European Archives of Psychiatry and Clinical Neuroscience (2022) 272:1391–1393
https://doi.org/10.1007/s00406-022-01511-8

EDITORIAL

New findings on attention/hyperactivity disorder: what is (not) known?

Vincent Millischer[1] · **Dan Rujescu**[1]

Published online: 7 November 2022

Attention deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder which is characterized by inattention, hyperactivity and/or impulsivity. It affects roughly one out of twenty children and often persists into adulthood. Overlapping symptoms with other psychiatric disorders often lead to difficulties in diagnosis and although efficient treatments like methylphenidate have been known for over fifty years, ADHD is still underdiagnosed and undertreated in many European countries, with a clear gender gap existing for both diagnosis and treatment. This leads to unnecessary suffering, as untreated ADHD can lead to several social problems, including poor academic achievement, social rejection, substance use and violence [1]. Finally, while there is a growing literature on related mechanisms, its neurobiology is still largely poorly understood. Several of these problems are addressed in this issue of European Archives of Psychiatry and Clinical Neuroscience, with a particular focus on this disorder.

Building up on the ever-growing evidence of overlap between ADHD and other psychiatric disorders, Hayashi et al. [2] examined the presence of autism spectrum disorder (ASD) symptoms in adults with ADHD without a clinical diagnosis of ASD and neurotypical controls. Patients scored significantly higher than controls on the Autism Diagnostic Observation Schedule, Second Edition (ADOS-2), with approximately one out of five meeting the ASD cut-offs. Even when only analysing patients not reaching the cut-off, these differences remained and could be observed in all domains: language and communication, reciprocal social interaction, social affect, and restricted and repetitive behaviours. In a single item analysis, the differences were particularly clear in domains of communication and social interaction. Overall, this study adds to the evidence of overlap between ADHD and ASD, possibly stemming from common biological and genetic causes and highlights the complex and heterogeneous nature of ASD symptoms in ADHD.

In another study, a group led by Pietro De Rossi and Stefano Vicari [3] examined the question how different patients with ADHD being recommended pharmacological treatment after the first assessment at a specialized centre were on a symptomatic level from those receiving other treatment options. Studying this question in a naturalistic sample of 715 children and adolescents with ADHD assessed for a first diagnosis, the authors found that patients being offered a pharmacotherapy with methylphenidate were significantly older and tested lower on IQ-scales and for adaptive skills. Furthermore, boys were more likely to be offered pharmacotherapy than girls, even if there was no difference in the above-mentioned variables between the two genders. Finally, the authors were able to show that both ADHD symptoms and non-ADHD psychopathological symptoms were higher in the treated group. Overall, the article paints the complex picture of patients being offered ADHD-specific treatment having overall higher symptom severity, but that the treatment decisions might also be influenced by other variables, not the least gender.

To study the effects of another suggested non-pharmacological treatment on inattention in children, Carucci et al. performed a randomized, double-blind placebo controlled trial for omega 3/6 dietary supplementation in a total of 160 children with mild to moderate inattentive ADHD [4]. No statistically significant effects were found for the main outcome, the inattention score of the ADHD-RS-IV after 6 months of treatment, nor for any secondary outcome. Omega 3/6 dietary supplementation being not more efficient than placebo at reducing inattention symptoms in ADHD, this study further supports the use of well-established treatments in this disorder.

✉ Dan Rujescu
dan.rujescu@meduniwien.ac.at

[1] Department for Psychiatry and Psychotherapy, Medical University of Vienna, Währinger Gürtel 18-20, 1090 Vienna, Austria

The importance of effective treatments is further supported by work by Hertz et al. [5] who analysed the predictive validity of ADHD symptoms in combination with the Violence Risk Appraisal Guide-Revised (VRAG-R) in a high-risk sample of young offenders. The VRAG-R is a risk assessment instrument developed to predict violent recidivism in adult offender samples, however had never been tested in youth. In their study, the authors were able to show, that the total sum of VRAG-R had good predictive validity for violent and general recidivism and re-incarceration in their younger sample, even if some of the items of the instrument seemed less adapted to a youth cohort than an adult group (e.g., marital status at time of index offence). Finally, the authors report that current ADHD symptoms – but not childhood ADHD symptoms – could improve the predictive validity beyond VRAG-R. Overall, their work validated the VRAG-R in youths, while supporting the necessity of its adaptation for this specific subgroup with the possibility of introducing screening for ADHD symptoms, introducing a possible modifiable risk factor to the screening method.

Yet another aspect of violent behaviour was studied by Eggart and colleagues [6] who performed a systematic review and meta-analysis on psychopharmacological treatment of non-suicidal self-injury in children and adolescents. Although self-harm is a very relevant clinical topic for all mental-health professionals and the authors performed a search for all classes of psychotropic drugs, only seven studies could be included. Four randomized-controlled trials on SSRI effects could be analysed in a quantitative manner. Pooling data from these studies, no effect could be found for SSRI on NSSI. Regarding other drugs, only retrospective and non-randomized studies were available for qualitative analyses. Overall, the study concludes that there is an urgent need for more and better-quality studies as the evidence in any direction is currently sparse currently no effective pharmacological treatment option for NSSI in adolescents is available.

Another systematic review and meta-analysis was performed by Vidor et al. [7] on magnetic resonance spectroscopy (MRS) studies assessing differences in brain metabolites between patients diagnosed with ADHD and healthy controls. Increasing the total sample size to 874 patients in 33 studies, this was the first meta-analysis was able to meta-analyse results for a few brain regions, based on age categories and laterality. This had previously not been possible, as regions often were analysed by too few studies and data had to be pooled. After correction for multiple testing, ADHD in children was associated with higher concentration of a composite of glutamate and glutamine in the right medial frontal area. Although the number of studies has increased over the last years, data for meta-analysis was too scarce for most of the regions. This led the authors to present a "map of opportunity" pointing out which areas still require more analysis to reach conclusive results and is therefore an important addition for the field.

A different approach to studying the neurobiology of ADHD was presented by Huang et al. The authors examined how long-range temporal correlations (LRTC) in different electroencephalograms frequency bands were associated with comorbid depression, depressive symptoms, and pharmacological intervention [8]. While showing that LRTC were present in subjects with ADHD, the authors did not find any associations with subphenotypes, therefore not supporting the use of LRTC as biomarker.

Finally, this issue features a third systematic review on imaging markers differentiation two important differential diagnoses of ADHD, namely borderline personality disorder (BPD) and major depressive disorder (MDD) [9]. Comparing grey matter volumes in young adults with BPD with healthy controls and patients suffering from MDD, the authors identified several common and distinct patter between the two disorders. However, given the relatively small number of adults with BPD included in the study, more research on the subject seems warranted as well.

This issue presents results on several new studies on ADHD, both with negative and positive results. It also supports the importance of systematically reviewing data to point out current knowledge gaps in the field and make it clear what is (not yet) known.

References

1. Faraone SV, Asherson P, Banaschewski T et al (2015) Attention-deficit/hyperactivity disorder. Nat Rev Dis Primers 1:15020
2. Hayashi W, Hanawa Y, Saga N et al (2022) ASD symptoms in adults with ADHD: a comparative study using ADOS-2. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-021-01362-9
3. De Rossi P, Pretelli I, Menghini D et al (2022) Clinical characteristics of children and adolescents with ADHD with or without methylphenidate prescription at their first diagnostic assessment. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-022-01386-9
4. Carucci S, Romaniello R, Demuru G et al (2022) Omega-3/6 supplementation for mild to moderate inattentive ADHD: a randomised, double-blind, placebo-controlled efficacy study in Italian children. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-022-01428-2
5. Gregório Hertz P, Müller M, Barra S et al (2021) The predictive and incremental validity of ADHD beyond the VRAG-R in a high-risk sample of young offenders. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-021-01352-x
6. Eggart V, Cordier S, Hasan A, Wagner E (2022) Psychotropic drugs for the treatment of non-suicidal self-injury in children and adolescents: a systematic review and meta-analysis. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-022-01385-w
7. Vidor MV, Panzenhagen AC, Martins AR et al (2022) Emerging findings of glutamate–glutamine imbalance in the medial

prefrontal cortex in attention deficit/hyperactivity disorder: systematic review and meta-analysis of spectroscopy studies. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-022-01397-6

8. Huang J, Ahlers E, Bogatsch H et al (2022) The role of comorbid depressive symptoms on long-range temporal correlations in resting EEG in adults with ADHD. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-022-01452-2
9. Cao Y, Xie H, Sun H et al (2022) Common and distinct patterns of gray matter alterations in young adults with borderline personality disorder and major depressive disorder. Eur Arch Psychiatry Clin Neurosci. https://doi.org/10.1007/s00406-022-01405-9