elderly CTLN2 patient successfully treated with medium-chain-triglyceride-supplemented formula

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Adalt-onset type 2 citrullinemia (CTLN2) is a glucose metabolism disorder and shows neuropsychiatric manifestations including aberrant behavior, nocturnal delirium, disorientation, consciousness disturbance and convulsive seizures. A 66-year-old Japanese man presented with recurrent episodes of neuropsychiatric manifestations and hyperammonemia. Liver cirrhosis or portosystemic shunt was not observed. An electroencephalograph showed generalized high voltage slow wave. We considered nonconvulsive status epilepticus and used antiepileptic agent with hyperammonemia treatment, but his symptoms were not improved. Further investigation showed high concentration of citrulline in both blood and urine, and high concentration of arginine in urine. Genetic analysis of SLE25A13 gene(cansative gene of CTLN2) was identified 24TCG (stop codon). Then we diagnosed that this case was having elderly onset CTLN2. He treated a low carbohydrate diet with Medium-Chain-Triglyceride (MCT)-supplemented Formula. His neuropsychiatric manifestations disappeared, and hyperammonemia was improved. MCT-supplemented formula is one of the effective treatments tool for elderly onset CTLN2 patients.

Disclosure: Nothing to disclose.

PP4258

A case of neuroachantosis

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Introduction: :A 27-year-old Iranian woman with psychiatric symptoms from 7 years ago because of choreathesosis symptoms was referred from a psychological ward for workup. She had a history of biting the tongue, tics, marked hyporeflexia and lower limb muscle wasting. She had one generalized tonic–clonic seizure attack during admission in the neurology ward.

Methods: In general appearance she was ill and cashectic. Marked scars of self-injury wounds in face and scalp were seen. She was hyporeflexic and quadriparetic with muscular atrophy dominantly in lower limbs. Cranial nerves exam was normal.She had mild ataxia and scanning speech. During the exam chorea-athetoic movements are seen in the limbs. She was anemic. Routine lab data (unless hematologic and mild increase in transaminases) ones were normal. MR showed atrophy of the caudate nucleus and putamen. Electro diagnostic evaluation showed mild to moderate axonal sensorimotor polyneuropathy. Peripheral blood smear showed red blood cell acanhtosis and mild hemolysis. She was treated during admission with atypical antipsychotic agent quatiapine and anti-choreic agent teterabeazine and valpraoat sodium for her seizures.Her symptoms became better but incomplete.

Conclusions: CNS manifestations of this disease as a neurodegenerative basal ganglia disease including.

(1) movement disorders,
(2) cognitive alterations, and
(3) psychiatric symptoms.

Progressive chorea syndrome similar to that seen in Huntington disease including the clinical triad of movement disorder, cognitive alterations, and psychiatric symptoms and seizures, mostly generalized.

Neuromuscular manifestations include a (mostly subclinical) sensorimotor axonopathy and muscle weakness or atrophy of different degrees.

Disclosure: Nothing to disclose.

PP4259

Peripheral neuropathy: rare manifestation in Henoch-Schönlein purpura

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Introduction: Henoch Schönlein Purpura (HSP) is a systemic vasculitis characterized by purpura, arthralgia or arthritis, abdominal pain and glomerulonephritis. Nervous system involvement mostly includes headaches, mental changes, seizures and focal neurological deficits. Peripheral nervous system dysfunction is very rare. We present a 35-year-old woman with HSP who suffered from peripheral neuropathy.

Case: A 35-year-old woman was admitted with a complaint of numbness in the hands and feet. She had a history of arthritis, palpable purpura concentrated on arms and legs, and gastrointestinal bleeding 10 years ago. Skin biopsy had been performed and with clinical features she had diagnosed as HSP. Since then, oral prednisolone had been given when she had symptoms and signs. Physical examination was normal. Neurological examination revealed hypoestesia with distribution of symmetrical globe and stocking type. Deep tendon reflexes of lower extremities were absent. Laboratory investigations were unremarkable. Electrophysiologic findings on both upper and lower extremities showed moderately reduced sensory nerve action potential amplitudes with normal latancies, suggesting mild axonal neuropathy mostly in peripheral sensory nerves. After initiation of the oral prednisolone therapy, she improved rapidly.

Conclusions: We present a case with HSP with peripheral nervous system involvement. Neurological manifestations are very rare in patients with HSP. Periheral nervous system dysfunction presents as polyneuropathy, mononeuropathy or mononeuropathy multiplex. Agressive dosage corticosteroids and cyclophosphamide are not advised for HSP patients with a peripheral or cranial neuropathy, since they are tend to full spontaneous recovery. In conclusion, although it is rare, neurologic involvement should be thought in HSP.

Disclosure: Nothing to disclose.

PP4260

The value of repeat CT imaging of the thorax in the diagnosis of neurosarcoidosis: report of a case

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Case report: A 36 year old woman presented with a 3 day history of diplopia. On examination there was a left oculomotor nerve palsy. Cerebral MRI demonstrated enhancement of the affected nerve. CSF showed a lymphocytosis with raised protein but normal glucose. Microbiological investigations were negative as was cytology. Serum and CSF angiotension converting enzyme (ACE) levels and CT thorax were normal. A diagnosis of possible neurosarcoidosis was made, and treatment started with prednisolone. Although the oculomotor palsy resolved within 3 weeks, MRI showed deterioration with new parenchymal lesions in both cerebellar hemispheres. The CSF was re-examined and found unremarkable. A repeat CT thorax identified an increase in size of several lymph nodes, biopsy of which confirmed a histopathological diagnosis of sarcoidosis. High dose steroids and methotrexate resulted in an ongoing good clinical response and progressive improvement in MRI appearances.

Discussion: Neurosarcoidosis can be difficult to confirm: there may be no disease outside the nervous system, and the neurological lesions may not be amenable to biopsy. Normal serum and CSF ACE levels do not exclude the diagnosis. High resolution CT imaging of the thorax is commonly performed in this condition, although rarely repeated. In this case, a repeat of this investigation demonstrated progression of appearances which allowed a definitive diagnosis to be made and avoided the risks of brain biopsy. Although the risks of radiation need to be borne in mind, repeat CT thorax after an interval should be considered in patients with an unconfirmed diagnosis of neurosarcoidosis.

Disclosure: Nothing to disclose.

PP4261

Celiac disease and leukoencephalopathy

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PP4262

Pain syndrome intensity, psychoemotional condition and quality of life in patients with multiple myeloma

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PP4263

Systemic diseases revealed by neuropsychiatric features

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PP4264

Rendu–Osler–Weber disease and prothrombin mutation in heterozygosity—imminent danger?

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PP4265

Hearing loss: Behçet's disease or Susac syndrome

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PP4266

Progressive dementia in a young women revealing mixed connective tissue disease

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PP4267

POEMS syndrome: a diagnostic and therapeutic challenge

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PP4268

Chronic paraneoplastic leukoencephalopathy associated with multiple myeloma: a rare association

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PP4269

Delayed onset of dementia and parkinsonism in a postoperatory hypoparathyroidism case

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PP4270

An autopsy case of multiple myeloma which revealed cerebellar ataxia and progressive dementia

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PP4271
A Creutzfeldt-Jakob disease patient treated with Korean medical treatment: a case report

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PP4272
Parkinson syndrome revealing a systemic lupus erythematosus disease: a case report and review of literature

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PP4273
Ischemic stroke revealing Wegenerś disease: one case study and review of literature

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PP4274
Adrenal tumor presenting as tetraplegia

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PP4275
Systemic lupus erythematosus manifested as drug-resistant mesial temporal lobe epilepsy

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PP4276
Loss of taste

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PP4277
Central nervous system (CNS) involvement in multiple myeloma (MM)

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Focused Workshops

Recent advances in multiple sclerosis research

FW1-1
Therapeutic antibodies in the treatment of MS

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Monoclonal antibodies (Ab) represent a rapidly growing field in multiple sclerosis (MS) therapy. The first approved Ab antibody approved for therapy of highly active MS was the anti-α4-integrin monoclonal antibody natalizumab that have been used in the treatment of more than 100,000 patients. Natalizumab therapy is associated with the risk of progressive multifocal leukoencephalopathy (PML), but today risk assessment can be used to guide treatment decisions. Recently, the anti-CD52 monoclonal Ab alemtuzumab was introduced in Europe and may be the most efficacious MS therapy available, but the treatment is associated with common serious adverse effects, mainly immune mediated thyroid disease. Several other candidates are under development, of which B-cell directed therapy with anti-CD monoclonal antibodies, ocrelizumab and ofatumumab, are prominent examples. Rituximab showed strong effects in relapsing-remitting MS, bur is not developed further as MS therapy. Also the monoclonal Ab anti-CD25 daclizumab are in phase III development. Animal models have suggested that anti-LINGO1 antibody has remyelinating potential, and phase 2 trials of the antibody are underway. Other interesting candidates are anti-IL-17 strategies, and interference with the complement pathway. Continued surveillance will be essential to establish the safety and clinical efficacy of these drugs in patients with relapsing-remitting MS.

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FW1-2
How stem cells speak with immune cells

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Advances in stem cell biology have raised great expectations that diseases of the central nervous system may be ameliorated by the development of non-haematopoietic stem cell medicines. Yet, the application of stem cells as therapeutics is challenging and the interpretation of some of the outcomes ambiguous. The initial idea that stem cell transplants work only via structural cell replacement has been challenged by the observation of consistent intercellular information exchange between the graft and the host. Sustained stem cell graft-to-host exchange of signals has led to remarkable trophic effects on endogenous brain cells and beneficial modulatory actions on innate and adaptive immune responses that ultimately promote the healing of the injured CNS. Among a number of promising candidate stem cell sources, mesenchymal/stromal stem cells (MSCs) and neural stem/precursor cells (NPCs) are being

extensively investigated for their capacities to signal to the immune system upon transplantation in experimental CNS diseases. Here, we focused on defining whether the form of cellular signalling mediated by extracellular membrane vesicles (EVs) exists for neural stem/precursor cells (NPCs), and on its molecular signature and functional relevance on target cells. We also investigated whether the EV cargo molecules are modulated by extracellular pro- or anti-inflammatory cytokines, determined the key elements responsible for this novel mechanism of EV-mediated intercellular communication, and finally reflected on the forthcoming challenges related to the translation of these exciting experimental proofs into ready-to-use clinical medicines for inflammatory CNS diseases.

Disclosure: Nothing to disclose.

Neuromuscular disorders: imaging, gender and carrier issues

FW2-1
MRI studies on limb girdle muscle dystrophies

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1. Introduction: Muscle MRI is a useful tool to study myopathies for many different reasons. First, it obtains images of the fatty infiltration of muscles of the body. The different studies performed in patients with a single disease, as for example limb girdle muscle dystrophy (LGMD) type 2B, have demonstrated that in general, every genetic disorder has a typical pattern of muscle involvement. This fact allows to obtain maps of muscle involvement on MRI in every disease and to design algorithms for the diagnosis of these diseases using muscle MRI. Second, as MRI technique is safe since it avoids the use of radiation, it can be repeated in a single patient many times without any risk. Based on this, natural history studies can be performed to know, which is the sequence of muscles involved in the different muscle diseases. Although this is possible, there are not so many prospective studies reported in the literature using muscle MRI in patients. Third, MRI is useful to identify which muscles are involved in a patient and guides on the site of choice to perform a muscle biopsy. This can be really helpful is those patients that have only hyperckemia without detectable muscle weakness in the clinical examination. Finally, MRI can become a biological marker of response to treatment in the near future, just in the moment in which many therapies form the different muscle dystrophies are under development. The first studies reported in the literature were performed using sequences that analyse the muscle of the lower limbs only, but at present new devices allow obtaining images of all the muscles of the body quickly. Whole body MRI can be obtained in less than 30 min. The MRI sequences that are commonly used are mainly three: T1, that differentiates healthy muscle from fatty infiltration, Dixon that quantifies the percentage of water and fat in every single pixel, and STIR, that allows to identify the presence of edema in muscles, and has been related with the presence of inflammatory infiltrates in the muscles. 2. Muscles involved in Dominant Inherited Muscle Dystrophies: There are not so many reports regarding the common pattern of muscle involvement of patients with dominant LGMD. However, based on the studies published some conclusions can be obtained. In the case of LGMD-1A (myotilinopathy) the studies reported have focused in lower limbs muscles, describing a frequent involvement of Soleus, medial Gastrocnemius and Tibialis Anterior in the legs and of Semimembranosus, Biceps Femoris (long head) and Adductor muscles in the thighs. Sartorius muscle can be also involved in these patients. This pattern is similar but different of patients with mutations in the desmin gene (cause of LGMD-1E). The main differences are that desmin patients have a preferential involvement of Semitendinosus, Sartorius and Gracillis, muscles in the thighs while Semitendinosus and Biceps are spared until later stages. In the legs, these patients have an involvement of Triceps Surae and of Peroneus muscles. Patients with LGMD-1B (laminopathies) with mutations in the gene that codifies for lamin A/C have a pattern of involvement similar to patients with Emery–Dreifuss muscle dystrophy produced by mutations in the Emerin gene. In general, they have an involvement of paravertebral muscles associated to a characteristic involvement of the thigs where the anterior muscles Vastus Lateralis, Medialis and Intermedius and the posterior muscles Semimembranosus, Biceps Femoris, Semitendinosus and Adductor Muscles are involved. There is a typical hypertrophy of rectus femoris and Gracilis and Sartorius are commonly unaffected. The pattern of involvement of muscles of the legs is unspecific, with involvement of Gastrocnemius Medialis and Soleus muscle. There are not enough data to support a common pattern of involvement in patients with LGMD-1C (caveolinopathies). There are some reports on the muscle MRI features of patients with the recently identified, LGMD-1D and LGMD-1F. Muscle MRI involvement of patients with mutations in the DNAJB6 gene that produces LGMD-1D, has been reported to be specific. An involvement of posterior muscles of the thighs such as Adductor Magnus, Semimembranosus and Biceps femoris associated to an involvement of soleus muscle in the legs are characteristic. Other muscles such as Gluteus, Vastus Intermedius or Gastrocnemius Medialis can be involved, but less severely. In the case of LGMD-1F (produced by mutations in the Transportin 3 gene) an involvement of Vastus Lateralis and Medialis in the thighs and of Gastrocnemius Medialis, Lateralis and of Soleus muscles in the legs have been reported. 3. Muscles involved in Recessive Inherited Muscle Dystrophies: In contrast with dominant inherited LGMD, many reports describing the features of muscle MRI involvement have been published. In the case of LGMD-2A (Calpainopathies) patients show prominent involvement of the gluteal and posterior compartment muscles of the thigh. The posterior compartment is also more severely involved in the legs, with a preferential involvement of Gastrocnemius Medialis and Soleus. Patients with mutations in the dysferlin gene (LGMD-2B) have also a characteristic progressive pattern of involvement. In the thighs, muscle pathology starts in the Adductor Magnus and then affected the Semimembranosus and the Vastus Lateralis muscles. In latter stages there is also an involvement of Vastus Intermedius and Medialis muscles and of Biceps and Semitendinosus muscles. Rectus femoris, Gracillis and Sartorius are commonly spared until very late stages. In the leg, the early involvement of the posterior compartment is characteristic. There are few reports on the MRI muscle involvement of patients with sarcoglycanopathies (LGMD 2C-D). In general there is a preferential involvement of the thighs (especially Vastus Intermedius, Medialis and Lateralis and also the posterior compartment), while legs muscles are spared. The pattern of involvement of patients with LGMD-2I (mutations in the FKRP gene) is also well documented. There is an initial involvement of the adductor muscles and the biceps femoris muscle that progress involving semimebranosus and semitendinosus muscles. Anterior muscles of the thighs are clearly less involved in these patients, however when involved, Vastus Medialis and Intermedius are the more infiltrated muscles. Regarding leg muscles, Gastrocnemii and Soleus are commonly affected while Tibialis Anterior is spared. In the case of LGMD-2 J, produced by mutations in the titin gene, the characteristic involvement of Tibialis Anterior is associated to atrophy of anterior muscles of thighs especially involving the vastus muscles with respect of Rectus anterior, gracillis and sartorius muscles. Finally, the characteristic pattern of involvement of patients with LGMD-2 N, produced by mutations in the ANO-5 gene, has also been published. In this case the pattern of involvement overlaps with that described in LGMD-2B patients.

4. Other limb-girdle muscle myopathies: 4a. Dystrophinopathies: In the case of Becker muscle dystrophy, the pattern and degree of involvement depends on the clinical symptoms of the patients. For example, there are publications reporting absence of fatty infiltration in patients without weakness or with mild weakness. In contrast in more affected patients, fatty infiltration of muscles in the arms and legs has been reported. In this case, the pattern of involvement is very similar between Duchenne and Becker patients. Pelvic muscles are affected, especially gluteus medius and maximus, while iliopsoas is less affected. In general, anterior and posterior muscles of the thighs are involved being adductor magnus, biceps femoris long head and semimembranosus the most commonly affected muscles. Fat infiltrates also vastus lateralis, mealis and intermedius muscles and less frequently rectus femoris. Legs muscles are less involved, but when affected, gastrocnemius medialis and soleus are the most commonly atrophic muscles. 4b. Facioscapulohumeral muscular dystrophy (FSHD): Patients with FSHD display two main features. First, asymmetry in the degree of involvement between left and right muscles is generally reported in all series. Second, there is not a common pattern of involvement since the muscles involved can be very heterogeneous between patients. However, periscapular, abdominal, semimembranosus and tibialis anterior are the most commonly affected muscles. 4c. Myotonic dystrophy type 2: There are not so many reports on the MRI findings in DM2 patients, however it has been reported that vastus lateralis is diffusely affected in these patients. In general, there is not an specific involvement and the degree of involvement is very broad ranging from a completely normal MRI in old patients to a diffuse involvement sparing the rectus femoris and preservation of calf muscles in younger patients. 4d. Pompe's disease: In the last years the MRI pattern of involvement of adult onset Pompe's patients has been very well characterized. There is a typical early involvement of paraverterbral and abdominal muscles associated to glutei and adductor muscles. Latter, the tongue, subscapularis, muscles of the posterior compartment of the legs and the Vastus muscles are involved. In general, muscles of the legs are spared.

Disclosure: Nothing to disclose.

FW2-2
Influence of gender in muscle disorders

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Torino, Italy

Objectives: To review of the sparse published papers on gender-related issues in muscle disorders, in order to highlight the most recent achievements and provide indications for clinical practice.

Results: Gender is a well-known, independent factor influencing phenotypic expression, course and therapeutical response of many human pathologies, of both acquired and genetic origin. In the broad field of neuromuscular disorders we can encounter gender-specific diseases, mainly related to the X-chromosome abnormalities, and gender-influenced disorders, which are more common in one sex or have a different course in each sex. Moreover, we have to deal with other gender-specific issues, such as fertility, pregnancy and delivery complications in women with muscle disorders. Well-known examples of the first group are the X-linked muscular dystrophies and myopathies, such as dystrophinopathies, emerinopathies, and centronuclear myopathy. In the recessive disorders, males usually present a defined, more severe phenotype, whereas females carrying one mutated allele may show very different clinical pictures, mainly related to the variable X chromosome inactivation, thus complicating the diagnostic procedures. When evaluating a female with muscle symptoms, the possibility of a carrier status for an X-linked disease should always be ascertained. Among the gender-influenced diseases, inflammatory myopathies are more frequent in females, as observed also in the majority of autoimmune diseases; namely, polymyositis and dermatomyositis incidence is evidently higher in females, with a ratio of 2.5:1. On the contrary, inclusion body myositis (IBM), which has a peculiar degenerative component, prevales in middle-aged and older men. This is consistent with other neurodegenerative diseases, in which the female gender may have a 'protective' role, as observed in some experimental autophagic pathological processes. Other examples include FSHD, with a more favourable clinical course in females, and Pompe's disease, in which female gender seems to be related to a better therapeutical response. Finally, pregnancy may cause deterioration of the clinical course in women with muscular weakness of different origin, especially due to the additional physiological changes: a strict monitoring of the cardiac, respiratory and motor function is therefore always necessary, associated to a surveillance of possible metabolic derangements. Child delivery options are challenging in muscle disorders: a natural delivery is not indicated when respiratory, abdominal or pelvic muscle are involved, whereas a Caesarean section may be safely performed with a spinal anesthesia to avoid intubation even in more affected women. A strict follow up in expert Centers is recommendable in all cases.

Conclusions: Gender differences in muscle diseases may have a more important role on outcomes and effects of therapies, such as observed in other medical disciplines. Gender-related variants in the pathogenetic processes, as well as in pharmacokinetics and pharmacodynamics, should always be addressed in the development of new therapeutical options.

Disclosure: Nothing to disclose.

FW2-3
Myopathies and cancer

M. de Visser
Amsterdam, The Netherlands

Paraneoplastic neurological disorders (PNDs) are a group of heterogeneous neurological disorders that occur in patients with cancer. They result from the remote effects of malignancy rather than from metastases or direct invasion of the nervous system by the tumour. Many PNDs are attributed to autoimmunity directed against the nervous system given the discovery that many PNS are associated with antibodies against neural antigens expressed by the tumour (onconeural antibodies),

PNDs typically present before the diagnosis of cancer. Hence, early clinical suspicion is of paramount importance. Overall, PNDs are rare.

Of the paraneoplastic neuromuscular disorders sensory peripheral neuropathy and Lambert-Eaton syndrome associated with small-cell lung cancer and myasthenia gravis with thymoma are well known.

The focus in this workshop will be on myopathies associated with cancer. The most frequent paraneoplastic myopathy is dermatomyositis. More recently, necrotizing autoimmune myopathy has also been recognized as a paraneoplastic myopathy. Diagnosis, treatment and prognosis will be discussed, as well as the risk of cancer and cancer screening. Some even more rare myopathies associated with cancer, such as amyloid myopathy will also be addressed. Patients with an established diagnosis of cancer may develop diffuse muscle atrophy

and weakness as part of their general catabolic state ('cancer cachexia').

Disclosure: Nothing to disclose.

Embolism to the brain—a preventable and treatable entity—European Stroke Organisation (ESO)/EFNS/ENS Joint Focused Workshop

FW3-1
High and medium risk sources of cardiac embolism to the brain

P. Michel
Lausanne, Switzerland

High and medium risk cardiac sources include atrial fibrillation (AF) and flutter with additional risk factors, mechanical prosthetic valves, acute transmural MI, aneurysmal left ventricular segment, mitral valve disease, low ejection fraction <35 %, left atrial or ventricular masses, left atrial tumours, and bacterial and nonbacterial thrombotic endocarditis (NBTE). The cardioembolic risk may be modified by a history of stroke, additional vascular risk factors, and multiple cardiac pathologies. The proportion of cardioembolic stroke is increasing, mainly due to the increased prevalence of AF in the aging population.

Clinically, cardioembolic stroke is characterized by abrupt onset and major severity and cortical symptoms (aphasia, hemianopia etc.) in supratentorial stroke. Radiologically, multiple arterial territories may be affected, either simultaneously or over time.

Structural cardioembolic sources are initially searched by transthoracic echocardiography. In the case of doubtful or negative findings, transoesphageal echocardiography, cardiac CT and MRI can be added. The earlier and the longer rhythm monitoring is performed, the more likely paroxysmal AF will be detected, with a 30 % detection rate at 3 years using an implantable event recorder (CRYSTAL study).

For AF and atrial flutter, the CHADS2VA2Sc and HAS-BLED scores should be used to estimate risks for ischemic stroke and haemorrhages. New oral anticoagulants (NOAC) reduce the intracranial haemorrhage rate by about 50 %, and therefore decrease overall bleeding and stroke recurrence risk in many patients. With these lower bleeding risks, Aspirin is no longer safer, but clearly less efficient than the NOAC. Most elderly and frail patients also benefit from anticoagulation. NOAC should be carefully adapted to age, renal function and concomitant antiplatelet treatment, and education for drug compliance is important.

In mechanical valves, the degree of anticoagulation by vitamin K antagonists (VKA) needs to be adapted to valve type, position and additional risk factors. For other high risk cardiac sources such as low ejection fraction, NBTE, left ventricular aneurysms and masses, or isolated mitral valve disease, anticoagulation has no or no proven benefit. For acute bacterial endocarditis and intracardiac tumours, antithrombotics may even be dangerous.

Prevention of cardioembolic stroke always includes prevention of atherosclerosis and cardiac disease by drugs and lifestyle modifications.

Disclosure: P. Michel has received through his institution (CHUV) within the last 3 years research grants from the Swiss National Science Foundation, the Swiss Heart Foundation, and Cardiomet-CHUV; speaker fees from Bayer, Boehringer-Ingelheim, Covidien and St. Jude Medical; honoraria from scientific advisory boards from Bayer and Pfizer; and consulting fees from Pierre-Fabre. He is member of the European Stroke Organisation Executive Committee and serves on the editorial board of Stroke and the International Journal of Stroke. He serves on the steering committee of BASICS, the International PFO-Consortium, the DSMB of SAFE, and the ICH-adjudication committee from CLOTBUST-ER.

FW3-2
Therapy of large cerebral artery strokes

C. Stapf
Paris, France

Large cerebral artery occlusion are the source of major stroke syndromes leading to high mortality and potentially severe long term morbidity.

Recommended acute treatment plans include stroke unit management, intravenous thrombolysis, and—in case of malignant MCA infarcts—therapeutic hemicraniectomy.

Acute endovascular therapy has failed to show clinical evidence for long-term benefit in several controlled clinical trials, but remains a promising treatment concept for acute proximal occlusions of the Circle of Willis arteries.

Current concepts of ongoing trial protocols will be discussed along with decision algorithms for individual patient management based on current knowledge.

Disclosure: Nothing to disclose.

Advances in restless legs syndrome (RLS)

FW4-1
RLS and cardiovascular disorders

U. Kallweit
Bern, Switzerland

Restless legs syndrome (RLS) is a frequent neurological and sleep disorder that follows a circadian trend defined by an uncontrollable urge to move the legs/limbs that worsens at rest in the evening or at night, often resulting in sleep disruptions, insomnia and daytime fatigue and sleepiness. In the majority of patients (70–90 %), periodic leg/limb movements in sleep (PLMS) occur. The etiology of RLS still remains incompletely understood. A deficient iron/dopamine transport and metabolism may underlie RLS. A sympathetic activation and hyperactivity in RLS, in particular in PLMS is suggested. Sleep disorders such as insomnia and obstructive sleep apnea (OSA) are established risk factors for hypertension and cardiovascular diseases (CVD). Some studies indicate a similar increase in hypertension and CVD risk due to RLS. Associations between RLS and hypertension, CVD, and related conditions are mainly linked to sympathetic activation and metabolic dysregulation. Current advances in the understanding of the relationship between RLS and cardiovascular diseases have important implications for the pathophysiology of RLS and also in reducing a potential CVD risk, in particular as for RLS an effective treatment is considerable.

Disclosure: Dr Kallweit is a member of Advisory Board RLS-UCB Pharma Germany.

FW4-2
RLS and associated conditions

J. Santamaria Cano
Barcelona, Spain

Restless legs syndrome (RLS) develops as a consequence of genetic factors, very important in idiopathic RLS, and non-genetic associated conditions. The threshold for RLS symptoms in patients

without a relevant genetic risk is higher than in those with a positive family history of the disorder. In this lecture I will review the conditions that are associated with RLS, the mechanisms underlying the appearance of RLS symptoms and the treatments to be used in these situations. One of the most common associated conditions is iron deficiency, with or without anaemia. Low serum levels of iron, and particularly of ferritin, occur in a significant percentage of RLS patients, and may be the ultimate cause of the development of RLS in a given period of life. All possible causes of iron deficiency are associated with RLS, including excessive physiologic (for instance hyper menorrhea) or pathologic blood loss (f.i. from the gut or stomach), pregnancy, renal insufficiency, etc. Iron is a cofactor of tyrosine hydroxylase, an enzyme essential for the synthesis of dopamine, which is implicated in the pathogenesis of RLS. Iron deficiency also contributes to the development of augmentation, an unexpected worsening of RLS symptoms that complicates the clinical course of these patients. Adequate identification of serum iron and ferritin levels is mandatory in all patients with RLS. RLS symptoms, and particularly, periodic leg movements of sleep (PLMS) or wakefulness (PLMW) occur in patients with a diversity of conditions including neurodegenerative disorders such as Parkinson's disease, Multiple System Atrophy, Friedrich's ataxia and other ataxias, as well as narcolepsy or spinal cord injury. RLS symptoms in these situations are not essentially different from those occurring in idiopathic RLS that is a disturbing dysaesthesia in the legs, favoured by rest, improving with movement and with a clear nocturnal predominance. However in some conditions, like in spinal injury, the typical set of 4 cardinal symptoms may not be apparent. I will review the evidence in favour of these associations and the difficulties to recognize and treat RLS in those patients.

Disclosure: Nothing to disclose.

FW4-3
Treatment: current advances

C. Trenkwalder
Kassel, Germany

When non-pharmacologic treatments such as regular sleep habits, moderate physical activity in the afternoon and sensory cues with massaging and cold bath are no longer efficient for symptom relief in RLS patients, pharmacological treatment should be started. Patients should classify for moderate to severe RLS according to IRLS (International RLS Study Group Severity Scale). Dopamine agonists (DA) such as pramipexole, ropinirole and transdermal rotigotine are considered the treatment of choice and are licensed in all European countries for treating moderate to severe RLS. Pregabalin, gabapentine and its pro-drug gabapentine enacarbil (only licensed in the US) and opioids may be alternative, but currently non-licensed treatments in Europe. Evidenced based medicine and a Cochrane report on dopamine agonist in RLS classified those agents efficient drugs when used in low dosages to alleviate RLS nocturnal symptoms, improve subjective and objective QoSleep and reduce periodic limb movements in sleep (PLMS). Pramipexole has been shown effective in the first night and also improved daytime symptoms including QoL, rotigotine has been effective for all those parameters both in short-term and in a 5-year study. Few side effects such as nausea or hypotension occur with DA, rotigotine can show local site reactions of the patch. Augmentation, an increase in severity of RLS during daytime and change of circadian rhythm of RLS during dopaminergic medication is the most important long-term side effect and seems to be more pronounced when short acting DA or levodopa are given in higher dosages and in patients with lower ferritin. Pregabalin can be used in RLS patients for improving symptoms and quality of sleep and eventually for pain relief. Side effects are mostly dizziness and somnolence increasing with dosage. Long-term and comparative studies are under way. A recent trial with oxycodon/naloxone sustained release in severely affected RLS patients who failed previous treatments significantly improved RLS symptoms and QoL in a 12-week placebo controlled and maintained this effect in a 1-year open phase. Side effects were mostly gastrointestinal with constipation and nausea. Before any treatment starts, ferritin levels should be checked, as iron deficiency even without anemia may significantly increase RLS symptoms. First studies on oral and i.v. iron show beneficial effects in RLS, either when ferritin is lower than 50 ng/ml, or even independent from ferritin levels. Treatment strategies in RLS should respect the severity of RLS symptoms, any pre-treatment and tolerability. Low dosages of dopaminergic drugs and a balanced iron metabolism with high normal ferritin va.

Disclosure: During 2012/13 Dr Trenkwalder worked with/received fees by Novartis, UCB, Mundipharma, Desitin, Teva Pharma Britannia, Glaxo-Smith-Kline, Vifor Pharma, GSK, RPS Research, Desitin, Boehringer Ingelh.

Misfolded proteins in diagnosis and monitoring of neurodegenerative diseases

FW5-1
Misfolded proteins in the diagnosis of Creutzfeldt-Jakob disease

A. J. Green
Edinburgh, UK

Objective: At present there is no disease-specific pre-mortem diagnostic test for Creutzfeldt-Jakob disease (CJD). Current diagnostic criteria rely on clinical features and the results of investigations such as EEG, MRI and the presence of 14-3-3 in the cerebrospinal fluid (CSF). These tests are not specific for CJD and none are able to detect all forms of CJD. Therefore a disease-specific test that will enable earlier and more accurate diagnosis is needed.

Methods: Real-time QuIC (RT-QuIC) is a recent adaptation of QuIC in which the seeded conversion of hamster recombinant PrP into aggregates of PrPSc is monitored in real-time. Thioflavin T (ThT) is included in the reaction and binds to the aggregated PrPSc causing a change in the ThT emission spectrum which is monitored using fluorescence spectroscopy. We undertook a retrospective study of the utility of CSF RT-QuIC using 124 CSF samples from neuropathologically confirmed sporadic CJD patients and 102 control patients.

Results: RT-QuIC had a sensitivity of 91 % and a specificity of 100 %, in comparison to a sensitivity of 95 % and a specificity of 63 % for CSF 14-3-3. Clinical factors such as length of disease duration, timing of lumbar puncture during disease course and age at onset of symptoms did not influence the CSF RT-QuIC sensitivity.

Conclusions: CSF RT-QuiC is a sensitive and highly specific pre-mortem diagnostic test for sporadic CJD. It is significantly more specific than existing CSF tests such as CSF 14-3-3.

Disclosure: Nothing to disclose.

FW5-2
Misfolded proteins in Parkinson's disease

T.F. Outeiro
Göttingen, Germany

Aggregation of alpha-synuclein (ASYN) in Lewy bodies and Lewy neurites is the typical pathological hallmark of Parkinson's disease (PD) and other synucleinopathies. Furthermore, mutations in the gene encoding for ASYN are associated with familial and sporadic forms of PD, suggesting this protein plays a central role in the disease. However, the precise contribution of ASYN to neuronal dysfunction and death is unclear. There is intense debate on the nature of the toxic species of ASYN. Little is still known about the molecular determinants of oligomerization and aggregation of ASYN in the cell. In order to clarify the effects of different mutations on the propensity of ASYN to oligomerize and aggregate, we assembled a panel of 17 described ASYN mutants and compared their behavior side-by-side. Altogether, our data shed light into the molecular effects of ASYN mutations in a cellular context, and establish a common ground for the study of genetic and pharmacological modulators of the aggregation process, opening new perspectives for therapeutic intervention in PD and other synucleinopathies.

Disclosure: Nothing to disclose.

FW5-3
Misfolded proteins in Alzheimer's disease

W. Scheper
Amsterdam, The Netherlands

Many neurodegenerative disorders are characterized by the accumulation of misfolded proteins that have a strong tendency to form protein aggregates. In Alzheimer's disease (AD) aggregates of Aβ are deposited in the plaques and aggregated tau protein is found in the neurofibrillary tangles (NFTs). Misfolded proteins are very toxic to cells, in particular the smaller or oligomeric aggregates. Therefore cells have developed protein quality control mechanisms to detect, prevent and clear misfolded proteins. Accumulation of misfolded proteins in the endoplasmic reticulum (ER) leads to activation of the unfolded protein response (UPR), a protein quality control mechanism that initially protects the cell against ER stress toxicity. We have previously shown that the UPR is activated in neurons in brains of patients with Alzheimer's disease (AD) and other tauopathies very early in pathology. In this lecture the connection between the UPR and the Aβ and tau aggregates in AD will be discussed as well as its implications for diagnostics and therapy.

Our work shows that although oligomeric Aβ sensitizes cells for ER stress, it is not a very potent activator by itself. The close association of the UPR and phosphorylated tau suggests a functional connection. Here we show that activation of the UPR is not a consequence of tau phosphorylation, but that UPR activation leads to tau phosphorylation, which is initially a reversible event. This is illustrated by our data that demonstrate that the UPR is also connected with physiological and reversible tau phosphorylation in hypometabolic animal models. We propose that phosphorylation of tau is part of the adaptive UPR. We present evidence that dysfunction of the autophagy/lysosomal system contributes to the persistence of the tau phosphorylation and oligomerization. Our data are in accordance with a model where early in AD pathogenesis the adaptive UPR is activated in response to metabolic disturbances, with tau phosphorylation as part of this response. Inability to restore homeostasis, for example by dysfunction of the autophagy/lysosomal system, ultimately leads to the formation of NFTs and neuronal loss.

Disclosure: Nothing to disclose.

Frontotemporal degeneration and motor neurone disease

FW6-1
Frontotemporal degeneration in ALS—clinical variants and limits

A. C. Ludolph
Ulm, Germany

The clinical syndrome of a combination between motor neuron degeneration and severe behavioral deficits has been first documented by Otto Dornblüth in 1889 (paralytisches Irresein). In the second half of the 20th century this established knowledge has been partially forgotten. In 2006, Manuela Neumann showed that a molecular signature (TDP-43) descriptively connects both, frontotemporal degenerations and motor neuron diseases. It has recently been demonstrated (Brettschneider et al., 2013; Braak et al., 2013; Brettschneider et al., 2014) that this signature is not only capable to define the temporal characteristics of both diseases, but also shows that there is a systematic spatial relationship between the clinical syndromes of frontal and motor disease. If the disease process of ALS is clinically associated with obvious frontal impairment (<10 %) of the patients, behavioral deficits dominate the clinical picture. This is also the case in the remaining patients which show more subtle behavioral deficits; the best assessment tool is currently the ECAS showing a characteristic pattern of alterations. On the other hand, subtle impairment of word fluency is often associated with ALS, independently from bulbar motor deficits. Whether frontal deficits influence judgement of the patient remains an individual decision; according to our data such an impairment is rather rare than frequent. The knowledge of cognitive and behavioral deficits being regularly associated with ALS leads to the conclusion that they are not an exclusion criterium for the diagnosis of ALS any more. Also, a clinical staging effort of both ALS and FTD must take into account that behavioral and motor features regularly contribute to both pictures. This will have an impact on future therapeutic measures targeting initiation and progression of both dieseases, ALS and FTD.

Disclosure: Nothing to disclose.

FW6-2
FTLD and ALS: diagnosis, biomarkers and therapeutic approaches

O. Hardiman
Dublin, Ireland

Until recently, ALS has been considered a single clinical entity characterized by a pattern of progressive upper and lower motor neuron degeneration, with respiratory failure as a terminal event. Diagnosis can be challenging, and A panel of "red flags" aimed at improving recognition in the earlier stages of the disease has been described. Although cognitive and behaviour impairment have not yet fully incorporated into the existing El Escorial diagnostic criteria, the existence of extra motor involvement as a core feature of ALS is increasingly recognized. There is evidence that the degree and of progression of cognitive and behavioural impairment in ALS is not uniform, underlining the evolving recognition of ALS as a heterogenous spectrum rather than in single pathologic entity.

One of the strongest predictors of cognitive or behavourial impairment in ALS is the presence of the C9ORF72 repeat expansion, which occurs in up to 10 % of those of European extraction with ALS, providing a useful stratification parameter for phenotyping and clinical trial stratification. Other diagnostic and prognostic biomarkers are under development including "wet" technologies such as proteomics and metabolimics; neurophysiologic markers including motor unit estimations (MUNE and MUNIX), spectral EEG and magnetic encephalography, and multimodal neuroimaging including MRI and PET. New strategies to provide accurate staging of both ALS and ALSFTD are underway, including modifications of the ALS Functional Rating Scale and the Edinburgh Cognitive Assessment Screen.

Despite over40 Phase II and Phase III clinical trials, no disease modifying therapies other than riluzole have been identified. Reasons for clinical trial failure include poor trial design, inadequately stratification and the absence of reliable pharmacodynamics biomarkers. Lessons learned from previous failure have led to modifications in clinical trial design. Improved stratification and the development of new therapeutic strategies are likely to herald a new therapeutic era for ALS, FTD and related neurodegenerations. New therapeutic approaches are likely to include small molecules that interfere with protein aggregation, gene therapies targeted at specific mutations, possible targeted therapies from stem cell and induced pluripotent cell lines that support both neuronal and glial cells populations, and recent oligonucleotides based technologies that target aberrant RNA processing. There is also increasing recognition that drug development should aim at multiple targets and that disease heterogeneity will require a menu of therapeutic approaches with appropriate pharmacodynamics biomarkers.

Disclosure: Prof. Hardiman has received honoraria from Biogen Idec and Novartis. She is on advisory boards for Cytokinetics, Novartis, Biogen and Teva. She is editor-in-Chief of the Journal ALS and the Frontotemporal Degenerations.

Neurological disorders in Southern Europe

FW7-1
The neurology of Behçet's disease and familial Mediterranean fever

F. Gülsen Akman Demir
Istanbul - Capa, Turkey

Two auto-inflammatory disorders that are prevalent in the Southern Europe are Behcet's disease (BD) and familial Mediterranean fever (FMF). Although there are variable figures in terms of prevalence both disorders have been reported to be seen in up to 1–4 per 1,000 population in endemic areas. Both the disorders may occasionally affect the nervous system; however, the former is more commonly seen in the neurology practice which is called neuro-Behcet's disease. In order to be diagnosed as BD, one must have recurrent oral aphtae plus any two out of uveitis, genital ulcers, skin lesions, or positive pathergy testing. About 5–10 % of the patients with BD may show neurological involvement. The majority of these present with a brainstem-diencephalic meningoencephalitis which is usually called parenchymal neuro-Behçet's. On the other hand, about a quarter of the patients with neurological involvement present with dural sinus thrombosis; more frequently in pediatric group. Males are more commonly affected than females. If untreated recurrent attacks cause early and progressive disability. However, treatment with immunosuppressant agents, usually is successful. Treatment of relapses consist of high dose steroids; azathioprine is the first line agent to prevent further relapses. Other cytotoxic drugs such as cyclophospamide, or biological agents such as interferon alpha or anti-TNF agents may also be considered. On the other hand FMF which is also a relatively common autosomal recessive disorder in the Mediterranean basin have less clear neurological implications. It is associated with a genetic defect in the control mechanisms of inflammation, and characterized by episodes of recurrent fever and abdominal pain. Arthritis, uveitis, or skin lesions may accompany. Consistent with polyserositis attacks episodes of aseptic meningitis may rarely be seen, as well as dural sinus thrombosis and pseudotumor cerebri. Optic neuritis has been described, and inflammatory CNS diseases such as multiple sclerosis might be more commonly seen in patients with FMF; however there is much controversy in this issue. Another debatable point is the possibility of increased inflammatory response due to the genetic mutation that may worsen otherwise unrelated conditions. Colchicine is used in milder forms; recently interleukin 1 antagonists seem to be effective in colchicine resistant FMF patients.

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Neuroimaging of language

FW8-1
Imaging aphasia in stroke patients

A. B. Hillis
Baltimore, USA

The neural networks that underlie language processing are remarkably consistent across individuals and across language tasks. That is, a subset of brain regions in left perisylvian cortex and surrounding areas of cortex, as well as some deep areas, such as left thalamus, are consistently engaged in most language tasks. But focal damage to one or more of these areas or to a white matter tract connecting a few of these areas to one another produces very different patterns of language impairment. And how the brain responds to recover from a focal lesion varies across individuals and across tasks. I will illustrate different patterns of recovery from aphasia caused by focal lesions due to acute stroke. These cases will show distinct mechanisms of recovery at different time points after stroke, as well as different patterns in individuals and tasks.

Disclosure: Nothing to disclose.

FW8-2
Imaging aphasia in dementia patients

M. Filippi
Milan, Italy

Neuroimaging is contributing to the phenotypic characterization of patients with neurodegenerative dementia. The detection of distinct patterns of atrophy on structural magnetic resonance imaging (MRI) and functional abnormalities using nuclear medicine techniques has improved our ability at establishing a correct diagnosis of primary progressive aphasia (PPA), and distinguishing PPA from patients with Alzheimer's disease. Preliminary studies in genetically and pathologically proven cases of PPA have suggested that MRI-defined atrophy patterns could assist in predicting in vivo the pathological subtype of frontotemporal lobar degeneration. Novel MRI

approaches, including diffusion tensor and functional MRI, have improved our understanding of the pathophysiology of the disease, and this should lead to the identification of additional useful markers of disease progression.

Disclosure: Nothing to disclose.

Update on atypical Parkinson's disease

FW9-1
Axial and bulbar parkinsonism

A. J. Lees
London, UK

There is a type of Parkinsonism that presents usually in individuals over 60 years of age with a disturbance of gait, postural instability and speech and swallowing disorders. Some cases also have early cognitive impairment. Responsiveness to L-dopa therapy is modest or absent. Early accurate diagnosis is difficult and as with many movement disorders often hinges around the company the syndrome keeps. The most common cause is Parkinson's disease when although limb signs may be relativeld mild a sequence effect may be demonstrable on finger tapping and hyposmia present on formal smell testing. Some cases also have early visual hallucinations and posterior cortical symptoms with difficulty drawing overlapping pentagons. Falls in the first 3 years are uncommon. Vascular Parkinsonism is suggested by a history of strokes, the presence of diabetes and hypertension and multiple subcortical lacunar infarcts and subcortical white matter ischaemia on MR imaging. Most of these cases have an intact pre-synaptic dopamine system, disproporitonately severe gait disturbance and an absent response to dopa. PSP-Parkinsonism may be suggested by the presence of frontal signs, slowness of vertical saccades and hypokinesia without motor decrement on finger tapping. The response to l-dopa is variable and a few of these cases also have a jerky limb tremor. Multiple system atrophy-Parkinsonism is suggested by rapid deterioration, early falls and cardiovascular failure. Imaging is of limited use in facilitating early diagnosis but can be helpful in picking up unusual secondary causes such as brain tumours, communicating hydrocephalus, cumulative head trauma and chronic manganism.

Disclosure: The author has no conflict of interest and has received no financial support.

FW9-2
Multiple system atrophy—clinical variations and autonomic problems

Gregor K. Wenning
Innsbruck, Austria

Multiple system atrophy is a rare neurodegenerative disease manifesting with progressive autonomic failure (PAF) including NOH and urogenital symptoms, poorly levodopa responsive parkinsonism, and cerebellar ataxia. Depending on symptom predominance patients may be categorized into pure MSA-P (no ataxia), predominant MSA-P (parkinsonism more severe than ataxia), predominant MSA-C (ataxia more severe than parkinsonism) and pure MSA-C (no parkinsonism). Most patients feature PAF, a further subtype of MSA-AF has therefore been abandoned. About 50 % of MSA patients develop PAF prior to motor onset. The survival is limited but about 10 % of MSA patients with delayed onset PAF may survive 12 years or longer. Few MSA patients may exhibit familial clustering and mutations in the CoQ2 gene have recently been reported in autosomal recessive pedigrees from Japan. However, most MSA patients appear to be non-familial. The underlying pathology is characterized by oligodendroglial alpha-synuclein inclusions that are associated with selective neuronal loss including SND and OPCA. Despite increasing lab work using in vitro and in vivo MSA models none of the interventions tested so far has been successful in disease modification trials except for autologous mesenchymal stem cells that appear to hold some promise. However, more work is needed before stem cell therapy can be recommended. In the meantime, considerable efforts have been taken to establish international MSA networks (e.g. www.esma-sg.org or MODIMSA = http://www.movementdisorders.org/about/leadership/committee_details.php?content_id=1184) that will allow rapid patient recruitment once feasible and effective therapies become available.

Disclosure: Nothing to disclose.

FW9-3
Therapeutic strategies for atypical parkinsonian conditions

J. J. Coutinho Ferreira
Lisbon, Portugal

Atypical parkinsonian syndromes comprise a heterogeneous group of disorders including multiple system atrophy (MSA), dementia with Lewy bodies (DLB), progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD). They correspond to rare and chronically debilitating conditions with limited response to dopaminergic and other antiparkinsonian medications. Although there have been advances in the genetics, molecular biology and neuroimaging of these disorders, efficacious treatments are still missing. The number of clinical trials based on disease-specific targets has increased in recent years, but results are disappointing, inconclusive or limited by the occurrence of adverse effects. A different therapeutic approach is to try to treat the most relevant signs and symptoms present in the phenotypical spectrum of atypical parkinsonian conditions. These include problems like postural instability, falls, cognitive deficit, orthostatic hypotension and urinary problems. Rehabilitation interventions are also being studied for the treatment of these clinical problems. Current therapeutic approaches are mainly extrapolated from studies and clinical use in Parkinson's disease patients.

Disclosure: Nothing to disclose.

Ischaemic stroke: a thrombo-inflammatory disorder?

FW10-1
Are platelet-immune cell interactions involved in reperfusion injury?

G. Stoll
Würzburg, Germany

Thrombolysis is the only approved therapeutic option in acute ischemic stroke. Patients may, however, develop progressive stroke despite sustained early reperfusion of previously occluded major intracranial arteries, a process referred to as "reperfusion injury". In the transient middle cerebral artery occlusion (tMCAO) model in mice, interference with early steps of platelet adhesion/activation by inhibition of the von Willebrand factor (vWF) receptor glycoprotein (GP) Ib, its ligand vWF, or the collagen receptor GPVI profoundly

limited infarct development. Although these findings strongly suggested that microvascular thrombus formation is the leading pathophysiological event in acute stroke, recent studies have shown that these molecules have the additional capacity to guide inflammatory processes, thereby providing an intriguing alternative mechanistic explanation for these observations. Accordingly, mice lacking T cells are also protected from acute stroke. T cell effects are antigen-independent, involve an unexpected detrimental Treg function and depend on the presence of platelets. Thus, acute ischemic stroke can be redefined as a thrombo-inflammatory disorder, and multifunctional molecules such as GPIb may provide new therapeutic targets linking inflammation and thrombus formation.

Disclosure: Our work was supported by the Deutsche Forschungsgemeinschaft (Bonn, Germany) SFB 688/B1. There are no relations to the pharmaceutical industry concerning the data covered in this talk.

FW10-2
The impact of delayed neuroinflammation to stroke outcome

Xabier Urra
Barcelona, Spain

Objectives: This lecture will focus on the deleterious and beneficial aspects of inflammation in stroke.

Methods: Critical review of the literature and recent data from ongoing unpublished experimental and clinical studies.

Results: Early after stroke sensors of the innate immune system are activated by brain ischaemia and tissue damage, leading to amplification of the inflammatory cascade. Later, activation of the adaptive arm of the immune system can also lead to deleterious antigen-specific autoreactive responses. The inflammatory response after stroke can build on top of chronic immune activation arising from systemic infections and inflammatory conditions that can hamper or boost endogenous repair mechanisms. While several anti-inflammatory strategies that have been effective for recovery in experimental stroke, none of them have been succesfully translated to clinical practice. Ongoing studies are exploring the effectiveness of different strategies to avoid the negative impact of inflammation including the use of inhibitors of the innate immune system, blocking specific leukocyte subtypes, inducing tolerance to neural antigens and administering stem cells as a source of trophic molecules to minimize damage and promote recovery.

Conclusions: Recent clinical and experimental studies have highlighted the complex interactions between the immune system and the central nervous system after stroke. A better knowledge of the beneficial and the deleterious aspects of autoimmunity and inflammation is needed in order to find effective immunomodulatory treatments for stroke.

Disclosure: Nothing to disclose.

FW10-3
Systemic effects of strokes on the immune system

A. Meisel
Berlin, Germany

In the acute course of the disease, stroke patients often develop bacterial infections, such as pneumonia. Clinical risk factors, such as dysphagia and unconsciousness are considered as the main causes of pneumonia by increasing the risk of aspiration. However, despite improved stroke care post-stroke infections remain an unsolved issue increasing morbidity and mortality of stroke patients. Over the last decade the concept of CNS-injury induced immunodeficiency syndrome (CIDS) has been established based on experimental and clinical findings. The crosstalk between CNS and immune system is mediated mainly by the autonomic nervous system. Stroke induces a hyperactivation of neuroendocrine stress pathways including the sympathetic nervous system and the hypothalamic–pituitary–adrenal axis leading to a rapid and long-lasting systemic suppression of cell-mediated immune responses within the first days after stroke onset increasing the susceptibility to bacterial infections. In particular, lymphopenia and lymphocytic dysfunction has been demonstrated to be essential causes of post-stroke infections. However, the first line of antibacterial defense is organized by cells of the innate immunity such as macrophages. The cholinergic anti-inflammatory reflex controls cells of the innate immunity. Acting as an adaptive response the cholinergic anti-inflammatory reflex prevents the organism from a potentially harmful excessing systemic inflammatory response to a local inflammatory challenge. Stroke might interfere with this tightly regulated mechanism via hyperactivation of the parasympathetic nervous system, thereby breaking down the antibacterial host-defense in lung causing post-stroke pneumonia. The local immune response in the lung is impaired via stimulation of the vagus nerve activating $\alpha 7$ nicotinergic acetylcholine receptors of alveolar macrophages and epithelial cells. Unraveling the underlying mechanisms of CIDS enables us to identify novel molecular targets for immunomodulation in order to prevent post-stroke infections. Moreover, novel immune markers identify patients at risk for post-stroke infections allowing a tailored preventive antiinfective treatment in order to improve stroke outcome.

Disclosure: Andreas Meisel is one of the inventors for a patent application on antiinfective agents and immunomodulators used for preventative therapy after an acute cerebrovascular accident, which has been filed to the European Patent Office (PCT/EP03/02246): patent owner Charite Universitaetsmedizin Berlin.

Impact of technology in neurorehabilitation of stroke and spinal cord injured subjects

FW11-1
Technology for enhancement of motor function in SCI-facts

R. Rupp
Heidelberg, Germany

Technology plays an important role in the rehabilitation of patients with impairments of the lower extremity due to disease or trauma of the central nervous system. The loss of mobility has devastating effects on the quality of life of the affected persons and their ability to remain independent in the community. In gait rehabilitation compensatory or restorative strategies are applied depending on the time after trauma and the level of impairment. Over the last 20 years advances in the understanding of the intrinsic capacity of the central nervous system for plasticity and recovery led to the establishment of task-oriented restorative therapies, first of all body weight supported treadmill training either manually assisted or with robotic devices. Although robotic therapies have not been shown to be superior to manual training regimes, therapists have been relieved from the exhaustive work of assisting the stepping movements. At this point, locomotion robots provide advanced therapeutic options such as intensive gait training at home and qualitative improvement of the training through the integration of real-time feedback including virtual reality. The effectiveness of robotic locomotion systems will only improve by consequent implementation of principles of motor

learning. For enhancement of mobility in individuals with severe sensorimotor impairment of the lower extremities compensatory strategies including the implementation of wheelchairs and more recently active exoskeletons need to be considered. Whether exoskeletons may represent an alternative to the cost-effective, efficient and socially accepted wheelchair needs be demonstrated. In general, more comparable clinical trials are needed to provide an objective basis, whether technology driven innovations in the field of neurorehabilitation are capable to outperform conventional approaches.

Disclosure: I am one of the patent holders of the locomotion robot "MoreGait" for home-based locomotion therapy, which will be part of my presentation.

FW11-2
Monitoring daily-life physical interaction with the environment after stroke

Peter Veltink
Enschede, The Netherlands

Objectives: Stroke is associated with impaired motor control, affecting performance of both upper and lower extremities. During rehabilitation, motor control is trained in order to prepare stroke survivors for their return to daily-life. The goal of rehabilitation is to optimize daily-life functional motor performance, however, in the clinical setting only motor capacity is evaluated. It is the objective of the EU project INTERACTION (FP7-ICT-2011-7-287351) to monitor the quality of motor performance of stroke survivors during daily-life.

Methods: A textile-integrated sensing system and measures to characterize the quality of performance of reaching and grasping as well as mobility during daily-life were developed. Both were evaluated in structured clinical experiments preceding daily-life evaluation in the final phase of the project. Currently, nine of a planned total of twenty individuals with a history of stroke have been included.

Results: While performing ADL tasks, the mean Center of Pressure shifted more to the non-affected side than during a 10 meter walk test and the subjects used their affected arm much less than they were able to according to their measured capacity. The asymmetry in gait and arm use during ADL tasks did not consistently correspond to the scores of standard clinical tests like the Berg Balance Scale and Fugl Meyer assessment.

Conclusions: Performance of daily-life ADL tasks may not correspond to clinically assessed motor capacity. This supports the need for assessment of the quality of motor performance during daily-life in stroke survivors.

Disclosure: Nothing to disclose.

FW11-3
Physiological requirements for the application of robots in neurorehabilitation

V. Dietz
Zurich, Switzerland

Impact of technology in neurorehabilitation of people with stroke and spinal cord injury There is an increasing impact of technology in the neurorehabilitation of people with stroke and spinal cord injury. This technology comprises robotic devices to support paretic limb movements, prostheses and ortheses. The advantages of these technologies, e.g. longer training times and standardized but individually adapted training and the limits will be discussed. However, also the challenges of neurorehabilitation technology will be discussed. A focus will be the basic physiological requirements and the need for an interaction between therapists, medical staff and engineers for an effective application of technology. The technology to assess and monitor the changes of movement disorders over the course of rehabilitation will be included.

Disclosure: Nothing to disclose.

New generation genetic techniques change diagnostic approach in clinical practice

FW12-1
Fundaments and clinical applications of next generation sequencing technologies

P. Nürnberg
Cologne, Germany

Next generation sequencing is a novel approach to sequence millions of different DNA fragments simultaneously thereby obtaining an unprecedented amount of information in a single experiment. In 2005 the first instrument from Roche 454 was heralded as a major breakthrough in sequencing technology with its capability of sequencing a complete bacterial genome of 20 Mb per run. Today's standard device is the HiSeq 2500 from Illumina with a capacity of 1 Tb per run, which is equivalent to 10 human genomes at 30× coverage. Although whole genome sequencing is feasible and has already been used in clinical settings, budget restrictions and challenges in data management still prevent a broader use. Instead of that, many clinical researchers focus on the 50–70 Mb in the genome that contain the information of the 25,000 genes, the so-called "exome". The need for enrichment of that part of the genome prior to sequencing may raise some additional problems but this is by far compensated through the reduction of computational load and data storage needs as well as the ease of data interpretation. The Cologne Center for Genomics has established a highly productive exome sequencing pipeline to assist clinicians in identifying the causal variants of genetically determined diseases. The heart of this pipeline is VARBANK (https://varbank.ccg.uni-koeln.de), which has been developed in cooperation with the Regional Computing Center Cologne. A major part of it is implemented on a 100 Tflop/s HPC-system. VARBANK combines state-of-the-art software to analyse the full spectrum of variants, including structural variants, with an easy-to-use graphical interface. VARBANK includes a database with tools for browsing, filtering and rating of variants. Features for copy number analysis, easy detection of de novo variants in parent-offspring trios, kinship/linkage analysis, gene coverage visualisation, and mutation burden analysis of particular genes are implemented. When developing VARBANK, we had users in mind, without great skills in bioinformatics, who work in a clinical environment and want to have full control over and permanent access to their genomic variant data that they may easily and selectively share with their colleagues. Thus, VARBANK has become a versatile platform for data analysis, interpretation, and sharing, with a high potential to be useful for diagnostic purposes in a clinical setting.

Disclosure: Nothing to disclose.

FW12-2
Examples of targeted and whole exome NGS in neurological practice

María-Jesús Sobrido
Santiago de Compostela, Spain

Next-generation sequencing (NGS) is a diagnostic tool that will dramatically transform clinical neurology. The power of NGS resides in the ability to perform fast, parallel analysis of many genes, avoiding a time-consuming, gene-by-gene query for the cause of a patienťs disease. Genomic technologies will have a special impact on the practice of neurology, where confronting symptoms that could be due to several dozen different causes is an everyday situation. Through whole exome sequencing (WES) the coding regions of all genes are analyzed, whereas targeted sequencing (TGS) implies that a given set of genes are simultaneously screened (e.g. the genes known to cause epilepsy). Whole genome sequencing (WGS) includes analysis of the coding and non-coding regions of an individual's genome. The results delivered by NGS laboratories are long lists of genetic variants present in a given person, i.e. nucleotide positions different from a reference sequence. These variants are then subject to bioinformatics algorithms and filtering criteria in light of the question being asked. High throughput genomic technologies have demonstrated their potential leading to an exponential knowledge of genes involved in human diseases. However in our experience, clinical interpretation and communication of NGS results remain the challenging steps in order to turn genomic information into best-practice decisions for the patients. As sequencing platforms and analysis pipelines improve, protocols are being developed to suit almost any customized diagnostic need. In this lecture we will present practical cases on how both WES and target gene sequencing can help us answer clinically relevant questions. The examples provided in this workshop will also serve as practical illustration of some medical and ethical issues that will have to be confronted as neurogenomics enters the clinic.

Disclosure: The author received consultation fees in a private Neurology practice. She is a shareholder in Genomic Consulting, a company related to the application of genomics in Medicine. Her research group received funding from Actelion Pharmaceuticals for research on genetics of rare neurological diseases.

FW12-3
Ethical and legal considerations of NGS and genetic databases for neuropsychiatric diseases

K. Melham
Oxford, UK

This talk addresses core ethical, legal and social (ESLI) issues that arise in the use of NGS and genetic databases in clinical practice. Delving more deeply into the usual—and still necessary—considerations of consent, withdrawal, privacy, feedback, benefit sharing and governance, the talk attends to the particular issues raised by the intersection of new sequencing technologies and genetic databases with the regulatory oversight of medical research. Implications for translation into clinical practice will be illustrated through practical examples. While not claiming exceptional status for either, I will argue that both NGS and genetic databases represent specific instances where the established ethical norms and practice of medical research may not be fit for emerging purposes. From the fiction of anonymity to the conflation of requirements for secondary use of data with those for invasive or interventional research, this talk assesses the ethical, legal and social requirements – and possibilities – of NGS and databases for genetic research, and explores how to handle the challenge of translation to clinical diagnostics.

Disclosure: Nothing to disclose.

Neuromyelitis optica (NMO) today

FW13-1
Pathology and pathogenesis

H. Lassmann
Vienna, Austria

Objectives: Although the association between neuromyelitis optica and auto-antibodies against aquaporin 4 is now well established, the mechanisms of lesions formation in the nervous system are so far incompletely understood. Pathological analysis of NMO lesions may offer some answers.

Methods: We performed a systematic neuropathological study on archival autopsy material from NMO patients, focusing on aspects of inflammation and tissue injury.

Results: We found profound inflammation by T-lymphocytes in early stages of NMO lesions. T-cell numbers were higher and their activation status increased in comparison to those seen in early lesions of acute multiple sclerosis. Regarding tissue injury different patterns were found, which included active astrocyte destruction by antibody and complement in the presence of granulocytes, primary astrocyte clasmatodendrosis in the absence of complement activation, as well as primary demyelination with relative preservation of astrocytes and axons.

Conclusions: Our data suggest that T-cell mediated inflammation plays a major role in initiating NMO lesions and that different immunological mechanisms lead to tissue injury even within different lesions of the same patient.

Disclosure: Nothing to disclose.

FW13-2
Diagnosis

Maria Assunta Rocca
Milan, Italy

Neuromyelitis optica (NMO) is a severe autoimmune inflammatory disorder of the central nervous system. Clinically, NMO is commonly characterized by recurrent optic neuritis and transverse myelitis. Historically considered a variant of multiple sclerosis (MS), after the identification in 2004 of a serological marker of NMO, the acquaporin-4 antibody (AQP4-Ab), or NMO-IgG, (Lennon, Wingerchuk et al. 2004) great improvement has been made in the understanding of the pathophysiological mechanisms of the disease, diagnostic work-up, and definition of the clinical spectrum and treatments. The previous clinical and laboratory findings have been included in the 2006 Revised Criteria for the diagnosis of NMO (Wingerchuk, Lennon et al. 2006). Most of NMO patients are seropositive for NMO-IgG which specifically targets AQP4. More recently, it has been discovered that some AQP4-Ab seronegative patients are characterized by the presence of antibodies against myelin oligodendrocyte glycoprotein (MOG-Abs) (Kitley, Waters et al. 2014). NMO patients generally show typical MRI findings, including the presence of contiguous spinal cord lesions extending over $\geq$3 vertebral segments, which may be hypointense on T1-weighted sequences and associated to varying degrees of Gd-enhancement and brain MRI not meeting diagnostic criteria for MS (Miller, Weinshenker et al. 2008) (Charil, Yousry et al. 2006; Miller, Weinshenker et al. 2008). These imaging features might help in the diagnostic work-up of NMO and they have also

been formally included in the 2006 Revised Criteria for NMO (Wingerchuk, Lennon et al. 2006). The majority of NMO patients has a normal brain MRI or only a few and non-specific T2-hyperintensities that may have a predilection for regions with a high expression of AQP4. These include lesions around the third and fourth ventricles in the hypothalamus and area postrema and surrounding the aqueduct of Sylvius. Lesions in the area postrema at the floor of the fourth ventricle are thought to be responsible for the characteristic prodrome of vomiting and hiccups that occurs in around 10 % of NMO patients at first presentation. However, such lesions in AQP4-rich regions only occur in between 5 and 10 % of patients. Other brain abnormalities seen in NMO include brainstem lesions, particularly of the centrodorsal medulla and the pons, and large, even tumefactive, hemispheric lesions. Advanced MRI techniques have been also applied in NMO, including magnetization transfer (MT) MRI and diffusion tensor (DT) MRI. MT MRI studies have suggested that this technique can contribute to distinguish patients with NMO from those with MS, since focal T2 lesion of the brain (whenever present) have higher MT ratio values in NMO than in MS patients (Filippi, Rocca et al. 1999), and, differently from MS, NMO patients have no abnormalities in the normal-appearing brain tissue (Filippi, Rocca et al. 1999). Conversely, cervical cord damage, quantified using MT MRI, is similar in NMO and MS patients (Filippi, Rocca et al. 1999). However, a DT MRI study disclosed more severe cervical cord damage in NMO than in MS patients (Benedetti, Valsasina et al. 2006). The assessment of brain normal-appearing white matter (NAWM) and gray matter (GM) damage in NMO patients gave conflicting Results: some authors found an isolated involvement of the GM (Rocca, Agosta et al. 2004), and others described an involvement of several WM tracts (Liu, Duan et al. 2012), which was more severe in the optic radiations and corticospinal tracts (Zhao, Zhou et al. 2012). As it is the case for MS patients, an increased recruitment of several cortical and subcortical areas has been also shown to occur in NMO patients using functional MRI and simple motor tasks (Rocca, Agosta et al. 2004). This lecture will discuss the actual challenges and more recent advances reached for the diagnosis of NMO and NMO-spectrum disorders, focusing the attention laboratory and MRI features that might improve our ability to correctly diagnose the disease.

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Disclosure: Nothing to disclose.

Biomarkers in neuroimmunology

FW14-1

Biomarkers in inflammatory demyelinating CNS disease

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Istanbul, Turkey

The research on biomarkers in inflammatory demyelinating central nervous system (CNS) diseases is very active. Although, the availability of banked biospecimens and new research technologies have increased the number of biomarker studies, very few biomarkers have been validated in inflammatory demyelinating CNS diseases. Because of the heterogeneity of this group of diseases, it is not easy to define an ideal biomarker which will be both predictive, diagnostic and prognostic.

Multiple sclerosis (MS) is the most common clinical form of inflammatory demyelinating CNS diseases. The pathogenesis of MS is complex. In addition, the clinical course of disease and response to treatment vary from patient to patient. The heterogeneity of MS presents a challenge to neurologists and increases the need for biomarker to guide them. Cerebrospinal fluid (CSF) might be a better biologic material to reveal the ongoing pathologic processes occurring in the brain and spinal cord. Because CSF is obtained by a lumbar puncture which is an invasive procedure, the collection of CSF is limited. Oligoclonal immunoglobulin G (IgG) bands and quantitative intrathecal Ig G synthesis in CSF are the most frequently used CSF biomarkers in MS. The presence of CSF oligoclonal bands or an increased Ig G index verifies evidence of an abnormal intrathecal B cell response. Cerebrospinal fluid oligoclonal bands are also found to be related with the risk of conversion to clinically definite MS.

Neuromyelitis optica (NMO) is an autoimmune inflammatory disease with predilection for the optic nerves and spinal cord. In 2004, Lennon and colleagues identified a highly specific autoantibody biomarker in the serum of NMO patients. The target antigen of NMO-Ig G was the astrocytic water channel aquaporin-4 which is the predominant water channel in CNS. This antibody was included in the diagnostic criteria of NMO and became the first useful diagnostic biomarker for distinction between patients with NMO and classical MS.

Disclosure: Nothing to disclose.

FW14-2

Biomarkers in neurodegenerative disease

Axel Petzold
London, UK

Objectives: Biomarkers provide information on diagnosis, prognosis and treatment effect in neurodegenerative diseases. Biomarkers are of interest to sponsors of drug trials because of their value as a high throughput outcome measure and as safety markers.

Methods: Methods used to study biomarkers rely on laboratory, imaging and electrophysiological techniques. These techniques provide complimentary information on structural integrity and function of the central nervous system.

Results: the prognostic value of a number of biological markers has been investigated. For clinicians relevant pre-analytical and analytical pitfalls will be reviewed in view of the results of multi centre validation studied. The prognostic information gained by

biomarkers for neurodegeneration will depend on the timing of sampling and pattern of the disease course.

Conclusions: it seems most unlikely that one single biomarker will fit all purposes. Therefore future longitudinal studies will need to make use of the synergistic value of biomarkers relying on different techniques. In order to convincingly show the benefit of a new treatment strategy, the effect needs to be demonstrated by more than one biomarker method.

Disclosure: Named inventor on patent WO/2012/005588.

FW14-3
Biomarkers in paraneoplastic syndromes

J. Honnorat
Lyon, France

Recently, a revised classification of paraneoplastic neurological syndromes (PNS) has been proposed according the associated biomarkers. PNS classification is not based anymore on the neurological symptoms or on the underlying tumor, but on the associated circulating autoantibodies and on the location of the targeted antigens. Indeed, evolution, response to treatment, and pathophysiology are radically different according to the associated autoantibodies. In some patients with autoantibodies targeting cell-surface antigens (NMDAR, AMPAR, GABABR, GABAAR, Lgi1, CASPR2, DNER, DPPX…), humoral immunity seems to play a direct role and a dramatic improvement is observed with immunomodulator treatments. In these patients, an associated tumor is less frequent. Conversely, patients with autoantibodies directed against intra-cellular targets (Hu, Yo, CV2/CRMP5, Ri…) are, in most cases, characterized by a high degree of irreversible neuronal death mediated by cytotoxic T-cells and do not improve after immunomodulator treatments. In these patients, an associated tumor is highly frequent and must be cured as soon as possible. A third group of patients can be identified with anti-GAD65 and anti-Amphiphysin antibodies. In patients with these autoantibodies, the efficiency of immunomodulator treatments is less clear as well as the type of immune response that could be a mix between humoral and cellular. In this last group, the antigen is intracellular, but patients may improve with immunomodulator treatments and associated tumors are rare. Thus, identification of associated autoantibodies should be prompt and the treatment guided according the identified autoantibody.

Disclosure: Nothing to disclose.

Nerve and muscle imaging

FW15-1
Ultrasound in entrapment and inflammatory neuropathies

E. Wilder-Smith
Singapore, Singapore

Objectives: To present the evidence surrounding the use of peripheral nerve ultrasound (US) in the detection of nerve entrapments and inflammatory neuropathies.

Methods: The literature and own experience in using US for the detection of nerve entrapments and inflammatory neuropathies is presented. Carpal tunnel syndrome (CTS), ulnar neuropathy at the elbow (UNE), peroneal neuropathy at the fibular head (PNF), radial nerve entrapment (RNE), meralgia paresthetica (MP), Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), multifocal motor neuropathy (MMN) and vasculitic neuropathy (VN) are considered.

Results: The composite sensitivity and specificity of ultrasound in the diagnosis of CTS are around 75 % and 85 % respectively. Some studies suggest including several sites of nerve enlargement and nerve vascularity further increases the usefulness of US. Personal experience suggests a significant role of US in the post-operative assessment of CTS. The US diagnosis of UNE ranges around 80 % sensitivity and 91 % specificity but needs more carefully designed studies taking into consideration the heterogenous nature of the condition. Diagnosis of PNF shows US sensitivity of 90 % and specificity of 69 % but importantly reveals 5 % due to intraneural ganglion cysts. Information on the sensitivity and specificity of RNE and MP is still sparse but suggests high usefulness.

The utility of US for the diagnosis of Guillain-Barré is not established. In CIDP, studies report sensitivity between 69 and 86 % when using multifocal nerve enlargement. A recent review suggests that when nerves are more extensively studied, nerves in CIDP are rarely normal. Conduction block has been shown associated with focal nerve swelling. Currently no data on US and disease prognosis exists. Studies in MMN reported around 90 % enlarged nerves outside typical entrapment sites, frequently at cervical plexus and root level. Several studies emphasize that the supplementary information on multifocal nerve enlargement in vasculitic neuropathy, may improve sampling of nerve biopsies.

Conclusions: Peripheral nerve ultrasound is a rapidly emerging tool for the assessment of the peripheral nervous system increasing the armamentarium of diagnostic tests available to the clinician.

Disclosure: Nothing to disclose.

FW15-2
MRI imaging of peripheral nerves

Martin Bendszus
Heidelberg, Germany

The diagnostic work-up of peripheral neuropathies largely depends on clinical and neurophysiological investigations. Recently, progress in magnetic resonance imaging (MRI) has led to new perspectives in the diagnostics of disorders of the peripheral nervous system (PNS). Experimental data show how MR neurography visualises axonal and demyelinating lesions of the PNS, and additionally may demonstrate denervation of the affected muscle. In clinical use, difficult cases of focal nerve compression, traumatic or inflammatory lesions can be solved by the combination of MR neurography and neurophysiology. In particular, the localisation of nerve lesions can precisely be determined by high-resolution MR techniques, redefining previously described compression neuropathies. Furthermore, MR neurography enables new insights in the pathophysiology of neuropathies, as for instance in for diabetic polyneuropathy or hereditary disorders like neurofibromatosis or amyloidosis. Finally, new functional techniques as diffusion tensor imaging (DTI) or peripheral nerve perfusion measurements shed new light on the pathophysiology of peripheral nerve disorders. In this overview, the basis for imaging findings in MR-neurography will be highlighted and relevant clinical results will be summarized. Moreover, a perspective of future techniques and applications of MR-neurography will be presented.

Disclosure: Nothing to disclose.

FW15-3
Muscle imaging in myopathies

B. Udd
Tampere, Finland

Muscle imaging is an important tool for the diagnosis and assessment of patients with myopathies and other neuromuscular disorders. The regular use of muscle MRI in clinical practice will help to provide more patients with a specific diagnosis and to accelerate the diagnostic process including the optimal choice for muscle biopsy. Algorithms of collated MRI data to define typical patterns of muscle involvement and the spectrum of pathology are already underway and continuously expanding. An all-European COST Action has also started to facilitate collaboration between clinical neuromuscular experts, radiologists, MRI physicists and computer vision specialists in order to provide web-based collections of muscle patterns of involvement to be used in the differential diagnostics. Because the value of muscle imaging for the diagnosis and assessment of neuromuscular patients has only recently been appreciated there is a shortage of trained radiologists to apply and further develop muscle imaging techniques. This means that, at present, the clinicians in neuromuscular clinics need to adopt a certain level of knowledge and understanding of the imaging results themselves to be used in the diagnostic work-up.

Disclosure: Nothing to disclose.

Narcolepsy update

FW16-1
What is the cause of narcolepsy?

Y. Dauvilliers
Montpellier, France

Narcolepsy with cataplexy is a disabling orphan disorder caused by a loss of hypothalamic hypocretin/orexin producing neurons. Recent advances in the identification of susceptibility genes and environmental exposures provide strong support that narcolepsy may be considered as an immune-mediated disease. A tight association has long been reported with the Human Leukocyte Antigen (HLA) DRB1*1501-DQB1*0602 haplotype with more recent associations with T-cell receptor alpha, purinergic receptor P2RY11 polymorphisms, Cathepsin H and Tumor necrosis factor (ligand) superfamily member 4. All these findings underline the importance of antigen presentation by HLA Class II to T cells in the pathophysiology of narcolepsy. Environmental factors may also be involved in NC, with streptococcus infections being frequently reported at disease onset with high titers of anti-streptolysin O. An association between H1N1 vaccination (mostly represented by Pandemrix®), and narcolepsy has been recently reported in children and adults, results that reinforce the hypothesis of an underlying autoimmune process in narcolepsy. However, unlike most of other autoimmune diseases, no antibodies against either nuclear proteins or hypocretin neurons have been reported in narcolepsy, but elevated Tribbles homolog 2 antibodies have been detected in some patients, close to disease onset. Intrathecal synthesis of immunoglobulins is rarely found and autopsy studies failed to report any T lymphocytes infiltration or increased HLA Class II expression in the hypothalamus in narcolepsy. However, the low sample size and the long time period between the disease onset and the study prevents any conclusion on the immune mechanisms involved in hypocretin-deficient narcolepsy. Significant decreased pro/anti-inflammatory cytokine profiles in serum and CSF were recently reported in narcolepsy, together with a Th2/Th1 serum cytokine secretion imbalance. Consistent with this finding and despite some controversies regarding efficacy of intravenous IgG in narcolepsy, we reported its positive effect to normalize both symptoms and CSF hypocretin-1 level in a single patient with narcolepsy.

Disclosure: Y. Dauvilliers has received funds for speaking and board engagements with UCB, Cephalon, Jazz, and Bioprojet.

FW16-2
Narcolepsy in children

Sona Nevsimalová
Prague, Czech Republic

Childhood narcolepsy has some specific features. Daytime sleep attacks are longer than in adults, and accompanied sometimes by sleep drunkenness. Muscle atonia in cataplectic attacks can be partial and expressed, in the youngest children, predominantly in facial muscles. Cataplexy, however, can be delayed for weeks, months, even years. Besides, hypnagogic hallucinations and sleep paralysis are difficult to diagnose in the youngest children. Narcolepsy–cataplexy is frequently marked by obesity, in some cases even by precocious puberty. In the most cases, pubertal age predisposes to the appearance of clinical symptoms, and often accounts for poor school performance. Personality and behavioral changes, frequently accompanied by depression, take share in the affected childreńs decreased quality of life.

Apart from clinical symptoms, multiple sleep latency test (MSLT) is the most important diagnostic tool in school children. Shorter mean sleep latency and higher sleep onset rapid eye movements (SOREMs) have been found at the beginning of the disease. Hypocretin deficiency is the best predictor of cataplexy developing later in life. Neuroimaging methods should exclude secondary (symptomatic) cases, particularly if cataplexy predominates. Treatment and management of pediatric cases should start as soon as possible, however, most of the medication used in adulthood is off label in childhood.

Narcolepsy in children long used to be an often undetected and underdiagnosed disease. However, the H1N1 Pandemrix experience contributed to our better recognition and earlier diagnosis, and facilitated our understanding of the autoimmune mechanisms of the disease.

Disclosure: Nothing to disclose.

FW16-3
Narcolepsy and other sleep disorders

J. Mathis
Bern, Switzerland

Narcolepsy-Cataplexy (NC) has been characterized by the tetrad of excessive daytime sleepiness (EDS), cataplexy, sleep paralysis and hypnagonic or hypnopompic hallucinations, later extended to a pentad, including also paradoxical insomnia. Since not all symptoms are present in the individual patient, narcolepsy may present in variable pleomorphic clinical pictures, leading to misdiagnosis. In the diagnostic process, the important differential diagnosis, particularly against idiopathic hypersomnia and non-organic hypersomnia must always parallel considerations on co-morbidities. The most prevalent co-morbidities are obstructive sleep apnea syndrome (OSAS), periodic limb movements (PLMS) and REM sleep behavior disorder (RBD), and at least one of these co-morbidities may appear in 40–80 % of narcoleptics, increasing with age. OSAS can be observed in about 10–30 % of narcolepsy patients, and in some of them the narcolepsy diagnosis was missed for many years. Since CPAP treatment in these patients is often not successful, a reconsideration of alternative causes is mandatory in residual EDS under CPAP (RES).

A PLMS index 15/h was found in up to 40 % of NC patients above the age of 40 years, but only 10 % of narcoleptic children had a PLMS-I above 5/h. Restless-legs (RLS) was diagnosed in 15–30 % of adult narcoleptics compared to 3 % in the control group, with no difference between males and females. RBD was found in about one-third of narcoleptic patients independent of age, with a greater prevalence in NC (37 %) compared to N (15 %). Anxiety disorder including panic attacks and social phobia and symptoms of mood disorders are found in one-third of narcolepsy patients, however it remains unclear if the prevalence of formal mood disorders diagnoses—including major depression—is increased. It remains to be demonstrated if anxiety and mood symptoms are secondary to the chronic symptoms of narcolepsy, or a direct consequence of the hypocretin deficiency.

Disclosure: Nothing to disclose.

Cognition in multiple sclerosis

FW17-1
The spectrum of cognitive impairment in multiple sclerosis

D. Langdon
London, UK

Cognitive impairment has been demonstrated in all stages and subtypes of Multiple Sclerosis. Large unselected samples have shown impairment in around 50 % of participants, with slightly lower prevalence in community samples and slightly more in clinic samples. Cognitive impairment tends to be most severe in the progressive forms and later in the disease. However, cognitive impairment is not closely tied to physical impairments and in some instances is clearly dissociated, for example in "benign" MS and the rare cognitive presentation. The cognitive domain most likely to be affected is information processing speed. There is some evidence that this may underlie other cognitive deficits in MS. Memory is also commonly affected. Visual processing and executive function are less likely to be impaired. Language is usually largely intact. Cognition is affected by other symptoms. For example fatigue influences cognitive performance, although the link between objective and self-report is complex and unreliable for both symptoms. Depression also reduces cognitive abilities, especially those requiring extensive working memory capacity.

Disclosure: Not received.

FW17-2
Cognition in paediatric MS

Maria Pia Amato
Florence, Italy

Multiple sclerosis (MS) is a chronic demyelinating disease of the CNS in which cognitive dysfunction, major depression and fatigue are common. While these problems are well documented in adults with MS, they are poorly understood in children and adolescents with the disease that represent 3–5 % of the whole MS population. Children and adolescents can be particularly vulnerable to MS-related cognitive issues since the disease occurs during key periods of age-expected brain growth, active primary myelination and maturation of neural networks, moreover during the learning curve and key formative years in the academic career. It has also to be considered that disease activity (clinical and MRI) is higher than in adults with MS, while, on the other hand, brain plasticity and ability for compensation is deemed to be more efficient in this age range. Similar to their adult counterparts, pediatric patients with MS are often cognitively impaired, with estimated figures of 30 % up to 50 % of the cases. Beyond deficits of information processing speed, memory and executive functions that overlap with those described in adults with MS, one peculiar aspect in some reports is involvement of language, usually spared in the adults. Intelligence Quotient (IQ) has also been reported in children who are younger at the disease onset, suggesting a special vulnerability of this subgroup. The study of large cohorts of patients is needed in the future to clarify whether the pattern of cognitive dysfunction in this population of patients may differ reflecting different developmental trajectories and depend on different classes of age and age at disease onset. Cognitive dysfunction in children has been documented in close proximity with disease onset and may progress in the absence of any significant physical disability. Cognitive outcomes may represent a more relevant indicator of the disease in this population given their profound impact on academic performance and lifestyle. Although neurologists may not be directly involved in interventions for psychosocial issues, sensitivity to such issues is important so that appropriate referral for assessment and treatment can be made. Therefore, addressing cognitive issues beyond disease duration, relapses and physical disability appears to be of critical importance for patient counselling, rehabilitation and therapeutic decisions making. To this aim, there is a critical, unmet need for the development of valid and reliable assessment tools that can be used in everyday practice and research, with good norms that cover different classes of age.

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FW17-3
Cognition as a prognostic parameter in MS: clinical imaging evidence

B. Brochet
Bordeaux, France

Objectives: To show the evidence of the prognostic value of cognitive impairment in patients at the early stages of MS. Methods: Teaching course.

Results: Multiple sclerosis (MS) is the most frequent chronic disabling non-traumatic neurologic disease in young adults in France. Relapsing-remitting MS (RRMS) represents the most frequent phenotype of this disease. Its diagnosis is based on the demonstration of the dissemination of lesions in space and time after a first typical clinical event called clinically isolated syndrome (CIS). The 2 main objectives of this thesis were, first to investigate the prediction of an early diagnosis of MS after a typical CIS, and second to support cognitive impairment as a potential useful prognostic marker in the early stages of MS. The first article reported the results obtained in a retrospective study including a homogeneous sample of 114 patients with a spinal cord CIS. The diagnosis of MS was predicted by 3 independent factors such as $\leq$40 years of age, positive oligoclonal bands in cerebrospinal fluid or raised IgG index, and $\geq$3 periventricular lesions at the time of the CIS. In the second article, the confirmation of the validity of these 3 identified predictive factors was provided in a large prospective study including 652 patients with CIS regardless of the anatomical location of the lesions. Notably, these factors achieved the same accuracy as the dissemination in space

criteria proposed in the McDonald criteria for the prediction of the diagnosis of MS. Once a MS diagnosis is established, the main challenge is to assess the severity of the disease, and early clinical predictors of the long-term disability are still lacking. The anatomical substratum of the disability accumulated in MS appears primarily reflect cumulative axonal loss. Cognitive impairment is frequent in MS even at the early stages of the disease, and has been associated with MRI markers of diffuse brain damage. Therefore, cognitive impairment appears like an interesting candidate as a prognosis factor at the early stages of MS. In the third article, the relationship between cognitive impairment and MRI parameters reflecting early diffuse brain damage and its change within the first 2 years after MS diagnosis has been confirmed in a 7-year longitudinal study of 44 newly diagnosed RRMS patients. In the fourth article, the prediction of the progression of disability over time by cognitive impairment detected after RRMS diagnosis in this sample of patients supported the prognostic value of cognitive deficits in early MS. In the fifth article, cognitive assessment was performed in 2 clinical phenotypes of MS such as RRMS and primary progressive MS (PPMS) with different prognoses. The extent and the severity of cognitive deficits were greater in 41 PPMS than in 60 RRMS patients supporting the relationship between cognitive impairment and widespread brain damage. In the sixth article, the prognostic value of cognitive dysfunction in MS was illustrated by the negative impact of cognitive deficits on quality of life and vocational status in 48 patients living with MS followed for 7 years. Finally, as cognitive deficits had the potential to predict early disability in patients with MS which is known to be relevant to predict the long-term disability in MS, their detection appear as a priority in managing patients with MS to adapt therapeutic strategies at the early stages of the disease. Information processing speed (IPS) is the main impaired cognitive domain in MS that had clinical implications. In the seventh article, a new in-house cognitive tool called the computerised speed cognitive test was assessed to detect slowness of processing speed in a validation study using samples obtained from 101 patients with MS and 415 healthy subjects. This test was clinically relevant with an excellent reliability, ecological validity, and predictive value for detecting IPS impairment in patients with MS.

Conclusions: clinical and imaging data suggest that cognitive impairment is a prognostic market in MS.

Disclosure: Nothing to disclose.

Stroke in early life—diagnostic and therapeutic challenges

FW18-1
Stroke and mimics in children and adolescents—what is different?

Fenella Kirkham
London, UK

Stroke and cerebrovascular disorders in childhood cause significant mortality and morbidity in childhood. Many acute neurological presentations, including hemiparesis, visual loss, seizures and coma, commonly have a vascular basis which may not be obvious on CT scan so emergency MRI with MRA of the intracranial and extracranial vessels and MRV is often required to distinguish between arterial and venous mechanisms and to exclude stroke mimics such as posterior reversible encephalopathy syndrome. Advances have been made in the classification of pediatric stroke, aided by clinical and radiological recognition of patterns of injury and differential outcomes dependent on timing of stroke occurrence. Perfusion and magnetic resonance wall imaging have helped in the determination of the cause of stroke. Focal arteriopathy of childhood is a new term proposed to refine the nomenclature of childhood arteriopathy. Risk factors for childhood stroke are multifactorial, and include infection, trauma, iron deficiency and haemoglobin oxygen desaturation as well as prothrombotic conditions. However, apart from vasculopathy in the vessel supplying the infarcted territory, causality remains difficult to prove. There is a high risk for recurrence of around 10 %, with vasculopathy and multiple prothrombotic disorders being independent risk factors for second stroke, making diagnosis in the acute phase important. Aspirin to attempt to reduce the recurrence risk is appropriate in the medium term for the majority of patients with arterial ischaemic stroke. Iron and B vitamin deficiencies should be excluded or treated. It is unusual for children with anterior circulation stroke to be triaged quickly enough (<4.5 h) for thrombolysis but this may occasionally be appropriate in posterior circulation occlusion associated with coma, where the time window is longer (<12 h). Anticoagulation carries relatively low risk and may be of benefit for children with venous sinus thrombosis (acutely and when at risk subsequently) or extracranial dissection. Surgical decompression may be life-saving in ischaemic as well as haemorrhagic stroke. Prevention is now possible in conditions where there is a high risk of childhood stroke such as sickle cell disease in which it is recommended to screen for asymptomatic arteriopathy with transcranial Doppler.

Disclosure: Nothing to disclose.

FW18-2
Arteriopathic causes of paediatric stroke

K. Braun
Utrecht, The Netherlands

Cerebral arteriopathies are the underlying cause in at least half of all children with arterial ischemic stroke (AIS). Arteriopathies are diagnosed twice as often in children as in young adults.

In contrast to what is often believed, well recognized arterial wall disorders—such as moyamoya, dissection and vasculitis—only account for a minority of arteriopathic stroke syndromes in children. The most frequently diagnosed childhood arteriopathic entity is 'transient cerebral arteriopathy' (TCA), which may be diagnosed in as many as 20–30 % of children with AIS, and in 30–40 % of those who were previously healthy. TCA is a monophasic, presumably inflammatory, unilateral, intracranial disease of the distal internal carotid artery and/or its branches. It causes mainly lenticulostriatal infarction. The diagnosis requires longitudinal vascular imaging. Repeated MRA shows eventual stabilization (with a residual arterial scar), improvement, or even normalization of the arterial abnormalities. After initial evaluation in the acute stage, the arteriopathy is often labelled as FCA (focal cerebral arteriopathy) until follow-up vascular imaging has demonstrated its non-progressive time course and TCA can be diagnosed. More than 40 % of children with TCA had chickenpox within 1 year prior to stroke (so called post-varicella angiopathy, PVA).

I will present the major cerebral arteriopathies in early life, and summarize overlap and differences between arterial diseases in children and young adults. The diagnostic strategy in these patients will be discussed, as well as the contribution of genetic evaluation.

Disclosure: Nothing to disclose.

FW18-3
To treat or not to treat—therapeutic dilemmas in paediatric stroke patients

C. Amlie-Lefond
Seattle, USA

In adults, clinical trials have resulted in evidence-based acute stroke treatments that improve neurological outcome: the use of tPA and the development of dedicated stroke units that provide standardized best practice acute care. Although most adults presenting with acute stroke do not receive tPA, the presence of acute stroke programs to ensure urgent access to tPA has enabled earlier initiation of evidence-based stroke treatment, improving stroke outcomes. These strategies include acute antithrombotic treatment, supportive care, prevention of complications, secondary stroke prevention, and rehabilitative care. Following arterial ischemic stroke, 10 % of children, and over 75 % will suffer long-term neurological deficits, some of which only emerge over months and years as the brain matures. Although it is well recognized that acute childhood stroke is a serious clinical challenge, the care of children with acute stroke is frequently poorly coordinated, reflecting minimal research on which to base treatment protocols. Stroke-specific recommendations directed at maximizing cerebral perfusion, neuronal protection and salvage, and prevention of early recurrence are used inconsistently in children, and recognition of childhood stroke is often delayed, even when stroke occurs in the hospital setting. The few children receiving tPA treatment, often do so outside of established safety guidelines used in adults. In the absence of evidence-based guidelines of care, the acute care of childhood stroke is fraught with therapeutic dilemmas which involve individualized interpretation of available data and extrapolation from adult experience aiming to balance the potential treatment risks and benefits. Critical questions regarding acute management of childhood stroke will benefit from developing research in the next decade, including optimal strategies for diagnosis, neuroimaging, the role of thrombolysis and protective strategies.

Disclosure: C. Amlie-Lefond will be discussing off FDA label use of TPA but has no financial conflicts.

Reflex epilepsies: one of our hidden ways to understand epileptogenesis

FW19-1
Visually-sensitive epilepsies: diversity in clinical expression and genetic background

Dorothee Kasteleijn-Nolst-Trenite
Utrecht, The Netherlands

Objectives: Visually-sensitive epilepsies constitute the major part of reflex epilepsies: a variety of visual stimuli like flickering sunlight, artificial light, TV, computer, videogames and black and white striped patterns can induce electroencephalographic and clinical seizures. Although visually- induced seizures are seen more often in the generalised epilepsies, their diversity is nevertheless huge both clinically and electrophysiologically. Recent genetic findings do emphasize this variability.

Conclusions: This presentation will discuss and illustrate the variability in visually induced epilepsies.

Disclosure: Nothing to disclose.

FW19-2
Genetics of reflex epilepsies: possible implications for physiopathology

Pasquale Striano
Genova, Italy

Objectives : Reflex seizures and epilepsies represent an ancient human model to understand basic mechanisms of epilepsy. The possibility to reproduce seizures in laboratory, to analyze the characteristics of effective stimulus, and to study the progression of clinical signs and EEG discharges, has greatly contributed to the understanding of some basic pathophysiological mechanisms. The recognition of provocative stimuli may contribute to the management of epilepsy.

Methods : I will review the literature focusing on the current understanding of Reflex Epilepsies (RE) and relative pathogenetic implications, hence contributing to the comprehension of mechanisms of epilepsy and epileptogenesis.

Results : RE have many intriguing subtypes depending on the trigger. Visually-sensitive epilepsies constitute the major part of RE but their diversity is even huge both clinically and electrophysiologically. There are recent efforts to elucidate their genetic background. Complex forms of RE such as reading or eating epilepsy pose many different questions and there are reported cases with various symptomatic etiologies indicating some acquired factors. Furthermore an experimental mouse model resembling eating epilepsy has been developed.

Conclusions : Reflex epilepsies (RE) provoked by specific external stimuli are important clues for investigating complex mechanisms of epileptogenesis. Future technical progress will hopefully offer the opportunity for further investigating cortical areas and brain networks involved in cerebral functions and in epileptic discharges, thus contributing to the comprehension of mechanisms of epilepsy and epileptogenesis.

Disclosure: Nothing to disclose.

FW19-3
Complex forms of reflex epilepsies: clinical and experimental clues for epileptogenesis

B. Baykan
Istanbul, Turkey

Although being very rarely observed, complex forms of reflex epilepsies (CRE) are important clues for investigating mechanisms of epileptogenesis. CRE have many intriguing subtypes depending on the daily life triggers such as reading, hot water (HWE) or eating epilepsy (EE). Some of them, like HWE and EE are predominant in males and show a clear predilection for specific geographic distribution. There are reported cases with various symptomatic etiologies besides cryptogenic ones indicating some acquired factors in addition to genetic predisposition. Feeling of ictal pleasure and self-induction are major associated features in HWE, requiring further attention. Evaluation of these patients inducing their own seizures could provide clues to the mechanisms underlying reflex seizures. The reported maneuvers and conditions necessary for triggering seizures are complex and long-lasting suggesting widespread involvement of temporal as well as parietal association cortices to reach a substantial threshold. Most of the CRE are focal epilepsies and associated with complexity of the triggering events and longer latency. In a well-documented study on rats, repeated hot water stimuli were shown to have a kindling-like effect, most notably on the amygdala, which produce progressive increases in convulsive responses to stimulation. Furthermore an experimental mouse model resembling EE has been

developed, in which mice treated with scopolamine after fasting for 48 h developed clonic convulsions soon after being allowed to eat. Development of seizures in fasted mice pretreated with atropin or biperiden clearly ruled out specific convulsant effect of scopolamin and suggested that the mechanism underlying this effect could be attributable to an antagonistic activity on muscarinic receptors. This animal model which showed resistance to most of the standard anti-epileptic drugs provided further support and insight, suggesting the importance of an initial precipitating injury in EE. Similarly seizures of EE in human occurred after a silent period following initial precipitating event. Moreover most of the CRE, like reading or thinking epilepsy could be considered as models of "system epilepsy" in which seizures are the result of hyperexcitability of a network of genetic and/or acquired origin, appearing only after a stimulus specific for this network occurred. Further clinical, electrophysiological, neuroimaging studies combined with genetic and epidemiological studies are needed to enlighten the pathophysiology of CRE.

Disclosure: Nothing to disclose.

Channelopathies affecting the peripheral nervous system

FW20-1
Muscle disorders associated with channelopathies

Michael G. Hanna
London, UK

Skeletal muscle channelopathies are rare disorders of muscle membrane excitability. Their episodic nature may result in diagnostic difficulty and delays in diagnosis. Advances in diagnostic clinical electrophysiology combined with DNA-based diagnosis has improved diagnostic accuracy and efficiency. Ascribing pathogenic status to identified genetic variants in muscle channel genes may be complex and functional analysis, including molecular expression, may assist. Accurate clinical and genetic diagnosis enables genetic counselling, advice regarding prognosis and aids treatment selection. An approach to accurate and efficient diagnosis is outlined. Importance of detailed clinical evaluation including careful history, examination and family history is emphasized. The role of specialized electrodiagnostics combined with DNA testing and molecular expression is considered. New potential biomarkers including muscle MRI using MRC Centre protocols are discussed. A combined diagnostic approach using careful clinical assessment, specialized neurophysiology and DNA testing will now achieve a clear diagnosis in most patients with muscle channelopathies. An accurate diagnosis enables genetic counselling, information regarding prognosis and treatment selection. Genetic analysis often identifies new variants of uncertain significance. In this situation functional expression studies as part of a diagnostic service will enable determination of pathogenic status of novel genetic variants.

Disclosure: Not received.

FW20-2
Peripheral nerve dysfunctions associated with channelopathies

Christian Krarup
Copenhagen, Denmark

Nerve fibre function is dependent on the concerted activation and inactivation of a number of ion-channels integrated in the axolemma. In myelinated fibres, the different channels are segregated at the node of Ranvier and at the internode. The homeostasis of ion concentrations, which is perturbed in connection with action potential propagation, is furthermore dependent on various ion pumps and exchangers that maintain the axon membrane potential. Abnormalities of ion channels and pump function may cause positive or negative symptoms including cramps, paresthesia, pain, sensory loss or weakness and may eventually lead to nerve fibre degeneration. Channelopathies may be hereditary or acquired. Hereditary channelopathies are rare disorders that may affect Na^+or K^+channels and include symptoms localized to the peripheral or the central nervous system or both. Acquired disorders that affect ion channels directly by blocking or indirectly through metabolic changes are more common. Autoimmune blocking of K^+-channels in peripheral nerve is well recognized. Furthermore, changes in ion-channel distribution may have functional implications in for example chronic demyelinating neuropathies and in regenerated fibres. Studies in hereditary motor and sensory neuropathies have also shown that aberrant ion-channels usually not present at the node of Ranvier may become expressed in dysmyelinating disease causing disturbed function confirming that transcriptional changes may lead to channelopathies. Conventional nerve conduction studies are not well suited to unravel changes in function associated with ion-channel or axon membrane dysfunction. NCS may show loss, slowing or repetitive firing of fibres but do not allow insight into the individual ion-channels or the membrane potential in vivo. Complementary studies of axonal excitability have become increasingly useful in the understanding of dysfunction of nerve fibres that are still able to conduct action potentials, even though they are affected by the underlying pathogenic mechanism. These methods use threshold tracking to assess changes in membrane potential and thus gain insight into different ion-channel functions. By combining different conditioning potential changes the accommodation associated with activation of ion-channels localized at the node of Ranvier and at the internode can be assessed. In this workshop, different examples of channelopathies and the understanding that has been obtained by studies of excitability will be discussed.

Disclosure: I have received speakers honoraria from Integra LifeSciences, Corp and research support from Integra LifeSciences, Corp and Shire.

FW20-3
Neuropathic pain and autonomic function in channelopathies

R. Liguori
Bologna, Italy

Objectives: An emerging group of peripheral neurological disorders causing pain and/or dysautonomia are associated with a ligand-gated ion channels (receptors) or a voltage-gated ion channels dysfunctions. These clinical conditions are frequently genetically determined but may also be acquired through autoimmune mechanisms.

Methods: Mutations in the SCN9A gene encoding Nav1.7 have been found to cause familial pain syndromes and there is increasing evidence for the involvement of TRP channel in human pain disorder. Autoimmune channelopathies have been recognised in some forms of peripheral pain and autonomic disturbances.

Results: The discovery of mutations in the SCN9A gene have revealed a wide spectrum of clinical phenotypes and determined the aetiology of a number of clinical syndromes. Gain-of-function mutations in the SCN9A gene cause erythromelalgia, paroxysmal extreme pain disorder and idiopatic small fiber neuropathy with dysautonomia. Furthermore, the first human TRP channelopathy underlying episodic pain syndrome has recently been reported. Peripheral autonomic disturbances involving the sympathetic as well as the parasympathetic systems have been associated, in a proportion of patients, with a high level of ganglionic AchR antibodies. In

addition, anti VGKC-complex antibodies have been detected in patients complaining neuropathic pain and dysautonomia.

Conclusions: Genetic analysis of the SCN9A and TRP genes has become an important diagnostic test in the characterization of pain syndrome. Autoimmune channelopathies have expanded rapidly to include peripheral neurological disorders like pain and dysautonomia. These clinical conditions may respond well to immunotherapies, and neurological damage may be minimized if diagnosis and treatment are instituted early.

Disclosure: Nothing to disclose.

Strategies to improve the outcome of CNS infections and autoimmune encephalitis

FW21-1
Bacterial meningitis

Diederik van de Beek
Amsterdam, The Netherlands

Bacterial meningitis kills or maims about a fifth of people with the disease. Rapid diagnosis and treatment of acute community-acquired bacterial meningitis reduces mortality and neurological sequelae, but can be delayed by atypical presentation, assessment of lumbar puncture safety, and poor sensitivity of standard diagnostic microbiology. Thus, diagnostic dilemmas are common in patients with suspected acute community-acquired bacterial meningitis. History and physical examination alone are sometimes not sufficient to confirm or exclude the diagnosis. Lumbar puncture is an essential investigation, but can be delayed by brain imaging. Results of cerebrospinal fluid (CSF) examination should be interpreted carefully, because CSF abnormalities vary according to the cause, patient's age and immune status, and previous treatment. Diagnostic prediction models that use a combination of clinical findings, with or without test results, can help to distinguish acute bacterial meningitis from other causes, but these models are not infallible. The effectiveness of widely available antibiotics is threatened by global emergence of multidrug-resistant bacteria. New antibiotics, such as fluoroquinolones, could have a role in these circumstances, but clinical data to support this notion are scarce. Additionally, whether or not adjunctive anti-inflammatory therapies (e.g., dexamethasone) improve outcomes in patients with bacterial meningitis remains controversial; in resource-poor regions, where the disease burden is highest, dexamethasone is ineffective. Other adjunctive therapeutic strategies, such as glycerol, paracetamol, and induction of hypothermia, are being tested further. Therefore, bacterial meningitis is a substantial and evolving therapeutic challenge. We review the dilemmas in the diagnosis of acute community-acquired bacterial meningitis, focus on strategies to optimise antibiotic efficacy in view of increasingly drug-resistant bacteria, and discuss the role of current and future adjunctive therapies.

Disclosure: Nothing to disclose.

FW21-2
Strategies to improve the outcome of viral encephalitis

J. Sellner
Salzburg, Austria

Encephalitis refers to an inflammatory process affecting the brain. The condition is rare, the recent estimate for the UK were 5.2-8.6 cases/100.000 inhabitants per year (1). A variety of viruses can cause encephalitis and the clinical spectrum presentation is broad. Herpes simplex virus (HSV) and varicella zoster virus (VZV) are most commonly involved in sporadic disease, while in about one-third of the patients the agent cannot be identified despite extensive diagnostic efforts.

Viral encephalitis continues to be associated with unacceptably high mortality and morbidity rates (2). Strategies to improve the outcome are therefore essential. In this talk, key steps and pitfalls in the management of a patient with an encephalitic syndrome will be introduced. These include, on the one hand, preventive measures. On the other hand, earlier recognition is likely by knowledge of signs and symptoms (and exceptions) indicating a potential encephalitic syndrome. Prompt initiation of antiviral and supportive treatment is an additional measure which define prognosis. Diagnostic strategies need to be individualized and will consider geographic location, season and exposure history. Moreover, consideration and management of intracerebral and systemic complications is essential for improving the outcome. Eventually, multimodal concepts for neurorehabilitation and continuous care are mandatory to reduce the burden of neurological sequelae on the patienťs life and that of their families.

1 Granerod et al. J Emerg Infect Dis 2013;19(9). doi: 10.3201/eid1909.130064.

2 Mailles A et al. Clin Infect Dis. 2012;54(10):1455-64.

Disclosure: Nothing to disclose.

FW21-3
Autoimmune encephalitis

M. Titulaer
Barcelona, Spain

Since the 1950s some clinical and pathological descriptions of paraneoplastic neurological syndromes were published. The field was boosted in the 1980-1990s when neuronal antibodies against intracellular antigens were discovered and cytotoxic T-cell mechanisms were identified. Unfortunately, most patients had a poor prognosis.

Recently new interest arose after the identification of various disorders, both paraneoplastic, but more often non-paraneoplastic, that occur with different antibodies against cell surface or synaptic antigens. This has changed the autoimmune encephalitides beyond rare, but intriguing syndromes to more commonly recognized diseases with a broad spectrum of neuropsychiatric symptoms, affecting patients at all ages. Most importantly, these new diseases respond in general very well to immunotherapy, making them diseases not to miss.

This talk will mainly focus on anti-NMDA receptor encephalitis, the most common of these new disorders, dealing with the clinical picture, treatment and outcome. Pitfalls in diagnosis will be discussed. Other encephalitis types like anti-AMPA receptor, anti-GABA(B) receptor and the most recently discovered anti-GABA(A) receptor encephalitis will be discussed shortly. Finally, encephalitis with anti-LGI1 and anti-Caspr2-antibodies will be covered, clarifying the picture of those disorders previously attributed to antibodies against voltage-gated potassium channel (VGKC). Pitfalls and open questions of the formerly known anti-VGKC encephalitis is dealt with.

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Therapeutic approaches in neurodegeneration with brain iron accumulation (NBIA)

FW22-1

Symptomatic treatment of NBIA

Nardo Nardocci
Milan, Italy

Neurodegeneration with brain iron accumulation (NBIA) constitutes a group of genetically determined disorders with brain iron accumulation. Phenotypically, they are characterized by prominent dystonia and parkinsonism associated with cognitive and psychiatric disturbances; onset can be from early childhood to adulthood, and the course of the disease, although invariably progressive, can be very variable, even within the same disease type. The clinical and the genetic spectrum of these conditions is continuously expanding, but still in a considerable proportion of patients no genetic alteration is identified (idiopathic NBIA). NBIA due to pantothenate kinase II (PANK2) defect, also named pantothenate kinase-associated neurodegeneration (PKAN) or NBIA type I, is the most common form, accounting for approximately half of all patients with NBIA. Treating NBIA disorders is a challenging issue that requires expertise and a comprehensive approach to the patient. Conventional pharmacotherapy and surgical treatment are primarily symptomatic, aimed to reduce abnormal movements and spasticity that represent the most disabling symptoms. Systemic Treatment. Several drugs may be efficacious for dystonia including anticholinergics, baclofen, typical and atypical neuroleptics, benzodiazepines, and L-dopa. Anticholinergic drugs, such as trihexyphenidyl, are the first line of the treatment of generalized and segmental dystonia Some patients need up to 60–80 mg per day of trihexyphenidyl but may experience dose-related blurred vision, drowsiness, confusion, memory difficulty, and hallucinations. Children usually tolerate higher doses than adults. The starting dose has to be low and increased very slowly so the accurate evaluation of efficacy requires some months. Antidopaminergic drugs. Although may be beneficial in the treatment of dystonia, the potential clinical benefit is usually limited by the development of side effects, especially sedation. Dopamine-depleting drugs, such as tetrabenazine, have proven useful in some patients with dystonia. Modest improvements with levodopa have been reported in patients with secondary and degenerative dystonias and in those patients with associated parkinsonism. As an exception to this, some patients with late-onset PLAN, MPAN, and with the very recently identified form of NBIA named beta-propeller-associated neurodegeneration (BPAN) have been reported to respond well to L-dopa treatment at short- and long-term follow-up. However, they may be prone to developing L-dopa-induced dyskinesia. Benzodiazepines (diazepam, lorazepam, and clonazepam) can provide additional benefit for patients whose response to anticholinergic drugs is unsatisfactory. Spasticity is common in most patients with NBIA and may vary in severity from a subtle neurological sign to severe spasticity causing pain and orthopedic deformities. The most used antispasticity drugs are those acting on a GABAergic system such as baclofen, gabapentin, and benzodiazepines and on alpha-2 adrenergic system such as tizanidine and those that block calcium release into the muscles such as dantrolene. It is important to note that there are no evidence-based guidelines for the choice and titration of these drugs but are based on clinical experiences. Psychiatric symptoms such as aggressive behavior, depression, nervousness, and irritability have been described in PKAN patients, especially in atypical cases and may require specific intervention; drugs such as benzodiazepine, selective serotonin receptor inhibitor, and antidepressant may be useful in children and adult patients. Few cases of NBIA presenting with clear psychotic symptoms (visual and auditory hallucination, ideation, and psychomotor agitation) have been described In the reported cases, symptoms resolved with olanzapine, clozapine, aripiprazole, and risperidone, and in these patients, the use of atypical neuroleptic is recommended. Obsessive–compulsive disorder and complex tics may be prominent symptoms especially in patients with late-onset PKAN, resembling Tourette syndrome. Focal Treatment: Botulinum-toxin injections are the treatment of choice in adult-onset focal and segmental dystonia In the context of NBIA, this local treatment may be helpful in reducing the most disabling symptoms, such as the oral mandibular or cranial involvement that can be frequently seen in NBIA, particularly in patients with PKAN. Surgical treatment: Among the surgical treatments, Intrathecal baclofen infusion has been reported as effective in patients with dystonia associated with spasticity; among them, it has also been reported to be effective in several patients with NBIA. In addition, a case series recently described the use of intraventricular baclofen in patients with treatment-refractory dystonia, including one child with PKAN. This patient's dystonia improved significantly with intraventricular baclofen administration. Intraventricular delivery of baclofen is of interest because delivery at this site may better treat upper-body and facialdystonia, such as blepharospasm and oromandibular dystonia that may be particularly disabling in NBIA patients. Deep Brain Stimulation will be discussed in other report. Physical and occupational therapy is indicated, particularly for only mildly symptomatic patients. Therapies to maintain normal joint mobility for as long as possible may be useful. Speech therapy is often indicated for PKAN-related dysarthria.

Disclosure: Nothing to disclose.

FW22-2

Therapeutic approaches in neurodegeneration with brain iron accumulation (NBIA)

Deep brain stimulation in NBIA-dystonia: rationale, evidence and pitfalls

L. Timmermann
Cologne, Germany

Neurodegeneration with Brain Iron Accumulation (NBIA) describes a heterogeneous group of diseases which often manifest clinically in pronounced secondary dystonia. The massive clinical picture leads in many patients to the situation that neither Botulinumtoxine-injections nor pharmacological interventions can substantially alleviate the suffering of the mostly pediatric patients. Therefore, deep brain stimulation (DBS) turned out in first mono-centric pilot studies to be a promising treatment option. In our first international retrospective approach, we tried to collect in a larger group of patients a representative cohort of NBIA patients undergoing DBS and demonstrated moderate improvement in dystonia as well as in quality of life. We can now confirm this data using the new German Registry for Pediatric DBS; again, showing a moderate improvement in dystonia after GPI DBS. We therefore started the international prospective trial on GPi DBS in dystonia with a natural restriction in the number of included patients. However, our prospective results are also promising in the reduction of dystonia, albeit showing again a lesser effect comared to GPi-DBS in primary dystonia. In all studies the number of adverse events seems to be significantly higher than in any other patient cohort. Taken together GPi-DBS is a relatively safe and moderately successful option for pediatric patients with NBIA-associated dystonia. The core challenge for the future is to collect internationally synchronized the data of these patients to improve outcome prediction for the individual patient and his/her family.

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FW22-3
Iron chelation therapy in NBIA: state of the art

Thomas Klopstock
Munich, Germany

Objectives: Since symptomatic treatment such as deep brain stimulation and antidystonic drugs lead only to some alleviation in NBIA, there is an urgent need for a causal treatment. Intriguingly, NBIA may be feasible for a causal therapy down-stream of gene therapy as it may be possible to biochemically address the accumulation of iron in the brain by iron chelation.

Methods: Literature review and presentation of the current status of TIRCON's randomized trial of deferiprone in Pantothenate Kinase-Associated Neurodegeneration (PKAN).

Results: Iron-chelating agents have been tried in single NBIA patients back to the 1970s without clear benefit. Early trials were limited by systemic iron deficiency before any neurologic benefit might have been realized. Unlike earlier iron chelators, deferiprone crosses the blood–brain barrier and removes intracellular iron. It may therefore be effective for all NBIA subgroups. Single NBIA cases have been treated with deferiprone. Forni reported regression of symptoms and reduction of brain iron in an adult with unspecified NBIA after 8 months. Pratini reported a patient with classic PKAN who had sustained improvement of dystonia after 1 year of deferiprone without remarkable side effects. In a pilot study of deferiprone in 10 PKAN patients, good tolerability and significant median reduction of globus pallidus iron of 30 % ($p = 0.008$) was found after 6 months treatment, but no change in clinical scores.

Conclusions: The promising results in these case reports and small pilot studies made us believe that the time has come for an appropriately powered efficacy trial of deferiprone in PKAN. This is currently conducted in the context of a large EU-FP7-funded collaborative project called TIRCON (Treat Iron-Related Childhood-Onset Neurodegeneration). The status of our randomized, placebo-controlled trial of deferiprone in PKAN will be discussed.

Disclosure: ApoPharma Inc., the manufacturer of deferiprone, is partner in TIRCON and sponsor of the clinical trial.

Toxic neuropathies: which are real, which are myth?

FW23-1
Chemotherapy-induced neuropathies

G. Cavaletti
Monza, Italy

Objectives: Chemotherapy-induced peripheral neurotoxicity (CIPN) is a frequent, potentially severe and dose-limiting side effect of cancer treatment. However, in several instances the real impact of CIPN on patients\' daily life seems to be not yet completely understood, and it is sometimes considered as an unavoidable event in the course of life-saving chemotherapy.

Methods: CIPN can be induced by several different classes of drugs that are widely used in the treatment of solid as well as hematological malignancies, such as platinum drugs, antitubulins and proteasome inhibitors, but also new targeted drugs. A revision of the mechanism at the basis of CIPN is necessary, since it is conceivable that structural properties of the various neurotoxic compounds contribute to variations in the pathogenetic mechanisms of the damage as well as in the type, severity of the clinical picture and incidence of CIPN.

Results and Conclusions: Unfortunately, so far no drugs capable of preventing the occurrence of CIPN or ameliorating its long-term course are available, and chemotherapy schedule modification is often required to limit its severity, thus preventing patients from receiving the most effective treatment of cancer. Moreover, also symptomatic therapy is often largely ineffective in reducing CIPN symptoms and further investigattion is highly required.

Disclosure: Nothing to disclose.

FW23-2
Neuropathies caused by infectious and industrial toxins

M. J. Donaghy
Oxford, United Kingdom

Diphtheria is the only infection which causes neuropathy by the means of a toxin, an RNA-inhibiting exotoxin secreted by Corynebacterium diphtheriae encoded by a phage. Primary infection usually occurs in the fauces and the initial paralysis occurs in the nearby bulbar musculature at a median delay of 10 days. Endotracheal intubation is necessary for severe bulbar failure and/or the respiratory muscle failure occurring in 20 %. Generalised polyneuropathy is commoner in childhood infections, is predominantly motor and demyelinating, follows the bulbar symptoms a median of 37 days from onset of infection, and recovers in most although 6 % remain unable to walk at 1 yr. A secondary bulbar failure occurs in 1/3 at a median of 40 days. Despite adequate bulbo-respiratory support 16 % die, usually from cardiac involvement. Antibiotics are the mainstay of treatment; the impact of antitoxin is unclear in established cases. Diphtheria remains endemic in the third world. Immunity wanes in vaccinated adults which allowed a return of Diphtheria to Russia and E Europe after 1993. Organophosphorus and Carbamate pesticides can cause neuropathy 1–3 weeks after single exposures, following the early cholinergic phase of acute paralysis associated with bronchosecretion, bradycardia and seizures. Neuropathy due to industrial compounds has become rare but can occur with intense exposure to acrylamide, carbon disulphide, dimethylaminoproprionitrile, ethylene oxide and methylbromide. Chronic industrial exposure to arsenic or inorganic mercury can produce mild, and often asymptomatic, predominantly sensory neuropathy. Lead has traditionally been regarded as causing a subacute motor disorder, but this reflects plumboporphyria whereas low dose industrial exposures result in mild sensory neuropathy as in poisoning with other heavy metals.

Disclosure: Nothing to disclose.

FW23-3
N-hexane neuropathy (short contribution)

Yesim Parman
Istanbul, Capa, Turkey

N-hexane causes a sensory-motor neuropathy that is common in occupationally exposed workers or glue-sniffers. N-hexane exposure results in a peripheral neuropathy with distal sensory loss, weakness, diminished or absent tendon reflexes and autonomic dysfunction, sometimes mimicking GBS. Concomitant degeneration of the distal corticospinal tracts and dorsal column can also occur showing signs of CNS involvement. Needle electromyography and nerve conduction studies are compatible with primarily axonal polyneuropathy with secondary segmental demyelination. Motor conduction velocities are usually the slowest in distal regions of the nerves. In the proximal nerve segments, when tested by magnetic stimulation of the nerve roots, this slowing is much less pronounced. Histopathologic studies show reduction of myelinated fibres with giant axons that are due to impaired axon transport. Cessation to exposure is the main treatment option but some cases continue to worsen even after the exposure is stopped (coasting). We still see some cases of n-hexane neuropathy especially in shoe-makers. The clinical, electrophysiologic and histopathologic features of these patients will be presented.

References

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Neghab M, Soleimani E, Khamoushian K. Electrophysiological studies of shoemakers exposed to sub-TLV levels of n- hexane. J Occup Health. 2012;54(5):376–82.

Disclosure: Nothing to disclose.

Special Sessions

EFNS/ENS/EFNA Awareness Session: Improving physician-patient communication

SPS1-1
Case-Study: Acquired Brain Injury

N. Steinhoff
Grimmenstein, Austria

At the Traumatic Brain Injury a complex and sudden impact leads to many simultaneous lesions of the central nervous system. This creates a sudden change of situation of life for the injured and the family. For communication in life several centres of the brain have to collude in order to make interactions between human or other beings possible. Corresponding to the complex injury of the brain through TBI several barriers arise in communication with the traumatic brain injured, concerning speech understanding and production, alertness, impetus, awareness, language, cultural problems, premorbid and emotional situation or the social environment. The environment and the injured have to adapt quickly to the new situation, which often creates new problems of interaction. But there is also a problem of time on the professional side and a lack of understanding TBI itself that reduces the capacity of perceiving the actual and in any case individual situation. Especially the nursing staff and caregivers are exposed to the sudden changes of moods and aggressive approach to communication. Most of communication problems are due to lack of training how to deal with the individual situation after TBI, This can go so far, that inadequate prognosis might be given to the TBI affected persons. Most of aggression and agitation are avoidable through professional training. The readaptation syndrome after TBI and its single factors are often resulting out of lack of transporting the most important information about TBI to the family and injured at the very beginning after TBI. The several steps of communication and its challenge after TBI shall be presented in this contribution and made visible through an example of a TBI injured person.

Disclosure: I disclose potential or actual conflicts of interest concerning this presentation.

European Basal Ganglia Club

SPS5-1
Aetiology and pathophysiology of focal dystonias

A. Berardelli
Rome, Italy

Primary focal dystonias are disorders characterized by involuntary muscle spasms causing abnormal postures and patterned movements. The various types of focal dystonias have different clinical, epidemiological and etiological features. Focal dystonias, however, share a number of factors. Shared features include genes, molecular and cellular pathways and anatomical circuits. Focal dystonias also share pathophysiological abnormalities. Loss of inhibition has been demonstrated by studies of spinal cord and brainstem reflexes (blink reflexes, reciprocal inhibition and long-latency reflexes). Reduced inhibition is also present at the level of primary motor cortex, as demonstrated by the abnormalities of intracortical inhibition, silent period and surround inhibition. Loss of inhibition contributes to the defect in focusing motor command and causes the abnormalities in cortical plasticity present in dystonia. Whether neurophysiological abnormalities depend on changes at cortical, brainstem and cerebellum is still unclear. Finally a defect in sensory and sensorimotor integration is another important abnormality of dystonia and may be responsible for some of the motor dysfunction. Differences and similarities in focal dystonia can be explained by a recently proposed conceptual model (Jinnah et al. 2013).

Disclosure: Nothing to disclose.

Mediterranean session—Jointly organised by EFNS/ENS and PAUNS (Pan Arab Union of Neurological Societies): Dementia and Alzheimer's disease

SPS7-1
Epidemiology of dementia—does the Mediterranean diet matter?

R. Gouider
Tunis, Tunisia

Introduction: Dementia is a major public health problem in Mediterranean populations. Its prevalence depends on the interaction of genetic and environmental risk factors including dietary habits.The Mediterranean diet is presented as a cultural and healthy model characterized by a plant-based dietary rich in anti-oxidants and polyunsaturated fatty acids.Its effects on preventing dementia are controversial.

Objective: To conduct a review of the epidemiological data concerning dementia in Mediterranean countries and assessing the influence ofthe adherence to Mediterranean diet on the risk of cognitive impairment and dementia.

Methods: Articles and reviews relevant to the topic were selected through a PubMed search using the search terms"Mediterranean diet","Nutrition","Dementia incidence" and "Cognitive decline". The search results included epidemiological and interventional studies.

Results: Data from population-based studies carried out in Mediterranean countriesshowshigher incidence rates of dementia in northern than in southern countries. Several epidemiological cohort studies found a relationship between Mediterranean diet and lower risk of cognitive decline and dementia. Higher adherence to Mediterranean diet seems to be associated with reduced risk of Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD). However, there are contrasting findings between studies about the impact of the Mediterranean diet on the risk of progression from MCI to AD.

Conclusion: Environmental risk factors such as dietary habits,interacting with genetic factors,may influence the epidemiology of dementia and contribute to the north–south gradient observed across Mediterranean countries. Indeed, Mediterranean diet appears to have a protective role against cognitive decline and progression to dementia.

Disclosure: Nothing to disclose.

SPS7-2
Transcultural approach in dementia

M. El Alaoui Faris
Rabat, Morocco

Objectives: As the elderly population increases faster in non-Western-countries than in Western-countries, the prevalence of dementia will increase more rapidly in these countries. We want to present the situation of dementia in these countries.

Methods: we studied the publications on dementia in non-Western countries, mostly in Asia, Africa and the Middle East, to know the state of knowledge of dementia in these countries.

Results: Although two-third of people with dementia live in non-western-countries, few studies concerning these countries. Prevalence of dementia in some of these countries is as high as in Western-countries, however, the diagnosis of dementia is often at an advanced stage of the disease and most people living with dementia have not received a formal diagnosis, one study in India suggesting that about 90 % of dementia remain unidentified. The delay and the lack of the dementia's diagnosis are probably due to several factors including lack of cognitive tests in native languages and on neuropsychological tests adapted to illiterate people. Furthermore, the perception of dementia in different cultures is decisive in the fact that families bring or not the patient in consultation, we need anthropological studies to understand this situation and to see how to use the resources of various cultures to help patients and their families.

Conclusions: Dementia in non-western-countries remains dangerously neglected by researchers and by policy makers. Clinical and epidemiological studies is likely to provide valuable information on patients living with dementia in these countries.

Disclosure: Nothing to disclose.

SPS7-3
Alzheimer's disease from pathophysiology to treatment?

M.N. Rossor
London, UK

Our understanding of the histopathology of Alzheimer's disease has expanded enormously over the last 20 years, although drug targets have to date proved disappointing. One of the challenges is that the hallmarks of AD, senile plaques and neurofibrillary tangles, show an association with cognitive impairment but not a close correlation with severity, particularly in the elderly. Nevertheless, the pathophysiology of amyloid deposition, driven by studies of familial Alzheimer's disease and of tau accumulation, have led to trials targeting these misfolded proteins. So far amyloid immunotherapy trials have failed to meet primary endpoints but there are a number of studies commencing which trial these drugs in early or premanifest cases. Numerous other potential targets that are being explored such as inflammation, and the unfolded protein response. Although current efforts are focused on disease modifying treatments, symptomatic treatments based on neurotransmitter modulation will remain an important approach to treatment, building on the current use of cholinergic enhancement and (cholinesterase inhibitors) and glutamate modulation (memantine). Finally, treatment of comorbidities which can alter synaptic function or indeed amyloid accumulation are important, as are non-pharmacological interventions.

Disclosure: Nothing to disclose.

Tournament

Tournament for Young Neurologists—basic

T101
Inhibition of oligodendrocyte differentiation, by immunoglobulin purified from serum of multiple sclerosis patients during relapse

A. Carotenuto[1], C. Santarpia[2], S. Damiano[2], R. Accetta[2], A. De Filippis[2], O. Iengo[2], P. Giuliano[2], G. Orefice[1], V.E. Avvedimento[3], M. Santillo[2], R. Paternò[2]
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Introduction: Multiple sclerosis (MS) is a chronic demyelinating disease affecting oligodendrocytes (OL) that originate from OL progenitor cells (OPCs). In chronic MS lesions, OPCs accumulate with loss of OL suggesting the existence of a differentiation block of OPCs, with consequent limited remyelination in MS. We found that, in serum of MS patients, there are antibodies that impair the OPCs differentiation; here we tested the hypothesis that the inhibition of OL differentiation is marked during relapses.

Methods: 72 MS patients and 64 subjects affected by other neurological inflammatory diseases (ONID) were enrolled. Human OL cell line MO3-13 were differentiated. IgG fraction purification from serum. The extent of OL differentiation was evaluated by measuring differentiation markers by Western blotting (Phospho-cyclic-AMP

response element binding protein, P-CREB) and by flow cytometry (Myelin basic protein, MBP) in MO3-13.

Results: Incubation of MO3-13 cells with the differentiation stimulus increased P-CREB and MBP protein levels, with 2.2 and 1.4 fold induction ($p < 0.05$) respectively, compared with undifferentiated cells. Cells incubated with 200 μg/ml of IgGs from ONID or MS patients during remission, did not modified P-CREB and MBP protein levels. On the contrary the incubation with IgGs from MS subjects, during a relapse, reduce P-CREB levels, with a 0.6 fold decrease ($p < 0.05$), and MBP levels, with a 0.5 fold decrease ($p < 0.001$).

Conclusions: IgG from MS patients, during the relapse, inhibit oligodendrocyte differentiation, impairing myelination. These results offer a new insight into the MS pathogenesis. Funded by Spin Off Prindex of the University "Federico II" of Naples.

Disclosure: Nothing to disclose.

T102

Hereditary spastic paraplegia in children: a network analysis of gait variables

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Introduction: Gait is sustained upon complex joint movement relationships, in which kinematic parameters may or not be linked in "building blocks" depending on their neurological context, and can be studied with network analysis. We show normal and hereditary spastic paraplegia (HSP) gait parameter configurations and their network properties.

Methods: 30 healthy and 19 HSP children were recruited in which 16 left and 16 right gait parameters (Schutte et al., 2000) were averaged from 4 to 5 cycles of instrumented gait analysis. A network for each group was generated (nodes: gait parameters; edge weights: bivariate Spearman's coefficients, network properties: following Rubinov and Sporns, 2010). Maintenance/appearance of new "building blocks" of parameters in HSP is also shown.

Results: HSP network is more integrated than normal, but paradoxically modularity is higher. Centrality of cadence is strong in both networks but range-of-knee-flexion centralizes in HSP. In HSP, the normal gait building block cadence/speed is enriched with range-of-knee-flexion, stance-time, and peak-dorsiflexion-in-stance. A second normal block mean-pelvic-tilt/minimum-hip-flexion is also enriched in HSP with time-to-peak-knee-flexion, knee-flexion-at-initial-contact and range-of-pelvic-tilt.

Conclusions: HSP gait network properties and their intrinsic relationships diverge from normalcy. Cadence is a preserved "hub" in gait control, to which the whole system adapts and to which ranges-of-knee-flexion is added in the spastic group. The tool points out the parameters that are selected by the motor neural command in HSP to comply with cadence requirements. This is supported by lower segregation in its network. Results are relevant for therapeutics since single parameter treatment might affect global network properties.

Disclosure: Nothing to disclose.

T103

Transplantation of next-generation directly-induced neural stem cells (iNSCs) in mice with experimental multiple sclerosis

G. Mallucci[1,2], *L. Peruzzotti-Jametti*[1], *Y.B. Lakes*[3], *E. Giusto*[1], *M. Donegà*[1], *A. Compston*[1], *F. Edenhofer*[3], *S. Pluchino*[1]

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Introduction: Limitations of current Neural Stem Cells (NSCs) therapies in humans are the source from which NSCs are derived and the allogeneicity of the graft. Recently, a method to directly obtain NSCs (iNSCs) from skin fibroblasts has been described [1]. We ought to compare the therapeutic potential of this new cell source with the established effects of adult NSCs in C57BL/6 J mice with experimental autoimmune encephalomyelitis (EAE).

Methods: Mouse embryonic fibroblasts from C57BL/6 J mice are isolated to directly obtain iNSCs, which are grown both as spheres and as adherent monolayers. Adult NSCs are derived from the subventricular zone of adult C57BL/6 J mice. Both cell lines are assessed for their self-renewal, daily growth rate, viability, clonal efficacy and cell differentiation in vitro. Expression of surface molecules is also assessed by FACS analysis. Either $1\hat{0}6$ iNSCs or $1\hat{0}6$ NSCs are then intracerebroventricularly transplanted in MOG-induced EAE mice and behavioural outcomes are assessed up to 30 days post transplantation.

Results: Adult NSCs and iNSCs share many common in vitro properties. Nonetheless, iNSCs tend to develop spheres of smaller diameter with a lower clonal efficacy and present a significantly increased expression of both CD44 and CX3CR1, compared to NSCs. Transplantation of either iNSCs or NSCs induce a remarkable clinical amelioration that is more pronounced in iNSCs transplanted mice.

Conclusion: Despites many similarities, iNSCs hold some peculiar features that suggest autologous iNSCs transplantation as the safest and most efficient stem cell therapy for Multiple Sclerosis.

1. Thier M., et al. (2012). Stem Cell, 10(4), 473–479.

Disclosure: European Neurological Society (ENS) supports this work.

T104

Identifying the causes of pharmacoresistant epilepsy through a genome-wide association study with pathway and network analysis: from complexity to coherence to centrality

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Introduction: A third of people with epilepsy are pharmacoresistant. As pharmacoresistance is a complex trait, a genome-wide pathway-level approach will be especially fruitful in its study.

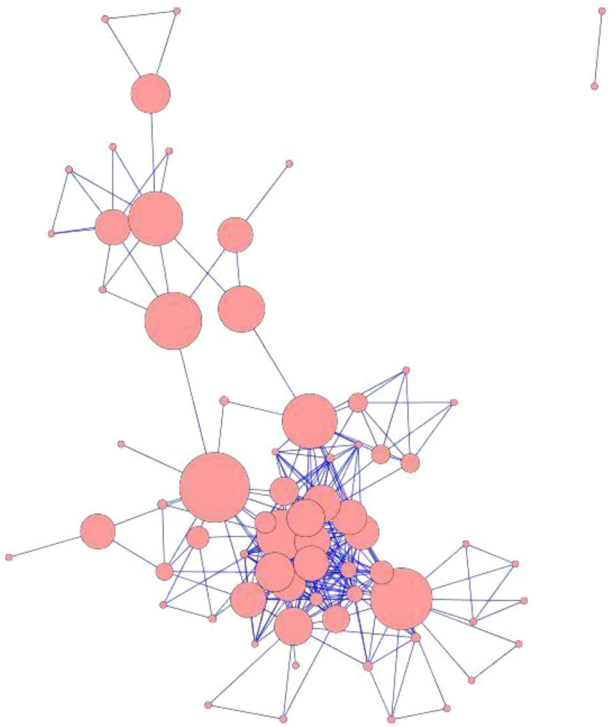
Methods: We performed a genome-wide association study (GWAS) of pharmacoresistant partial epilepsy, with discovery and replication cohorts including, in total, 421 cases and 2624 normal population controls, and 5,519,310 genotyped and imputed SNPs.

Results: At the single variant level, there was no overlap in the top results of the two cohorts. However, at the gene-set and pathway level, there was clear replication of results between the two cohorts:

(1) there was a striking correlation between the discovery and replication cohorts in the gene-set analysis results (Pearson's correlation coefficient = 0.8, one-sided p-value $<2.2 \times 10^{-16}$), and
(2) there was a highly significant overlap between the enriched pathways for the discovery and replication cohorts (hypergeometric distribution p-value $<3.7\text{x}10^{-17}$).

For the combined 'mega-analysis', there were 71 enriched pathways. We showed using network analysis that these enriched pathways form a highly interconnected network in which each pathway is directly connected, on average, to 8.4 other pathways. The enriched pathways, therefore, form a coherent whole and it can be expected that changes in one pathway in this network will have a cascading effect on the rest of the network. Finally, we identified, using betweenness centrality network analysis, the most important central pathway in this network: signalling by NGF.

Figure: The central network of interconnected pathways. Each node represents a pathway. Node sizes are proportional to their betweenness centrality.



Conclusion: We have performed the first ever GWAS of pharmacoresistant partial epilepsy and identified the most central pathway underlying this phenotype.

Disclosure: Nothing to disclose.

T105

Differentiation of neurological disorders of gait using automated classification systems

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Introduction: Clinical gait analysis has so far been limited in its role as a differential diagnostic tool due to the huge amounts of generated data and the absence of specific analysis criteria. Automated pattern recognition systems are available, but its value for drawing a diagnosis in neurological patients is not clear. We determined the accuracy of diagnoses of pathological gait disorders using automated pattern recognition techniques.

Methods: Clinically confirmed cases of postural phobic vertigo (N = 30), cerebellar ataxia (N = 30), progressive supranuclear palsy (N = 30), bilateral vestibulopathy (N = 30), and healthy subjects (N = 30) wereincludled. 136 discreet measurements using a GAITRite® carpet were obtained from each subject. Subjects were randomly divided into training cases and validation cases. Sensitivity and specificity of k-nearest neighbor (KNN), naive-bayes classifier (NB), artificial neural networks (ANN) and support vector machines (SVM) in classifying the validation cases were calculated.

Results: ANN and SVM had the highest overall sensitivity with 90.6 % and 92 % respectively. Overall specificity of all the methods was high, ranging from 94.2 % for NB to 98.1 % for SVM. SVM and ANN showed high false negative rates for bilateral vestibulopathy cases (20 % and 26 % respectively); while KNN and NB had high false negative rates for progressive supranuclear palsy cases (76.7 % and 40 % respectively) and high false positive rates for cerebellar ataxia (31.3 % and 48.1 % respectively).

Conclusions: SVM and ANN differentiate gait patterns of several distinct clinical disorders with high sensitivity and specificity compared to KNN and NB. SVM and ANN appear to be a promising diagnostic tool for gait disorders.

Disclosure: Nothing to disclose.

T106

Recovery of visual body motion perception and underlying cerebro-cerebellar network plasticity

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Introduction: Visual processing of body motion is essential for everyday life activities such as car driving, motor learning or social interaction. Recent findings indicate that visual perception of action is deficient in patients with damage to the cerebellum (Sokolov et al. *Cereb Cortex* 2010), likely through perturbation of reciprocal functional and structural communication with the superior temporal sulcus, STS (Sokolov et al. *Neuroimage* 2012, Sokolov et al. *Cereb Cortex* in press), the major cortical hub for action observation. However, compensatory potential after cerebellar damage remains unknown.

Methods: Through combination of neuropsychological and psychophysical assessment, functional MRI and effective connectivity analysis, we conducted a follow-up study of visual body motion perception in a

patient SL undergoing neurosurgery for left cerebellar dysplastic gangliocytoma (WHO grade I) and six healthy matched controls.

Results: Visual sensitivity to body motion before neurosurgery was substantially impaired in patient SL ($\chi^2 = 9.54$, $p < 0.01$). Postoperatively, significant improvement was noted, with the sensitivity reaching the level of controls at 24 months after neurosurgery ($\chi^2 = 1$, n.s.). Functional MRI indicated a postoperative midline shift of cerebellar activity during body motion processing ($p < 0.001$). Psychophysiological interaction analysis of effective connectivity demonstrated intact cerebellar communication with an area in the STS ($p < 0.05$), but shifted to the anterior as compared to normalcy.

Conclusions: Cerebellar lesions may induce substantial shifts within a cerebro-cerebellar circuitry enabling complete recovery of a higher cognitive function. Further research is required to confirm the outcome and clarify whether this plasticity mechanism may be generalizable.

Disclosure: Nothing to disclose.

Tournament for Young Neurologists—clinical

T201

Epilepsy during pregnancy: a prospective population-based cohort study of prevalence, incidence, treatment and predictors of depressive symptoms

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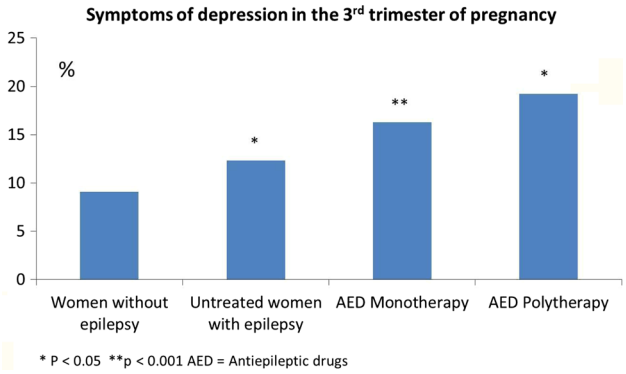
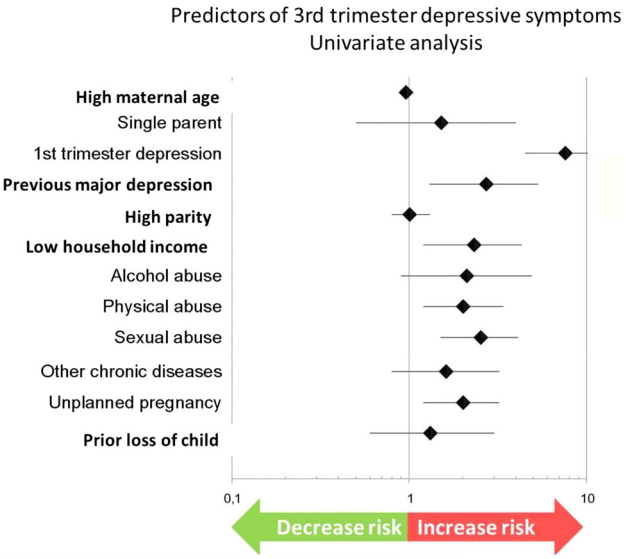
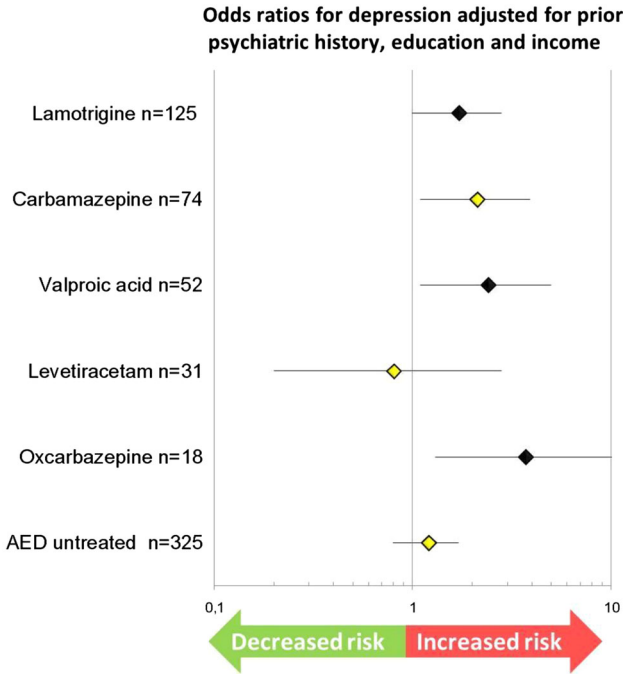
Introduction: We have investigated the prevalence, incidence, treatment and risk factors of third trimester depressive symptoms (DS) in pregnant women with and without epilepsy (WwE and WwoE).

Methods: All 101,769 pregnancies in the prospective Norwegian Mother and Child Cohort Study were included. Pregnant women reported on epilepsy, psychosocial factors and use of antidepressive and antiepileptic drugs (AEDs) in week 18. Serum concentrations of lamotrigine, valproate, levetiracetam and carbamazepine were measured. DS were reported around week 30 using a validated screening tool.

Results: Epilepsy was present in 713 cases. Point prevalence of DS was 14.1 % in WwE and 9.1 % in WwoE ($p < 0.001$, Adjusted Odds Ratio (OR) 1.5 (1.2–1.9)). The incidence during 3rd trimester was 8.4 % and 5.4 % ($p > 0.001$). Depressed WwE more seldom received antidepressives than WwoE (6.9 % vs. 14.3 %, $p < 0.05$). Use of topiramate, oxcarbazepine, carbamazepine and valproic acid was associated with an increased risk of DS (OR adjusted for psychiatric history 2.1–8.2 (1.1–28.4)). There were no relation between AED serum levels and DS. Low household income, unplanned pregnancy, prior depression and prior physical and sexual abuse were related to depressive symptoms in both groups. Sexual/Physical abuse and a psychiatric history were independent risk factors and doubled the risk of DS.







Conclusions: DS are frequent during pregnancy in WwE and seldom receive treatment with antidepressives. No antiepileptic drug was found to protect against these symptoms in WwE. Other risk factors of DS during pregnancy are similar between women with and without epilepsy.

Disclosure: Nothing to disclose.

T202

Regional hippocampal involvement in pediatric multiple sclerosis: a radial mapping MR study

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Introduction: Regional hippocampal volume (HV) changes in pediatric multiple sclerosis (MS) patients seem to correlate with clinical, neuropsychological and MRI metrics.

Methods: From 53 pediatric MS patients and 18 healthy controls (HC), brain dual-echo and 3D T1-weighted images were acquired. Global HV was computed using a manual tracing procedure. Regional HV changes were assessed using a radial mapping analysis. Patients with abnormal performance in $\geq$2 tests of the Brief Neuropsychological Battery for Children were classified as cognitively impaired (CI).

Results: Global HV was reduced in patients versus HC ($p < 0.001$), but not significantly correlated with clinical and MRI measures. In patients, radial atrophy affected the cornu Ammonis (CA1), subiculum and dentate gyrus (DG) subfields of both hippocampi, mostly on the right side ($p < 0.001$). Radial hypetrophy of the DG subfield was found in both hippocampi, mostly on the left side. Regional HV changes correlated significantly with clinical and MRI metrics. Twenty-one (39.6 %) patients were CI. Global HV did not differ between CI versus CP MS patients. Compared to CP patients, CI ones had areas of radial atrophy of the subiculum and DG subfields of the right hippocampus ($p < 0.001$). Significant correlations were found between regional HV changes and memory, attention and language abilities.

Conclusions: Hippocampal subregions have different vulnerability to MS-related damage, possibly reflecting differential susceptibility to inflammatory insults and neurodegenerative processes. These results support the feasibility of MR-based radial mapping for the development of reliable markers of disease progression in MS.

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T203

The impact of neuromyelitis optica spectrum disorder on pregnancy outcome

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Introduction: Neuromyelitis Optica Spectrum Disorder (NMOSD) predominantly affects women and is often active during childbearing years. Although recent studies have demonstrated increased post-partum disease activity, no studies have investigated the impact of NMOSD on pregnancy.

Objective: To investigate the association between NMOSD and spontaneous miscarriage or preeclampsia.

Methods: We retrospectively examined the medical and obstetric history of 60 women with aquaporin-4 (AQP4) antibody-mediated NMOSD and at least one pregnancy, registered in UK, Portugal and Japan. Multivariate logistic regression assessed the association between NMOSD, maternal age and medical history on odds of adverse pregnancy outcome.

Results: Spontaneous miscarriage and preeclampsia rates were 12.9 % and 11.5 %, respectively. In pregnancies after NMOSD onset, these rates were 37.5 % and 17.7 % respectively. Univariate logistic regression identified maternal age and pregnancy after NMOSD onset as risk factors for miscarriage. Multivariate analysis revealed that pregnancy after, or immediately preceding, NMOSD onset was associated with increased odds of miscarriage independent of the risk associated with maternal age (OR 4.88–7.27, 95 %CI 1.18–34.2, $p < 0.05$). No association existed between maternal age or NMOSD onset and preeclampsia, although preeclampsia incidence was higher than reported in multiple sclerosis and population studies.

Conclusions: Pregnancy after or immediately preceding NMOSD onset is associated with increased risk of miscarriage, independent of the risk associated with increased maternal age. There is an increased risk of preeclampsia in women who develop NMOSD. AQP4 is expressed in human placenta, and growing evidence implicates AQP4-antibody-mediated inflammation of the placenta in both complications. These conclusions have important clinical relevance.

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T204

A reflection on plasticity research in writing dystonia

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Introduction: Much attention has focused on the hypothesis that there is enhanced plasticity of sensorimotor circuits in dystonia. The most common experimental method to assess plasticity is paired associative stimulation (PAS). Excessive, non-focal effects of PAS were observed in early studies of dystonia, however, these large effects have not been uniformly replicated. Furthermore in healthy subjects, it is now appreciated that responses to PAS are highly variable and may not have the spatial specificity that was found in initial studies.

Methods: In this work we present new data from 15 patients with writing dystonia.

Results: As in healthy individuals, we found the effects of PAS to be highly variable in size and direction. A review of previous studies examining PAS in focal hand dystonia confirms that this is not unusual and highlights the range of effects that have been seen. We also note that methodological details of the data analysis may have favoured findings of enhanced plasticity.

Conclusions: We conclude that evidence is currently divided as to whether PAS responses in dystonia are excessive and/or non-specific. We propose that greater focus on individual neurophysiological profiles will allow the identification of subject-specific interventions that may not be apparent at group level. Although our conclusions are limited to the PAS paradigm in writing dystonia, the degree of variation observed in other plasticity protocols suggests that similar problems may affect other studies using different neurophysiological paradigms.

Disclosure: Nothing to disclose.

T205

Gut microbiota are associated with Parkinson's disease and clinical phenotype—a case–control study

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Introduction: In the course of Parkinson's disease (PD), the enteric nervous system (ENS) and parasympathetic nerves are amongst the structures most frequently and earliest affected by alpha-synuclein pathology. Accordingly, gastrointestinal dysfunction is an important non-motor symptom in PD and often present years before motor symptom onset. Recent research has shown that intestinal microbiota interact with the autonomic and central nervous system via diverse pathways including the ENS and vagal nerve. The role of gut microbiota in PD has not been previously investigated.

Methods: We compared the fecal microbiomes of 72 PD patients and 72 control subjects by pyrosequencing of the bacterial 16S rRNA gene. Associations between clinical parameters and microbiota were analyzed using generalized linear models taking into account potential confounders.

Results: On average, the abundance of Prevotellaceae in feces of PD patients was reduced by 77.6 % as compared with controls ($Q = 0.031$). Relative abundance of Prevotellaceae of $\leq$6.5 % had 86.1 % sensitivity and 38.9 % specificity for PD (AUC = 0.664 [95 % CI 0.556–0.771]; $P = 0.004$). A logistic regression classifier based on the severity of constipation and the abundance of four bacterial families identified PD patients with 66.7 % sensitivity and 90.3 % specificity (AUC = 0.832 [95 % CI 0.766-0.897]; $P < 0.001$). The relative abundance of Enterobacteriaceae was positively associated with the severity of postural instability and gait difficulty ($P < 0.001$).

Conclusions: The intestinal microbiome is altered in PD and is related to motor phenotype. This may point to a role of intestinal microbiota in the etiopathogenesis of PD and could be a potential biomarker.

Disclosure: Nothing to disclose.

T206

Percutaneous tibial nerve stimulation for the treatment of the overactive bladder in patients with neurological disease

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Introduction: Percutaneous Tibial Nerve Stimulation (PTNS) is a minimally-invasive neuromodulation technique effective for managing the overactive bladder(OAB). The objective of this study was to evaluate the safety and efficacy of PTNS in neurological patients reporting OAB.

Methods: In this prospective evaluation over 18 months, patients for whom first line antimuscarinic treatment was either ineffective or intolerable underwent a standard 12-week course of PTNS (Urgent-PC, Uroplasty) at a tertiary care centre. Symptoms were evaluated using standardised bladder questionnaires (ICIQ-OAB and ICIQL-UTS-QoL) and bladder diaries and data analysed.

Results: Of forty-nine consecutive patients (33 females; mean age 56 years; range20-85), 44 completed treatment. Compared to baseline, significant improvements ($p < 0.05$) were noted in the following domains (relative improvement): urinary urge(23 %), incontinence severity(25 %), 24-h urinary frequency (10 %) and day-time frequency(11 %), total OAB scores (15 %) and related-bother(11 %), quality of life(12 %) and related-bother(14 %). Using a 7-point Likert scale (best score 7), patients found the treatment to be comfortable (6.1 $\pm$ 1.2), were satisfied with the treatment (6.23 $\pm$ 1.07) and would recommend it to a friend (6.36 $\pm$ 0.90) (mean score $\pm$ SD). Twenty-four patients opted to continue with top-up treatments and patients reporting improvement in quality of life at week 12 more often attended top-up treatments ($n = 16$)($p < 0.05$); mean top-up interval was 45 days(7–155 days). No adverse effects were reported.

Conclusions: PTNS is a safe treatment and associated with significant improvements in OAB symptoms, quality of life and related-bother in patients with a neurogenic bladder.

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