European Archives of Psychiatry and Clinical Neuroscience (2024) 274:1–2
https://doi.org/10.1007/s00406-023-01756-x

EDITORIAL

How to embrace transdiagnostic concepts when neurodevelopmental disorders become harbingers of adult psychopathology?

Sebastian Walther[1]

Published online: 27 December 2023

Neurodevelopmental disorders are less prevalent than adult-onset mental health issues, but are associated with poor outcomes and low quality of life. Furthermore, neurodevelopmental psychopathology may become comorbid to or predisposing for psychotic, affective, or substance use disorders. Collectively, obsessive compulsive disorder (OCD), attention deficit hyperactivity disorder (ADHD), and autism spectrum disorders (ASD) may exert shared and distinct pathways to other psychopathology. For example, OCD, ADHD, and ASD have specific abnormalities of psychomotor behaviors [1]. Likewise, neurodevelopmental disorders show overlaps between other physiological measures or dimensions of psychopathology, e.g. reduced cognitive control or impulsiveness. Furthermore, transdiagnostic psychopharmacological strategies have been applied to some of these disorders, such as OCD and ADHD. Phenomenological and behavioral similarities suggested common pathobiology. However, a recent large-scale ENIGMA meta-analysis failed to demonstrate shared differences between control subjects and ADHD, ASD, or OCD patients [2]. Instead, specific cortical (ASD) and subcortical (ADHD) abnormalities were substantiated. Thus, despite some commonalities, the differences between the neurodevelopmental disorders are critical for psychiatry.

When treating patients, the knowledge of comorbid or premorbid neurodevelopmental conditions may help to improve diagnosis and to guide specific treatment. Currently, the field struggles to integrate this knowledge into treatment. In this issue, the journal covers multiple studies on ADHD, ASD, and OCD, spanning genetics, neuroimaging, and interventions.

✉ Sebastian Walther
Sebastian.walther@unibe.ch

[1] Translational Research Center, University Hospital of Psychiatry and Psychotherapy, University of Bern, Murtenstrasse 21, 3008 Bern, Switzerland

Four articles in the current issue discuss aspects of ADHD. Lou et al. report from an EEG study, that children with ADHD show increased prestimulus alpha oscillations during a visual context perception task [3]. The increased preparatory activity was associated with better task performance but was unaffected by modulation through methylphenidate administration. This finding suggests that children with ADHD increase visual perception to compensate for cognitive impairment. Another paper introduces a protocol for non-invasive brain stimulation in ADHD. Mauche et al. present the study protocol from a German multicenter randomized clinical trial testing the effect of five sessions of anodal transcranial direct current stimulation (tDCS) over the right dorsolateral prefrontal cortex (DLPFC) to treat ADHD symptoms in adults [4]. This study holds promise for augmenting pharmacotherapy and psychotherapy approaches in adult ADHD.

The current issue also includes three articles on autism spectrum disorders, focusing on neurobiology and psychometric test properties. Liloia et al. conducted a neuroimaging meta-analysis of regional homogeneity in subjects with pediatric autism [5]. Summarizing data from 11 experimental samples with 455 autism spectrum individuals and 474 controls, they detected decreased regional homogeneity in the fMRI signal in 3 clusters: (1) paracentral, (2) ventromedial prefrontal cortex, and (3) posterior cingulate cortex. These areas are typically serving functions such as motor behavior/interoception, mentalizing, and autobiographical memory. Thus, meta-analytic evidence from neural activity suggest specific local decreases in ASD subjects. Another report by Huang et al. investigated the specificity of instruments assessing autism severity in children [6]. Authors found that the clinical administered childhood autism rating scale—high functioning version (CARS-HF) performs best when administered in children with low autism severity. In this case, the CARS ratings also correlate with caregiver report of social responsiveness. In contrast, in children with high autism severity, these measures poorly correlate. Authors

suggest to specifically select the optimal instrument when assessing autism symptom severity.

Finally, four articles report on OCD, including phenomenology and brain imaging. Yang et al. performed a meta-analysis of grey matter volume and resting state brain activity in patients with OCD and healthy controls [7]. They included 83 studies (41 resting state fMRI and 42 voxel-based morphometry) and found specific alterations of resting state brain activity and grey matter volume. The 1780 OCD patients had more resting state activity than the 1991 control subjects in bilateral inferior frontal gyri, medial prefrontal cortex and bilateral medial cingulate cortex, but at the same time, they had hypoactivity in the cerebellum, paracentral lobule, and inferior parietal cortex. Grey matter was increased in bilateral thalamus, right striatum and cerebellum, but decreased in frontal cortical areas. Findings suggest specific alterations in brain areas responsible for cognitive control and motor behavior. Morgenroth et al. conducted a phenotyping and genotyping analysis in 91 patients with schizophrenia who were treated with clozapine [8]. They investigated the association between clozapine treatment and the presence of obsessive compulsive symptoms or OCD, and they explored the associations between OCD comorbidity and polygenetic risk scores for schizophrenia, OCD, or clozapine treatment. They found a substantial proportion of patients presenting with obsessive compulsive symptoms (40%), while 28% even qualified for comorbid OCD. There was no association with polygenetic risk scores in this cohort. This study adds to the growing literature of comorbid OCD in psychosis. Whether childhood-onset OCD might be the ouverture to a psychotic prodrome was explored by Borrelli et al., who studied prodromal psychotic symptoms in individuals with OCD [9]. They focused on cognitive-perceptual basic symptoms (COPER) and high-risk criterion cognitive disturbances (COGDIS) and the age of OCD onset. In 90 outpatients with OCD, they found that COPER and COGDIS correlated with OCD severity scores. Importantly, 29% qualified for COPER and 27% for COGDIS risk criteria. Subjects with OCD onset before age 10 (very early onset) demonstrated more prodromal symptoms than the adult onset group. In sum, data suggest an association of OCD symptoms and psychosis across the age span.

Dimensional psychiatry approaches are excellent in broadening our perspectives on the development of psychopathology. Recent studies managed to identify the interaction of symptom dimensions on pathobiology, such as autistic and schizotypal traits on hippocampal perfusion [10]. In clinical practice, however, we still need to focus on categories and individuals. The broader perspective may lead to transdiagnostic treatment approaches that when applied in everyone might fall short of specific action (e.g. "one size fits all"). Therefore, it will be critical to recognize transdiagnostic neurodevelopmental origins while searching for syndrome specific solutions (i.e. "think global but act local"). One solution could be the augmentation of psychotherapy with psychopharmacology and non-invasive brain stimulation, offering individual variation within broader treatment concepts.

Data availability There is no data associated with this article.

References

1. Walther S, Mittal VA (2022) Motor behavior is relevant for understanding mechanism, bolstering prediction, and improving treatment: a transdiagnostic perspective. Schizophr Bull 48(4):741–748
2. Boedhoe PSW, van Rooij D, Hoogman M et al (2020) Subcortical brain volume, regional cortical thickness, and cortical surface area across disorders: findings from the ENIGMA ADHD, ASD, and OCD working groups. Am J Psychiatry 177(9):834–843
3. Luo X, Dang C, Guo J et al (2023) Overactivated contextual visual perception and response to a single dose of methylphenidate in children with ADHD. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-023-01559-0
4. Mauche N, Ulke C, Huang J et al (2023) Treatment of adult attention-deficit hyperactivity disorder (ADHD) with transcranial direct current stimulation (tDCS): study protocol for a parallel, randomized, double-blinded, sham-controlled, multicenter trial (Stim-ADHD). Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-023-01652-4
5. Liloia D, Manuello J, Costa T, Keller R, Nani A, Cauda F (2023) Atypical local brain connectivity in pediatric autism spectrum disorder? a coordinate-based meta-analysis of regional homogeneity studies. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-022-01541-2
6. Huang CY, Chen KS, Lee KY, Lin CH, Chen KL (2023) Different autism measures targeting different severity levels in children with autism spectrum disorder. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-023-01673-z
7. Yang Z, Xiao S, Su T et al (2023) A multimodal meta-analysis of regional functional and structural brain abnormalities in obsessive-compulsive disorder. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-023-01594-x
8. Morgenroth CL, Kleymann P, Ripke S et al (2023) Polygenetic risk scores and phenotypic constellations of obsessive-compulsive disorder in clozapine-treated schizophrenia. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-023-01593-y
9. Borrelli DF, Ottoni R, Provettini A et al (2022) A clinical investigation of psychotic vulnerability in early-onset obsessive-compulsive disorder through cognitive-perceptive basic symptoms. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-022-01543-0
10. Nenadic I, Meller T, Evermann U et al (2023) Modelling the overlap and divergence of autistic and schizotypal traits on hippocampal subfield volumes and regional cerebral blood flow. Mol Psychiatry. https://doi.org/10.1038/s41380-023-02302-w