Child's Nervous System (2023) 39 (Suppl 1):S1–S10
https://doi.org/10.1007/s00381-023-05914-3

ABSTRACTS

Posterior Fossa Society Publication

Published online: 8 May 2023

Friday 9 September 2022

Abstracts listed in presenting order, unless stated otherwise

Radiology Session

Cerebellar-PAG "survival circuits" and the core symptoms of cerebellar mutism syndrome (CMS)

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CMS patients exhibit a varying aggregate of transient and lasting symptoms, and our understanding of which neuronal systems underpin which symptoms is poor. A recent evaluation of medulloblastoma patients in our hospital identified apraxia as one in a "core" cluster of CMS symptoms that co-occurs with speech impairment[1]. We evaluated patterns of surgical damage in these patients using advanced segmentation and analysis techniques to find that damage to the fastigial nuclei had a strong association with CMS diagnosis. Additionally, magnetization transfer imaging was used to evaluate myelin degradation in specific midbrain targets of the cerebellum in CMS patients. We found that the ventral periaqueductal grey (PAG) was among the significantly affected areas in CMS. This region is evolutionarily conserved in mammals and plays a critical role in the gating of conspicuous behaviours. Several recent studies have demonstrated the functional link between the fastigial nuclei and PAG, as well as the role of specific PAG cell populations in initiating "survival functions" like freezing of motion and suppression of vocalization[2-4]. Together, this recent information may help illuminate the specific neuronal dysfunction that leads to these core CMS symptoms. Here we will review this evidence, place it in the context of our broader understanding of CMS etiology, and highlight newly relevant questions for the future.

1. Khan, R.B., et al., Clinical features, neurologic recovery, and risk factors of post-operative posterior fossa syndrome and delayed recovery: A prospective study. Neuro Oncol, 2021.

2. Al-Afif, S., et al., Long-term impairment of social behaviour, vocalizations and motor activity induced by bilateral lesions of the fastigial nucleus in juvenile rats. Brain Struct Funct, 2019.

3. Vaaga, C.E., et al., Cerebellar modulation of synaptic input to freezing-related neurons in the periaqueductal gray. Elife, 2020.

4. Tschida, K., et al., A Specialized Neural Circuit Gates Social Vocalizations in the Mouse. Neuron, 2019.

Advanced MRI in Medulloblastoma Patients with and without CMS during Treatment and Follow-up

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Postoperative cerebellar mutism syndrome (CMS) occurs in about 25% of paediatric patients after medulloblastoma resection. While the symptoms of CMS are well documented, its pathophysiology and mechanism are poorly understood [1]. We prospectively followed a large sample of paediatric patients [2] with newly diagnosed medulloblastoma on an institutional protocol (SJMB12, ClinicalTrials.gov: NCT 01878617) with advanced brain MRI, including Dynamic Susceptibility Contrast-enhanced (DSC) and Magnetization Transfer (MT) imaging. Longitudinal results between patients with and without CMS were compared. The study was IRB approved and written informed consent was given by each participant. DSC and MT results are reported here for three time points: TP1 – after surgery before radiation therapy, TP2 – at the end of chemotherapy, and TP3 – at 1.5-year follow-up. Images from 159 (105/54) patients (non-CMS/CMS) at age 11.4±0.25 years were analysed. CBV and CBF were calculated for each brain lobe and various ROIs (26 cerebellar, 56 cortical/Brodmann Area, and 8 Basal Ganglia); values were generally lowest at TP1 for both patient groups across the brain, except for cerebellum regions where CBF, CBV, and MT ratio (MTR) decreased over time. Compared to non-CMS patients, CMS patients had significantly lower CBF, CBV and MTR values in cerebellar regions at all TPs, with the largest difference at TP3. These long-term differences in cerebellar regions with CMS patients correlate with abnormal neurological findings in these patients [2], even after regaining of speech. Surprisingly, CMS patients had significantly lower MTR and CBV values in both left and right hippocampi at TP1 (when speech was lost) but not at later TPs (when speech was regained).

References: [1] Patay Z (2015) Childs Nerv Syst 31:1853-58 ; [2] Khan RB, et al. (2021), Neuro Oncol 23(9):1586-96

Neurological Manifestations of Postoperative Cerebellar Mutism Syndrome in Paediatric Patients with Medulloblastoma are Strongly Associated with Disruption of the Dentato-Thalamo-Cortical Pathway: A Diffusion Tractography Study

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The dentato-thalamo-cortical (DTC) tracts of 83 post-operative paediatric medulloblastoma (MB) patients were reconstructed using diffusion tractography. Robust forms of disruption of the DTC tracts include thinning or absence, hence 4 patterns were established in patients: bilateral DTC absence, right (unilateral) DTC absence, left (unilateral) DTC absence, and intact DTC bilaterally. The associations between DTC disruption and neurological symptoms were analysed by using biostatistical methods. Evaluated categories of neurological deficits were dysmetria, ataxia, and mutism. The most severe symmetric dysmetria was observed in the patients with bilateral DTC absence; asymmetric dysmetria occurred in patients with unilateral DTC absence. Ataxia was evaluated by using the modified Scale for Assessment and Rating of Ataxia (SARA) and was worst in patients with bilateral DTC tract absence; The SARA score was significantly associated with the loss of left ($p < 0.001$) and right ($p < 0.001$) DTC volumes. Mutism was strongly associated with DTC disruption. The odds ratio of having mutism was 156 for patients with bilateral DTC absence, 14.8 for patients with unilateral right DTC absence, and 7.4 for patients with unilateral left absence compared to that for patients with bilateral intact DTC. A logistic model suggested that both left and right DTC volumes were negatively associated with the odds ratio of having mutism. A strong association between bilaterally intact DTC tracts and the lack of neurological deficits was observed. The odds ratio for being neurologically asymptomatic was 16.8 for patients with bilaterally present DTC tracts compared to patients with bilaterally absent ones. This finding suggests that bilaterally intact DTCs are indispensable for patients to remain asymptomatic after surgery. In conclusion, the disruption of the DTCs, especially their absence, is likely the principal injury causing mutism and other neurological deficits in MB patients after surgery. Upstream effects of DTC disruption need further research.

Predicting Cerebellar Mutism Syndrome using Lesion-Symptom mapping

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Background: Survival rates for paediatric cancers have greatly improved in this century, and this includes brain tumours. This increases the importance of understanding and preventing the development of treatment-related effects in the paediatric population. About 25% of patients who undergo cerebellar tumour resection develop a constellation of deficits in cognition, affect and executive function, known as cerebellar mutism syndrome. A recent study by Albazron et al, involving 195 subjects included showed that lesion anatomy was a critical variable for CMS, showing that: 1) damage to the cerebellar outflow pathway increases the risk of CMS ten-fold, and 2) a data driven lesion symptom map identified a region maximally associated with CMS.

Objective: We aim to further evaluate the relationship of lesion location and the onset of severe cognitive and affective symptoms following paediatric cerebellar tumour resection. Specifically, our goal was to test the results of the Albazron study in an independent cohort, with pre-registered anatomical hypotheses. In particular, we hypothesized that subjects with CMS would have lesions that overlap with the cerebellar outflow pathway and the CMS lesion symptom map to a greater extent than patients whom did not develop CMS.

Methods: This was an observational study that included data from 56 patients under 21 years of age who underwent cerebellar tumour resection. Each patient had a post-surgical MRI and clinical assessment to determine the presence or absence of CMS. Each tumour resection cavity was manually segmented and transformed to a common template brain. The intersection of the lesion with the cerebellar output pathway and the CMS lesion symptom map was quantified and compared between individuals that did or did not develop CMS.

Results: Out of 56 patients, 10 developed CMS (18%). As hypothesized, the lesions of individuals with CMS overlapped with the cerebellar outflow pathway and the data-driven lesion symptom map to a greater extent than individuals that did not develop CMS (p=0.0271 & p=0.013, respectively).

Conclusion: Our analysis provides further support that the anatomy of the resection site is a critical variable in the development of CMS and it can predict the development of CMS across independent cohorts.

Scoring Session

Acute neuropsychological predictors of long-term language abilities in children with post-surgical CMS/CCAS

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Aim: While speech, behavioural, affective, and neurological status of children with CMS/CCAS are variable in the acute stage, their predictive value concerning long-term language abilities is unclear. This study aims to characterize long-term language abilities of children with CMS/CCAS and their acute predictors.

Methods: Forty-seven files of patients with CMS/CCAS who received surgery for a posterior fossa tumour at age 4-17 were analysed retrospectively. Post-operative speech, affect and neurological status (swallowing, cerebellar, brainstem, and motor function) were coded in the first two weeks after surgery, using a scale from Catsman-Berrevoets and Aarsen (2010), adapted by Kingma (2021). Duration of mutism was noted. Scores for verbal fluency on average 9 weeks after surgery, and verbal fluency, verbal learning, verbal intelligence, and auditory intelligence capacity beyond 1 year after surgery were gathered. Spearman correlations between acute scores and follow-up data were computed.

Results: Inter-rater agreement in the acute stage was low for acute scores on speech (n.s.), and moderate for scores on affect (r=0.6) and sub-scores including speech and affect (r=.6). Long-term impairments in language were observed in verbal intelligence, verbal learning, and auditory intelligence capacity.

Longer duration of mutism was associated with poorer verbal fluency at follow-up (r=-0.7). Greater severity of acute speech and affect deficits was associated with longer mutism (r=-0.4) and poorer long-term verbal learning (r=-0.5). Greater severity of acute speech (r=-0.6) and swallowing deficits (r=-0.7) correlated with poorer verbal fluency 1 year after surgery. The total score in the acute checklist showed a weak correlation with duration of mutism (r=0.4) and verbal fluency weeks after surgery (r=0.4).

Conclusion: Acute speech and affect patterns may predict duration of mutism and long-term verbal impairments prevalent in children with CMS/CCAS beyond 1-year after surgery. Options for sharpening the criteria for assessment in the acute stage to improve reliability will be discussed.

Saturday 10 September 2022

Surgery Session

Cerebellar mutism syndrome (CMS) following posterior fossa surgery in children below 18 years, what we have learnt over the last 10 years

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Objective: The aim is to evaluate our institutional experience with tumour resection in the posterior fossa in children and the incidence of CMS postoperatively, and to analyse association with multiple risk factors, such as tumour entity, size and location, surgical approach, usage of ultrasonic cavitation device and hydrocephalus.

Methods: All patients below 18 years, who received a tumour resection in the posterior fossa between January 2010 and March 2021 were included for retrospective analysis. Various data points, including demographic, tumour-associated, clinical, radiological, surgery-associated, complications and follow-up data were collected and statistically evaluated for association with CMS.

Results: 60 patients were included with a median age of 8 years (range 0-18). Integrated diagnosis showed 48% pilocytic astrocytoma, 32% medulloblastoma, 10% anaplastic ependymoma and 13% other tumour entities. Complete resection was achieved in 68%, 23% underwent subtotal resection and 7% underwent partial resection.

43% were operated using a telovelar approach, 8% using a transvermian approach and 48% using other approaches. 16% developed CMS postoperatively, following telovelar approach in 15% and 60% following a transvermian approach. Medulloblastoma patients and midline tumours showed a higher incidence of CMS, though not significant. Tumour size and infiltration of the brainstem did not differ significantly in our cohort.

Presence of acute hydrocephalus was associated with a significantly higher risk for developing CMS (p 0.01) as well as need for a ventriculoperitoneal shunt (p 0.04). Usage of an ultrasonic cavitation device was not associated with CMS. All patients with CMS showed marked improvement during follow up but with residual deficits.

Conclusion: Our CMS rates compare to those described in literature. CMS was not only associated with a transvermian approach, but also occurs using a telovelar approach, but to a lesser extent. Presence of acute hydrocephalus prior to tumour surgery is associated with higher incidence of CMS.

Feasibility of cerebello-cortical stimulation for intraoperative neurophysiological monitoring of cerebellar mutism

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Background: Cerebellar mutism can occur in a third of children undergoing cerebellar resections. Recent evidence proposes it may arise from uni- or bilateral damage of cerebellar efferents to the cortex along the cerebello-dento-thalamo-cortical pathway. At present, no neurophysiological procedure is available to monitor this pathway intraoperatively. Here, we specifically aimed at filling this gap.

Methods: We assessed 10 patients undergoing posterior fossa surgery using a conditioning-test stimulus paradigm. Electrical conditioning stimuli (cStim) were delivered to the exposed cerebellar cortex at interstimulus intervals (ISIs) of 8–24 ms prior to transcranial electric stimulation of the motor cortex, which served as test stimulus (tStim). The variation of motor-evoked potentials (MEP) to cStim + tStim compared with tStim alone was taken as a measure of cerebello-cortical connectivity.

Results: cStim alone did not produce any MEP. cStim preceding tStim produced a significant inhibition at 8 ms ($p < 0.0001$) compared with other ISIs when applied to the lobules IV-V-VI in the anterior cerebellum and the lobule VIIB in the posterior cerebellum. Mixed effects of decrease and increase in MEP amplitude were observed in these areas for longer ISIs.

Conclusions: The inhibition exerted by cStim at 8 ms on the motor cortex excitability is likely to be the product of activity along the cerebello-dento-thalamo-cortical pathway. We show that monitoring efferent cerebellar pathways to the motor cortex is feasible in intraoperative settings. This study has promising implications for paediatric posterior fossa surgery with the aim to preserve the cerebello-cortical pathways and thus prevent cerebellar mutism.

National multicentered retrospective review of clinical and intraoperative features associated with the development of cerebellar mutism after paediatric posterior fossa tumour resection

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Background: Cerebellar mutism (CM) is a condition characterized by a significant lack or loss of speech in children following posterior fossa (PF) surgery. The biological origin of CM remains largely unclear and

remains the subject of ongoing debate. The more important observation is however, that despite multidisciplinary interventions, the outcome is less favourable than previously described.

Methods: A national multi-centred retrospective review of all the children undergoing PF resection in 4 midsized Canadian academic paediatric institutions was undertaken. Patient, tumour, and surgical factors associated with the post-operative development of CM was reviewed. The study retrospectively identified patients developing CM with an internal control population consisting of patients who did not develop post-operative CM.

Results: 258 patients across the 4 centers over a 10-year period (2010-2020) were identified. The average age of the cohort was 6.73 years and 42.2% of children were female. Frozen section was available in 90.3% of cases. Most of the final tumour histology in children developing CM was medulloblastoma (35.7%), pilocytic astrocytoma (32.6%), ependymoma (17.1%) and exophytic glioma (1.2%). Intraoperative impression of adherence to the floor of the 4th ventricle was negative in 47.7%, positive in 36.8% of cases. Intra-operative surgeon's assessment as gross total resection occurred in 69.8% of cases. Intraoperative abrupt changes in blood pressure and/or heart rate was identified in 19.4% and 17.8% of cases. CM was experienced in 19.5% of patients (N=50). The clinical resolution of CM as mainly assessed by a neurosurgeon (86%) and was complete, significant resolution, slight improvement, no improvement, and deterioration in 56.0%, 8.0%, 20.0%, 14.0%, 2.0% respectively.

Conclusion: As a devastating surgical complication, identifying and understanding the biological origin of CM is the first step to complication avoidance. Maximal safe resection irrespective of intra-operative pathology remains the goal to avoid the devastating complication of CM.

Application of Rotterdam post-operative cerebellar mutism syndrome prediction model to patients operated for medulloblastoma in a single institution

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Post-operative cerebellar mutism syndrome (CMS) develops in up to 30% of children with medulloblastoma. A score of ≥100 in a Rotterdam model (RM) predicts a 66% risk of CMS in patients with posterior fossa tumours (1). We have previously reported that surgical experience contributes to CMS risk. Our aim was to study incidence of CMS in high-risk patients by retrospectively applying the RM to patients that had first tumour resection at our institution and were enrolled on SJMB12 protocol (NCT01878617). All participants got structured serial neurologic evaluations.

CMS was categorized into type 1 (complete mutism) and type 2 (paucity of speech). Rotterdam score was calculated based on pre-operative imaging parameters. Of the 40 (14 female, 26 male) study participants, 4 (10%) had CMS (3 CMS1, 1 CMS2). Median age at tumour resection was 11.7 years. Tumour location was midline in 30 (75%), right lateral 6 (15%) and left lateral 4 (10%). Median Evans index was 0.3 (0.2-0.4) and 34 (85%) were ≥0.3 (indicative of hydrocephalus). Median tumour volume was 50 cm3 (2-180.6). Gross total resection was achieved in 35 (87.5%), near total in 4 (10%) and subtotal in 1. Twelve tumours were SHH, 7 WNT, and 29 NWNS. Median RM score was 90 (25-145). Eighteen participants had a score of ≥100 and 16.7% of these (n=3) developed CMS. Scores for the 4 with CMS were 85, 125, 145 and 145. At our institution, the incidence of CMS in those that had RM of ≥100 was much lower than reported risk of 66%. This data supports our hypothesis that neurosurgical experience is a significant risk factor in the development of CMS.

1. Bae D, et al. Preoperative prediction of postoperative cerebellar mutism syndrome. Validation of existing MRI models and proposal of the new Rotterdam pCMS prediction model. Childs Nerv Syst. 2020;36:1471-1480.

SIOPE-MB6 – Integration of a randomized surgical question into a Pan-European prospective clinical trial protocol for standard risk medulloblastoma

Mynarek M[1], Bailey S[2], Clifford S[2], Doz F[3], Rutkowski S[1], Padovani L[4], Kwiecien R[5], Mosseri V[6], Beccaria K[7], Thomale U[8], Aquilina K[9], Sehested A[10], Puhr A[11], Milde T[12]

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Neurocognitive impairment is one of the key late effects in survivors of childhood medulloblastoma and a major concern for patients, families and treating physicians. All key aspects of the therapy required for the treatment for medulloblastoma (surgical resection, chemotherapy and radiotherapy) may influence the neurocognitive performance of survivors of the disease.

In order to address this many trials have focused on the reduction of the dose of radiotherapy administered to the brain and spine (craniospinal radiotherapy, CSI) in favourable and standard risk patients. However, so far only a few studies have investigated the possibility of reducing the degree of neurocognitive impairment caused by tumour resection. Cerebellar mutism syndrome (CMS) is a frequent complication of surgery for medulloblastoma. CMS is in turn associated with reduced neurocognitive performance in survivors. Retrospective data (mainly in high-risk metastatic medulloblastoma) suggest that a surgical approach aiming at tumour debulking with subsequent adjuvant chemotherapy followed by definitive surgery may be associated with improved neurosurgical outcome compared to the standard-of-care initial maximal safe tumour resection. Prospective or randomized studies to test this hypothesis have not been performed.

The embryonal tumour group as part of the SIOP-E brain tumour group is currently discussing a trial concept in which in patients with non-metastatic medulloblastoma will be randomized to either receive initial maximal safe tumour resection (standard arm) or debulking surgery/biopsy with defined hydrocephalus management followed by two cycles of carboplatin/etoposide chemotherapy followed by definitive surgery (experimental arm) with the aim of reducing the incidence and severity of cerebellar mutism syndrome and hence neurocognitive sequelae in survivors.

In this presentation, the trial concept will be presented and different outcome parameters will be discussed.

CCAS Session

Evaluating the diagnostic validity of the Cerebellar Cognitive Affective Syndrome (CCAS) in paediatric posterior fossa tumour patients

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Objective: The aim of this case-control study was to investigate the severity of the Cerebellar Cognitive Affective Syndrome (CCAS) in patients treated for paediatric posterior fossa tumours (PFT) and evaluate its diagnostic validity and predictive value for long-term effects.

Method: Using neuropsychological test data of 56 patients with PFT (mean age: 14 years), the deficit severity in the core CCAS domains executive functions, verbal functions, visuo-spatial skills, emotion/behaviour was assessed. Neuropsychological and academic long-term outcomes of patients with CCAS were compared to two control groups of PFT patients (treated with either surgery or surgery followed by radio-/chemotherapy) without the syndrome. Risk factors associated with various deficits were considered.

Results: All but one PFT patient suffered from slight to severe impairments in at least one CCAS domain, while complete CCAS occurred in 35.7%. Seven years after tumour diagnosis CCAS patients performed worse in information processing, logical reasoning, verbal functions, visuospatial skills, and executive functioning and required more special educational support compared to the control groups. CCAS patients performed equally poor as patients treated with chemo-/radiotherapy in tasks measuring information processing speed. Risk factors were significantly associated with deficits in information processing speed but not CCAS emergence.

Conclusion: Deficits in the core CCAS domains are commonly found in PFT patients, but varying in severity, which suggests the syndrome to be continuous rather than dichotomous. However, the validity of CCAS diagnosis was low and unspecific. The exclusion of relevant functions typically impaired in PFT patients (e.g., information processing) resulted in difficulties being overlooked.

Speech Therapy Session

Team Approach for Education and Support of Postoperative Paediatric Cerebellar Mutism Syndrome in the Preoperative and Immediately Postoperative Phase

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Postoperative paediatric cerebellar mutism syndrome (CMS) is a known complication following surgical resection of posterior fossa tumours. However, minimal information exists describing the progression of this syndrome and how to best support these patients. At Ann & Robert H. Lurie Children's Hospital of Chicago, the brain tumour team has been fortunate enough to work together for years. Throughout the time that this team has been collaborating, a typical protocol has been developed for children at most risk for postoperative paediatric CMS, refined with each patient experience, to the current model. Much of what has been written about postoperative paediatric CMS (and varying terminology) has focused on potential risk factors, surgical approach, and causes, as well as definitively defining the condition. We have instead focused on the impact of this constellation of symptoms. The team has focused on supporting the patient and families, and how we as caregivers can prepare, educate and support families through this difficult diagnosis and early management of CMS. There is much work to be done in describing and quantifying postoperative paediatric CMS. In the care of children with paediatric brain tumours in the preoperative and immediately postoperative phases, a team approach is paramount. When discussing expectations following surgery, consistent messaging and communication of hope are essential. Furthering multidisciplinary understanding of postoperative paediatric CMS will provide a framework upon which additional work can be built.

Verbal fluency as a window to language processing changes in children with post-operative CMS/CCAS

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Objective: Several studies report language difficulties in children with post-operative CMS/CCAS, using general language measures. The current study uses a critical variable approach to verbal fluency data to examine whether children treated for posterior fossa tumours exhibit impaired linguistic abilities at specific levels of language processing and whether this changes over time.

Methods: Data were accessed retrospectively from University Medical Center Groningen clinical files of children with CMS and/or CCAS. Verbal fluency data were extracted for analyses from the files of 17 patients at 2 points in time (on average, 8 weeks after surgery and after 1 year after surgery). The word properties analysed were typicality, concreteness, imageability, familiarity, frequency, age of acquisition, length in phonemes, phonological neighbourhood, length in syllables, syllable stress and consonant clusters. Patient mean values for each word property were statistically compared to those of healthy age- and gender-matched control children, both in group and individual analyses. Furthermore, longitudinal analyses explored potential quantitative differences between 2 assessment points, for each word property. More patient and control data will be gathered and added to this study.

Results: Current results are preliminary, as the sample size will increase. Children with CMS and/or CCAS used words with significantly fewer phonological neighbours than their controls, 1 year after surgery. Individual analyses showed heterogeneous patterns of language impairment across children. A significant increase in word count and mean typicality of words was observed between the first and the second assessment.

Conclusion: The findings at group level may indicate a problem in the phonological output lexicon in the children with CMS and/or CCAS. However, language profiles of these children are often heterogeneous, and thus an individual diagnosis of language difficulties is necessary. The increased typicality values might indicate that the quantitative recovery in verbal fluency is accompanied by recovery in semantic processing.

Characterising the spontaneous language outcomes in people who underwent cerebellar tumour surgery: differential outcomes in participants who did and did not experience postoperative cerebellar mutism

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Background: Following cerebellar tumour surgery, children may present with symptoms of impairment of spontaneous language. Nonetheless, the language processing deficits underlying these impairments are poorly understood. Also, the differences in language outcomes between children who experience postoperative cerebellar mutism syndrome (pCMS) and children who do not are still unclear. The present study aimed to characterise the language impairments of children who underwent cerebellar tumour surgery as reflected by measures of spontaneous language. A distinction was made between participants who experienced pCMS and those who did not.

Methods: Twelve participants who underwent cerebellar tumour surgery (age range = 3-24 years) were compared to 39 non-language-impaired controls. Follow-up time since surgery ranged between 11 months and 12;3 years. Spontaneous oral language samples were gathered during a structured interview and picture description tasks. Nouns and verbs produced were rated for psycholinguistic variables (e.g., word frequency). Standard spontaneous language measures (e.g., mean length of utterance) were calculated. Variables reflected lexical, semantic, phonological and morphosyntactic processing. This allowed us to identify the impaired language processing levels.

Results: The outcomes of every participant who underwent cerebellar tumour surgery were compared against their controls using individual case statistics. Nine out of 12 (75%) participants showed impairments across different levels of language processing. Three out of these nine participants were diagnosed with pCMS. Participants who experienced pCMS had predominantly morphosyntactic and semantic impairments, while the spontaneous language impairments of the non-pCMS-group were more evenly distributed across multiple levels of language processing. A large inter-individual heterogeneity was observed both in the presence and severity of the observed language impairments.

Conclusion: Both participants who did and did not experience pCMS following cerebellar tumour surgery may show long-term spontaneous language impairments. A comprehensive postoperative language assessment seems necessary, given the large inter-individual heterogeneity in the language outcomes.

Preoperative word-finding difficulties in children with Posterior Fossa tumours

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Posterior fossa tumour surgery in children implicates a high risk of severe speech and language impairments. Most studies focus on predictors of postoperative impairment, while to date there are only few studies investigating preoperative language functions. The lack of precise knowledge about the impact of the tumour itself on children's speech and language before surgery makes it difficult to evaluate to which degree postoperative deviations are caused by surgery or were already present preoperatively. One type of impairment that has been reported both pre- and postoperatively is word-finding difficulties, and children with preoperative word-finding difficulties are at higher risk for developing Cerebellar Mutism Syndrome. We first present an investigation of preoperative word-finding difficulties in Swedish children with posterior fossa tumours (n=24, age: 5;9-13;4 years), using the Swedish subset of the Nordic-European CMS study. To evaluate difficulties, we compare accuracy and speed on a confrontation naming test with performance in typically developing Swedish children (n=222, age: 5;9-13;4 years), and we examine whether the impact of the tumour changes across development.

Having established degree of difficulties, we then investigate the impact of tumour histology and location on preoperative word-finding ability in a large sample of children with posterior fossa tumours, analysing data from the Swedish, Danish, Norwegian, British, Hungarian, Italian and Latvian subsets of the Nordic-European CMS study (n=203, age: 2;1-17;8 years). Word-finding difficulties have implications for the child's well-being and participation in everyday life, and understanding its predictors is important for prognosis and treatment.

Sunday 11 September 2022

Neuropsychology Session

Neurocognitive outcome, academic achievement and occupation in a consecutive sample of paediatric cerebellar tumour long-term survivors

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Introduction: Tumours of the cerebellum are known to impact distinct neuropsychological domains beside motor function, with cerebellar mutism syndrome (CMS) being one of the most frequent complications. Moreover, survivors of cerebellar tumours are at high risk for developing adverse long-term sequelae in terms of academic achievement, neurocognitive and occupational outcome. This connection between the cerebellum and neurocognitive performance has increased the scientific interest in the role of the cerebellum regarding higher cognitive functioning.

Patients and Methods: A consecutive sample of 93 paediatric cerebellar tumour patients was analysed, all treated between 2001 and 2015. Eight patients were diagnosed with CMS (8.6%). Most common histologies were pilocytic astrocytoma, medulloblastoma and ependymoma. All patients completed a comprehensive standard-of-care neuropsychological test-battery. Median time between diagnosis and follow-up assessment was four years. Comparisons were made for different histologies, CMS and different treatments.

Results: The results indicate that all patient groups showed difficulties in various neurocognitive domains, even patients with low grade gliomas. All participants suffering from post-operative CMS needed a

special form of educational/occupational support, compared to 33% in the total sample. Moreover, CMS patients showed significantly lower neurocognitive functioning in certain domains (divided attention, information processing speed) years after diagnosis.

Conclusion: All patients turned out to be at high-risk for neurocognitive late effects, not only those with CMS. Cerebellar tumour affects academic achievement and increases the need for special support services. Finally, the results highlight the importance of sophisticated neurocognitive assessment in all PFT patients, accompanied by distinct counselling regarding education.

Rehabilitation Session

Sociocultural variables have a major impact on participation in patients treated for paediatric posterior fossa tumours

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Objective: This study investigates the severeness of participation barriers in patients surviving paediatric posterior fossa tumours (PFT) many years after treatment. In the past, etiological studies on adverse outcome have primarily focused on pathobiological risk factors. The current analysis aims to investigate the importance of environmental variables.

Method: On average, ten years after diagnosis educational and social difficulties of 42 patients surviving paediatric PFT (mean age 17 years) were inquired using a self-constructed questionnaire following the Psychosocial Resource-Orientated Assessment (PREDI). Educational or social participation barriers were defined by self- and/or proxy-reported difficulties in school or in peer relationships. Accordingly, the children and adolescents were categorized into groups of adequate and limited participation. Subsequently, the study identified potential pathobiological (treatment type, hydrocephalus, tumour relapse, gender, age at diagnosis, seizures, cerebellar mutism) and environmental (parental and maternal education, siblings, main language, discrepancies between personal and environmental values, regular physical activity, private living space) risk factors and investigated whether patients with adequate and limited participation differed in the number of risk factors.

Results: Almost one decade after treatment two-thirds of patients experienced educational and/or social difficulties. Patients with limited participation were more frequently associated with environmental factors such as low maternal education degree, siblings, main language other than German, discrepancies between societal and personal values and irregular physical activity, as well as the pathobiological risk factors treatment type, hydrocephalus, tumour relapse, cerebellar mutism, and seizures. These variables significantly discriminated between patients with and without limited participation.

Conclusion: Limited participation in patients treated for paediatric PFT is common. Next to pathobiological, also environmental risk factors play a major role in educational and social participation barriers. This highlights the fact that solely considering pathobiology is not sufficient when investigating risk factors for the emergence of late sequelae. Future etiological studies must adopt a biopsychosocial perspective.

Posters

Abstracts listed in alphabetical order by presenting author

Neuro-ophthalmological findings in children and adolescents with medulloblastoma - a retrospective analysis

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Background: Medulloblastoma represents the most common malignant paediatric brain tumour. Ophthalmic complications are possible sequelae.

Methods: Paediatric medulloblastoma (MB) patients treated at the Medical University of Vienna from January 2012 to August 2021 were analysed and their last ophthalmic assessment was reviewed.

Results: Fifty-six MB patients could be included (71.4% non-WNT/non-SHH, 16.1% SHH-activated, 8.9% WNT-activated, 3.6% non-specified). Mean age at diagnosis was 7.2 years (range 0-19). Median follow-up to last ophthalmological assessment was 19.7 months (range 0.1-93.2). Thirty-four children underwent tumour resection at our hospital, their tumour localizations were: vermis (55.9%), floor of the 4th ventricle (26.5%), cerebellar hemispheres (11.8%), lateral recess (5.9%). Symptoms at presentation were evaluable for 51 children: 92.2% had symptoms of elevated intracranial pressure, 76.5% ataxia and 21.6% visual disturbances. Postoperative posterior fossa syndrome was observed in 11.1% of 54 children. 98.2% had chemotherapy as part of their initial treatment and all children older than four years (85.7%) received postoperative irradiation of the posterior fossa. In 13 (23.2%) intraventricular chemotherapy was applied. At the last follow-up 21 patients experienced relapse after primary treatment.

At the final assessment, frequent neuro-ophthalmological abnormalities included: oculomotor disturbance (75%), esotropia (35.7%) including abducens palsy (12.5%), other cranial nerve palsies (21.4%), horizontal gaze-evoked nystagmus (51.8%), spontaneous nystagmus (16.1%), ocular tilt reaction (21.4%), and optic disc abnormalities (14.3%). Good visual acuity (≥20/25) was maintained in 62.5% patients. Visual field and optical coherence tomography was successfully performed in 75% and 66.1% of patients, respectively. Optic pathway lesions were detected in 4 patients (7.1%), including two cases with occipital metastases, one with optic nerve metastasis and one with leptomeningeal carcinomatosis. Orthoptic treatment with prisms and strabismus surgery was required in 14.3% and 7.7% of children, respectively.

Conclusion: Children with MB frequently suffer from neuro-ophthalmological late-effects. Regular monitoring is warranted to initiate appropriate management.

A 4-year neurocognitive follow-up of children with a posterior fossa tumour

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Survivors of a posterior fossa tumour during childhood often demonstrate a broad spectrum of neurocognitive and psychosocial difficulties later in

life. However, the trajectories of these difficulties throughout treatment and survivorship have rarely been studied. We sought to determine these neurocognitive and psychosocial trajectories throughout treatment and survivorship, and the impact of radiotherapy (RT) on them.

Thirty-eight children with a brain tumour located in the posterior fossa and diagnosed at the University Hospitals Leuven were included. In addition, these children had at least 3 neurocognitive assessments between their diagnosis and their 18th birthday and assessments were conducted every 2 years. The first assessment was conducted at the earliest possible moment after diagnosis and before the start of any adjuvant therapy. Mean age at diagnosis was 7.62 years. The most common diagnosis was pilocytic astrocytoma (n=23) and medulloblastoma (n=10). Ten patients received craniospinal RT, all of them were patients with a medulloblastoma and 23 patients received focal RT.

Repeated measures were used to analyse the evolution of intelligence, memory, processing speed, visuomotor functioning, executive functions, internalizing and externalizing problems. The between subject factor was type of irradiation (no, focal and craniospinal).

For intelligence a borderline significant interaction effect was found with the craniospinal group demonstrating the steepest decline (p=0.065). A significant time effect was found for memory (p=0.007), processing speed (p=0.009) and executive functions (p=0.006), the overall group performed better over time.

In addition to the expected decrease in general intelligence in craniospinal irradiated patients, we demonstrate an improvement across other neurocognitive domains. The assessment of neurocognitive functioning shortly after diagnosis is often challenging. Several factors, such as hydrocephalus can have then an impact. Our data show that different neurocognitive trajectories can be observed. Longitudinal studies are needed to better predict these neurocognitive trajectories.

Paediatric Neuropsychological Outcomes of Cerebellar Mutism Following Posterior Fossa Tumour Resection

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Cerebellar mutism syndrome (CMS), also referred to as posterior fossa syndrome, is a possible complication of posterior fossa tumour resection. Symptomology has included various combinations of ataxia, cognitive dysfunction, personality and behaviour change, emotional lability and irritability, hypotonia, dysphagia, dysarthria, and mutism. The purpose of this poster is to review the neuropsychological outcomes following posterior fossa tumour resection when CMS is present. Literature was obtained through searches in the following databases: PsycINFO, PsycARTICLES, ERIC, and MEDLINE with Full Text. The search was limited to peer-review publications and used a combination of the following terms: 'cerebellar mutism or posterior fossa syndrome' and 'resection' and 'neuropsychology or neuropsychological or cognitive or intelligence or executive functioning or executive functions or language or attention or concentration or memory or visual-spatial or motor or sensory' and 'posterior fossa tumour', and 'children or adolescents or youth or child or teenager or paediatric or paediatric or kids'. A total of 33 articles were found with 22 relevant empirical articles. Articles were not considered relevant if they focused on cerebellar mutism in individuals who have not undergone posterior fossa tumour resection, didn't focus on neuropsychological outcomes, were focused on adults, or were reviews of the literature. Although cerebellar mutism is a relatively common finding following posterior tumour resection, most of the published studies have relatively small number of participants or are case studies which limits generalizability. Additional research is needed including on risk and resiliency factors, as well as tumour type and characteristics. Given the multifunctional role of the cerebellum, paediatric neuropsychologists should conduct comprehensive assessments with this population. Implications for researchers and practitioners will be discussed.

The realities of a rehabilitation journey following posterior fossa syndrome

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Rehabilitation following a diagnosis of Posterior Fossa Syndrome can be complex and lengthy. We will share case examples of children and young people who have been through a full rehabilitation journey from initial diagnosis to long term follow up, including their opinions about the highlights and pitfalls of their experience. We will focus on their individual strengths and needs throughout their rehabilitation pathway, and also present their long term outcomes. We will highlight that there is a large variability in offer, intensity, resources and knowledge across the rehabilitation journey for CYP with this diagnosis.

Medulloblastoma, cerebellar mutism syndrome and disability

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Introduction: Medulloblastoma is the paradigm of CNS tumours, treated with intensity (surgery, chemotherapy and radiotherapy), survivors have significant cognitive and motor sequelae. Cerebellar mutism syndrome, develops in children after surgery for midline cerebellar or intraventricular tumours and compromises several neurologic and neurocognitive signs.

The aim of this retrospective study is to determine the most frequent sequelae in patients with medulloblastoma treated in the last 10 years in our center, and correlate the severity of the same with the presence of the cerebellar mutism syndrome.

Patients and Methods: Retrospective review of the medical records of patients with medulloblastoma treated in our center in the last 10 years, analysing the sequelae present immediately after surgery, one year and two years after surgery.

Results: Of the total number of patients with posterior fossa tumour, 29% were medulloblastoma.

All patients were evaluated after surgery and received physiotherapy, occupational therapy and speech therapy according to their needs.

The most frequent and permanent sequelae at two years of follow-up were ataxia (81%), ocular affectation (62.5%), cognitive impairment (100%) and 50% were dependent for basic activities of daily living.

Sixty-eight percent, had a paediatric postoperative cerebellar mutism syndrome having good evolution with early rehabilitation treatment. Two years after surgery, patients with cerebellar mutism syndrome

had more ataxia (77.7%), hypotonia (56.2%), ocular affectation (75%), severity of cognitive deficits and functional dependence (55%).

Conclusions: Children with medulloblastoma have a high survival but will have permanent motor and cognitive deficits over time that can produce a significant level of disability and dependence. Cerebellar mutism syndrome is a common complication in the treatment of medulloblastoma, increasing sequelae and long-term disability.

Besides improving the side effects of the treatments, the integration of rehabilitation in the therapeutic team from the beginning is key to improving these conditions.

Single centre experience of Posterior Fossa Syndrome from a tertiary paediatric oncology centre

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Posterior Fossa Syndrome (PFS) occurs after surgical resection of posterior fossa (PF) tumour in 8-31% of cases; characterised by transient mutism, emotional lability, ataxia, cranial nerve deficits and cognitive difficulties occurring 1-3 days post operatively, recovery can be incomplete.

Aim: To explore the incidence and recovery of PFS in our centre.

Methodology: Retrospective data was collated and reviewed on patients aged 0-16 years, presenting with PFS over a 15year period (2006 -2021).

Results: 112 patients underwent posterior fossa surgery, 24 (16 male, 8 female) were with diagnosed with PFS (21%). Median age at diagnosis 8 years 2 months (range 2years 8 months – 14years 11 months). Diagnoses; 17 medulloblastomas, 5 pilocytic astrocytomas 2 ependymomas,.8/24 had metastatic disease at presentation. Tumour was unilateral in 6 and midline in 18. Complete tumour excision was achieved in 19/24. 16 subsequently received additional oncological treatment. All patients experienced symptom onset within 2 days of neurosurgery, 6 had reduced speech and 18 had mutism. 16 patients showed behavioural changes and 17 had ataxia.

Follow up data was available on 19/24; 3 died of progressive disease, 2 transferred elsewhere. Median follow up was 21 months (range 12months – 11 years 4 months). 3 (16%) patients recorded complete recovery with a rehabilitation length of stay of <30days (2 pilocytic astrocytomas, 1 ependymoma), 17 recovered functional speech, 11 had significant mobility issues with 8 wheelchair dependent outside the home (10 medulloblastomas and 1 pilocytic astrocytoma).

Conclusion: The retrospective data demonstrates our incidence is within the reported range. Patients with complete recovery had shorter duration of mutism followed by rapid physical recovery. While malignant and metastatic tumours were associated with worse PFS, this was not exclusive. The variety of data documentation makes specific categorization of PFS challenging and a standardized assessment and recording tool would improve future analysis.

Clinical case study: a 14 year old boy with Posterior Fossa Syndrome presenting after cerebellar haemorrhage

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Posterior fossa syndrome (PFS) is well documented as occurring following neurosurgery for cerebellar tumour resection however there is little in the literature related to non neuro oncology PFS incidence. This case demonstrates features of PFS occurring in a 14 year old boy post-neurosurgery to the cerebellum for a small deep cerebellar arteriovenous malformation.

At onset he was mute with severe agitation and confusion, bulbar dysfunction necessitating tube feeding, abnormal eye movements, 4 limb weakness and severe ataxia affecting trunk and limbs. He required intensive neurorehabilitation over 6 months. At last follow up, 5years post surgery, he remains moderately ataxic with ongoing difficulty with bulbar function and speech.

Post-Operative Paediatric Cerebellar Mutism Syndrome; A National audit of Speech & Language Therapy Intervention

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Background: Post-Operative Paediatric Cerebellar Mutism Syndrome is a condition in which children and young people (CYP) develop mutism or reduced speech following surgery to the posterior fossa region of the brain to remove a tumour. Incidence is estimated to be 11-29% and risk varies depending on the type of tumour. Currently, little is known about the most effective SLT interventions for this population with no particular approach having been studied and therefore no evidence base to refer to. Consequently, there are no published guidelines to support Speech and Language Therapists (SLTs) in selecting the most effective interventions for those with POPCMS.

Methods: 8 Principal Treatment Centres (PTCs) for children with cancer in England contributed towards this study and each provided data for up to 5 patients. Medical, surgical and SLT data was collected and analysed using combined statistical and descriptive methods to identify patterns and variations in SLT intervention nationally.

Results: The data of 31 patients was collated and analysed; 21 males and 10 females with a median age of 7 years 1 month. Patients were seen a median of 11 times by a Speech and Language Therapist (SLT) and waited a median of 8 days for their first SLT contact following neurosurgery. 71% of patients received input solely from a SLT and outcomes measures for SLT intervention were only used for 10% of all individuals.

Conclusion: The results of this study show variation in SLT intervention nationally for individuals with POPCMS which reflects the limited literature and published guidelines for this patient group. Further research in to specific SLT interventions as national consensus and development of guidelines to inform SLT decision making would be of benefit.

Language outcomes in children who underwent surgery for a posterior fossa tumour: A systematic review of the literature

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Introduction: Following surgical resection, children with a posterior fossa tumour may have spoken or written language impairments, such as word-finding and reading difficulties. The present systematic review synthesises the literature regarding the expressive and receptive postoperative language outcomes in this clinical population. Furthermore, the influence of several variables related to child (e.g., age at diagnosis), tumour (e.g., tumour type) and tumour treatment (e.g., radiation dosage) characteristics is investigated. For this second aim, we are particularly interested in the influence of the emergence and duration of pCMS on the language outcomes. Potential benefits of this work are the identification of shortcomings in the literature and a starting point toward formulating guidelines for postoperative language assessment in this clinical population.

Methods: A comprehensive literature search is conducted in Covidence, including studies with participants who underwent posterior fossa surgery during childhood (< 18 years) and were at least two years old at the time of the postoperative language assessment. The methodological quality of the included studies is assessed using an adapted version of the Joanna Briggs Institute checklist. Studies of reduced quality (score < 50%) are excluded. Included studies are narratively synthesised and language outcomes are organised per level of language processing (e.g., phonology, morphosyntax). Also, the influence of several variables on the language outcomes is considered. A critical evaluation of the administered assessment tools is conducted.

Preliminary results & conclusion: A total of 70 studies met the inclusion criteria. These studies are narratively synthesised. It is already clear that a broad spectrum of language impairments was reported, but that these are characterised by a large interindividual heterogeneity. Furthermore, a preoperative language assessment is missing in the majority of the included studies, which could provide us with an important baseline. Final results will be available in September