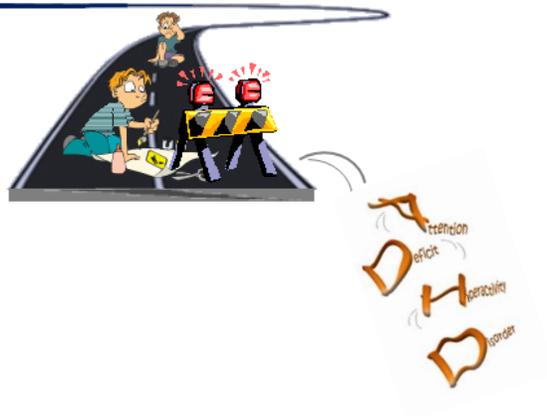


# NEWSLETTER



## INDICE:

Dalle banche dati bibliografiche

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Scarpellini F, Bonati M.

**TRANSITION CARE FOR ADOLESCENTS AND YOUNG ADULTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): A DESCRIPTIVE SUMMARY OF QUALITATIVE EVIDENCE**

*Child Care Health Dev. 2022;1-13*

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## BIBLIOGRAFIA ADHD OTTOBRE 2022

Appl Neuropsychol Child. 2022 Oct;11:567-78.

**OSMOTIC RELEASE ORAL SYSTEM-METHYLPHENIDATE HYDROCHLORIDE (OROS-MPH) VERSUS ATOMOXETINE ON EXECUTIVE FUNCTION IMPROVEMENT AND CLINICAL EFFECTIVENESS IN ADHD: A RANDOMIZED CONTROLLED TRIAL.**

**Tas Torun Y, Isik Taner Y, Güney E, et al.**

**Objectives:** The aim of this study to compare the clinic efficacy and effects of osmotic release oral system-methylphenidate and atomoxetine on executive function in children and adolescents with attention deficit hyperactivity disorder by a open-label, prospective, randomized controlled trial.

**Methods:** The study was performed by 95 cases between ages 6 and 12 years who were diagnosed as attention-deficit/hyperactivity disorder (ADHD) and also 40 control individuals. In this study, Conners' Teacher Rating Scale (CTRS) was used in order to evaluate the efficacy of the treatment. Executive functions were assessed by the performance-based neuropsychological tests and ecological behavioral rating scales. Stroop test, cancellation test, and serial digit learning test were applied to performance based neuropsychological tests. Behavior Rating Inventory of Executive Function tests (BRIEFs) were used as behavioral assessment scales.

**Results:** Among the ADHD groups, a reduction of over 40% in the CTRS subtest scores used to evaluate the efficacy of the treatment was considered to be an improvement, and no significant difference was found for both drugs. Both Osmotic Release Oral System-Methylphenidate Hydrochloride (OROS-MPH) and atomoxetine (ATX) significantly improved scores in neuropsychological tests.

**Conclusion:** Atomoxetine and OROS-MPH treatments have shown similar efficacy in clinical recovery and improvement on executive functions. However, disturbances in executive functions observed in children with ADHD are persistent despite treatment, when compared with the control group

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Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

Arch Dis Child. 2022;107:A322-A323.

**ADHD AND GIRLS; HEARING THEIR STORIES: A QUALITATIVE EXPLORATION OF THE EXPERIENCES OF GIRL BEING DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Pountney L, Liang H.**

**Aims Background** Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder which commonly presents in childhood. It is widely recognised that there exists a significant difference in the referral and diagnostic rates between boys and girls. Current literature suggests that girls with ADHD often go unrecognised or are misdiagnosed. If left undiagnosed children with ADHD can experience long term social, academic and emotional difficulties. To date no UK study has specifically focussed on hearing from girl's themselves in order to understand more about their experiences of living with symptoms of, or being diagnosed with, ADHD. This is essential to enhance our understanding of ADHD in girls and to improve recognition, referral rates and the diagnostic process for this vulnerable group.

**Objectives** The objective of this qualitative study was to explore the views and feelings of the girls and their families about their experience of being diagnosed with ADHD. We aimed to explore the girls' own perception of their difficulties, how they manifested and their impact upon their lives, to explore their experience of being referred for an assessment and of the diagnostic services involved in their care, to ascertain if there were any barriers to them receiving their diagnosis and to identify ways in which the girls and parents felt that the diagnostic process and care for girls could be improved.

**Methods** Participants were invited to participate in the study via an advertisement broadcast across the social media platforms of nine UK ADHD charities. Semi-structured interviews were held over Microsoft Teams with participants until data saturation. The data was thematically analysed using an inductive approach.

**Results** 14 semi-structured interviews were conducted, seven with girls aged between 6-16 years old and seven with at least one parent. Analysis of these interviews identified key themes relating to girls being referred and diagnosed, including: misconceptions about how ADHD presents in girls (within families, schools and the wider society), service design barriers and communication failures. The girls often felt misunderstood which impacted upon friendships, their wellbeing and their educational attainment. Parents frequently felt judged by professionals and wider society. Solutions for improving recognition of ADHD in girls included improving awareness within society, especially in school staff. Solutions for enhancing the diagnostic pathway included developing child-centered collaborative services and providing parents with a guide to early support services after symptom recognition, increased childfocussed ADHD education and peer support for girls.

**Conclusion** Misconceptions about how ADHD presents in girls continue to be a significant barrier to them accessing diagnostic services and appropriate care. This alongside service design issues negatively affected their patient journey. Enhanced education for schools is essential for earlier recognition of those experiencing possible symptoms of ADHD. Consulting with girls with ADHD and their families is important as we seek to develop and commission services that improve recognition of ADHD in girls and access to services for this patient group

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Arch Dis Child. 2022;107:A320-A321.

**ADHD IN DOWN'S SYNDROME – A SCOPING EXERCISE.**

**Perera S, Katangodage D.**

**Aims** 1. Literature survey on ADHD in Down's syndrome 2.To evaluate the prevalence of Attention Deficit hyperactivity Disorder (ADHD ) and Autism in Down's Syndrome using Light House Child development center Down's Syndrome data base. 3.Describe the clinical presentation and comorbidity of the ADHD children with Down's syndrome in the clinic setting.

**Methods** 1. Literature Survey on Down's Syndrome was done using the terms' ADHD/OR 'attention deficit hyperactivity disorder'/Or ' Attention Deficit Disorder with Hyperactivity/', 'autism Spectrum Disorder'/or 'autism or ASD or 'Autistic Disorder' or 'aspergerΓêù' and 'down's Syndrome/', 'down syndrome or' trisomy 21' in Medline, EMBASE and PsycINFO. only English Language articles since 2017 were reviewed. 2. The Down's Syndrome data base at the Light House Child Development center was searched for Children and

young people (upper limit of the age was 25 years) with a diagnosis of ADHD and Or autism. Their clinical presentations and comorbidity were noted.

**Results** 1. Literature survey - identified 23 articles in PsycINFO .171 articles in EMBASE (humans) and 51 articles in Medline. 55 articles were used for this focused review. we aim to present the findings at the meetings. 2.The Down's syndrome data base interrogation revealed that out of the 80 children and young people, aged 25 or younger, 15 were under 5 years of age and excluded from the study. records of one child who moved out of the area was not available. Two (02) had ADHD, Eleven (11) had Autism Spectrum Disorder (ASD). Hypothyroidism was identified in Twelve (12) patients. Other medical conditions on record include, Type 1 diabetes, coeliac disease, Hirschprungs, obesity and scoliosis. All ADHD and ASD children on the data base have Intellectual disability. One child with ADHD (Diagnosed at six years of age and started on 10mg Extended release MethylPhenidate preparation is currently(13.5 yrs) on 60mg O.D. he has Circadin 6 mg for sleep on set insomnia. The young person diagnosed at the Age of 14.5yrs did not tolerate ADHD medication but tolerates Crushed Circadin

**Conclusion** The Data base exploration in January 2022 revealed 1.6% had ADHD and 17. 2% ASD in children and young people with Down's syndrome aged 5-25 Yrs. The prevalence of ADHD and ASD in the Southend on Sea Down Syndrome data base at the Light House Child Development Center in comparison to a population based study in Sweden with 60 Down's syndrome children and young people (Ulrika Wester Oxelgren et al in Developmental Medicine & Child Neurology 2017)(ADHD 14%, ASD 47%) is very low. Limitations of the study- Number of children with ADHD is too small to comment on the variability of the type of presentation and the treatment response. A UK wide Down's Syndrome Data base review may help to ascertain the true prevalence of ADHD in Down Syndrome

Arch Dis Child. 2022;107:A322.

**VIRTUAL MEDICATION REVIEWS IN CHILDREN AND YOUNG PEOPLE (CYP) WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) DURING THE COVID-19 PANDEMIC – A LOCAL SERVICE USER EXPERIENCE SURVEY.**

**Matthews YY, Wong M.**

**Aims** Traditional in-person ADHD medication review is part of the Neurodevelopmental Service led by a community paediatrician at a district general hospital in North Wales. Consequent to COVID-19 pandemic lockdown in March 2020, the service was delivered virtually to limit infection risk, via telephone and web-based video Attend Anywhere platform. Although aligned with the European ADHD Guidelines Group recommendations, there was no past report of user experience on such contingent service delivery. A survey was therefore designed to evaluate user satisfaction and preference on the new locally implemented virtual ADHD medication review clinics in CYP during the COVID-19 UK-wide lockdown.

**Methods** Families with ADHD CYP who had attended their first virtual ADHD medication consultation between 6 April to 12 May 2020 were surveyed via telephone in August 2021. Parent/carer and/or CYP with ADHD were requested for consent to provide independent satisfaction and preference ratings scores (5 very satisfied/strongly agreed, 4 satisfied/ agreed, 3 neutral, 2 unsatisfied/disagreed and 1 very unsatisfied/strongly disagreed). Demography and clinical data were retrieved from respective clinic review letters. Microsoft Excel 2016 was used to analyse anonymised survey data.

**Results** Among nine clinics over the 6-week surveyed period, 47% (30/64) of the families of ADHD CYP of which 73% (22/30) male, were available and completed the survey. Responses were provided by all except one (29/30) mother and 37% (7/22 male and 4/8 female) of the surveyed ADHD cohort. The median (range) age in years for male was 13 (9 to 19) and female 14 (9 to 16). Their ADHD diagnosis ranged from 1 to 10 years with 63% identified with co-morbidities. Forty-percent experienced sleep issues with a-third benefiting for melatonin use. Among 93% of the cohort taking stimulants, 20% warrant medication only for schooling. Collective ratings were based on 10 telephone, 9 video and 11 both modes of virtual consultations. Greater satisfaction was reported from mothers than children on the quality of virtual consultations with highest ratings in screen (95% vs 86%) compared to access (70% vs 64%) and audio (79% vs 64%). Preferences on consultation modes for both mothers and children were similar with highest ratings for face-to-face (79% vs 82%), followed by video (61% vs 70%) and lowest via telephone (57% vs 55%) call.

**Conclusion** This parental and ADHD CYP survey results on the local virtually delivered ADHD medication reviews during the COVID-19 nationwide crisis, revealed despite high satisfaction on the quality of virtual

consultations, greater for video screen than telephone audio only call, both users expressed greater preference for in-person consultations. Following COVID-19 de-escalation, while resuming the user preferred in-person ADHD medication review clinic service, video-link consultations with its past trial-established advantages and this survey of high user satisfaction in its quality, should be retained as an alternative clinic delivery mode

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Arch Dis Child. 2022;107:A321-A322.

**A COMMUNITY STUDY ON IMPROVING THE MONITORING OF ADHD PATIENTS ON STIMULANT MEDICATION AT A NORTHAMPTONSHIRE GP PRACTICE.**

**Liao J.**

**Aims** 1. Improve the monitoring of patients with ADHD on medication in the community by measuring height, weight, BP and heart rate at the specified time intervals 2. Improve compliance with the NICE guidelines on diagnosis and management of ADHD 3. Identify adverse effects of stimulant medication such as growth restriction, hypertension and tachycardia in the paediatric population

**Methods** Data gathered on SystemOne software using specific inclusion criteria included all patients on ADHD medication and paediatric growth charts were reviewed. Data was collected and analysed on Excel and subgroup analysis was performed on the paediatric ADHD population under 18 years old. Parameters collected included sex, date of birth, age, current ADHD medication (dexamphetamine, atomoxetine or dexamfetamine) and baseline measurements (weight, height, blood pressure and heart rate) and whether they were monitored by Child Health Specialist Service (CHSS) or GP practice. A re-audit was conducted 2 months after initial audit results were disseminated at the practice meeting and interventions implemented which included reminder letters sent to patients to book appointments for reviewing height, weight, heart rate and blood pressure.

**Results** 47 patients were identified on clinical reporting using search string criteria (figure 1). 16/47 had discontinued ADHD medications. Of the 31 patients: 27 were taking methylphenidate, 3 were taking atomoxetine, and 1 patient was taking dexamfetamine for narcolepsy and did not have a diagnosis of ADHD, but was still subject to the same monitoring requirements and therefore included for data analysis (figure 1). 3/31 (10%) were female and 28/31 (90%) were male. 16/31 were paediatric cases under 18 years old and 15/31 were over 17 years old. Before intervention, 52% (16/31) of the total population were regularly monitored by CHSS or GP and this increased to 69% (20/29) after interventions were implemented at the local GP practice reflecting a 33% increase in pickup rate. This was largely due to a 127% increase in monitoring rate by the GP practice. Subgroup analysis of the paediatric population showed that 15/16 were on methylphenidate and 1 was on atomoxetine. There was a 75% increase (from 4/16 to 7/16) in monitoring after the interventions were implemented. 5 (31%) paediatric patients were identified with falling centiles in weight and required closer monitoring. 3/5 patients' weight values were between the 2nd-9th centile. Monitoring of the parameters were conducted by health care assistants (38%), doctors (17%) and nurses (7%).

**Conclusion** Monitoring rates for patients on ADHD drugs improved by 127% after interventions were implemented as part of this quality improvement project. GP monitoring rates for children improved by 75% (figure 2) and 5 children with falling weight centiles were identified after the re-audit and red flagged for further review. 69% of the total ADHD population served by this GP practice were monitored, up from 52% previously. There was a significant portion (31%) of the ADHD population served by this practice who did not engage with the service and were not monitored as a result. Although this small study had a large impact, novel approaches are still required to engage the poor responders

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Arch Dis Child. 2022;107:A323.

#### **MINDFULNESS MEDICATION IN ADHD.**

**Finlay F, Virani S.**

**Aims** ADHD is highly heterogeneous with a multi-factorial aetiology, diverse neurocognitive impairments and co-occurring problems, as well as positive traits such as creativity. Self-control deficits in everyday life, including problems controlling impulses, switching attention, regulating emotional responses, initiating and organizing tasks, impact functioning of children with ADHD. In children self-control ratings are an important predictor for health, wealth, academic, occupational and crime outcomes years later, therefore, improving self-control is important. Evidence-based interventions for children with ADHD include medication and behavioural treatments, although both have limitations and medication may have side effects. Other interventions merit further exploration and the aim of this literature review was to look at mindfulness meditation as an intervention.

**Methods** A literature search was conducted to look at the benefits of mindfulness meditation in ADHD

**Results** Mindfulness training is an intervention based on eastern meditation techniques. It helps increase awareness of the present moment, enhances non-judgmental observation, strengthens ability to control attention, retain focus and reduce distraction, and increases awareness of emotions making impulsive actions less likely. There is a growing body of research on the effectiveness of mindfulness for children, adolescents and adults with various psychopathologies, including anxiety and depression and sleep disorders. In adults, numerous studies have found that mindfulness interventions have a significant positive effect on ADHD symptoms, with improvements in executive functioning and self-reported emotion dysregulation. Various studies in children and adolescents also report positive outcomes. Zylowksa (2008) found that self-reported ADHD symptoms and performance on several neurocognitive attention tasks improved after mindfulness training in a mixed group of children and adults. A study by van der Oord (2012) involving 22 children showed a significant reduction in ADHD behaviour following an eight week mindfulness programme, delivered in a group format, and a reduction in parental stress. However teacher ratings showed non-significant effects. A further study with an eight week mindfulness programme (van de Weijer-Bergsma 2012) involving 10 adolescents and their parents found a self-reported reduction in attention and behaviour problems, with improved executive functioning. There were also improvements in performance in attention tests, and a reduction in parental stress in fathers but not mothers. In a study involving 25 children, aged 7-11 years, Santonastaso (2020) found that mindfulness orientated meditation had positive effects on neuropsychological measures and ADHD symptoms, the authors suggesting it as a promising tool for ameliorating cognitive and clinical manifestations of ADHD.

**Conclusion** As mindfulness-based training has become more popular, there is a need to examine whether it is beneficial for individuals with ADHD. Although most studies have small sample sizes, there is an emerging body of evidence that mindfulness training is an effective approach in children and adolescents with ADHD, maintenance strategies being required for long term effectiveness. Studies point toward improved planning, cognitive flexibility and better interactions within families. However, there are no published studies comparing the efficacy of mindfulness interventions with standard pharmacological treatment. The outcome of such studies in future will be of interest

Autism. 2022.

#### **"INSTRUMENTS ARE GOOD AT ELICITING INFORMATION; SCORES ARE VERY DANGEROUS": THE PERSPECTIVES OF CLINICAL PROFESSIONALS REGARDING NEURODEVELOPMENTAL ASSESSMENT.**

**Coughlan B, Woolgar M, Weisblatt EJJ, et al.**

Clinical judgement is a crucial part of autism and attention deficit hyperactivity disorder (ADHD) assessments. This study aims to harness insights from psychology and sociology to explore clinical perspectives and assessment practices of autism and attention deficit hyperactivity disorder. Qualitative interviews were conducted with health care professionals (n = 17). Interviews were conducted between January and May 2019. Data were analysed using a thematic approach. Themes were sorted into two interrelated categories (1) approaches to diagnosis (2) elements of diagnosis. Approaches to diagnosis were comprised of the following subthemes: nature of diagnosis, application of diagnosis: natural and pragmatic, revisiting conceptualisations: sub-optimal practice & unhelpful diagnoses, autism and attention deficit hyperactivity

disorder. Elements of diagnosis contained three related subthemes: contextualising standardised assessments, triangulating material, organisational factors. There is sometimes a pragmatic as well as nosological dimension to diagnosis. Competing desires for consistency and utility add further complexity to neurodevelopmental assessment. Lay abstract: Autism and attention deficit hyperactivity disorder are common behaviourally diagnosed conditions. One of the key aspects of diagnosis is clinical judgement. Yet despite decades of research, it is only in recent times that researchers have started exploring clinicians' perspectives on diagnosing these conditions. We aimed to add to this body of knowledge by conducting interviews with 17 experienced health care professionals in the United Kingdom to hear their perspectives on diagnosing autism and attention deficit hyperactivity disorder. Clinicians reflected that for some children and young people, diagnosis is reasonably straightforward; however, in other situations, decisions are made on more pragmatic grounds (i.e. will this be helpful). We identified some differences of opinion between professionals and organisation which adds to the complexity of applying a diagnosis. We recommend several areas for future research and point to some practical and philosophical implications of the work

Behav Brain Res. 2023;437.

**DYNAMIC FUNCTIONAL CONNECTIVITY CHANGES OF RESTING-STATE BRAIN NETWORK IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Zhu Z, Wang H, Bi H, et al.**

Patients with attention-deficit/hyperactivity disorder (ADHD) have shown abnormal functional connectivity and network disruptions at the whole-brain static level. However, the changes in brain networks in ADHD patients from dynamic functional connectivity (DFC) perspective have not been fully understood. Accordingly, we executed DFC analysis on resting-state fMRI data of 25 ADHD patients and 27 typically developing (TD) children. A sliding window and Pearson correlation were used to construct the dynamic brain network of all subjects. The k-means+ clustering method was used to recognize three recurring DFC states, and finally, the mean dwell time, the fraction of time spent for each state, and graph theory metrics were quantified for further analysis. Our results showed that ADHD patients had abnormally increased mean dwell time and the fraction of time spent in state 2, which reached a significant level ( $p < 0.05$ ). In addition, a weak correlation between the default mode network was associated in three states, and the positive correlations between visual network and attention network were smaller than TD in three states. Finally, the integration of each network node of ADHD in state 2 is more potent than that of TD, and the degree of node segregation is smaller than that of TD. These findings provide new evidence for the DFC study of ADHD; dynamic changes may better explain the developmental delay of ADHD and have particular significance for studying neurological mechanisms and adjuvant therapy of ADHD

Biomedizinische Technik. 2022.

**ANALYSIS OF EEG BRAIN CONNECTIVITY OF CHILDREN WITH ADHD USING GRAPH THEORY AND DIRECTIONAL INFORMATION TRANSFER.**

**Ekhlas A, Nasrabadi AM, Mohammadi M.**

Research shows that Attention Deficit Hyperactivity Disorder (ADHD) is related to a disorder in brain networks. The purpose of this study is to use an effective connectivity measure and graph theory to examine the impairments of brain connectivity in ADHD. Weighted directed graphs based on electroencephalography (EEG) signals of 61 children with ADHD and 60 healthy children were constructed. The edges between two nodes (electrodes) were calculated by Phase Transfer Entropy (PTE). PTE is calculated for five frequency bands: delta, theta, alpha, beta, and gamma. The graph theory measures were divided into two categories: global and local. Statistical analysis with global measures indicates that in children with ADHD, the segregation of brain connectivity increases while the integration of the brain connectivity decreases compared to healthy children. These brain network differences were identified in the delta and theta frequency bands. The classification accuracy of 89.4% is obtained for both in-degree and strength measures in the theta band. Our result indicated local graph measures classified ADHD and healthy subjects with

accuracy of 91.2 and 90% in theta and delta bands, respectively. Our analysis may provide a new understanding of the differences in the EEG brain network of children with ADHD and healthy children

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BMJ Open. 2022;12.

**TRAINING INHIBITORY CONTROL IN ADOLESCENTS WITH ELEVATED ATTENTION DEFICIT HYPERACTIVITY DISORDER TRAITS: A RANDOMISED CONTROLLED TRIAL OF THE ALFI VIRTUAL REALITY PROGRAMME.**

**McKay E, Kirk H, Coxon J, et al.**

**Introduction** Attention deficit hyperactivity disorder (ADHD) is characterised by significant deficits in attention and inhibition. These deficits are associated with negative sequelae that emerge in childhood and often continue throughout adolescence. Despite these difficulties adolescents with ADHD often demonstrate poor treatment compliance with traditional interventions (eg, psychostimulant medication). Virtual reality (VR) presents an innovative means of delivering engaging cognitive interventions for adolescents with ADHD and offers the potential to improve compliance with such interventions. The current parallel, randomised controlled trial aims to evaluate the effects of a VR intervention (Alfi) designed to improve inhibition in adolescents with ADHD.

**Methods and analysis** A sample of 100 adolescents (aged 13-17) with elevated ADHD symptoms will be recruited from secondary schools and ADHD organisations located in the state of Victoria, Australia. Participants will be randomly assigned to either an 8-week VR intervention or a usual care control. The VR intervention involves the completion of 14 sessions, each 20 min in duration. Participants will complete computerised assessments of inhibition and risk-taking preintervention and immediately postintervention. Parents/guardians will complete online questionnaires about their child's ADHD symptoms and social functioning at each of these timepoints. The primary outcome is change in inhibition performance in adolescents who received the intervention from preintervention to postintervention compared with adolescents in the control condition. Secondary outcomes include change in risk-taking, ADHD symptoms and social functioning in adolescents who received the intervention from preintervention to postintervention compared with adolescents in the control condition. If the intervention is shown to be effective, it may offer a supplementary approach to traditional interventions for adolescents with ADHD experiencing inhibitory control difficulties.

**Ethics and dissemination** This trial has ethics approval from the Monash University Human Research Ethics Committee (HREC) (21530) and the Victorian Department of Education and Training HREC (2020\_004271). Results will be disseminated through peer-reviewed journals, conference proceedings and community activities. Individual summaries of the results will be provided to participants on request.

**Trial registration number** ACTRN12620000647932

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Brain Sciences. 2022;12.

**A CROSS-SECTIONAL COMPARATIVE STUDY OF SLEEP DISTURBANCES IN CHILDREN WITH ADHD AND MATCHED CONTROLS.**

**Joseph AA, Gupta A, Hazari N, et al .**

**Background:** Systematic reviews conducted on sleep disturbances in attention deficit hyperactivity disorder (ADHD) have found inconsistent results due to the presence of several moderating variables which were not controlled for in previous studies. The aim of this study was to examine sleep disturbances in children with ADHD compared to their typically developing peers after controlling for moderating variables (age, sex, medication status, body mass index, and psychiatric and medical comorbidities).

**Methods:** ADHD was diagnosed using DSM-IV-TR criteria (Diagnostic and Statistical Manual of Mental Disorders) and Conners Parent Rating Scales. Children recruited (aged 6-12 years) for the ADHD group (n = 40) met the following criteria: IQ > 80, unmedicated, and no psychiatric or medical comorbidities. The control group consisted of age- and sex-matched typically developing peers (n = 40). Sleep was assessed subjectively (through parent reported questionnaires and sleep logs) and objectively (using video polysomnography).

**Results:** 65% of children with ADHD had a sleep disorder, as compared to 17% of controls. The ADHD group reported more sleep disturbances and disorders, both on subjective measures and objective measures.

**Conclusions:** Sleep disturbances and primary sleep disorders in children with ADHD exist independent of moderating variables and differences in sleep assessment methods, thereby bolstering support for previously documented literature on the ADHD and sleep connection

Brain Sciences. 2022;12.

**CLOCK GENES PROFILES AS DIAGNOSTIC TOOL IN (CHILDHOOD) ADHD: A PILOT STUDY.**

**Anatra A, Reis O, Wagner H, et al .**

Attention deficit hyperactivity disorder (ADHD) is a very common disorder in children and adults. A connection with sleep disorders, and above all, disorders of the circadian rhythm are the subject of research and debate. The circadian system can be represented on different levels. There have been a variety of studies examining 24-h rhythms at the behavioral and endocrine level. At the molecular level, these rhythms are based on a series of feedback loops of core clock genes and proteins. In this paper, we compared the circadian rhythms at the behavioral, endocrine, and molecular levels between children with ADHD and age- and BMI-matched controls, complementing the previous data in adults. In a minimally invasive setting, sleep was assessed via a questionnaire, actigraphy was used to determine the motor activity and light exposure, saliva samples were taken to assess the 24-h profiles of cortisol and melatonin, and buccal mucosa swaps were taken to assess the expression of the clock genes BMAL1 and PER2. We found significant group differences in sleep onset and sleep duration, cortisol secretion profiles, and in the expression of both clock genes. Our data suggest that the analysis of circadian molecular rhythms may provide a new approach for diagnosing ADHD in children and adults

Brain Sciences. 2022;12.

**NEUROFEEDBACK FOR THE EDUCATION OF CHILDREN WITH ADHD AND SPECIFIC LEARNING DISORDERS: A REVIEW.**

**Patil AU, Madathil D, Fan YT, et al.**

Neurofeedback (NF) is a type of biofeedback in which an individual's brain activity is measured and presented to them to support self-regulation of ongoing brain oscillations and achieve specific behavioral and neurophysiological outcomes. NF training induces changes in neurophysiological circuits that are associated with behavioral changes. Recent evidence suggests that the NF technique can be used to train electrical brain activity and facilitate learning among children with learning disorders. Toward this aim, this review first presents a generalized model for NF systems, and then studies involving NF training for children with disorders such as dyslexia, attention-deficit/hyperactivity disorder (ADHD), and other specific learning disorders such as dyscalculia and dysgraphia are reviewed. The discussion elaborates on the potential for translational applications of NF in educational and learning settings with details. This review also addresses some issues concerning the role of NF in education, and it concludes with some solutions and future directions. In order to provide the best learning environment for children with ADHD and other learning disorders, it is critical to better understand the role of NF in educational settings. The review provides the potential challenges of the current systems to aid in highlighting the issues undermining the efficacy of current systems and identifying solutions to address them. The review focuses on the use of NF technology in education for the development of adaptive teaching methods and the best learning environment for children with learning disabilities

Child Care Health Dev. 2022;1–13.

**TRANSITION CARE FOR ADOLESCENTS AND YOUNG ADULTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): A DESCRIPTIVE SUMMARY OF QUALITATIVE EVIDENCE.**

**Scarpellini F, Bonati M.**

The review presents a summary of available evidence about transition care of ADHD patients from all service users' perspectives. Common barriers, and suggestions for improvement ADHD of transition care, were extrapolated from qualitative research, including case notes studies, and were exposed. A comprehensive search of the PubMed, Embase, PsychInfo and Web of Science databases for articles published up to October 2021 was conducted to summarize recent evidence on the experiences of all stakeholders involved in the transition process. Reviews, other chronic conditions and different meaning of transition were excluded. Authors extracted data and assessed study quality independently. Findings were discussed taking into consideration barriers and suggestions from all service users' perspectives. Findings from 23 studies with different context and methods were collected and summarized. Most of the studies were conducted in UK, using interviews and questionnaires, and addressed to the physicians. The lack of information about ADHD as a condition and about transition process were the barriers most reported, while joint working and sharing transition protocols were the suggestions pointed out by all stakeholders. Despite different perspectives, all stakeholders exposed similar needs. The review reveals an evident need for defining and evaluating the effectiveness of transition programmes from child to adult ADHD services

Child Neuropsychol. 2022.

**INCIDENCE AND RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND LEARNING DISABILITY BY ADULTHOOD AFTER TRAUMATIC BRAIN INJURY IN CHILDHOOD: A POPULATION-BASED BIRTH COHORT STUDY.**

**Brown AW, Esterov D, Zielinski MD, et al.**

The aim of this study was to understand the risk of developing attention-deficit/hyperactivity disorder (ADHD) or learning disability (LD) after childhood traumatic brain injury (TBI) in a population-based birth cohort. Cases of TBI for children from birth to 10 years were confirmed and stratified by severity of injury. For each TBI case, two age-matched and sex-matched referents without TBI were identified from the same birth cohort. Presence of ADHD and LD before age 19 were confirmed using medical and/or school records. Associations between TBI exposure and subsequent ADHD or LD were assessed in multivariable Cox regression models, adjusting for maternal age, education, and race. The incidence rate of TBI before age 10 was 1,156 per 100,000 person-years. Children who had a TBI before age 10 were more likely to have met the research criteria for ADHD (hazard ratio [HR], 1.68; 95% CI, 1.15-2.45) or LD (HR, 1.29; 95% CI, 1.00-1.68) by age 19. No statistically significant associations were shown between TBI and ADHD or LD when restricted to definite and probable TBI cases (consistent with moderate to severe and mild TBI, respectively) and their referents. Significant associations were shown when the analysis was confined to possible TBI cases (consistent with concussive TBI) and their referents (ADHD: HR, 2.05; 95% CI, 1.31-3.20; and LD: HR, 1.42; 95% CI, 1.05-1.91). Increased risk for developing ADHD and LD by adulthood was shown particularly for children with the least-severe injuries, indicating that factors other than trauma-related altered brain function likely contribute to this risk

Clin EEG Neurosci. 2022.

**NEW ELECTROGRAPHIC MARKER? EVALUATION OF SLEEP SPINDLES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Ozbudak P, et al.**

**Introduction:** Attention deficit and hyperactivity disorder (ADHD) is one of the most common developmental disorders in childhood which lasts lifelong. Sleep structure and sleep spindle features are disorganized in ADHD. In this study, we aimed to look for a new, simple, inexpensive, and an easily detectable electrographic marker in the diagnosis of ADHD by using electroencephalography (EEG).

**Method:** We included treatment free 35 patients with ADHD and 32 healthy children (HC) who were examined by polysomnography (PSG) and EEG for sleep disorders. The ADHD group were separated into three groups according to predominant presentations of ADHD. We determined the sleep staging and slow and fast sleep spindles, calculated each spindle's amplitude, frequency, activity, duration and density at non rapid eye movement (REM) sleep stage 2.

**Results:** Slow sleep spindle's amplitude, duration, density and activity are significantly higher in ADHD group (most significant in ADHD-I) than the HC group ( $p < 0,05$ ). Sleep spindle's features are not statistically significant between in ADHD subgroups.

**Conclusions:** In children with ADHD, slow sleep spindles showed higher amplitude, activity, density and duration in the frontal regions. These results indicate that slow sleep spindles in children with ADHD may reflect executive dysfunction and slow frontal spindles may be useful as a new electrographic marker in children with ADHD. This is the first study of its kind evaluating all aspects of sleep spindles in ADHD patients

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CNS Spectr. 2022;27:134-35.

**SUCCESSFUL AGOMELATINE MONOTHERAPY FOR AN ADOLESCENT WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND COMORBID MIGRAINE.**

**Naguy A, Alamiri B.**

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Cogn Affect Behav Neurosci. 2022 Oct;22:1183-98.

**DISTINCT NEURAL PROFILES OF FRONTOPIRIETAL NETWORKS IN BOYS WITH ADHD AND BOYS WITH PERSISTENT DEPRESSIVE DISORDER.**

**Vilgis V, Yee D, Silk TJ, et al.**

Working memory deficits are common in attention-deficit/hyperactivity disorder (ADHD) and depression—two common neurodevelopmental disorders with overlapping cognitive profiles but distinct clinical presentation. Multivariate techniques have previously been utilized to understand working memory processes in functional brain networks in healthy adults but have not yet been applied to investigate how working memory processes within the same networks differ within typical and atypical developing populations. We used multivariate pattern analysis (MVPA) to identify whether brain networks discriminated between spatial versus verbal working memory processes in ADHD and Persistent Depressive Disorder (PDD). Thirty-six male clinical participants and 19 typically developing (TD) boys participated in a fMRI scan while completing a verbal and a spatial working memory task. Within a priori functional brain networks (frontoparietal, default mode, salience), the TD group demonstrated differential response patterns to verbal and spatial working memory. The PDD group showed weaker differentiation than TD, with lower classification accuracies observed in primarily the left frontoparietal network. The neural profiles of the ADHD and PDD differed specifically in the SN where the ADHD group's neural profile suggests significantly less specificity in neural representations of spatial and verbal working memory. We highlight within-group classification as an innovative tool for understanding the neural mechanisms of how cognitive processes may deviate in clinical disorders, an important intermediary step towards improving translational psychiatry

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Cogn Affect Behav Neurosci. 2022 Oct;22:969-83.

**EXPLORATION HEURISTICS DECREASE DURING YOUTH.**

**Dubois M, Bowler A, Moses-Payne ME, et al.**

Deciding between exploring new avenues and exploiting known choices is central to learning, and this exploration-exploitation trade-off changes during development. Exploration is not a unitary concept, and humans deploy multiple distinct mechanisms, but little is known about their specific emergence during development. Using a previously validated task in adults, changes in exploration mechanisms were investigated between childhood (8-9 y/o, N = 26; 16 females), early (12-13 y/o, N = 38; 21 females), and late

adolescence (16-17 y/o, N = 33; 19 females) in ethnically and socially diverse schools from disadvantaged areas. We find an increased usage of a computationally light exploration heuristic in younger groups, effectively accommodating their limited neurocognitive resources. Moreover, this heuristic was associated with self-reported, attention-deficit/hyperactivity disorder symptoms in this population-based sample. This study enriches our mechanistic understanding about how exploration strategies mature during development

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Complement Ther Med. 2022;67.

**DIET AND PHYSICAL EXERCISES FOR PRESCHOOLERS WITH ADHD AND THEIR MOTHERS: AN INTERVENTION STUDY.**  
**Hassan MM, Nuaim AA, Osman SR, et al.**

**Background:** Attention deficit hyperactivity disorder (ADHD) is a serious public health problem. Diet-focused approaches and physical exercise can be used to complement other ADHD management techniques.

**Objective:** To determine the prevalence of ADHD symptoms among preschoolers in nursery schools and to evaluate the educational interventions toward nutrition and physical exercise in mothers and their preschoolers with ADHD symptoms.

**Research methodology:** A two-phase sampling method was employed. First, a cross-sectional survey was conducted to determine the prevalence of ADHD symptoms in four nursery schools (400 preschoolers aged between 3 and 6 years). Second, an intervention study (a quasi-experimental research design with one group completing the pre-test and the post-test) was performed on 36 preschoolers having ADHD symptoms and their mothers by using the educational intervention for mothers and photos and games about nutrition and physical exercise for the preschoolers with ADHD; mothers of four children out of the 40 refused to participate in the study. Data were analyzed using SPSS version 20. The paired t-test was used to determine significant differences between the groups. Differences were considered significant at  $P < 0.05$ .

**Results:** Of the 400 preschoolers, 10% had high ADHD symptoms. The mean score of mothers knowledge of nutrition and physical exercise improved after the implementation of the program ( $p = 0.01$ ). In addition, preschoolers with ADHD enjoyed the session with photos and games ( $p = 0.01$ ).

**Conclusions and Implications:** Educational intervention significantly improved the knowledge of the mothers. Moreover, preschoolers with ADHD symptoms enjoyed the session with photos and games. This intervention appears to be feasible and promising for further investigation of its effects

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Disabil Health J. 2022.

**THE EFFECT OF PHYSICAL ACTIVITY ON QUALITY OF LIFE AND PARENTING STRESS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED CONTROLLED TRIAL.**

**Zhang Z, Li R, Zhou Z, et al.**

**Background:** Poorer quality of life (QoL) is commonly observed in children with Attention-deficit/Hyperactivity Disorder (ADHD). Parents of children with ADHD also perceived elevated levels of parenting stress. Previous research has documented the positive effects of physical activity (PA) on managing ADHD symptoms. It is critical to implement ADHD management with broader functioning from both children's and parents' perspectives.

**Objective:** This study aimed to examine whether PA would exert an influence on the QoL of children with ADHD and parenting stress of their parents.

**Methods:** Forty-three children with ADHD (6-12 years) were randomly assigned to the PA intervention and waitlist control groups. Children in the intervention group participated in a 12-week PA program. Parent-reported QoL and parenting stress were assessed before and immediately after the intervention. Analysis of covariance with a mixed factorial design of 2 (time: before vs. after intervention)  $\times$  2 (group: PA intervention vs. waitlist control) was conducted to examine changes in QoL and parenting stress over the 12 weeks.

**Results:** Compared to the control group, parents of children in the intervention group reported significant reduced overall parenting stress ( $p = .021$ ,  $\Delta = 0.142$ ) and child domain of parenting stress ( $p = .024$ ,  $\Delta = 0.138$ ) after the intervention. No significant improvement in QoL was documented in either group.

**Conclusions:** The participation of PA intervention positively impacts parenting stress perceived by parents of children with ADHD, which provides further evidence of the family-wide benefits of the PA intervention

Drug Saf. 2022;45:1277-78.

**ADHD MEDICATION USE AND PSYCHIATRIC COMORBIDITY, TRAUMA AND MORTALITY IN CHILDREN AND YOUNG ADULTS: A COHORT STUDY FROM QUEBEC, CANADA.**

**Lunghi C, Vasiliadis HM, Rahme E, et al.**

**Introduction:** Among the Canadian provinces, Quebec showed one of the highest trends in increased diagnostic rates of attention-deficit/ hyperactivity disorder (ADHD) between 2000 and 2012 (1). Recent prevalence estimates of ADHD are 6.6%, 18.9%, and 15.5% for those aged 11, 12-17, and 18-24 years, respectively (2). Prescription rates for ADHD medications in Quebec have increased from 1.9 to 7.7% between 2000 and 2020 (3). The comorbidity and health outcomes of individuals using ADHD medications have not been described in Quebec.

**Objective:** The aim of this study was to describe the prevalence of comorbidity, trauma-related events and mortality according to ADHD medication use.

**Methods:** Data were drawn from the Quebec Integrated Chronic Disease Surveillance System of the National Public Health Institute of Quebec (4) between 2000 and 2020. The cohort included residents covered under the public drug insurance plan between April 1st, 2000, and March 31st, 2020. Individuals between 1 and 24 years entered the cohort at either a first physician claim, hospital diagnosis of ADHD, or an ADHD medication claim. Medications included amphetaminederivatives, methylphenidate-based psychostimulants and non-psychostimulants (5). The study population was categorized concerning the presence of an ADHD medication and diagnosis [ADHD medication only, n = 34,528; ADHD diagnosis only, n = 20,574; both an ADHD medication and diagnosis, n = 59,610 (the majority had medications and diagnosis within 90 days)]. We estimated prevalence rates of psychiatric comorbidities, trauma-related events (ambulatory records), and mortality rates (all-cause; trauma-related without suicide) according to the presence of ADHD medication and ADHD diagnosis. Differences were based on 99% confidence intervals (CIs) around estimates.

**Results:** The prevalence of lifetime psychiatric comorbidities in individuals with ADHD medication only, diagnosis only and both medication and diagnosis were 78.5%, 65.8%, and 79.3%, respectively. Traumatic-related events were present in 48.3% of individuals with ADHD medication only, 49.4% of those with ADHD diagnosis only, and 59.0% of those with both. The prevalence of all-cause mortality was higher in those with ADHD diagnosis only (0.33% vs 0.19% in ADHD medication only, and 0.17% in both diagnosis and medication). Similar results among groups were found for traumarelated mortality, being 0.06% among individuals with ADHD medications, 0.05% among those with diagnosis only, and 0.07% among those with both.

**Conclusion:** Differences exist in the psychiatric comorbidities, traumatic- related events and mortality between individuals using ADHD medications and those who do not. Within-subject analyses are underway and will allow for assessing the association between ADHD medication use, suicide behaviours, trauma and mortality

Drugs and Therapy Perspectives. 2022;38:77-83.

**VILOXAZINE FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A NEW FORMULATION FOR A NEW INDICATION.**

**Balasundaram MK, Singh A.**

Viloxazine (SPN-812), an age-old antidepressant, has recently been approved by the US FDA for the treatment of attention-deficit hyperactivity disorder (ADHD) in children aged 6-17 years, at a dose range of 100-400 mg/day. Viloxazine acts primarily by norepinephrine reuptake inhibition and may also modulate the serotonergic system. The efficacy of viloxazine for the treatment of ADHD in children aged 6-17 years has been demonstrated in a series of short-term clinical trials. The most common adverse events include somnolence and gastrointestinal upset, while the FDA has issued a black-box warning regarding suicidal

ideation or behavior. This article summarizes the information regarding viloxazine based on previously published narrative reviews, preclinical studies, and blinded controlled clinical trials

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Egyptian Pediatric Association Gazette. 2022;70.

**RELATION BETWEEN LATROPHILIN 3 (LPHN3) GENE POLYMORPHISM (RS2345039) AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN.**

**Elsadek A, Soliman D, Behiry E, et al.**

**Background:** The most prevalent psychological disorder in children is attention deficit hyperactivity disorder (ADHD). Latrophilin 3 (LPHN3) is a G protein-coupled receptor family member. It is brain specific and related to attention deficit hyperactivity disorder (ADHD) genetic susceptibility. This study aimed to assess the association of LPHN3 gene with ADHD and its types.

**Methods:** The subjects were 2 groups: group I, thirty patients with ADHD, and group II, thirty healthy individuals as a control group. The process of polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was used to establish the genetic association of ADHD with the polymorphic gene LPHN3 (rs2345039).

**Results:** The ADHD group included 20 male and 10 females; the mean age was 9.8-11.8 years. LPHN3 rs2345039 polymorphism genotypes distribution showed a statistical significant difference between ADHD and controls ( $P = 0.01$ ). In the ADHD group, individuals with CG genotype were 5.8-folds to have ADHD than CC individuals. Also, those with GG genotype were about six times more likely to have ADHD than CC ones. All of these relationships were significant statistically ( $P = 0.024$  and  $= 0.018$ , respectively). Individuals carrying the G allele were 2.6 times more likely to develop ADHD than those carrying the C allele (OR = 2.6, 95% CI = 1.3-5.6,  $P$  value = 0.01).

**Conclusion:** Our results demonstrate an association between latrophilin 3 (LPHN3) gene rs2345039 and ADHD. Moreover, LPHN3 polymorphisms tend to have a key role in triggering the condition and exacerbating its severity

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Eur J Clin Pharmacol. 2022;78:1095-104.

**A VIEW OF RESPONSE AND RESISTANCE TO ATOMOXETINE TREATMENT IN CHILDREN WITH ADHD: EFFECTS OF CYP2C19 POLYMORPHISMS AND BDNF LEVELS.**

**Demirci E, Sener EF, Gul MK, et al.**

**Objective:** Although several genes have previously been studied about the treatment of Attention Deficit Hyperactivity Disorder (ADHD), the number of studies investigating the effects of genes on atomoxetine (ATX) treatment is very limited. In this study, we aimed to investigate the effect of CYP2C19 polymorphisms, which have a role in ATX biotransformation, on the treatment response and also to assess whether there is a relationship between BDNF and treatment response in children and adolescents with ADHD.

**Methods:** One hundred children with ADHD and 100 healthy controls (HCs) were included in this study. The treatment response was assessed 2-months after the start of the ATX treatment. DNA samples from peripheral venous blood were replicated using PCR and analyzed using the ILLUMINA next-generation sequencing method. The resulting fastq files were analyzed using BaseSpace® Variant Interpreter Program. Plasma BDNF levels were evaluated with ELISA kits.

**Results:** Treatment response was found to be lower in both heterozygous and homozygous carriers of the c.681G > A (CYP2C19\*2) polymorphism. When the BDNF level was compared, it was found to be significantly higher in the ADHD group compared to HCs. Also, BDNF has a stronger predictive value for assessing resistance to ATX treatment.

**Conclusions:** To our knowledge, this is the first study to assess the effects of CYP2C19 polymorphisms and BDNF levels together on ATX treatment in children. Further studies with an extensive population are needed to better understand the effects of CYP2C19 polymorphisms on treatment and side effects, as well as the effects of BDNF levels

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Eur Neuropsychopharmacol. 2022;64:63-71.

**LONG-TERM METHYLPHENIDATE EXPOSURE AND 24-HOURS BLOOD PRESSURE AND LEFT VENTRICULAR MASS IN ADOLESCENTS AND YOUNG ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Buitelaar JK, Loo-Neus GHH, Hennissen L, et al.**

Young people with attention deficit hyperactivity disorder (ADHD) are now being treated with psychostimulant medication for longer than was previously the case and are increasingly likely to remain on methylphenidate into adolescence and adulthood. This study was designed to determine whether the long-term use of methylphenidate (MPH, immediate release or extended release) increases blood pressure and left ventricular mass (LVM) identified by echocardiography in adolescents and young adults with ADHD aged 12-25 years. In a five-site cross-sectional design two groups were compared for 24-hour blood pressure and heart rate (HR) registrations and LVM: 1) adolescents and young adults with ADHD who had been treated with MPH for > 2 years (N=162, age mean (SD) 15.6 (3.0)), and 2) adolescents and young adults with ADHD who had never been treated with methylphenidate (N=71, age mean 17.4 (4.2)). The analyses were controlled for propensity scores derived from age, sex, height, weight, and 19 relevant background variables. A blood pressure indicative of hypertension (>95th percentile) was observed in 12.2% (95% confidence interval 7.3-18.9%) of the participants in the MPH treated group and in 9.6% (95%CI 3.2-21.0%) of the MPH naïve group, with overlapping intervals. The 24-hour recorded systolic blood pressure (SBP) and HR were significantly higher during daytime in medicated individuals with ADHD than in those with unmedicated ADHD, but were similar in both groups during the night. 24-hour diastolic blood pressure (DBP) did not differ between both groups during either daytime or at night. LVM, corrected for body-surface area (LVMBSA), also did not differ between the two groups (p=0.20, controlling for confounders). Further, MPH daily dose and duration of treatment were unrelated to LVMBSA, SBP, and DBP. Long-term MPH use in adolescents and young adults with ADHD is associated with small but significant increases of SBP and HR during daytime. Given the current sample size, the proportions of hypertension do not differ significantly between MPH treated and MPH-naïve individuals with ADHD. Future studies with larger samples, longer treatment duration, and/or with within-subject designs are necessary. The results do, however, further support recommendations that highlight the importance of monitoring blood pressure and HR during MPH treatment

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Eur Psychiatry. 2022;65.

**ASSESSING THE RELATIONSHIP BETWEEN MATERNAL RISK FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER AND FUNCTIONAL CONNECTIVITY IN THEIR BIOLOGICAL TODDLERS.**

**Kerr-German A, White SF, Santosa H, et al.**

**Background.** Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder associated with increased risk for poor educational attainment and compromised social integration. Currently, clinical diagnosis rarely occurs before school-age, despite behavioral signs of ADHD in very early childhood. There is no known brain biomarker for ADHD risk in children ages 2-3 years-old.

**Methods.** The current study aimed to investigate the functional connectivity (FC) associated with ADHD risk in 70 children aged 2.5 and 3.5 years via functional near-infrared spectroscopy (fNIRS) in bilateral frontal and parietal cortices; regions involved in attentional and goal-directed cognition. Children were instructed to passively watch videos for approximately 5 min. Risk for ADHD in each child was assessed via maternal symptoms of ADHD, and brain data was evaluated for FC.

**Results.** Higher risk for maternal ADHD was associated with lower FC in a left-sided parieto-frontal network. Further, the interaction between sex and risk for ADHD was significant, where FC reduction in a widespread bilateral parieto-frontal network was associated with higher risk in male, but not female, participants.

**Conclusions.** These findings suggest functional organization differences in the parietal-frontal network in toddlers at risk for ADHD; potentially advancing the understanding of the neural mechanisms underlying the development of ADHD

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Evid -Based Complement Altern Med. 2022;2022.

**A STUDY ON THE EFFECTS OF A CARTOON TEXT VERSION OF HEALTH EDUCATION MANUAL WITH SANDPLAY ON THE PSYCHOLOGICAL STATUS AND COGNITIVE FUNCTION OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**He L, Huang L.**

**Purpose.** The study aimed to examine the effects of a cartoon text version of a health education manual with sandplay on the psychological status and cognitive function of children with attention deficit hyperactivity disorder (ADHD).

**Methods.** Eighty cases of children with ADHD admitted from February 2019 to September 2021 were selected for the study. They were numbered according to the order of consultation, and after obtaining family consent, they were divided into the control group (n = 40) and the observation group (n = 40) using the random number table method. The control group received only medication and verbal health education, while the observation group received a cartoon text version of the health education manual together with sandplay on top of the above, and both groups were treated for 30 weeks. The attention test results and the Swanson, Nolan, and Pelham-IV rating scales (SNAP-IV) were used to assess the effectiveness of the treatment for both groups of children. The awareness rate of health education knowledge of children and their families in both groups was counted. The Conners Parent Symptom Questionnaire (PSQ) and the Combined Raven's test (CRT) were used to assess the psychological status and cognitive functioning of the children in both groups.

**Results.** After treatment, the response time, the number of errors, and the number of missed alarms in the attention test results were lower in the observation group than in the control group ( $P < 0.05$ ). After treatment, the inattention, antagonism and defiance, and impulsiveness and hyperactivity scores on SNAP-IV were lower in the observation group than in the control group ( $P < 0.05$ ). After treatment, the knowledge of disease and treatment, medical and nursing cooperation, safety and protection, and dietary precautions were higher in the observation group than in the control group ( $P < 0.05$ ). After treatment, the learning problems, conduct problems, psychosomatic problems, anxiety, impulsivity-hyperactivity, and hyperactivity index scores on the PSQ were lower in the observation group than in the control group ( $P < 0.05$ ). After treatment, the A, B, C, D, and E theme scores in the CRT were higher in the observation group than in the control group, and the IQ score was also higher in the observation group than in the control group ( $P < 0.05$ ).

**Conclusion.** The cartoon text version of the health education manual with sandplay can significantly improve the attention deficit, hyperactive behaviour, psychological status, and cognitive function of children with ADHD on the basis of pharmacological treatment, which has a good clinical application

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Front Behav Neurosci. 2022 Sep;16.

**PHYSICAL ACTIVITY AND THE DEVELOPMENT OF GENERAL MENTAL HEALTH PROBLEMS OR ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) SYMPTOMS IN CHILDREN AND ADOLESCENTS: A CROSS-LAGGED PANEL ANALYSIS OF LONG-TERM FOLLOW-UP EPIDEMIOLOGICAL DATA.**

**Ganjeh P, Hagmayer Y, Meyer T, et al.**

Studies have shown that physical activity (PA) can provide a helpful, low-risk, and cost-effective intervention for children and adolescents suffering from mental health problems. This longitudinal study aimed to assess whether PA prevents the development of mental health problems, such as attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. Data were analyzed from the German Health Interview and Examination Survey for Children and Adolescents (KiGGS) collected from more than 15.000 children and adolescents at three different time points over a period of more than 10 years. Parents scored the PA of the study participants on three frequency levels according to WHO recommendations, and mental health

problems were assessed by means of the Strengths and Difficulties Questionnaire (SDQ). The total problem score (SDQ-Total) and the hyperactivity/inattention symptoms sub-scale (SDQ-H/I) were used in an autoregressive cross-lagged model to examine their relationship with PA. The results showed that PA of boys and girls at preschool age was inversely associated with the occurrence of mental health problems and, in particular, ADHD symptoms about 6 years later. Higher levels of PA were associated with better general mental health and fewer ADHD symptoms at the next time point (Wave 1). These effects were not observed from preadolescence (Wave 1) to adolescence (Wave 2), neither for girls nor for boys. These findings indicate that medium-to-high PA may be a supportive factor for good mental health in children in preschool and elementary school. Future studies will have to show whether PA may be a helpful add-on for interventional programs for improving general mental health and alleviating ADHD symptoms among children and adolescents

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Front Human Neurosci. 2022;16.

**SWEET BUT SOUR: IMPAIRED ATTENTION FUNCTIONING IN CHILDREN WITH TYPE 1 DIABETES MELLITUS.**

**Lancrei HM, Yeshayahu Y, Grossman ES, et al.**

Children diagnosed with type 1 diabetes mellitus (T1DM) are at risk for neurocognitive sequelae, including impaired attention functioning. The specific nature of the cognitive deficit varies; current literature underscores early age of diabetes diagnosis and increased disease duration as primary risk factors for this neurocognitive decline. Forty-three children with T1DM were evaluated for Attention Deficit/Hyperactivity Disorder (ADHD) symptomatology using the MOXO continuous performance test (MOXO-CPT) performed during a routine outpatient evaluation. The study cohort demonstrated a significant decline in all four domains of attention functioning. The effect was most pronounced with early age at T1DM diagnosis, a longer disease duration and with poorer glycemic control (represented by higher HbA1c values). With increased disease duration (of 5 plus years), acute hyperglycemia was associated with inattention in the real-time setting. These findings highlight the need for routine screening of neurocognitive function in children with T1DM so that early intervention can be employed during this crucial period of cognitive development

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Frontiers in Pediatrics. 2022;10.

**THE RELATIONSHIP BETWEEN DIABETES MELLITUS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.**

**Ai Y, Zhao J, Liu H, et al.**

**Background:** This study aims to investigate the prevalence estimate of diabetes mellitus (DM) among people with attention deficit hyperactivity disorder (ADHD) as well as the prevalence of ADHD among those with DM. In addition, the impact of ADHD on glycemic control in patients with DM was also assessed using a systematic review and meta-analysis of currently available published data.

**Materials and methods:** The PubMed, Embase, Web of Science, and PsycInfo databases were searched for potential studies. Two reviewers independently selected studies according to the inclusion and exclusion criteria. All pooled analyses were conducted using the random-effects models on Review Manager 5.3.

**Results:** Seventeen observational studies were included. The pooled results showed an increase in the prevalence of DM among patients with ADHD versus those without ADHD [type 1 DM OR: 1.37 (95% CI: 1.17-1.61); type 2 DM OR: 2.05 (95% CI: 1.37-3.07)]. There was an overall 35% increase in the prevalence of ADHD among patients with type 1 DM [OR: 1.35 (95% CI: 1.08-1.73)]. Children with type 1 DM and ADHD had higher levels of hemoglobin A1c [standardized mean of differences: 0.67 (95% CI: 0.48-0.86)], and prevalence of hypoglycemic and ketoacidosis index compared with those without ADHD.

**Conclusion:** Our study revealed the bidirectional associations between ADHD and DM. Patients with ADHD and type 1 DM comorbidities were more likely to have poorer diabetes control. More studies are needed to confirm this association and elucidate the underlying mechanism

Frontiers in Pediatrics. 2022;10.

**PLANNING PROCESSING IN ADHD WITH COMORBID READING DISABILITIES IS WORSE THAN IN ADHD: BASED ON DAS-NAGLIERI COGNITIVE ASSESSMENT SYSTEM.**

**Zhang Z, Feng J, Xue Y, et al.**

**Objective:** To explore and compare the cognitive processing weakness of children with Attention deficit hyperactivity disorder (ADHD) and comorbid reading disabilities (RD) (ADHD+RD) and children with ADHD only using the Das-Naglieri Cognitive Assessment System (DN:CAS).

**Methods:** Eighty-eight children with ADHD who visited the hospital for the first time from September 2021 to November 2021 and had a Full scale intelligence quotient (IQ) of  $\geq 85$  on the Wechsler Intelligence Scale for Children revised in China (C-WISC) were selected (Age: 6-12 years; Grade: 2-6). Based on comorbidity with RD and the subtypes of ADHD (e.g., Inattention dominant type, ADHD-I, Hyperactivity/Impulse dominant type, ADHD-H and Combined type, ADHD-C), these children were divided into the ADHD+RD group (n = 30) and ADHD group (n = 58) as well as the corresponding subgroups. Clinical data on gender, age, grade, IQ scores, and DN:CAS processing scores were compared between both groups/subgroups. Spearman's correlation test was used for correlation analysis of results of interest.

**Results:** No differences in age, grade, male-to-female ratio, verbal IQ, performance IQ, and full scale IQ were observed between the ADHD+RD group and ADHD group as well as the corresponding subgroups ( $P > 0.05$ ). Children in the ADHD-C+RD subgroup had lower scores in Planning processing of DN:CAS than those in the ADHD-C subgroup ( $P = 0.040$ ). However, there were no significant difference between the ADHD-I+RD subgroup and ADHD-I subgroup in Planning scores of DN:CAS assessment; The grade of ADHD-C+RD and ADHD-I+RD subgroups were positively correlated with the Planning scores of DN: CAS ( $r = 0.599$ ,  $P = 0.030$  and  $r = 0.508$ ,  $P = 0.044$ , respectively). The grade of ADHD-C subgroup was positively correlated with the Planning and Simultaneous processing scores of DN: CAS ( $r = 0.409$ ,  $P = 0.042$  and  $r = 0.406$ ,  $P = 0.044$ , respectively).

**Conclusion:** Our study confirmed that children of ADHD-C with comorbid RD have a more severe Planning processing weakness compared to children with ADHD-C only. Among the children of ADHD-C+RD, ADHD-I+RD and ADHD-C, such a Planning processing impairment may improve with increasing educational skills

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Front Psychiatry. 2022;13.

**SELF-REPORTED MATERNAL PARENTING STRESS FROM 9 M IS LONGITUDINALLY ASSOCIATED WITH CHILD ADHD SYMPTOMS AT AGE 12: FINDINGS FROM A POPULATION-BASED BIRTH COHORT STUDY.**

**Endo K, Stanyon D, Yamasaki S, et al.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) develops in early childhood and carries lifelong impact, but early identification and intervention ensure optimal clinical outcomes. Prolonged or excessive parenting stress may be a response to infant behavioral differences antecedent to developmental disorders such as ADHD, and therefore represents a potentially valuable inclusion in routine early-life assessment. To investigate the feasibility of using routinely-collected self-reported maternal parenting stress as a risk marker for child ADHD, this study investigated the longitudinal association between maternal parenting stress from 1 to 36 months after childbirth and child ADHD in early adolescence.

**Methods:** The sample comprised 2,638 children (1,253 girls) from the Tokyo Teen Cohort population-based birth cohort study. Mothers recorded parenting stress five times from 1 to 36 months following childbirth in the Maternal and Child Health Handbook, a tool used for routine early-life assessment in Japan. Nine years later, mothers evaluated their child's ADHD symptoms at 12 y using the hyperactivity/inattention subscale from the Strength and Difficulties Questionnaire.

**Results:** Approximately 7.5% of parents reported that they had parenting stress at 36 m after childbirth. 6.2% of children were evaluated as above the cut-off for ADHD symptoms at 12 y. Parenting stress at 1 and 3-4 m was not associated with child ADHD symptoms at 12 y. However, child ADHD symptoms at 12 y was significantly associated with parenting stress at 9-10 m (unadjusted OR = 1.42,  $p = .047$ , 95% CI [1.00, 2/00]), 18 m (unadjusted OR = 1.57,  $p = .007$ , 95% CI [1.13, 2.19]) and 36 m (unadjusted OR = 1.67,  $p = .002$ , 95% CI [1.20, 2.31]). These associations remained after adjustment for child's sex, age in months and family income.

**Conclusions:** We identified associations between parenting stress at 9-10, 18 and 36 m after childbirth and child ADHD symptoms at 12 years old. Self-reported parenting stress data may have utility as an early indicator for ADHD risk. Participation in early-life health checks, assessment of parenting stress, and tailoring support to family needs should be promoted for early identification and intervention for ADHD

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Front Psychiatry. 2022;13.

**CORRELATION RESEARCH OF SUSCEPTIBILITY SINGLE NUCLEOTIDE POLYMORPHISMS AND THE SEVERITY OF CLINICAL SYMPTOMS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Xu Y, Lin S, Tao J, et al.**

**Objective:** To analyze the correlation between susceptibility single nucleotide polymorphisms (SNPs) and the severity of clinical symptoms in children with attention deficit hyperactivity disorder (ADHD), so as to supplement the clinical significance of gene polymorphism and increase our understanding of the association between genetic mutations and ADHD phenotypes.

**Methods:** 193 children with ADHD were included in our study from February 2017 to February 2020 in the Children's ADHD Clinic of the author's medical institution. 23 ADHD susceptibility SNPs were selected based on the literature, and multiple polymerase chain reaction (PCR) targeted capture sequencing technology was used for gene analysis. A series of ADHD-related questionnaires were used to reflect the severity of the disease, and the correlation between the SNPs of specific sites and the severity of clinical symptoms was evaluated. R software was used to search for independent risk factors by multivariate logistic regression and the corplot package was used for correlation analysis.

**Results:** Among the 23 SNP loci of ADHD children, no mutation was detected in 6 loci, and 2 loci did not conform to Hardy-Weinberg equilibrium. Of the remaining 15 loci, there were 9 SNPs, rs2652511 (SLC6A3 locus), rs1410739 (OBI1-AS1 locus), rs3768046 (TIE1 locus), rs223508 (MANBA locus), rs2906457 (ST3GAL3 locus), rs4916723 (LINC00461 locus), rs9677504 (SPAG16 locus), rs1427829 (intron) and rs11210892 (intron), correlated with the severity of clinical symptoms of ADHD. Specifically, rs1410739 (OBI1-AS1 locus) was found to simultaneously affect conduct problems, control ability and abstract thinking ability of children with ADHD.

**Conclusion:** There were 9 SNPs significantly correlated with the severity of clinical symptoms in children with ADHD, and the rs1410739 (OBI1-AS1 locus) may provide a new direction for ADHD research. Our study builds on previous susceptibility research and further investigates the impact of a single SNP on the severity of clinical symptoms of ADHD. This can help improve the diagnosis, prognosis and treatment of ADHD

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Front Psychiatry. 2022;13.

**SEXUALITY IN ADULTS WITH ADHD: RESULTS OF AN ONLINE SURVEY.**

**Hertz PG, Turner D, Barra S, et al.**

Establishing a secure sexual identity is a major developmental goal of an individual's transition from childhood to adolescence and the years that follow. Attention deficit/hyperactivity disorder (ADHD) as a neurodevelopmental disorder defined by the core symptoms of inattention, hyperactivity, and impulsivity, but also with emotional dysregulation, oppositional behaviors, or disorganization appearing early in life, can affect several areas of an individual's personal and social development, including sexual health. Yet, the scientific knowledge about the relationship between ADHD and sexual functioning is still scarce. Using an anonymous online survey, we compared different sexual behaviors including risky sexual behaviors, hypersexual behaviors, and sexual dysfunctions between 206 individuals with (n = 139) and without (n = 76) ADHD. Individuals with ADHD reported significantly more hypersexual behaviors than non-ADHD individuals, whereas no differences were found concerning risky sexual behaviors or sexual dysfunctions. In women with ADHD, hypersexual behaviors, sexual risk-taking as well as sexual dysfunctions were closely related to symptoms of emotional dysregulation, impulsivity, and oppositional symptoms. In men with ADHD, the associations between ADHD symptomatology and the sexuality-related measures were less clear, however, signs of emotional dysregulation seemed to be relevant as well. Since individuals with ADHD seem to be at

an increased risk of some peculiarities in sexual behavior, sexuality-related issues should be routinely addressed during clinical consultations to provide more holistic treatment in order to enhance individual well-being and quality of life

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Front Psychiatry. 2022;13.

**EXECUTIVE FUNCTIONS MEDIATE THE ASSOCIATION BETWEEN ADHD SYMPTOMS AND ANXIETY IN A CLINICAL ADOLESCENT POPULATION.**

**Haugan ALJ, Sund AM, Thomsen PH, et al.**

**Objective:** Attention-deficit/hyperactivity disorder (ADHD) is associated with a high prevalence of anxiety disorders in children and adolescents. The reasons for this association are poorly understood. Preliminary findings with young adults have suggested that executive functions and functional impairment may mediate the relationship between symptoms of ADHD and mixed anxiety and depressive symptoms. The objective of this study was to explore whether ADHD symptoms, executive functions and functional impairment predict anxiety in a clinical adolescent population. In addition, we investigated the possible mediating role of executive functions and functional impairment in this relationship.

**Method:** One hundred adolescents with ADHD and their parents completed the ADHD Rating Scale IV (ADHD RS-IV), the Behavior Rating Inventory of Executive Function (BRIEF), and the Weiss Functional Impairment Rating Scale (WFIRS) in relation to an RCT study. The adolescents also completed the Screen for Child Anxiety-Related Emotional Disorders (SCARED). Analyses were conducted using regression and a serial multiple mediator model.

**Results:** In the regression analyses, parent-rated ADHD symptoms were unable to predict anxiety, but ADHD inattention symptoms predicted anxiety in the self-ratings. Executive dysfunction and functional impairment predicted anxiety in both the parent- and self-reports. In the mediation analyses ADHD symptoms alone did not predict anxiety, but executive dysfunction mediated this relationship as expected. Functional impairment mediated this relationship indirectly through executive functions. The results were similar in the parent- and self-reports.

**Conclusion:** The results pinpoint executive dysfunction as an important treatment target for alleviating anxiety in adolescents with impairing ADHD symptoms

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Hum Brain Mapp. 2022.

**INFORMATION-BASED MULTIVARIATE DECODING REVEALS IMPRECISE NEURAL ENCODING IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER DURING VISUAL SELECTIVE ATTENTION.**

**Li D, Luo X, Guo J, et al.**

Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in school-age children. Attentional orientation is a potential clinical diagnostic marker to aid in the early diagnosis of ADHD. However, the underlying pathophysiological substrates of impaired attentional orienting in childhood ADHD remain unclear. Electroencephalography (EEG) was measured in 135 school-age children (70 with childhood ADHD and 65 matched typically developing children) to directly investigate target localization during spatial selective attention through univariate ERP analysis and information-based multivariate pattern machine learning analysis. Compared with children with typical development, a smaller N2pc was found in the ADHD group through univariate ERP analysis. Children with ADHD showed a lower parieto-occipital multivariate decoding accuracy approximately 240-340 ms after visual search onset, which predicts a slower reaction time and larger standard deviation of reaction time. Furthermore, a significant correlation was found between N2pc and decoding accuracy in typically developing children but not in children with ADHD. These observations reveal that impaired attentional orienting in ADHD may be due to inefficient neural encoding responses. By using a personalized information-based multivariate machine learning approach, we have

advanced the understanding of cognitive deficits in neurodevelopmental disorders. Our study provides potential research directions for the early diagnosis and optimization of personalized intervention in children with ADHD

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Int J Dev Neurosci. 2022.

**HOW DOES BRAIN STRUCTURE AND FUNCTION ON MRI DIFFER IN CHILDREN WITH AUTISM SPECTRUM DISORDER, DEVELOPMENTAL COORDINATION DISORDER, AND/OR ATTENTION DEFICIT HYPERACTIVITY DISORDER?**

**Kangarani-Farahani M, Izadi-Najafabadi S, Zwicker JG.**

**Aim:** The purpose of this study was to systematically review the neural similarities and differences in brain structure and function, measured by magnetic resonance imaging (MRI), in children with neurodevelopmental disorders that commonly co-occur to understand if and how they have shared neuronal characteristics.

**Method:** Using systematic review methodology, the following databases were comprehensively searched: MEDLINE, EMBASE, CINAHL, CENTRAL, PsycINFO, and ProQuest from the earliest record up to December 2021. Inclusion criteria were (1) peer-reviewed studies, case reports, or theses; (2) children under 18 years of age with at least one of the following neurodevelopmental disorders: autism spectrum disorder (ASD), attention hyperactivity deficit disorder (ADHD), developmental coordination disorder (DCD), and their co-occurrence; and (3) studies based on MRI modalities (i.e., structural MRI, diffusion tensor imaging [DTI], and resting-state fMRI). Thirty-one studies that met the inclusion criteria were included for quality assessment by two independent reviewers using the Appraisal tool for Cross-Sectional Studies (AXIS).

**Results:** Studies compared brain structure and function of children with DCD and ADHD (n = 6), DCD and ASD (n = 1), ASD and ADHD (n = 17), and various combinations of these co-occurring conditions (n = 7). Structural neuroimaging (n = 15) was the most commonly reported modality, followed by resting-state (n = 8), DTI (n = 5), and multimodalities (n = 3).

**Interpretation:** Evidence indicated that the neural correlates of the co-occurring conditions were more widespread and distinct compared to a single diagnosis. The majority of findings (77%) suggested that each neurodevelopmental disorder had more distinct neural correlates than shared neural features, suggesting that each disorder is distinct despite commonly co-occurring with each other. As the number of papers examining the co-occurrence of ASD, DCD, and/or ADHD was limited and most findings were not corrected for multiple comparisons, these results must be interpreted with caution

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Int J Environ Res Public Health. 2022;19.

**THERAPEUTIC APPROACHES FOR ADHD BY DEVELOPMENTAL STAGE AND CLINICAL PRESENTATION.**

**Galvez-Contreras AY, Vargas-de la Cruz I, Beltran-Navarro B, et al.**

Attention Deficit Hyperactivity Disorder is a neurodevelopmental disorder with three presentations: inattentive, hyperactive/impulsive and combined. These may represent an independent disease entity. Therefore, the therapeutic approach must be focused on their neurobiological, psychological and social characteristics. To date, there is no comprehensive analysis of the efficacy of different treatments for each presentation of ADHD and each stage of development. This is as narrative overview of scientific papers that summarize the most recent findings and identify the most effective pharmacological and psychosocial treatments by ADHD presentation and age range. Evidence suggests that methylphenidate is the safest and most effective drug for the clinical management of children, adolescents and adults. Atomoxetine is effective in preschoolers and maintains similar efficacy to methylphenidate in adults, whereas guanfacine has proven to be an effective monotherapy for adults and is a worthy adjuvant for the management of cognitive symptoms. The psychosocial treatments with the best results in preschoolers are behavioral interventions that include training of primary caregivers. In adolescents, the combination of cognitive and cognitive-behavioral therapies has shown the best results, whereas cognitive-behavioral interventions are the most

effective in adults. Pharmacological and psychosocial treatments must be adjusted to the ADHD presentation and its neurocognitive characteristics through the patient's development

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JAMA Network Open. 2022;5:E2236364.

**ASSOCIATION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DIAGNOSIS WITH ADOLESCENT QUALITY OF LIFE.**

**Kazda L, McGeechan K, Bell K, et al.**

**Importance:** Appropriate diagnosis of attention-deficit/hyperactivity disorder (ADHD) can improve some short-term outcomes in children and adolescents, but little is known about the association of a diagnosis with their quality of life (QOL).

**Objective:** To compare QOL in adolescents with and without an ADHD diagnosis. Design, Setting, and

**Participants:** This cohort study followed an emulated target trial design using prospective, observational data from the Longitudinal Study of Australian Children, a representative, population-based prospective cohort study with biennial data collection from 2006 to 2018 with 8 years of follow-up (ages 6-7 to 14-15 years). Propensity score matching was used to ensure children with and without ADHD diagnosis were well matched on a wide range of variables, including hyperactive/inattentive (H/I) behaviors. Eligible children were born in 1999 to 2000 or 2003 to 2004 and did not have a previous ADHD diagnosis. All incident ADHD cases were matched with controls. Data were analyzed from July 2021 to January 2022. Exposures: Incident parent-reported ADHD diagnosis at age 6 to 7, 8 to 9, 10 to 11, 12 to 13, or 14 to 15.

**Main Outcomes and Measures:** Quality of life at age 14 to 15 was measured with Child Health Utility 9D (CHU9D) and 8 other prespecified, self-reported measures mapped to the World Health Organization's QOL domains. Pooled regression models were fitted for each outcome, with 95% CIs and P values calculated using bootstrapping to account for matching and repeat observations.

**Results:** Of 8643 eligible children, a total of 393 adolescents had an ADHD diagnosis (284 [72.2%] boys; mean [SD] age, 10.03 [0.30] years; mean [SD] H/I Strengths and Difficulties Questionnaire score, 5.05 [2.29]) and were age-, sex-, and H/I score-matched with 393 adolescents without ADHD diagnosis at time zero. Compared with adolescents without diagnosis, those with an ADHD diagnosis reported similar QOL on CHU9D (mean difference, -0.03; 95% CI, -0.07 to 0.01; P =.10), general health (mean difference, 0.11; 95% CI, -0.04 to 0.27; P =.15), happiness (mean difference, -0.18; 95% CI, -0.37 to 0.00; P =.05), and peer trust (mean difference, 0.65; 95% CI, 0.00 to 1.30; P =.05). Diagnosed adolescents had worse psychological sense of school membership (mean difference, -2.58; 95% CI, -1.13 to -4.06; P <.001), academic self-concept (mean difference, -0.14; 95% CI, -0.02 to -0.26; P =.02), and self-efficacy (mean difference, -0.20; 95% CI, -0.05 to -0.33; P =.007); displayed more negative social behaviors (mean difference, 1.56; 95% CI, 0.55 to 2.66; P =.002); and were more likely to harm themselves (odds ratio, 2.53; 95% CI, 1.49 to 4.37; P <.001) than adolescents without diagnosis.

**Conclusions and Relevance:** In this cohort study, ADHD diagnosis was not associated with any self-reported improvements in adolescents' QOL compared with adolescents with similar levels of H/I behaviors but no ADHD diagnosis. ADHD diagnosis was associated with worse scores in some outcomes, including significantly increased risk of self-harm. A large, randomized clinical trial with long-term follow-up is needed.

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J Autism Dev Disord. 2022;52:4651-64.

**DEVELOPMENT AND VALIDATION OF THE ASSESSMENT OF BULLYING EXPERIENCES QUESTIONNAIRE FOR NEURODIVERGENT YOUTH.**

**Morton HE, Gillis JM, Zale EL, et al.**

Bullying victimization is a prevalent concern for neurodivergent (e.g., autistic, ADHD) youth. Bullying assessment methods vary widely and there is currently no questionnaire specific to neurodivergent youth. The Assessment of Bullying Experiences (ABE) was created to fill this gap. The ABE questionnaire was completed by 335 parents of school-age youth characterized as autistic, having ADHD, or community comparison. Exploratory and Confirmatory Factor Analysis identified a four-factor solution, aligning with verbal, physical, relational, and cyber victimization. Construct validity analyses indicate the ABE converges

with an existing bullying questionnaire and diverges from disruptive behavior or internalizing symptoms. The ABE questionnaire is a valid measure of bullying that furthers understanding of nuance in peer victimization for neurodivergent youth and informs group-specific intervention

J Autism Dev Disord. 2022.

**ADAPTIVE BEHAVIOR IN YOUNG AUTISTIC CHILDREN: ASSOCIATIONS WITH IRRITABILITY AND ADHD SYMPTOMS.**  
**Carpenter KLH, Davis NO, Spanos M, et al.**

Attention-deficit/hyperactivity disorder (ADHD) symptoms affect 40%–60% of autistic children and have been linked to differences in adaptive behavior. It is unclear whether adaptive behavior in autistic youth is directly impacted by co-occurring ADHD symptoms or by another associated feature of both autism and ADHD, such as increased irritability. The current study examined relationships between irritability, ADHD symptoms, and adaptive behavior in 3- to 7-year-old autistic children. Results suggest that, after adjusting for co-occurring ADHD symptoms, higher levels of irritability are associated with differences in social adaptive behavior specifically. Understanding relationships between irritability, ADHD, and adaptive behavior in autistic children is critical because measures of adaptive behavior, such as the Vineland Scales of Adaptive Functioning, are often used as a proxy for global functioning, as well as for developing intervention plans and measuring outcomes as primary endpoints in clinical trials

Journal of Clinical Medicine. 2022;11.

**SLEEP-RELATED BREATHING DISORDERS IN CHILDREN: RED FLAGS IN PEDIATRIC CARE.**  
**Blumer S, Eli I, Kaminsky-Kurtz S, et al.**

**Objectives:** In recent years, we have witnessed a growing interest in pediatric sleep-related breathing disorders (SRBD). Although a Pediatric Sleep Questionnaire (PSQ) exists and was found reliable in screening SRBD in children, many of the children remain underdiagnosed. The aim of the present study was to define anamnestic and clinical findings that can serve as red flags indicating the presence of SRBD in children.

**Methods:** 227 children aged 4–12 years old were evaluated with regard to the following parameters: (i) anamnestic variables (e.g., general state of health, oral habits, bruxism, esophageal reflux, sleep continuity, snoring); (ii) clinical parameters (e.g., oral mucosa, palate, tonsils, tongue, floor of the mouth, angle classification, gingival health, caries risk) and (iii) presence of SRBD (through the PSQ).

**Results:** Significant differences between children with and without SRBD were observed regarding continuous sleep, developmental delay, mouth breathing, and snoring. Taking medications for ADHD increased the odds of SRBD in children by over seven times, non-continuous sleep increased the odds of SRBD by six times, mouth breathing increased the odds by almost five times, and snoring increased the odds by over three times.

**Conclusions:** Child caregivers from various fields (dentists, orthodontists, pediatric physicians, school nurses) should actively inquire about disturbed sleep, medications for ADHD, snoring, and mouth breathing among their young patients. Initial screening through a few simple questions may help raise red flags that can assist in the early detection of SRBD in children and lead to proper diagnosis and treatment

J Dev Behav Pediatr. 2022 Sep;43:386-92.

**PRIMARY CARE DIAGNOSIS AND TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN SCHOOL-AGE CHILDREN: TRENDS AND DISPARITIES DURING THE COVID-19 PANDEMIC.**

**Bannett Y, Dahlen A, Huffman LC, et al.**

**Objective:** The aim of this study was to assess rates of primary care provider (PCP) diagnosis and treatment of school-age children with attention-deficit/hyperactivity disorder (ADHD) during the COVID-19 pandemic compared with pre-pandemic years and to investigate disparities in care.

**Method:** We retrospectively analyzed electronic health records from all primary care visits (in-person and telehealth) of children aged 6 to 17 years seen between January 2016 and March 2021 in a community-based primary health care network (n = 77,298 patients). Study outcomes are as follows: (1) number of primary care visits, (2) number of visits with ADHD diagnosis (ADHD-related visits), (3) number of PCP prescriptions for ADHD medications, (4) number of patients with first ADHD diagnoses, and (5) number of first PCP prescriptions of ADHD medications. Interrupted time series analysis evaluated changes in rates of study outcomes during 4 quarters of the pandemic year (March 15, 2020–March 15, 2021) compared with pre-pandemic years (January 1, 2016–March 14, 2020). Patient demographic characteristics during pre-pandemic and pandemic years were compared.

**Results:** ADHD-related visits dropped in the first quarter of the pandemic year by 33% (95% confidence interval, 22.2%–43.6%), returning to pre-pandemic rates in subsequent quarters. ADHD medication prescription rates remained stable throughout the pandemic year. Conversely, rates of first ADHD diagnoses and first medication prescriptions remained significantly lower than pre-pandemic rates. The proportion of ADHD-related visits for patients living in low-income neighborhoods was lower in the pandemic year compared with pre-pandemic years.

**Conclusion:** Ongoing treatment for school-age children with ADHD was maintained during the pandemic, especially in high-income families. Socioeconomic differences in ADHD-related care emphasize the need to improve access to care for all children with ADHD in the ongoing pandemic and beyond

Journal of Managed Care and Specialty Pharmacy. 2022;28:S65.

**EARLY REAL-WORLD UTILIZATION OF JORNAY PM (DELAYED-RELEASE/EXTENDED-RELEASE METHYLPHENIDATE) FOR THE TREATMENT OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER: DEMOGRAPHIC, DOSING, AND PERSISTENCE DATA FROM A LARGE US CLAIMS DATABASE ANALYSIS.**

**Morgan D, Anupindi V, Faraone S, et al.**

**BACKGROUND:** JORNAY PM (formerly HLD200) is an evening-dosed, delayed-release and extended-release methylphenidate (DR/ER-MPH) launched in June 2019 for the treatment of attention-deficit/hyperactivity disorder (ADHD) in individuals aged 6 years.

**OBJECTIVE:** To report real-world demographic/clinical characteristics and treatment patterns in patients initially prescribed DR/ER-MPH in its first year of availability compared with two established stimulants, osmotic release oral system (OROS) MPH and lisdexamfetamine dimesylate (LDX).

**METHODS:** A retrospective analysis was conducted of patients initially prescribed DR/ER-MPH, branded OROS MPH, or LDX from June 2019-2020 using US professional fee (Dx) and prescription claims (Rx) databases (New Data Warehouse, IQVIA). Data were de-identified and complied with HIPAA requirements; therefore, institutional review board approval was not required. Demographic/clinical data included age, sex, and prior ADHD medication use. Dosing data were calculated from persistent patients (those without a gap of > 1x fill duration over 12 months, allowing for summer drug holidays in patients 22 years). Demographic/clinical data were compared between groups using the standardized mean difference (SMD), with absolute SMD 0.1 indicating significance. Persistence data were compared using a paired t-test.

**RESULTS:** A total of 8,854 patients taking DR/ER-MPH, 56,200 patients taking OROS MPH, and 175,772 patients taking LDX were included. In the DR/ER-MPH group the mean age was 16.9 years and 63.2% of patients were male; 9.8% of patients had no ADHD medication prescriptions prior to initiating DR/ER-MPH treatment. Compared to OROS MPH/LDX, the DR/ER-MPH group was younger (SMD = -0.39/-0.76), had a higher proportion of males (SMD = 0.16/0.44), and fewer patients were treatment-naïve (SMD = -0.39/-1.16). With DR/ER-MPH, a higher proportion achieved 12-month persistence (25.7% vs 22.8%/22.2%; both P < 0.0001). In persistent patients, the mean daily dose of DR/ER-MPH was 53.8 mg.

**CONCLUSIONS:** Patients initially prescribed DR/ER-MPH in its first year of availability were generally younger than patients prescribed established medications and were typically not treatment-naïve. Mean prescribed doses of DR/ER-MPH in persistent patients were lower than those in clinical trials. Yet, patients demonstrated higher persistence to DR/ER-MPH treatment compared with OROS MPH and LDX, perhaps in part due to its unique evening administration and/or dose-dependent duration effect

Journal of Managed Care and Specialty Pharmacy. 2022;28:S65-S66.

**IMPROVEMENTS IN AN OBJECTIVE MEASURE OF ATTENTION FUNCTION WITH A DIGITAL THERAPEUTIC IS ASSOCIATED WITH IMPROVEMENTS IN ACADEMIC PERFORMANCE MEASURES IN PEDIATRIC ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Palko L.**

**BACKGROUND:** Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders in childhood and adolescence, current prevalence is around 6.1 million children/adolescents in the US. Attention problems can have particularly detrimental effects on school performance.

**OBJECTIVE:** Studies have shown that attention difficulties in first graders were related to decreasing reading and math achievement over time. AKL-T01 is a digital treatment delivered through a videogame interface and designed to improve attentional control. In a prior randomized controlled trial 4 weeks of treatment improved measures of objective attention Test of Variables of Attention, Attention Comparison Score, TOVA ACS.

**METHODS:** STARS-Adjunct was an open label study in 206 children 8-14-year-old. Here, we present exploratory analysis from STARS-Adjunct to examine the association between changes in objective measures of attention TOVA ACS and academic performance Mathematics Fluency and Calculation Tests MFaCTs, Test of Silent Reading Efficiency and Comprehension TOSREC.

**RESULTS:** Change in TOVA ACS scores from baseline after 4 weeks of AKL-T01 treatment was positively correlated with change in MFaCTs scores in the overall cohort (Pearson's  $r = 0.30$ ,  $P < 0.0001$ ) and the attentional impairment subgroup (Pearson's  $r = 0.35$ ,  $P = 0.002$ ). Correlations between change in TOVA ACS and TOSREC scores were weaker but still significant.

**CONCLUSIONS:** The present study found that changes in attention were associated with changes in academic performance, supporting the role of attention in mediating functional impact in patients with ADHD. This finding suggests a far transfer from improving objective attention function to measures related to academic skills

Journal of Managed Care and Specialty Pharmacy. 2022;28:S62-S63.

**TREATMENT PATTERNS AMONG PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND COMORBID ANXIETY OR DEPRESSION IN THE UNITED STATES - A RETROSPECTIVE CLAIMS ANALYSIS.**

**Gagnon-Sanschagrin P, Schein J, Childress A, et al.**

**BACKGROUND:** Patients with attention-deficit/hyperactivity disorder (ADHD) often have psychiatric comorbidities such as anxiety and depression that may confound diagnosis and affect treatment outcomes and costs.

**OBJECTIVE:** Describe treatment patterns and healthcare costs among commercially insured patients with ADHD and comorbid anxiety or depression in the US.

**METHODS:** Patients with ADHD initiating pharmacologic treatments were identified from IBM MarketScan Data (2014-2018). The index date was the first observed ADHD treatment. Comorbidity profiles (anxiety or depression) were assessed during the 6-month pre-index baseline period using DSM-5 definitions. Treatment changes (discontinuation, switch, add-on, drop) were examined during the 12-month study period. Adjusted odds ratios (ORs) of experiencing a treatment change were estimated. Adjusted annual healthcare costs were compared between patients with and without treatment changes. Results were stratified by age group (children [ages 6-12], adolescents [ages 13-17], adults [ages 18+]).

**RESULTS:** Among 172,010 patients with ADHD (children:  $n = 49,756$ ; adolescents:  $n = 29,093$ ; adults:  $n = 93,161$ ), the proportion of patients with anxiety and depression increased with age from childhood to adulthood (anxiety: 11%, 18%, 23%; depression: 3%, 16%, 19%). Although stimulants were the most prevalent first treatment observed in all 3 populations, children were observed to have a greater increase in non-stimulant use when anxiety or depression was present (eg, non-stimulant use in children was 9.7% in the overall ADHD population with/without comorbidities, 19.6% for those with anxiety, and 19.8% for those with depression). Compared to patients without the comorbidity profile, those with the comorbidity profile experienced a significantly higher odds of a treatment change (ORs of a treatment change in children, adolescents, adults were 1.37, 1.19, 1.19 for those with anxiety and 1.37, 1.30, 1.29 for those with

depression). Excess costs associated with a treatment change were generally higher among patients with a comorbidity profile than the overall population with ADHD. Among patients with 3 + treatment changes, annual excess costs per child, adolescent, and adult was \$2,234, \$6,557, and \$3,891 for those with anxiety and \$4,595, \$3,966, and \$4,997 for those with depression.

**CONCLUSIONS:** Over 12 months, patients with ADHD and comorbid anxiety or depression were significantly more likely to experience a treatment change than those without these psychiatric comorbidities and incurred higher excess costs associated with a treatment change than the overall ADHD population

J Paediatr Child Health. 2022;58:1753-59.

**OBESITY AND NEURODEVELOPMENTAL AND MENTAL HEALTH CONDITIONS AMONG ADOLESCENTS AGED 10-17 YEARS: THE NATIONAL SURVEY OF CHILDREN'S HEALTH 2017-2018.**

**Buro AW, Salinas-Miranda A, Marshall J, et al.**

**Aim:** Adolescents have a high prevalence of obesity and neurodevelopmental and mental health co-occurring conditions. This study examined the association between obesity and several co-occurring conditions autism spectrum disorder (ASD); intellectual disability; learning disability; stuttering, stammering or other speech problems; developmental delay; attention-deficit hyperactivity disorder; epilepsy or seizure disorder; cerebral palsy; depression; anxiety; and Tourette Syndrome in adolescents aged 10-17 years (n=26 266) using 2017-2018 National Survey of Children's Health data.

**Methods:** This cross-sectional study used 2017-2018 National Survey of Children's Health data (n=27 328); 2 tests were conducted to compare the prevalence of obesity and several co-occurring conditions. Multiple logistic regression was conducted to adjust for age, gender, race/ethnicity and household income.

**Results:** Obesity prevalence was 15.3%. Adolescents with ASD (25.1%) and epilepsy/seizure disorder (27.8%) had the greatest obesity prevalence. Adjusting for socio-demographic characteristics, odds of obesity were higher in those with ASD (odds ratio (OR) 1.7, confidence interval (CI) 1.2-2.6), learning disability (OR 1.5, CI 1.2-2.0), epilepsy or seizure disorder (OR 2.2, CI 1.2-3.8) and depression (OR 2.0, CI 1.6-2.5). For all regression analyses, odds of obesity were higher among adolescents who were non-Hispanic Black, Hispanic and low-income.

**Conclusions:** The increased prevalence of obesity in adolescents with ASD, learning disability, epilepsy or seizure disorder, and depression demonstrates the need to attend to their nutrition and physical activity needs. Future research should examine obesity risk factors among adolescents with specific neurodevelopmental and mental health conditions, as well as racial or ethnic minority and low-income populations, to properly tailor obesity prevention services

J Psychiatr Res. 2022;155:302-12.

**TRANSCRANIAL DIRECT CURRENT STIMULATION (tDCS) IN CHILDREN WITH ADHD: A RANDOMIZED, SHAM-CONTROLLED PILOT STUDY.**

**Schertz M, Karni-Visel Y, Genizi J, et al.**

**Background:** ADHD is a common neurodevelopmental disorder with a pediatric prevalence of 5.2%. While medication treatment for ADHD is effective, it does not address all symptoms and a small but notable subgroup does not respond to medications. Adverse effects limit its use and some parents and participants resist use of medication. Thus, limitations of medication treatment for ADHD motivate searching for other therapeutic options. Transcranial Direct Current Stimulation (tDCS) has been suggested as a treatment for children with ADHD, with mixed results to date. Protocol variables employed, including combined use of cognitive training (CT) and scheduling of sessions, may explain diverse findings to date. The aim of this study was to examine safety, feasibility and efficacy of tDCS combined with CT provided three-times-per week for one-month to treat children with ADHD.

**Methods:** In a double blind, randomized, sham-controlled pilot study, 25 children with ADHD were randomized to receive 12 sessions of either anodal tDCS or sham-tDCS for 20 min combined with CT three-times-per-week for four weeks. The tDCS anode was over left dorsolateral prefrontal cortex (DLPFC) and

cathode over vertex. Assessments were obtained prior to, after 6 sessions, 12 sessions and one-month after intervention.

**Results:** No significant post-intervention differences were found between those receiving tDCS or sham-tDCS. Both groups demonstrated significant improvement on questionnaire measures of ADHD and executive function with mixed results seen on computerized performance measures. Overall, adverse effects were mild with no significant difference between groups. However, three children, all from the tDCS group, experienced headaches with two requiring temporary cessation and one requiring removal from the study.

**Conclusions:** Anodal tDCS to the DLPFC using the above protocol in children with ADHD did not demonstrate additional treatment benefits beyond that of CT

J Psychiatr Res. 2022;156:36-43.

**LOWER PLASMA CONCENTRATIONS OF SHORT-CHAIN FATTY ACIDS (SCFAs) IN PATIENTS WITH ADHD.**

**Yang LL, Stiernborg M, Skott E, et al.**

Short-chain fatty acids (SCFAs), produced during bacterial fermentation, have been shown to be mediators in the microbiota-gut-brain axis. This axis has been proposed to influence psychiatric symptoms seen in attention deficit hyperactivity disorder (ADHD). However, there is no report of plasma SCFA concentrations in ADHD. The aim of this study was to explore the plasma concentrations of SCFAs in children and adults with ADHD and the possible factors that could influence those levels. We collected data on age group, sex, serum vitamin D levels, delivery mode, body mass index, diet, medication and blood samples from 233 ADHD patients and 36 family-related healthy controls. The concentrations of SCFAs and the intermediary metabolite succinic acid, were measured using liquid chromatography-mass spectrometry. Adults with ADHD had lower plasma concentrations of formic, acetic, propionic and succinic acid than their healthy family members. When adjusting for SCFA-influential factors among those with ADHD, children had lower concentrations of formic, propionic and isovaleric acid than adults, and those who had more antibiotic medications during the last 2 years had lower concentrations of formic, propionic and succinic acid. When adjusting for antibiotic medication, we found that among children, those currently on stimulant medication had lower acetic and propionic acid levels, and adults with ADHD had lower formic and propionic acid concentrations than adult healthy family members. In all, our findings show lower-than-normal plasma concentrations of SCFAs in ADHD explained in-part by antibiotic medication, age and stimulant medication. Whether or not this is of clinical significance is yet to be explored

J Psychopathol Behav Assess. 2022;44:725-37.

**ADHD BEHAVIORS AND SOCIAL FUNCTIONING IN PRESCHOOL CHILDREN: THE MODERATING ROLE OF EMOTION RECOGNITION.**

**Krasner A, Dennis M, Shoulberg EK, et al.**

This study examined the moderating role of emotion recognition on the association between preschoolers ADHD behaviors and social functioning outcomes. Sixty preschoolers (48.3% female; Mage = 3.94, SDage = .56) were recruited from Head Start-affiliated classrooms. Teacher-rated ADHD behaviors and an objective measure of children's emotion recognition were assessed at the beginning of the school year. Teacher ratings of social functioning outcomes were obtained approximately three months after the start of school. Hierarchical regressions examined the unique and interactive effects of ADHD behaviors and emotion recognition on preschoolers social functioning outcomes (i.e., oppositional behaviors, peer behavior problems, and social-emotional school readiness). The interaction between ADHD behaviors and emotion recognition predicted oppositional behaviors, peer behavior problems and social-emotional school readiness such that higher levels of emotion recognition appear to buffer the negative association between ADHD behaviors and adaptive social functioning. Preliminary considerations for interventions aimed at promoting preschoolers social functioning are discussed

Journal of Psychopathology and Clinical Science. 2022 Oct;131:793-807.

**ASSESSING GENERAL VERSUS SPECIFIC LIABILITY FOR EXTERNALIZING PROBLEMS IN ADOLESCENCE: CONCURRENT AND PROSPECTIVE PREDICTION OF SYMPTOMS OF CONDUCT DISORDER, ADHD, AND SUBSTANCE USE.**

**Perkins ER, Joyner KJ, Foell J, et al.**

This study explored the generality versus specificity of two trait-liability factors for externalizing problems—disinhibition and callousness—in the concurrent and prospective prediction of symptoms of conduct disorder, attention-deficit/hyperactivity disorder (ADHD), and substance use (i.e., alcohol use disorder and history of illicit substance use). Disinhibition involves an impulsive, unrestrained cognitive-behavioral style; callousness entails a dispositional lack of social-emotional sensitivity. Participants were European adolescents from the multisite IMAGEN project who completed questionnaires and clinical interviews at ages 14 (N = 1,504, Mage = 14.41, 51.13% female) and 16 (N = 1,407, Mage = 16.46, 51.88% female). Disinhibition was related concurrently and prospectively to greater symptoms of conduct disorder, ADHD, and alcohol use disorder; higher scores on a general externalizing factor; and greater likelihood of having tried an illicit substance. Callousness was selectively related to greater conduct disorder symptoms. These findings indicate disinhibition confers broad liability for externalizing spectrum disorders, perhaps due to its affiliated deficits in executive function. In contrast, callousness appears to represent more specific liability for antagonistic (aggressive/exploitative) forms of externalizing, as exemplified by antisocial behavior. Results support the utility of developmental-ontogenetic and hierarchical-dimensional models of psychopathology and have important implications for early assessment of risk for externalizing problems.

**General Scientific Summary**—This study suggests that assessing dispositional traits of disinhibition and callousness in adolescence can provide important predictive information about later-emerging behavior problems. Further, these trait-risk factors differ in the specificity of their relations with externalizing psychopathology, with disinhibition promoting overall risk and callousness predicting risk for conduct problems in particular

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**28.1 ADHD AND BIPOLAR DISORDER: A COMPLEX AND MISUNDERSTOOD COMORBIDITY.**

**Wilens TE.**

**Objectives:** Controversy exists as to the nature, evidence, clinical presentation, and therapeutics of individuals with ADHD and bipolar disorder. In this Symposium, a timely review and new information covering the historical context of the issue, evidence of the association, clinical presentation, and pharmacotherapeutic strategies will be presented.

**Methods:** Data ascertained from multiple controlled longitudinal and registry studies of ADHD describing the emergence of bipolar disorder and overlap data will be presented. The characteristics of bipolar disorder in adolescents and adults found to have ADHD will be presented. Pharmacotherapeutic strategies including the effects of sequencing treatment with stimulants, and the overall effects of stimulants and nonstimulants on ADHD and bipolar disorder, will be presented.

**Results:** Data support the coexistence of bipolar disorder and ADHD, which may be a developmental marker of early-onset bipolar disorder. Medication treatment of ADHD in patients with bipolar disorder has good outcomes when there is stabilization of the mood prior to the ADHD intervention. Stimulants and nonstimulants appear effective and relatively well-tolerated in treating ADHD in bipolar disorder.

**Conclusions:** ADHD is associated with early-onset bipolar disorder, and the existence of the 2 disorders has important clinical connotations. Individuals with ADHD and bipolar disorder can be treated pharmacologically. ADHD, BRD, PPC

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### 31.2 NEURAL AND CLINICAL ALTERNATIONS IN ADHD IN YOUTH WITH AND WITHOUT A FAMILIAL RISK FOR BIPOLAR DISORDER.

*DeBello MP, Du L, Tallman M, et al.*

**Objectives:** We used proton magnetic resonance spectroscopy (1H MRS) and structural MRI to compare baseline clinical and neural characteristics among youth who have ADHD with and without a family history of bipolar disorder (BP) and healthy comparison (HC) youth, and differences in clinical changes between youth who have ADHD with and without a family history of BP, following treatment with mixed amphetamine salts-extended release (MAS-XR).

**Methods:** Three groups of psychostimulant-free youth (10-18 years old) were enrolled: 1) youth with ADHD with at least 1 biological parent or sibling with bipolar I disorder (high risk, HR); 2) youth with ADHD without a first- or second-degree relative with a mood or psychotic disorder (low risk, LR); and 3) HC youth. All youth with ADHD were treated with 12 weeks of MAS-XR. Bilateral ventrolateral prefrontal cortex (VLPFC) 1H MRS and structural MRI scans and symptom ratings (including the ADHD Rating Scale [RS]) were performed. Graph-based network analysis from structural MRI data were used to interrogate topological properties of brain networks. ANOVAs were used to compare MRI characteristics across groups and change in symptom ratings over 12 weeks between ADHD groups.

**Results:** A total of 149 youth (HC n = 49; LR n = 50; HR n = 50) were enrolled. At baseline, HR youth exhibited greater manic, depressive, and ADHD hyperactive/impulsive symptom severity. Although VLPFC metabolite levels did not differ across groups, left VLPFC choline (Cho) levels correlated with the ADHD RS total score in LR, but not HR, group (group interaction,  $p = .0017$ ). LR and HR groups exhibited similar differences compared with HC in the default-mode and central executive networks. Greater topological alterations in the salience network (SN) were found in the HR group compared with the LR and HC groups. Following MAS-XR treatment, HR youth exhibited lower remission rates (ADHD-RS total score 18) (61% vs 92%;  $p < .0001$ ) and 50% less improvement in global functioning compared with LR youth ( $p < .0001$ ).

**Conclusions:** The identified alterations in the salience network of the HR youth may represent a prodromal phenotype relevant to the risk for developing BP. Our findings also indicate differences in clinical characteristics and response to treatment with MAS-XR between LR and HR youth, suggesting that attentional deficits in HR youth may represent an early phenotype of BP that is distinct from other ADHD presentations. ADHD, BRD, IMAGS

J Am Acad Child Adolesc Psychiatry. 2022;61:S126.

### 2.1 PHARMACOLOGICAL STRATEGIES IN ADHD: FOCUS ON PRAGMATIC INTERVENTIONS.

*Wilens TE.*

**Objectives:** Increasingly complex cases of children with ADHD are presenting to child and adolescent psychiatrists, requiring practitioners to learn new strategies for sequencing treatment, the management of refractory core-ADHD symptoms, and the treatment of comorbidity(ies).

**Methods:** A systematic review of the literature from historic, recently completed, and ongoing trials was completed to elucidate data on stimulant and nonstimulant treatments for ADHD. Data on combination therapies were also reviewed.

**Results:** The literature combined with the clinical experience indicates that alterations in the use of traditional stimulants in existing and novel release forms, atomoxetine, viloxazine, alpha agonists, the use of alternative agents, and combinations of medications can enhance a patient's ADHD response.

**Conclusions:** Pharmacological strategies will be reported for those who: 1) have not responded to traditional agents; and 2) present with comorbidity(ies). Both empirically derived data and illustrative cases will be used in this pragmatic presentation. ADHD, CM, TREAT

J Am Acad Child Adolesc Psychiatry. 2022;61:S132.

**5.2 WHAT'S NEW IN ADHD, SUBSTANCE USE DISORDERS, AND SUICIDE PREVENTION?**

*Wilens TE.*

**Objectives:** ADHD, substance use, and suicidality are among the most prevalent and serious behaviors that child and adolescent psychiatrists treat. This talk provides a timely update on contemporary data related to the care of youth with these presentations.

**Methods:** A selected review of the literature focused on ADHD, substances (opioids), and suicide was undertaken. Studies and editorials focused on relevant issues related to the understanding, prevention, and care of young people with these disorders were reviewed.

**Results:** This talk focuses on longer-term persistence data in ADHD, as well as recommended accommodations, developmental profiles of comorbid irritability, and the pharmacotherapy of aggression in ADHD. Recent guidelines on the treatment of youth with opioid use disorders will be reviewed. Issues related to racial considerations in the prevention of youth suicide will be highlighted.

**Conclusions:** Emerging contemporary findings related to ADHD, substances (opioids), and suicide prevention will be presented. ADHD, SUD, S

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J Am Acad Child Adolesc Psychiatry. 2022;61:S312-S313.

**23.3 TRENDS IN THE DIAGNOSIS AND TREATMENT OF ADHD IN INDIVIDUALS WITH AN OPIOID USE DISORDER.**

*Yule AM.*

**Objectives:** ADHD in childhood is a risk factor for the development of a substance use disorder (SUD). SUD, particularly opioid use disorders (OUDs), are associated with substantial morbidity and mortality. This study examines trends in the prevalence and treatment of ADHD among individuals with an OUD in the United States.

**Methods:** Using a nationally representative claims-based database of commercially insured people aged 13 to 64 years in the United States, we identified patients diagnosed with OUD with at least 6 months of continuous enrollment between 2007 and 2017. Patients with ADHD had at least 2 previous claims with an ADHD diagnosis within the same year. We defined concurrent prescribing of ADHD stimulant and medication for OUD (MOUD; buprenorphine, methadone, or naltrexone) as the receipt of stimulant prescription and MOUD treatment within 30 days of each other. We then tested the association between demographic characteristics and mental health diagnoses and receipt of a concurrent stimulant and MOUD among people aged 13 to 64 years using multivariable regression.

**Results:** Among 387,980 individuals with an OUD, the diagnosis of co-occurring ADHD increased from 5% to 15% between 2007 and 2017. Treatment of ADHD, primarily with stimulant medication, also increased to 52% by 2017. Among individuals on MOUD, concurrent receipt of stimulant medication increased from 2% to 8% between 2007 and 2017. Concurrent receipt of stimulant medication in this group was associated with younger age and female sex. Mental health diagnoses were associated with increased likelihood of concurrent stimulant receipt: ADHD (adjusted OR [aOR] = 22.63; 95% CI, 21.58-23.73), psychotic disorders (aOR = 1.18; 95% CI, 1.04-1.35), mood disorders (aOR = 1.43; 95% CI, 1.37-1.49), and anxiety disorders (aOR = 1.11; 95% CI, 1.06-1.16). Co-occurring SUD was associated with a decreased likelihood of concurrent stimulant receipt (aOR = 0.73; 95% CI, 0.69-0.76).

**Conclusions:** ADHD diagnosis and treatment in patients with OUD have increased over time. Although concurrent treatment with stimulants and MOUD tripled during the study period, only a minority of those with ADHD on MOUD treatment received a stimulant prescription. Further study of the benefits and risks of ADHD treatment in patients with OUD is needed. SUD, ADHD, PPC

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#### POSTSECONDARY EDUCATION IN PEOPLE WITH ADHD AND CONTROLS.

**Hechtman L, Rostain AL.**

**Objectives:** This Clinical Perspectives will explore postsecondary education in people with and without ADHD and possible predictors and support needed for their success or failure at university.

**Methods:** Sabrina Burr, PhD, will explore the characteristics of people with and without ADHD who go on to enroll in postsecondary education compared to those who do not. She will use data from the MTA. George DuPaul, PhD, will report on a 4-year prospective study of college students with (N = 228) and without (N = 228) ADHD. ADHD symptoms, sexual behavior, and grade point average (GPA) are all explored, as are needed supports. Lily Hechtman, MD, will describe postsecondary education and its predictors from data of 7 longitudinal controlled prospective follow-up studies. Factors that predict postsecondary educational outcomes are explored.

**Results:** Dr. Burr found that students with ADHD who enrolled in postsecondary education had less severe ADHD and better school performance in core subjects compared to those who did not. The need for academic support to address their disability was evident. Dr. DuPaul found that students with ADHD exhibited significant difficulties with inattention, hyperactivity, impulsivity, risky sexual behavior, and lower grade point averages relative to controls across 4 years, regardless of medication status. Students with ADHD required transitional support and psychosocial intervention throughout college. Dr. Hechtman found that, generally, people with childhood ADHD are less likely than matched controls to go on to postsecondary education or complete a university degree. Factors that predict postsecondary educational outcomes include IQ, executive functioning, comorbidity (eg, ODD, conduct disorder, substance abuse disorder, anxiety, depression), and psychosocial adversity (eg, poverty, abuse, neglect). Medication use, which is often intermittent, is not a strong predictor in most studies.

**Conclusions:** These studies suggest that people with ADHD can succeed in enrolling in and completing their postsecondary education, but they face greater challenges and require more educational and psychological supports to do so. ADHD, COLST

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#### 23.4 ADHD SYMPTOMS AND SMOKING OUTCOMES IN A RANDOMIZED CONTROLLED TRIAL OF VARENICLINE FOR ADOLESCENT TOBACCO CESSATION.

**Green R.**

**Objectives:** Many adult daily smokers try their first cigarette during adolescence. ADHD in adolescents has been associated with an increased risk for cigarette smoking in comparison to peers without ADHD. Despite examinations into neurobiological and psychosocial mechanisms underlying this comorbidity, the impact of ADHD on smoking cessation among adolescents has been less well-studied. This presentation will present data from a clinical trial examining ADHD symptoms as a moderator of smoking cessation following varenicline treatment in adolescents.

**Methods:** An overview of a double-blind, placebo-controlled trial of varenicline for adolescent smoking cessation will be provided. The trial included treatment-seeking daily cigarette smokers ages 14 to 21 years (N = 157) randomized to receive a 12-week course of varenicline or placebo, added to weekly smoking cessation counseling. At pretreatment assessment, participants were administered a self-report measure of ADHD symptoms, the ADHD Rating Scale (ADHD-RS). High (≥5) vs low (<5) ADHD-RS symptom counts in both hyperactive/impulsive (HI) and inattention (IA) domains were examined as predictors of smoking outcomes. Generalized mixed effects regression models were utilized to assess the association of baseline ADHD-RS with smoking outcomes during study treatment.

**Results:** Participants with high IA symptoms at baseline were less likely to achieve 7-day point prevalence abstinence (PPA) at weekly visits (relative risk [RR] = 2.38; 95% CI, 1.46-3.88; p = .001) and reported higher average cigarettes per day ( = 1.28; standard error [SE] = 0.49; p = .009) during active treatment, compared to those with low IA symptoms. In contrast, high HI symptoms did not predict differences in 7-day PPA (RR = 1.42; 95% CI, 0.82-2.43; p = .21) or cigarettes per day ( = .79; SE = 0.48; p = .099), compared to low HI symptoms. These findings were not modified by varenicline vs placebo treatment assignment.

**Conclusions:** Current findings suggest that ADHD IA symptoms are associated with poorer smoking cessation among adolescent smokers. These findings warrant additional investigation into how ADHD symptoms may be accounted for in smoking cessation interventions for adolescents. NIC, ADHD, TREAT

J Am Acad Child Adolesc Psychiatry. 2022;61:S301.

### 16.2 DOPAMINE TRANSPORTER AND CYP2D6 GENE EFFECTS ON ADHD IN THE METHYLPHENIDATE AND ATOMOXETINE CROSSOVER STUDY.

**Stein MA.**

**Objectives:** Despite 25 years of ADHD pharmacogenetic studies, there are few reliable predictors to guide treatment. The dopamine transporter (DAT1) is a primary pharmacodynamic target for methylphenidate (MPH) with known genetic variation hypothesized to impact response, while CYP2D6 variation impacts atomoxetine (ATX) kinetics. We examined genetic variation in DAT1 and CYP2D6 with dose response in youth diagnosed with ADHD exposed to both medications.

**Methods:** Dose-response relationships were examined for ATX and MPH and genotype-based metabolizer groups for DAT1 (9/9, 9/10, 10/10) or CYP2D6 (poor [PM], intermediate [IM], normal [NM], or ultrarapid [UM]) over a 4-week period in 199 youth with ADHD (mean age 10.4 years [2.7 SD]; 24% female) participating in a double-blind crossover study. Treatment followed an escalating, dose-optimization approach (MPH: 18, 36, 54, and 72 mg; ATX: 0.5, 1.0, 1.4, and 1.8 mg/kg). Changes in the ADHD-Rating Scale (ADHD-RS) total score over time was the primary outcome measure examined. Weekly ratings of ADHD symptoms and impairment (ADHD-RS and Clinical Global Impression [CGI]) were obtained by blinded raters.

**Results:** Therapeutic improvement were observed for both drugs, beginning at week 3 for ATX and week 2 for MPH. Youth with greater severity at baseline had greater reduction in symptoms over time. Prior stimulant exposure was associated with less symptom improvement to ATX. The DAT1 genotype significantly modified dose relationships with ADHD-RS total scores for ATX ( $p = .029$ ), such that 9/9 subjects did not respond as doses were increased. For weeks 1 and 2 (corresponding to dosages of 18 mg and 36 mg, respectively), the DAT1 9/9 group did not display typically observed dose-dependent decreases in ADHD symptoms until higher doses were administered. There was a significant CYP2D6 genotype-by-time interaction ( $p = .035$ ) at week 3, whereby UMs had greater symptom improvement to ATX vs non-UMs. UM responders had nominally greater ATX dose increases from week 2 to week 3 as compared to non-UMs.

**Conclusions:** Most children with ADHD with the most common genotypes respond well to both medications. DAT1 and CYP2D6 genotypes influenced dose relationships in a minority of patients. Future studies using whole-genome approaches will examine predictors of tolerability and discontinuation, which may have more clinical utility than studies focusing on acute symptomatic response. ADHD, PDS, PPC

J Am Acad Child Adolesc Psychiatry. 2022;61:S38.

### 27.3 POSTSECONDARY EDUCATION AND ITS PREDICTORS IN PEOPLE WITH AND WITHOUT ADHD FROM CONTROLLED PROSPECTIVE FOLLOW-UP STUDIES.

**Hechtman L.**

**Objectives:** Postsecondary education and its predictors will be described in people with and without ADHD from 7 longitudinal, controlled, prospective follow-up studies: the Montreal Study, the New York Study, the Milwaukee Study, the Pittsburgh Study, the Massachusetts Study, the Berkeley Girls Study, and the MTA.

**Methods:** Using data from the 7 studies outlined above, postsecondary education will be described in the ADHD and control subjects, and possible predictors of this outcome will be described and evaluated. The predictors explored include IQ, socioeconomic status (SES), severity and persistence of ADHD, comorbidities, and treatment.

**Results:** Generally, adults with adulthood ADHD have lower educational attainments when compared to matched control subjects. They repeat more grades, drop out of school more often, and are less likely to complete high school, go on to university, or to complete university degrees. Factors that predict this education outcome include persistence of ADHD symptoms, IQ, cognitive executive functioning, comorbidity

(eg, ODD, conduct disorder [CD], substance use disorder, and anxiety and mood disorders), and psychosocial adversity such as poverty, abuse, and neglect. Medication treatment (which is usually intermittent) is not a clear-cut predictor in most studies.

**Conclusions:** Controlled prospective follow-up studies clearly show that individuals with ADHD in childhood are less likely than matched-control subjects to receive a postsecondary educational degree. Predictors include persistence of ADHD, IQ, executive functioning, SES, and comorbidity, such as ODD, CD, substance use disorder, anxiety, and depression. Medication treatment, often intermittent, is not a strong predictor. ADHD, COLST

J Am Acad Child Adolesc Psychiatry. 2022;61:S312.

### **23.2 PROBLEMATIC ALCOHOL USE IN ADULTHOOD AS A FUNCTION OF ADHD IN CHILDHOOD, PARENTAL KNOWLEDGE IN ADOLESCENCE, AND IMPAIRMENT IN YOUNG ADULTHOOD.**

**Molina BSG.**

**Objectives:** Children with ADHD are at increased risk for alcohol-related problems in adulthood (Lee et al, 2011). Research examining this risk in adolescence and young adulthood has described mediational pathways through ADHD symptom persistence, delinquency, and social and academic impairment (Molina et al, 2012; 2014), with stronger associations when parents are less well informed about their teen's daily activities. Whether these processes extend into adulthood is unknown. This study tested whether young adult functioning and ADHD symptom persistence continued to mediate ADHD-related risk for problematic alcohol use at age 30 years and whether parenting in adolescence exerted lasting effects.

**Methods:** Participants from the Pittsburgh ADHD Longitudinal Study (N = 255; 57% = childhood ADHD; 82% = White; 92% = male) were interviewed during adolescence, at age 25 years (or 27/29 for ADHD symptom persistence), and at age 30 years. Participant-/parent-reported delinquency, parent-reported social impairment, participant-/parent-reported ADHD symptom persistence, and participant-reported highest level of education at age 25 years were tested as mediators in the relation between childhood ADHD and past-year heavy drinking (average of binge drinking/drunkenness) and alcohol problems at age 30 years. Adolescent-reported parental knowledge was tested as a moderator of these pathways.

**Results:** Childhood ADHD predicted higher social impairment ( $+1 = .37$ ;  $p < .001$ ) and ADHD symptom persistence ( $+1 = .37$  to  $.38$ ;  $p < .001$ ) and lower educational attainment ( $+1 = -.49$  to  $-.52$ ;  $p < .001$ ) at age-25. Childhood ADHD predicted lower age-30 heavy drinking ( $+1 = -.14$ ;  $p < .05$ ) with no mediation. Prediction of more age-30 alcohol-related problems was mediated by age-25 social impairment, ADHD symptoms, and education. Parental knowledge in adolescence did not moderate any pathways.

**Conclusions:** Social skill deficits common in ADHD may exacerbate risk for interpersonal alcohol problems (eg, fights and damaged friendships) that we previously shown are especially elevated for individuals with ADHD histories. Coupled with our earlier studies in adolescence, symptom persistence and academics (eg, tutoring and organizational support) should be addressed across development to reduce alcohol problem risk. ADHD, SUD, ALC

J Am Acad Child Adolesc Psychiatry. 2022;61:S323.

### **30.4 THE EFFECT OF ASD FEATURES ON NEUROCOGNITIVE CHANGE WITH NEUROFEEDBACK IN ADHD: NEW ICAN DATA.**

**Painter QA, Ging-Jehli N, Arnold LE, et al.**

**Objectives:** The objectives are to examine how ASD features change with theta-beta ratio (TBR) neurofeedback (NF) in children with ADHD and how they affect cognitive outcomes.

**Methods:** Children aged 7 to 10 years in the International Collaborative ADHD Neurofeedback (ICAN) RCT received either active TBR NF (n = 78) or control (sham) NF (n = 55) for 38 sessions. To assess treatment effects on cognition, they performed an Integrated Visual and Auditory Continuous Performance Test (IVA2-CPT) at baseline and at mid- and end-treatment. The diffusion decision model decomposed IVA2-CPT performance into encoding time (Ter) and drift rate indexing efficiency/quality of information integration (v).

Those receiving active NF improved more in  $v$  than controls. Although no child had an ASD diagnosis (all were selected for ADHD), ASD features were gleaned from parent and teacher reports at baseline and at mid- and end-treatment. We used a series of multivariate regressions to examine the change in the number of ASD features with treatment, the effects of those changes on cognitive components, and whether these changes and effects were treatment dependent.

**Results:** ASD symptoms decreased from baseline to treatment end ( $t[137.4] = 3.11$ ;  $p < .0001$ ). The ASD improvement difference between the NF and control groups was not significant. The overall efficiency of responses ( $v$ ) improved only for participants who received active NF treatment and whose ASD symptoms decreased more than the grand average from mid- to end-treatment ( $+d = -.038$ ;  $SD = 0.016$ ,  $p = .018$ ). Additionally, those who received NF and had average ASD improvement showed a faster encoding time ( $Ter$ ) from mid-treatment to treatment end ( $+d = .038$ ;  $SD = 0.018$ ;  $p = .042$ ), while the controls showed a slowing of  $Ter$  ( $+d = -.033$ ;  $SD = 0.014$ ;  $p = .021$ ).

**Conclusions:** ASD features improved significantly during treatment, whether active NF or control, with a marginal trend of advantage for NF. Although the speed of cognitive responses improved from mid- to end-treatment for children who received active NF and had average ASD improvement, the accuracy and efficiency of information integration improved only for children who both received active NF and had greater ASD improvement, possibly reflecting ASD mediation of the cognitive effects of NF. ADHD, ASD, NEPSYC

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#### 4.2 BLOOD MINERAL LEVELS: A ROLE IN TREATMENT RESPONSE TO MULTINUTRIENTS FOR ADHD AND EMOTIONAL DYSREGULATION: THE MADDY RCT.

**Robinette LM, Hatsu IE, Srikanth P, et al.**

**Objectives:** The Micronutrients for ADHD in Youth (MADDY) study was an 8-week double-blind RCT of broad-spectrum multinutrients (BSMN) for children with ADHD with emotional dysregulation (ages 6-12 years). The primary outcome, the Clinical Global Impressions-Improvement (CGI-I) scale, showed 3 times as many responders (54%) with BSMN as placebo (18%). Because the minerals lithium (Li), manganese (Mn), iron (Fe), copper (Cu), zinc (Zn), selenium (Se), and magnesium (Mg) are in the BSMN formula, this research explored: 1) changes in blood mineral levels with supplementation of 78 children (46 BSMN, 32 placebo); and 2) baseline levels as moderators of treatment response.

**Methods:** A linear fixed-effects model with clustered standard error for site quantified the within-group change from baseline to end of the RCT and the between-group difference (BSMN vs placebo). The primary outcome for moderator analyses was the odds of treatment response defined by week-8 CGI-I of 1 or 2 (very much or much improved). Logistic regression models were used for moderator analyses with baseline blood mineral levels entered as potential moderators.

**Results:** From baseline to week 8, blood Li increased significantly more with BSMN than placebo (+17.29ppb [95% CI, 13.35-21.23];  $p < .0001$ ); but Cu decreased significantly more than placebo (-39.48ppb [95% CI, -70.70 to -8.26];  $p = .01$ ). Se showed a trend of greater increase with multinutrients (+5.53ppb [95% CI, -2.77 to 15.94];  $p = .17$ ). Other minerals were comparable between groups: Zn (+34.54ppb [95% CI, -48.09 to 117.16];  $p = .4$ ), Mg (+.0003ppb [95% CI, -.002 to .002];  $p = .75$ ), Mn (+.04ppb [95% CI, -.19 to .26];  $p = .74$ ), Fe (-33.92ppb [95% CI, -278 to 210.16];  $p = .79$ ). In a different analytic approach comparing percentage change in log-transformed levels, the significance levels did not change. For all minerals, baseline levels did not moderate treatment response in the moderator analyses.

**Conclusions:** Although some minerals changed after supplementation, BSMN may be beneficial to children with ADHD and irritability regardless of baseline mineral status, suggesting that attempts to use blood levels to select treatment candidates may waste effort, time, and expense. With regard to next steps, Li, Se, Fe, and Cu should be investigated further as potential mediators of treatment response. ADHD, SAC, MCS

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### 30.2 NETWORK CONNECTIVITY CHANGES UNDERLYING RESPONSES TO TRIGEMINAL NERVE STIMULATION IN ADHD: RCT RESULTS.

*Loo SK, Jurgiel J, McGough JJ.*

**Objectives:** External trigeminal nerve stimulation (TNS) is a noninvasive method of brain modulation that received FDA device clearance in 2019 for treatment of children aged 7 to 12 years with ADHD. Children randomized to active TNS exhibited significantly greater improvements in ADHD symptoms ( $p < .005$ ) than sham and increased EEG power in the right frontal (F4) and frontal midline (Fz) brain regions. This presentation examines changes in resting-state functional connectivity to more fully characterize the neural mechanisms underlying TNS treatment related improvements in ADHD.

**Methods:** Sixty-two children aged 8 to 12 years with K-SADS diagnosed ADHD were randomly assigned to 4 weeks of nightly active or sham TNS treatment. The primary outcomes were the clinician-rated ADHD Rating Scale (ADHD-RS) and the Clinical Global Impression (CGI) scales. The secondary outcomes included cognitive measures, weekly ratings of behavioral executive functions (Behavior Rating Inventory of Executive Function [BRIEF]), and EEG measures at pretreatment and posttreatment. Cortical source-level resting-state functional connectivity was estimated from 128-channel EEGs using the groupSIFT program within the EEGLAB data analysis platform.

**Results:** After 4 weeks of treatment, the active TNS group exhibited stronger connectivity between the anterior and posterior nodes of the default mode network (DMN) and lower connectivity between the frontal and medial nodes of the salience and executive control networks than the sham group ( $p$  s range = .004-.008). Lower connectivity among edges involving the right frontal nodes (right insula, right lateral prefrontal cortex) were significantly associated with improved ADHD symptomatology ( $r$  s range = .29-.35;  $p = .02-.05$ ) at the end of treatment. TNS responders trended toward stronger connectivity within the DMN ( $p = .06$ ), which correlated with greater improvement in ADHD symptoms ( $r = .33$ ;  $p = .03$ ) and better parent-rated executive function (BRIEF working memory [WM]  $r = -.30$ ;  $p = .05$ ).

**Conclusions:** The neural mechanisms underlying the TNS treatment effects in ADHD involve normalization of connectivity within several resting-state networks (DMN, salience, executive control), particularly those involving mid- and right-frontal connections. ADHD, NM, TREAT

J Am Acad Child Adolesc Psychiatry. 2022;61:S331.

### 35.3 SCORES ON THE NOVEL MEASURE OF IMPULSIVE AGGRESSION ASSOCIATED WITH THE USE OF MEDICATION FOR AGGRESSION, IRRITABILITY, AND ADHD.

*Langfus J.*

**Objectives:** The aims of this presentation are to evaluate: 1) the reliability and criterion validity of a brief new scale measuring aggression and irritability in a large, nationally representative sample of youths; and 2) invariance across race and sex groups.

**Methods:** A representative US sample of parents of children aged 6 to 18 years ( $N = 1163$ ) completed a new measure of mood and behavior problems. Latent class analysis of expert ratings identified 43 items measuring impulsive aggression (IA). Exploratory factor analysis (EFA) assigned items to 2 highly correlated scales. Confirmatory factor analysis (CFA) and item-reliability curves were used to select a short form of items with representative content coverage. Area under the receiver operating characteristic curves (AUROCs) evaluated the scores predictive power to identify children medicated for ADHD, irritability, and aggressive behavior. Multigroup CFA evaluated invariance across biological sex and race.

**Results:** EFA guided the selection of 16 items; CFA indicated a good fit (Tucker-Lewis Index [TLI] = .984; root mean square error of approximation [RMSEA] = .068) for 2 highly correlated ( $r = .88$ ) factors, each high internal consistency ( $\alpha > .88$ ). IRT analyses indicated good precision across severity levels ranging from high normal to severely clinically elevated. Treating the items as a single scale, higher scores predicted receiving medication for aggression (AUROC = .78), irritability (AUROC = .73), and ADHD (nonstimulant AUROC = .69, stimulant AUROC = .67). Finally, multigroup CFAs showed evidence of strong invariance across race and sex groups.

**Conclusions:** This new screener shows high internal consistency and good criterion validity against clinically relevant outcomes. It also shows promise in terms of measurement equivalence across race and biological

sex groups, reducing potential measurement bias in treatment and services research. Having an unbiased, free tool would help clinicians identify children who might most benefit from treatment for aggression. Treatment sensitivity is the next feature to check. BRD, DEMF, OTH

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### 23.1 POSSIBLE SENSITIZATION EFFECTS OF AMPHETAMINE TREATMENT IN DRUG-NAIVE YOUTH WITH ADHD.

*Ivanov I.*

**Objectives:** Emerging evidence of sensitization following stimulant administration in humans represents a challenge for understanding the relationship between stimulant treatment for ADHD and the subsequent development of substance use disorders (SUD). We have proposed a hybrid model that the majority of youth with ADHD greatly benefit from treatments with stimulants, which are in turn protective against the development of SUD; however, a much smaller number may have heightened vulnerability, based on altered responsiveness of the brain reward system either at baseline or in response to stimulant treatment. To investigate this model, we used functional neuroimaging paired with ratings of reward sensitivity and sensation seeking, to assess changes in activation of the brain reward system and behavioral indices thought to underlie SUD risk in drug-naïve youth at high risk (HR) and low risk (LR) for SUD before and after treatment with stimulant medication.

**Methods:** We conducted an open clinical trial of mixed amphetamine salts (mean: 17.69 mg; SD = 3.8) for 52 days (SD = 37) paired with pre- to post-fMRI in 16 children with ADHD aged 8 to 12 years (LR: N = 7, ADHD only; HR: N = 9, ADHD + severe ODD/OCD). Participants were assessed using the Kirby scale (delay discounting), and the Urgency, Premeditation, Perseverance, Sensation Seeking (UPPS) scale at baseline and posttreatment; fMRI scans were obtained while performing 2 reward tasks (anticipation, conflict, reward, and passive avoidance tasks).

**Results:** We found significant group effects for delay discounting, suggesting that HR and LR participants are different at baseline ( $F_{1,13} = 6.160$ ;  $p = .028$ ;  $n_2 = .322$ ). In addition, there were trends for differential response to treatment, with worsening of delay discounting posttreatment in the HR group. Similarly, the groups showed different patterns of change with regard to sensation seeking on the UPPS scale, with interaction effects at the trend level ( $F_{1,13} = 3.066$ ;  $p = .103$ ;  $n_2 = .191$ ). Neuroimaging analyses are ongoing.

**Conclusions:** Behavioral indices of sensation seeking and delay discounting yield conflicting results; identification of neurobiological profiles at baseline and posttreatment may offer a more specific view of possible sensitization effects. Potential implications for clinical practice will be discussed. ADHD, IMAGS, STIM

J Am Acad Child Adolesc Psychiatry. 2022;61:S282.

### 4.1 NEW POST-RCT OPEN-LABEL OUTCOMES OF BROAD-SPECTRUM MULTINUTRIENTS FOR CHILDREN WITH ADHD AND EMOTIONAL DYSREGULATION: MADDY 16-WEEK RESULTS.

*Leung BMY, Srikanth P, Hatsu IE, et al.*

**Objectives:** Following the 8-week placebo-controlled RCT phase of the Micronutrients for ADHD in Youth (MADDY) study reported last year, all participants were offered the option to continue in an 8-week open-label (OL) extension. We examined change in symptoms of ADHD/emotional dysregulation by the original active (multinutrient) and placebo groups in the OL phase (weeks 8 to 16).

**Methods:** In the OL phase, participants, parents, and clinicians remained blind to the randomization of the RCT. Data from 126 children at baseline, 123 at week 8, and 99 at week 16 were analyzed using McNemar's 2 test for the clinician-rated Clinical Global Impression-Improvement (CGI-I) dichotomized outcome of responders and nonresponders and linear mixed-effects model with a random effect for subject nested within site for the parent-rated Child and Adolescent Symptom Inventory-5 (CASI-5) composite score.

**Results:** The clinician-rated CGI-I showed a significant increase in the proportion of treatment responders (CGI-I = 1-2) from week 8 (18%) to week 16 (64%) in the group originally assigned to placebo ( $p = .0003$ ). There was also a significant increase in the proportion of responders from week 8 (54%) to week 16 (66%)

in the multinutrient group ( $p = .04$ ). The mean change from week 8 to week 16 in the CASI-5 composite score was not different between the multinutrient (0.20; 95% CI, 0.11-0.29) and placebo (0.21; 95% CI, 0.11-0.32) groups. In overall mean change from baseline to week 16, there was a large improvement for both groups but no between-group difference for multinutrient (0.51; 95% CI, 0.42-0.60) vs placebo (0.50; 95% CI, 0.40-0.60) on the CASI-5.

**Conclusions:** After 8 weeks of multinutrients, children who initially took placebo for 8 weeks almost caught up with those who initially took multinutrients and continued an additional 8 weeks for a total of 16 weeks; they had >3 times the proportion of responders as when taking placebo. Children who took multinutrients for 16 weeks had a 12% further increase in proportion of responders compared to 8 weeks. Thus, most multinutrient benefit shows in the first 8 weeks but may have modest further improvement on continued supplementation. ADHD, CAM, DBD

J Am Acad Child Adolesc Psychiatry. 2022;61:S322.

### 30.1 EEG LEARNING PARAMETERS IN THE ICAN DOUBLE-BLIND RCT OF NEUROFEEDBACK FOR ADHD.

**Roger deBeus P, Cowley B, Ptukha A, et al.**

**Objectives:** The objective is to explore which neurofeedback (NF) session parameters, such as EEG data, movement, and muscle artifact, identify NF learners vs nonlearners in the International Collaborative ADHD Neurofeedback (ICAN) randomized double-blind trial.

**Methods:** A total of 142 children aged 7 to 10 years with combined or inattentive ADHD completed 19 to 38 NF sessions of either real theta/beta ratio (TBR) downtraining ( $n = 84$ ) or sham (control) treatment ( $n = 58$ ) of equal duration, intensity, and appearance based on prerecorded EEGs of a different child. EEG and artifact data were obtained from the training software (EEGer; EEG Software LLC, Northridge, CA) used for the intervention. To identify how each group responded to NF as a stimulus, we examined the dependence between the variance and expected values of the single-session variability for both TBR values and TBR session slopes. We compared groups using the 2-sample Kolmogorov-Smirnov (KS) test. Further, a linear model was fitted to estimate how average-session TBR values change with the duration of overall days of training length. Slopes (negative = learners) were fitted across sessions using Welch's t test to identify differences between groups.

**Results:** The analysis of within-session TBR variability indicated a significant between-group effect (KS  $D = 0.39$ ;  $p < .0001$ ) in favor of the active NF over the control group. Slope variability also showed a significant effect (KS  $D = 0.36$ ;  $p < .001$ ) favoring active NF. Overall days of training showed a positive slope (nonlearners) for the control group and negative slope (learners) for the active NF group. TBR slope values across sessions were significantly different between groups ( $t [118.2] = -1.96$ ,  $p .05$ ), with more negative (learner) values in the active NF group.

**Conclusions:** Learning analyses showed TBR within-session and across-session slopes and variability thereof reduced for the active NF group compared to controls; distributions of TBR slope values differed between groups, with significantly more decreases in active NF. The control group's TBR slope increase with the overall days of training may reflect habituation to the training and boredom. These results confirm treatment randomization and fidelity. Additional further analyses will be presented using continuous-time structural equation modeling to better estimate the NF learning process. ADHD, TREAT

J Am Acad Child Adolesc Psychiatry. 2022;61:S37.

### 27.1 PATHS TO POSTSECONDARY EDUCATION ENROLLMENT AMONG ADOLESCENTS WITH AND WITHOUT CHILDHOOD ADHD.

**Burr SM, LeFevre JA, Arnold LE, et al.**

**Objectives:** Despite the long-term deficits associated with ADHD, some adolescents with ADHD enroll in postsecondary education (PSE). Postsecondary students represent a relatively high-functioning segment of the population, but students with ADHD continue to experience academic difficulties in higher education. Beyond admittance to postsecondary programs, do adolescents with ADHD histories who enroll in

postsecondary studies differ from those who do not? We aimed to determine whether symptoms and academic functioning are distinct developmentally from childhood through adolescence between adolescents with and without ADHD who did and did not enroll in PSE.

**Methods:** Using data from the MTA (N = 749; 79% boys), including both ADHD and normative comparison groups, and latent curve modeling, we explored developmental trajectories of ADHD symptoms, standardized achievement, and school grades.

**Results:** Adolescents who eventually enrolled in PSE had less severe ADHD symptoms; however, among those with ADHD histories, the differences were modest and trajectories similar over time. For all adolescents, standardized achievement trajectories declined as much as two-thirds of an SD from ages 9 to 17 years, but there was no critical time period in which the groups began to differ from one another. In high school, for adolescents with ADHD histories, school performance in core subjects remained stable, whereas grade point averages (GPAs) declined for those who did not enroll in PSE and improved for those who did enroll. Despite this improvement, among adolescents who did enroll in PSE, adolescents with ADHD histories continued to have lower GPAs than their peers without ADHD histories.

**Conclusions:** Overall, school performance was more important than standardized achievement test scores and ADHD symptoms for understanding the academic trajectories of adolescents with ADHD histories. These results reinforce a well-established need for equity in education to ensure that students who would otherwise excel academically are not disadvantaged by their disability. Based on our findings, interventions when students transition to middle school that are specifically targeted toward improving school performance may be critical. ADHD, COLST, ADOL

J Am Acad Child Adolesc Psychiatry. 2022;61:S282.

**MICRONUTRIENTS AS TREATMENT AND PREVENTION: NEW FINDINGS FROM 2 RCTs (MADDY AND NUTRIMUM) FOR ADHD, EMOTIONAL DYSREGULATION, AND ANTENATAL DEPRESSION.**

**Arnold LE, Jensen PS.**

**Objectives:** The objectives are to examine 16-week outcomes, mineral effects, and glyphosate effects from an RCT of broad-spectrum multinutrients (BSM) for inattention and emotional dysregulation (ED) and report maternal and infant effects of gestational BSM.

**Methods:** A total of 126 children aged 6 to 12 years with ADHD and ED were randomized to BSM (all known vitamins and essential minerals at doses between the recommended dietary allowance [RDA]/reference daily intake [RDI] and upper limit) vs placebo for 8 weeks, yielding 54% responders (Clinical Global Impression-Improvement [CGI-I] = 1-2) with BSM vs 18% with placebo. All children took BSM at weeks 9 to 16. Primary analysis was repeated at week 16. Blood minerals were checked at baseline and week 8. Baseline urinary glyphosate concentration was compared between responders and nonresponders (CGI-I >3). A total of 88 medication-free depressed second-trimester women were randomly assigned to 12 weeks BSM vs control containing only iodine and B2. After week 12, all took BSM. Maternal depression was rated at baseline and week 12; infant function was tested at 2 weeks postbirth. A total of 44 healthy controls (HCs) and 14 mothers taking gestational antidepressants (AD) were recruited for infant comparisons.

**Results:** In the ADHD group originally assigned to BSM, the responder rate increased to 66% at week 16. Those initially assigned to 8-week placebo, who took BSM for the final 8 weeks, increased to 62% responders. Both increases were significant. From baseline to week 8, blood lithium increased while copper decreased; zinc, magnesium, manganese, iron did not change significantly. No baseline mineral level moderated treatment response. Urinary glyphosate was associated with treatment response. Among depressed mothers, 69% taking gestational BSM were responders, more than placebo (39%). BSM infants had significantly higher gestational age (d =.74) and infant length (d =.83) than AD infants. BSM infants performed better than AD (d =.7-2.0) and HC infants (d =.2-.7) on Brazelton orientation, motor, autonomic stability, and state regulation.

**Conclusions:** BSM appears beneficial to children with ADHD and ED regardless of baseline mineral status. The response to BSM is sustained for 16 weeks. Most effects appear by 8 weeks, but modest additional benefit seems to accrue with additional time. Glyphosate burden may interfere with response to BSM or be a marker of BSM nonresponse. BSM appears to benefit both gestational depression and subsequent infants function. DBD, ADHD, RCT

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J Am Acad Child Adolesc Psychiatry. 2022;61:S333-S334.

### **37.1 A CLUSTER RCT TO REDUCE STIMULANT DIVERSION AND ASSOCIATED RISK FOR ADOLESCENTS WITH ADHD STIMULANT-TREATED IN PRIMARY CARE.**

**Molina BSG.**

**Objectives:** Diversion (sharing, selling, or trading) of prescription stimulants supports the nonmedical use of ADHD medications by adolescents. Despite the typicality of pediatricians prescribing stimulants for their patients with ADHD, evidence-based strategies to reduce diversion and risk are not available to these primary care providers.

**Methods:** Seven pediatric practices in southwestern Pennsylvania were assigned to receive a workshop on stimulant diversion prevention (SDP) or continue treatment as usual (TAU) in a cluster-randomized controlled trial (NCT03080259). Electronic surveys were completed by 341 adolescent stimulant-treated patients at baseline and again at 6, 12, and 18 months posttraining for both groups. Patient reports were analyzed to determine SDP efficacy.

**Results:** Intent-to-treat analyses using generalized estimating equations, adjusting for practice effects and baseline levels, compared SDP vs TAU at the follow-up assessments. Patient-reported diversion was infrequent at baseline (1% TAU; 0% SDP) and thereafter (6.7% TAU; 3.7% SDP, across follow-ups), and the perceived risk of harm and intent to divert were at low risk levels, yielding no group differences. Among secondary outcomes, the results showed increased provider use of diversion prevention strategies, parent-patient communication about diversion, and increased patient expectations of negative social consequences from diversion in the SDP vs TAU groups. Three indirect (mediating) associations were observed, no iatrogenic (adverse) effects resulted, and strong provider satisfaction was reported.

**Conclusions:** Overall, the current study demonstrated that a brief, 1-hour training of pediatric primary care providers and their staff resulted in a small amount of benefit, and no negative effects, to the risk of stimulant diversion by adolescent patients treated for ADHD. The low-risk nature of the sample prevented the detection of stronger effects on our a priori outcome variables. Additional research with older, higher-risk patients is warranted. Providers reported strong satisfaction with the training which, coupled with lack of iatrogenic effects, highlights palatability of the workshop for prescribers who wish to address concerns about stimulant misuse and diversion with their patients. STIM, SUD, NIDA

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J Am Acad Child Adolesc Psychiatry. 2022;61:S311.

### **22.3 WORKING MEMORY AND REACTION TIME VARIABILITY MEDIATE THE RELATIONSHIP BETWEEN POLYGENIC RISK AND ADHD-LIKE TRAITS: EVIDENCE FROM A GENERAL POPULATION SAMPLE.**

**Bellgrove M.**

**Objectives:** Endophenotypes are heritable and quantifiable traits indexing genetic liability for a disorder. Here we examined which potential cognitive endophenotypes (working memory, response inhibition, and reaction time variability) statically mediate the relationship between the genetic risk for ADHD and ADHD-like traits reported in a large population-based sample.

**Methods:** The total sample comprised of genetic, cognitive, and behavioral data for up to 2221 participants aged 11 to 12 years from the ABCD. Polygenic risk scores (PRS) quantified ADHD genetic risk. ADHD-like traits were quantified as Bartlett factor scores, calculated with Attention Problems items from the Child Behavior Checklist, and Effortful Control items from the Early Adolescent Temperament Questionnaire Revised. Candidate cognitive endophenotypes were quantified using task-based measures. Working memory was defined as the accuracy of the emotional n-back task, and response inhibition and reaction time

variability were estimated from the stop-signal task. After corrections for multiple testing, cognitive measures associated with ADHD-like traits and PRSs were evaluated as potential mediators.

**Results:** Higher ADHD PRSs were associated with more pronounced ADHD-like traits ( $R^2 = 0.02$ ). Lower working memory performance, poorer response inhibition, and increased reaction time variability were associated with more pronounced ADHD-like traits. Higher ADHD PRSs were associated with poorer working memory accuracy ( $\beta$  [95% CI] =  $-0.09$  [ $-0.13, -0.05$ ];  $p < .001$ ) and increased reaction time variability ( $\beta$  [95% CI] =  $0.12$  [ $0.07, 0.16$ ];  $p < .001$ ) but not response inhibition. Working memory performance and reaction time variability partially mediated the relationship between ADHD PRS and ADHD-like traits (proportion mediated: 15% and 18%, respectively).

**Conclusions:** These findings indicate that working memory and reaction time variability can be understood as endophenotypes underlying the relationship between the genetic risk for ADHD and its behavioral traits in a population-based sample. GS, COG, ADHD

J Am Acad Child Adolesc Psychiatry. 2022;61:S101-S102.

#### **BALANCING THE BENEFIT AND RISK OF LONG-TERM TREATMENT WITH STIMULANTS IN ADHD.**

**Baweja R, Wilens TE, Childress AC.**

**Objectives:** Approximately 5% of school-aged youth are prescribed ADHD medication in the United States. Treatment with central nervous system (CNS) stimulants is associated with decreases in the risks of a wide range of ADHD-associated functional outcomes including motor vehicle crashes and depression. The most common adverse effects associated with stimulants are their impact on sleep, weight, growth, and cardiovascular (CV) parameters. This Clinical Perspectives highlights the benefits of long-term use of stimulants and the most common physical adverse events (weight, growth, sleep, and CV effects) associated with use of stimulants.

**Methods:** Presenters use a combination of reviewing current research literature, clinical case examples, current practice guidelines, consensus statements, and best clinical practices. Presenters will discuss the long-term functional outcomes related to ADHD pharmacotherapy and summarize the findings for assessing and managing physical adverse events associated with stimulants in the treatment of pediatric ADHD.

**Results:** The presenters of this Clinical Perspectives are national experts who will share the benefits of long-term stimulant use and its impact on weight, growth, sleep, and CV parameters, as well as management strategies. In the first talk, Timothy Wilens, MD, presents the long-term outcomes related to the pharmacotherapy of ADHD. In the second talk, James Waxmonsky, MD, discusses the impact of stimulants on growth and weight trajectories in children and systematic methods to promote healthy rates of height and weight gain. Margaret Weiss, MD, discusses the relationship between stimulant medications and sleep in children and adolescents with ADHD and management strategies for emergent sleep problems. Paul Hammerness, MD, presents a comprehensive review of CV impacts of stimulant medications in children and adolescents with ADHD. As the final talk in the session, Ann Childress, MD, integrates these presentations and discusses their clinical implications with a focus on how they inform management of ADHD.

**Conclusions:** ADHD pharmacotherapy is associated with decreases in the risks for ADHD-associated functional outcomes. Although some physical adverse events with stimulants are time-limited, others may persist chronically. This presentation will increase participants' awareness and understanding of the benefits and risks of long-term stimulant use for ADHD. ADHD, PPC, STIM

Kobe J Med Sci. 2021;67:E125-E136.

#### **OFFERING NEUROFEEDBACK AS AN INTERVENTION FOR CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN INDONESIA: A FEASIBILITY STUDY.**

**Subandriyo APEP, Jongmsa MLA, Wijaya DA, et al.**

**BACKGROUND:** EEG Neurofeedback training is an accepted non-pharmacological therapy for attention deficit/hyperactivity disorder (ADHD). Although stimulant medication is known to decrease ADHD symptoms, possible adverse effects, concerns about prolonged drug use on neural development, and problems related

to the compliance with the medications are often reported. In Indonesia, research on the feasibility of EEG Neurofeedback to treat ADHD is still lacking. The current study aimed to investigate whether setting up an EEG neurofeedback training program for children with ADHD would be feasible in Indonesia.

**METHODS:** Nine children (aged 6-12 years) participated in the study. ADHD was diagnosed using the Vanderbilt ADHD Diagnostic Rating Scale (VADRS). Children received twenty-five sessions of sensorimotor rhythm (SMR) neurofeedback training twice a week. Each session consisted of a 3-minute baseline, followed by 5\*3 minutes of training. IQ scores and VADRS scores were collected at baseline, after completion of the intervention, and at 3 months follow-up, while school reports were provided by the schools. The EEG spectral content was determined for all 25 training sessions. In addition, a Go/No-Go Task, was administered at the first 5 training sessions, and at session 10, 15, 20 and 25.

**RESULTS AND CONCLUSION:** An overview of all the collected data is provided descriptively, given the small group size. One child dropped-out during the training because of parental request, but the remaining eight children completed the full intervention program. Descriptive data suggested improvement with respect to both the ADHD symptomatology and performance IQ. These findings are in line with previous studies. Although a control arm was not included, we propose that the abovementioned SMR neurofeedback protocol may still be offered as a suitable non-pharmacological intervention for children with ADHD in Indonesia and deserves further research

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Mol Psychiatry. 2022.

**WORKING MEMORY AND REACTION TIME VARIABILITY MEDIATE THE RELATIONSHIP BETWEEN POLYGENIC RISK AND ADHD TRAITS IN A GENERAL POPULATION SAMPLE.**

**Moses M, Tiego J, Demontis D, et al.**

Endophenotypes are heritable and quantifiable traits indexing genetic liability for a disorder. Here, we examined three potential endophenotypes, working memory function, response inhibition, and reaction time variability, for attention-deficit hyperactivity disorder (ADHD) measured as a dimensional latent trait in a large general population sample derived from the Adolescent Brain Cognitive DevelopmentSM Study. The genetic risk for ADHD was estimated using polygenic risk scores (PRS) whereas ADHD traits were quantified as a dimensional continuum using Bartlett factor score estimates, derived from Attention Problems items from the Child Behaviour Checklist and Effortful Control items from the Early Adolescent Temperament Questionnaire-Revised. The three candidate cognitive endophenotypes were quantified using task-based performance measures. Higher ADHD PRSs were associated with higher ADHD traits, as well as poorer working memory performance and increased reaction time variability. Lower working memory performance, poorer response inhibition, and increased reaction time variability were associated with more pronounced ADHD traits. Working memory and reaction time variability partially statistically mediated the relationship between ADHD PRS and ADHD traits, explaining 14% and 16% of the association, respectively. The mediation effect was specific to the genetic risk for ADHD and did not generalise to genetic risk for four other major psychiatric disorders. Together, these findings provide robust evidence from a large general population sample that working memory and reaction time variability can be considered endophenotypes for ADHD that mediate the relationship between ADHD PRS and ADHD traits

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Neural Plast. 2022;2022.

**RESTING-STATE fMRI WHOLE BRAIN NETWORK FUNCTION PLASTICITY ANALYSIS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Tang Y, Zheng S, Tian Y.**

Attention deficit hyperactivity disorder (ADHD) is a common mental disorder in children, which is related to inattention and hyperactivity. These symptoms are associated with abnormal interactions of brain networks. We used resting-state functional magnetic resonance imaging (rs-fMRI) based on the graph theory to explore the topology property changes of brain networks between an ADHD group and a normal group. The more refined AAL\_1024 atlas was used to construct the functional networks with high nodal resolution, for detecting

more subtle changes in brain regions and differences among groups. We compared altered topology properties of brain network between the groups from multilevel, mainly including modularity at mesolevel. Specifically, we analyzed the similarities and differences of module compositions between the two groups. The results found that the ADHD group showed stronger economic small-world network property, while the clustering coefficient was significantly lower than the normal group; the frontal and occipital lobes showed smaller node degree and global efficiency between disease statuses. The modularity results also showed that the module number of the ADHD group decreased, and the ADHD group had short-range overconnectivity within module and long-range underconnectivity between modules. Moreover, modules containing long-range connections between the frontal and occipital lobes disappeared, indicating that there was lack of top-down control information between the executive control region and the visual processing region in the ADHD group. Our results suggested that these abnormal regions were related to executive control and attention deficit of ADHD patients. These findings helped to better understand how brain function correlates with the ADHD symptoms and complement the fewer modularity elaboration of ADHD research

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Nord J Psychiatry. 2022;76:497-506.

**ASSESSING SUSTAINED ATTENTION OF CHILDREN WITH ADHD IN A CLASS FLOW VIDEO TASK.**

***Yildirim Demirdogen E, Esin, Turan B, et al.***

**Objective:** The aim of the study was to evaluate sustained attention performance of children with ADHD and effect of distractors on sustained attention through an eye-tracking during a class-flow video task.

**Method:** Data were collected using an eye-tracking during a class-flow task conducted with 60 children (ADHD and control groups). Two areas of interest were determined in the task, these are relevant (teacher and whiteboard) and irrelevant (any regions outside the relevant area) areas. The task also included distractors in relevant and irrelevant areas, comprising a brief conversation and dropping of a pencil, respectively. Proportion of total fixation duration on areas of interest (PFDAOI) was used to assess sustained attention.

**Results:** Children with ADHD had lower PFDAOI in the relevant area during the whole class than children in the control group. After the relevant area distractor, PFDAOI increased in relevant area in ADHD group, indicating these children may have better attention after the distractor. However, children with ADHD also showed increased PFDAOI in the irrelevant area following the irrelevant area distractor, indicating that it negatively affected them. There was no significant change in the control group following the distractors.

**Conclusion:** These findings indicate that children with ADHD have poor sustained attention performance during the whole class. Moreover, distractors in distinct areas could affect children with ADHD differently. Thus, students with ADHD could benefit from increased stimuli in the relevant area and this can be a guide for classroom arrangements to improve the academic functionality of these children

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Nutrients. 2022;14.

**CHANGES IN EATING BEHAVIORS FOLLOWING TASTE EDUCATION INTERVENTION: FOCUSING ON CHILDREN WITH AND WITHOUT NEURODEVELOPMENTAL DISORDERS AND THEIR FAMILIES: A RANDOMIZED CONTROLLED TRIAL.**

***Thorsteinsdottir S, Njardvik U, Bjarnason R, et al.***

Fussy-eating children often display problematic behaviors around mealtimes, such as irritation, opposition, or may even throw tantrums. This may lead to reduced food variety and poor nutritional profiles, which may increase parents worries about their children's diet, particularly when the children also have neurodevelopmental disorders (ND) such as Autism Spectrum Disorder (ASD) and Attention-Deficit/Hyperactive Disorder (ADHD). To investigate the effect of Taste Education on problematic mealtime behaviors, 81 children aged 8-12 years, with ND (n = 33) and without (n = 48), and their parents, participated in a 7-week Taste Education intervention. Children were matched on age, sex, and ND, and allocated at random into Immediate-intervention and Delayed-intervention groups. Parents completed the Meals in Our Household Questionnaire (MiOH). To examine changes in MiOH-scores, repeated-measures analysis-of-variance with time-points were used, with condition as factors (Immediate intervention and Delayed

intervention). Baseline measures were adjusted for, and a robust linear mixed-model was fitted. Results showed superior outcomes for Intervention compared to waiting on all measures of MiOH, with stable effects through six-month follow-up. Differences were non-significant between children with and without ND. The Taste Education program suggests a promising, simple, and non-intrusive way to reduce children's problematic mealtime behaviors in the long term

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Nutrients. 2022;14.

**EFFECTIVITY OF SAFFRON EXTRACT (SAFFR-ACTIV) ON TREATMENT FOR CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD): A CLINICAL EFFECTIVITY STUDY.**

**Blasco-Fontecilla H, Moyano-Ramirez E, Martínez-González O, et al.**

Attention Deficit/Hyperactivity Disorder is the most prevalent neurodevelopmental disorder worldwide. Choice treatment includes psychostimulants, but parents tend to be reluctant to administer them due to side effects, and alternatives are needed. Saffron extract is a natural stimulant that has been proven safe and effective for treating a variety of mental disorders. This study compares the efficacy of saffron and the usual treatment with methylphenidate, using objective and pen-and-paper tests. We performed a non-randomized clinical trial with two groups, methylphenidate (n = 27) and saffron (n = 36), in children and adolescents aged 7 to 17. Results show that the efficacy of saffron is comparable to that of methylphenidate. Saffron is more effective for treating hyperactivity symptoms, while methylphenidate is more effective for inattention symptoms

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Pediatrics. 2017;140:S178.

**ASSOCIATION BETWEEN MEDICATION PRESCRIPTION FOR ATOPIC DISEASES AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Padron GT, Hernandez-Trujillo VP.**

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PLoS ONE. 2019;14.

**A NETWORK ANALYSIS APPROACH TO ADHD SYMPTOMS: MORE THAN THE SUM OF ITS PARTS.**

**Silk TJ, Malpas CB, Beare R, et al.**

In interpreting attention-deficit/hyperactivity disorder (ADHD) symptoms, categorical and dimensional approaches are commonly used. Both employ binary symptom counts which give equal weighting, with little attention to the combinations and relative contributions of individual symptoms. Alternatively, symptoms can be viewed as an interacting network, revealing the complex relationship between symptoms. Using a novel network modelling approach, this study explores the relationships between the 18 symptoms in the Diagnostic Statistical Manual (DSM-5) criteria and whether network measures are useful in predicting outcomes. Participants were from a community cohort, the Children's Attention Project. DSM ADHD symptoms were recorded in a face-to-face structured parent interview for 146 medication naïve children with ADHD and 209 controls (aged 6-8 years). Analyses indicated that not all symptoms are equal. Frequencies of endorsement and configurations of symptoms varied, with certain symptoms playing a more important role within the ADHD symptom network. In total, 116,220 combinations of symptoms within a diagnosis of ADHD were identified, with 92% demonstrating a unique symptom configuration. Symptom association networks highlighted the relative importance of hyperactive/impulsive symptoms in the symptom network. In particular, the motoric-type symptoms as well as interrupts as a marker of impulsivity in the hyperactive domain, as well as loses things and does not follow instructions in the inattentive domain, had high measures of centrality.

Centrality-measure weighted symptom counts showed significant association with clinical but not cognitive outcomes, however the relationships were not significantly stronger than symptom count alone. The finding may help to explain heterogeneity in the ADHD phenotype

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Psychiatry and Clinical Psychopharmacology. 2018;28:160.

**UNEXPECTED COMPLICATION AFTER METHYLPHENIDATE IN A BOY WITH ATTENTIONDEFICIT/ HYPERACTIVITY DISORDER: HICCUPS.**

***Kara T, Akaltun I.***

Attention-deficit/hyperactivity disorder (ADHD) is a chronic condition with adverse impacts on school/work life involving symptoms of inattention and hyperactivity-impulsivity. It is the most commonly diagnosed and treated childhood onset psychiatric disorder, with a prevalence in children and adolescents of 5.9-7.9%. Immediate-release methylphenidate (MPH) (Ritalin) is the first MPH-based pharmacotherapy approved by the Food and Drug Administration (FDA) for the treatment of ADHD. Hiccups is sudden and involuntary contractions of the diaphragm and intercostal muscles. The condition is generally benign and self-limiting, but may be chronic under some circumstances. We report a case of hiccups developing following treatment in a boy started on MPH therapy with a diagnosis of ADHD. Case presentation: A 7-year-old boy was the second of three children and was in the second year of school. He was brought by his parents to our clinic due to hyperactivity, easy boredom and irritability, academic failure, forgetfulness, and difficulty in organizing tasks and activities. ADHD was diagnosed on the basis of DSM-5 diagnostic criteria following psychiatric assessments, and IR-MPH was initiated. Two days later, the patient was brought back to our clinic by his mother. The mother stated that on the previous day, she had given the patient his medication after breakfast and sent him to school, but that the school had called 1-2 hours subsequently, and his teacher informed her that hiccups had developed, and that this condition was persisting. The hiccups stopped 1-2 hours after the mother collected the patient from school, and she did not give him the medication again. We told the mother to administer the medication when they returned home, but that the drug could be modified if hiccups recurred. The child was brought back the next day, and we were informed that hiccups had recommenced when the drug was administered, and stopped after 3-4 hours. The hiccups persisted 3-4 hours after medication administration, and this being repeated suggested that the MPH might have been the cause. MPH was therefore stopped, and atomoxetine therapy was started. The pathogenesis of hiccups is complex and has not yet been fully clarified. The neurotransmitters reported to be involved in the development of hiccups are dopamine, serotonin and GABA. Changes in their states are known to play a significant role in hiccups' development, and drugs that affect these neurotransmitters are effective in the treatment of the condition. MPH principally affects catecholaminergic activity in the prefrontal cortex and striatum. It produces this effect by increasing dopamine transmission through more than one mechanism. MPH increasing the level and effect of extracellular dopamine. In addition, MPH mediates the stimulation of the  $\alpha$ -2 noradrenergic receptor and the dopamine D1 receptor in the cortex. Hypo-/hyperdopaminergic states are reported to play a role in the development of hiccups. It was thought that MPH could trigger hiccup by increasing dopamine. We think that the possible relationship between MPH and hiccups should be carefully monitored by physicians

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Psychiatry and Clinical Psychopharmacology. 2018;28:244-45.

**FIRST DOSE-INDUCED ANGIOEDEMA DUE TO PHOSPHATIDYLSERINE - A COMPLEMENTARY ADHD TREATMENT.**

***Citir BG, et al.***

Attention-deficit/hyperactivity disorder (ADHD), characterized by attention problems, hyperactivity, and impulsivity, is a common paediatric psychiatric disorder. Multimodal treatment approaches including psychosocial and medical interventions are used in the treatment of ADHD. Complementary treatment is a nonmedical choice of other treatment options. Rare allergic reactions due to stimulants and complementary treatments have been reported. Here, we present a case with the diagnosis of ADHD suffered from an angioedema, an unexpected adverse effect, due to monotherapy of phosphatidylserine use. Case

presentation: Our case is a 6-year-old boy who was brought to our outpatient clinic with complaints of hyperactivity, paying less attention to the lessons, and fights with his friends. He has no developmental delays. There was no child psychiatric application before. The parents and his teacher filled out the scales; Disruptive Behavior Disorders Screening and Evaluation Scale and Conners Parent Rating Scale. After psychiatric and psychometric assessment, the diagnosis of ADHD was considered. Stimulant was recommended but his parents did not approve a medication. Therefore, phosphatidylserine was offered. The parents gave consent on the use of a herbal drug. Phosphatidylserine (150 mg/day) was started together with the psychosocial interventions. Unfortunately, the parents reported that their child had experienced some side effects even with a single dose use of phosphatidylserine. Parents had noticed swelling on the lips and face of the child and they brought him to an emergency unit as quick as possible. Angioedema was resolved after a pheniramine maleate injection. The phosphatidylserine use was stopped after that single dose. In spite of the inadequate efficacy, fish oil, herbal-based treatments, and trace elements are commonly used in the treatment of ADHD when the parents are unreluctant to the use of stimulants. However, adverse effects of these alternative treatments have been reported. In our case, phosphatidylserine use led to an allergic reaction. As far as we know, we have not come across a similar case with phosphatidylserine. Clinicians should be careful for unexpected side effects even prescribing herbal alternative treatments

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**ASSOCIATIONS OF CHILDHOOD AND CURRENT ADHD SYMPTOMS WITH PAIN IN WOMEN WITH FIBROMYALGIA: MEDIATOR ROLE OF DEPRESSION AND ANXIETY .**

**Karaf H, et al.**

**Objective:** Childhood attention-deficit/ hyperactivity disorder (ADHD) symptoms may persist, co-occur with anxiety, depression, and other psychiatric symptoms in later life. Despite the fact that cognitive functions are impaired in patients with fibromyalgia and there is a high rate of psychiatric comorbidity in these patients, little is known about childhood and current ADHD symptoms and their effects on pain in these patients. This study aimed to determine whether childhood and current ADHD symptoms were higher than control group and whether these symptoms predicted pain in patients with fibromyalgia.

**Methods:** Sixty-four patients who were followed up with fibromyalgia diagnosis in a physical therapy and rehabilitation and a specific pain outpatient clinic and 58 healthy individuals who have similar socio-demographic features were included in the study. A sociodemographic and clinical data form, Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), Adult ADHD Self-Report Scale (ASRS), Wender Utah Rating Scale (WURS), Fibromyalgia Impact Questionnaire (FIQ) were administered to participants.

**Results:** BDI, BAI, ASRS, and WURS scores were found to be significantly higher in the fibromyalgia group than the control group. WURS scores were found to be a significant predictor of pain in patients with fibromyalgia. Our results also showed that both BDI and BAI scores significantly mediated the association between childhood ADHD symptoms and pain.

**Conclusions:** Childhood and current ADHD symptoms are found to be higher in patients with fibromyalgia than the control group. Childhood ADHD symptoms may contribute to development and exacerbation of pain in fibromyalgia. Taking the ADHD symptoms into account has an important role in the treatment of patients with fibromyalgia who have frequent cognitive symptoms. Our findings also suggested that the strong relationship between childhood ADHD symptoms and pain can be explained by the presence of depression and anxiety symptoms in these patients

Psychiatry and Clinical Psychopharmacology. 2018;28:22.

**SYSTOLIC AND DIASTOLIC MYOCARDIAL PERFORMANCE IN PATIENTS USING METHYLPHENIDATE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DIAGNOSIS: A TISSUE DOPPLER IMAGING STUDY.**

**Kara T, et al.**

**Objective:** Many children with Attention-Deficit/ Hyperactivity Disorder (ADHD) are treated with psychotropic medications. It is known that psychostimulants have cardiovascular effects. The effects on heart rate and blood pressure and tachyarrhythmia are well defined. However, acute cardiomyopathy and pericarditis due to the use of methylphenidate (MPH) have rarely been reported. The purpose of this study is to show the relationship between the use of MPH and cardiac functions.

**Methods:** The study was conducted with 102 participants. A total of 51 patients were included in the study group, aged 6-18 years, using MPH derivatives (immediate-release-IR, extended release-ER) for at least 6 months. Twenty-two of the participants were using MPH with IR/ER: 50/50 and 29 with IR/ER: 22/78. All participants were administered the Barkley Stimulant Side Effects Rating Scale (SERS) by the researchers for the evaluation of drug side effects. Participants were also assessed using the Tissue Doppler Echocardiography (also called Tissue Doppler Imaging-TDI), a useful echocardiographic technique for assessing global and regional myocardial systolic and diastolic function. The obtained data were compared statistically.

**Results:** There was a statistically significant difference in the distribution of iso-volumetric contraction time (IVCT) between the case and control groups ( $p: 0.049$ ). IVCT values of all patients using MPH were found to be statistically significantly shorter than those who did not use it. It was observed that the IVCT changed depending on the type of MPH used. Participants using IR / ER: 22/78 had IVCT:  $54.4 + 8.9$  and IR / ER: 50/50 participants had IVCT:  $48.9 + 10.1$ . In addition, there was a statistically significant positive correlation between the IVCT scores and the symptoms of Stares a lot or daydreams ( $r = 0.398$ ,  $p = 0.004$ ) and uninterested in others ( $r = 0.321$ ,  $p = 0.021$ ) (Spearman's rho  $p < 0.05$ ).

**Conclusions:** MPH is the most commonly used psychostimulant drug in the treatment of ADHD in children and adolescents. It is a potent central nervous system stimulant that exerts its effects by increasing pre-synaptic levels of dopamine and norepinephrine. Previous studies have shown that extended release MPH increases heart rate, systolic blood pressure, diastolic blood pressure, and corrected QT (QTc) interval. Methamphetamine has been found to increase cardiomyopathy probability by 3.7 fold. The exact mechanism through which methamphetamine or methylphenidate exerts myocardial pathology remains unclear. But it is thought to be due to mainly direct catecholamine effects on cardiac myocytes. Increased catecholamine levels are thought to be due to myocardial overexpression of adrenoceptors, which may lead to pathological changes in cellular hypertrophy, apoptosis, and contractile function. In our study, MPH users were also found to have shorter IVCT. As the IR release rate increased, this shortening in IVCT was found to be increased. We think that monitoring of cardiac pathology of MPH users is important. We consider that there is a need for more comprehensive and longitudinal studies on the potential cardiovascular effects of MPH

Psychiatry and Clinical Psychopharmacology. 2018;28:217.

**REMISSION OF NOCTURNAL ENUREZIS AFTER METHYLPHENIDATE TREATMENT IN A BOY WITH 9 YEARS OF AGE.**

**Kara T, Yilmaz S.**

Attention-deficit/hyperactivity disorder (ADHD) is the most frequently seen childhood neuropsychiatric disorder. Methylphenidate (MPH) is a first-line drug in the pharmacological treatment of ADHD. Enuresis is defined as urinary incontinence at least twice a week for 3 months after 5 years of age without organic causes. It is termed as nocturnal enuresis (NE) if it occurs only during night-time sleep. NE has an important clinical and psychological burden and leads social, psychological, and emotional distress which reduces the quality of life. Enuresis is reported to co-exist in up to 30% of children with ADHD. Here, we report a case who showed a significant improvement in NE with MPH which was given for the ADHD treatment. Case presentation: A 9-year-old boy was brought to the outpatient clinic by his parents with the complaints of overactivity, difficulty in organizing tasks, losing items, impulsive behaviours, low school success, and night-time bed wetting. Night-time bed wetting was noticed which was present since very early ages with a frequency of almost every night. The patient was consulted with the paediatric urology clinic and organicity was excluded. The patient was diagnosed with ADHD and NE on the basis of DSM-5 diagnostic criteria. For

ADHD treatment, long-acting MPH with a dose of 0.5 mg/kg was started. At his first month visit, improvement was noticed both in ADHD symptoms and in NE complaints. When the MPH dose was increased to 1 mg/kg, together with the ADHD symptoms NE complaints ceased. The family stated that they had to cessate the MPH medication one week ago, because they had gone a holiday outside the city and forgotten to bring the medication with them. The patient was experiencing bed wetting in almost every night for the last one week in which no MPH was taken. After restarting the MPH treatment, both ADHD and NE complaints ceased again. MPH leads the blockage of dopamine and norepinephrine reuptake and so indirectly causes an increase in extracellular dopamine and norepinephrine levels. Dopamine may mediate the alertness effect of MPH in the central nervous system. Dopaminergic cell groups send descending projections to the spinal motor neurons and play a neuro-regulatory role in various spinal functions including motor control. It is suggested that dopaminergic drugs may influence the micturition physiology not only in the CNS, but at the peripheral level as well and the dopaminergic effect may contribute to the smooth muscle tonus of the lower urinary tract. The enhancement of therapeutic dopamine function through these dopaminergic effects of MPH has been thought to play a role in the treatment of enuresis. A noradrenergic effect on the bladder may lead to relaxation in the detrusor muscle and subsequent decrement in the bladder contractility and this eventually causes an increase in bladder capacity. Besides, this effect may cause sphincter contraction and a decrease in the rate of urinary incontinence. In conclusion, MPH can be considered as an alternative treatment in NE cases that do not respond to traditional medical treatment in children with/without ADHD

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Psychiatry and Clinical Psychopharmacology. 2018;28:341.

#### **EEG SIGNATURES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: CLINICAL CORRELATES.**

##### ***Cak HT.***

Attention-deficit/hyperactivity disorder (ADHD) affects 5-10% of all school-aged children and the heterogeneity in clinical presentation, treatment response, and outcome requires valid biomarkers that can assist diagnosis, predict developmental outcomes, and monitor treatment response. Neurophysiological measures have been a major focus of research in ADHD. Brain electrical activity can be recorded via electroencephalography (EEG) during rest or while performing a cognitive task. EEG offers a different way of neural assessment from blood flow-dependent measures and it measures neuronal postsynaptic electrical fields. In the ADHD literature, excess theta activity, increased theta/beta ratio (TBR), and reduced amounts of alpha activity are often reported findings and have been interpreted as signs of immature brain activity or hypoarousal, but are insufficient as a diagnostic biomarker. On the other hand, high TBR and excess theta activity are thought to be possible positive prognostic markers and excess beta activity or beta spindles negative prognostic markers for stimulant treatment response. Only a handful of studies investigated the behavioural correlates of proposed EEG markers in ADHD. Positive relation between theta activity and inattention symptoms in adults and children, negative relation between theta activity and hyperactivity/impulsivity symptoms in children and decreased frontal theta and increased frontal beta activity in parent improved ratings of parent reported ADHD symptoms in children using psychostimulants have been reported. Additionally spindling excessive beta activity is specifically associated with impulse control problems. Frontal alpha asymmetry, the difference in alpha-band activity over right vs. left frontal hemispheres, is also proposed to be associated with reduced reward responsiveness, aggression, and difficulties with inhibition. There appears to be increased slow-wave and decreased fast-wave activity in ADHD and other forms of externalizing behaviour. It can be hypothesized that slow waves are associated with subcortical motivational systems and fast waves with cortical cognitive systems. In our current study, 80 right-handed, psychotropic medication naïve, 6-10 years old boys with a total IQ score of 75 or more, newly diagnosed with ADHD according to DSM-5 criteria were recruited. Detailed psychiatric evaluation, clinician- and parent-rated scales, along with WISC-IV and Bruininks-Oseretsky Test of Motor Proficiency, was administered and eyes open and closed resting state Electroencephalography (EEG) recordings were taken. As expected theta activity and TBR were negatively correlated with age but could only reach statistical significance at the temporal lobe. Theta and beta activity were not correlated with parent reported psychiatric symptoms nor cognitive measures but children with ADHD Inattentive Type had significantly higher theta activity at frontal and parietal electrodes. Additionally, left TBR was negatively correlated with clinician rated inattention symptom severity. As for original findings, bilateral coordination and upper limb coordination scores were

significantly negatively correlated with theta activity and overall TBR was significantly negatively correlated with total motor proficiency, more significant at the left hemisphere. Fine motor integration, manual dexterity, bilateral coordination, balance and upper limb coordination were significantly negatively correlated with left hemisphere TBR. To the best of our knowledge, this is the first study to demonstrate the association of TBR with motor skills in ADHD.

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#### **THEORY OF MIND IN CHILDREN AND PSYCHOPATHOLOGY.**

**Sahin B.**

Theory of Mind (ToM) is a social cognition skill demonstrated its importance in the last 40 years with psychiatric clinical trials. ToM is seen as an effective and necessary skill in the social functioning of human who is a social creature with the ability to recognize the mental states and emotions of others. In the first six years of life, ToM has been associated with many fields. Many tests are used in the evaluation of ToM. First-order false-belief tasks assess the ability of the person to understand what he or she knows, at the simplest level that the other person does not know. Second-order false-belief tasks; the ability of a third person to predict the thoughts of a second person about a thought. The Hinting Task is one of the advanced ToM tasks. It tests the ability to predict the true intention behind the indirectly spoken verbal expressions. Faux Pas and Reading the Mind in the Eyes Tasks are considered to be the most complex ToM skill and these tests are accepted as a sensitive measurement tool of ToM deficits. The first psychopathology studies have been carried out in children with Autism Spectrum Disorders (ASD), and the studies about ToM skills in the diagnosis of neurodevelopmental disorders are becoming more and more interesting. In addition to impulsive control, attention, and other neurocognitive problems in the Attention-deficit/ hyperactivity disorder (ADHD), children have emotional problems and interpersonal problems with parents, siblings, peers, and teachers. Social dysfunction is considered one of the most debilitating aspects of ADHD. It was found that 22% of children with ADHD had deficits in social functioning and this was significantly higher than the control group. Social dysfunction is very important for short- and long-term prognosis of children with ADHD. The relationship between ADHD and social cognitive deficits including emotional face recognition and prosodic perception has been clearly demonstrated. It is unclear whether impairment of emotion recognition and ToM deficits in ADHD are comparable to ASD in terms of severity. It is important to investigate whether social cognitive disorders in ADHD are independent abnormalities or secondary to neurocognitive skill abnormalities affecting social cognitive tasks of neuropsychiatric patients. We will present our study of social cognition in children presenting with ADHD, Specific Learning Disorder, and ASD diagnoses.

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#### **NOCTURNAL ENCOPRESIS AFTER METHYLPHENIDATE USE IN A SEVEN-YEAR-OLD BOY.**

**Onder A, Adanir AS, Kavurma C, et al.**

Encopresis is defined by involuntary or intentional recurrent faecal incontinence according to the DSM-5. Although the exact aetiology of encopresis was not known, studies showed that it was associated with a large number of psychiatric disorders. But nocturnal encopresis is often caused by an organic cause and requires detailed medical examination. This article will discuss the occurrence of nocturnal encopresis after the use of methylphenidate. Case presentation: M.U.B. is seven years old. He is a student in the second class. He came to the outpatient clinic with his mother because of complaints of inattention, hyperactivity, and academic failure. It was observed that he was very active and constantly spoiling the goods on the table in the policlinic. He spelled out and read slowly when he wanted to read. The story taken from her mother showed that he had been active since kindergarten, there had been a lot of complaints from the school due to his hyperactivity in first grade. No illness was described in the general medical story. His developmental stages were normal. He gained toilet training in time. There was no medical or psychiatric illness in the family. In the next interview, he was diagnosed ADHD - Combined Type and Specific Learning Disorder after evaluating Teacher Information Form, Turgay Disruptive Behavior Disorders Screening Scale and

intelligence test results. Long-term methylphenidate treatment started with 10 mg after blood transfusion, blood pressure and height weight measurement. We learned that hyperactivity and attention problems decreased in the control after two weeks but he started to defaecate every night when he took the drug. Constipation was not described. A week after the medication was discontinued, there is no repetition of the complaint about the defaecation. Methylphenidate treatment was resumed after the neurology and paediatric consultation requested no abnormality. Because the complaint of defaecation restarted after a week, the treatment was stopped and the treatment with atomoxetine was switched on. After one month of treatment with atomoxetine, we learned that attention and hyperactivity problems decreased and now he was compatible in school. Later on, he never had a complaint of defaecation again in his next controls. We are still following him regularly in our outpatient clinic. To our knowledge, the present case is the first case where nocturnal encopresis is seen after methylphenidate used in the literature. In the cases with attention-deficit/hyperactivity disorder and comorbid encopresis, the efficiency of the methylphenidate treatment has been showed in both the symptoms of attention-deficit/hyperactivity disorder and encopresis. There is a case report showing the effect of methylphenidate in imipramine and sertraline resistant encopresis without attention-deficit/hyperactivity disorder. Methylphenidate is believed to provide this effect on encopresis with executive functions, impulse control, and increased awareness of internal stimuli. It is unclear which mechanism of methylphenidate treatment led to nocturnal encopresis in our case. However, the reduction in complaints with the withdrawal of methylphenidate and recurrence in complaints after we restart methylphenidate shows that that side effect is caused by methylphenidate treatment

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#### **ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) DIAGNOSIS: DIVA AND OTHER DIAGNOSTIC TOOLS.**

##### ***Cipil A.***

Adult attention-deficit/hyperactivity disorder (ADHD) is a relatively common, often unrecognized disorder. It affects 4.4% of adults in United States, but most adults with ADHD live with the symptoms and suffer the devastating effects of ADHD in their lives without identifying the source of their struggles. Instead, their difficulties are attributed to their own shortcomings. Many adults who suffer from untreated ADHD avoid diagnosis or treatment due to the negative stigmatization associated with ADHD. Mental health workers sometimes dismiss ADHD and define it as little more than laziness which is targeted as a marketing opportunity by pharmaceutical companies. However, many years of scientific research confirms adult ADHD does indeed exist, and that ADHD diminishes adults' quality of life. DIVA semi-structured interview allows a thorough evaluation of the diagnostic criteria of DSM-IV-TR for ADHD in adulthood, as well as in childhood. It is divided into two domains, each applicable for childhood (before age 12) and for adulthood: The DSM-IV criteria for inattention, and for hyperactivity/impulsivity. Adult ADHD Self-Report Scale-V1.1 Screener (ASRS-V1.1): The 6-item ASRS-V1.1 designed as a tool to help screen for ADHD in adults (aged 18 years and older). The 6 questions are consistent with the DSM-IV criteria and address the manifestation of ADHD in adults. The paper version requires 1-2 min to complete. Respondents are required to use a 5-item Likert scale to indicate the frequency of occurrence of symptoms (0 = never; 1 = rarely; 2 = sometimes; 3 = often; 5 = very often). According to the convention, if the respondent has 4 or more responses marked in the darkshaded boxes of the copyrighted paper-version of the Screener (or in Part-A of the ASRS Symptom Checklist), then the current symptom profile of the individual is considered to be highly consistent with ADHD diagnosis in adults. Accurately diagnosing ADHD is critically important, as highlighted by the findings of Barkley and colleagues and Biederman and colleagues. These studies demonstrate that missed diagnosis and the absence of treatment were associated with educational, occupational, and social impairments in adaptive functioning, as well as an increased risk of substance use disorder. Because of the high prevalence rate of ADHD relative to other Axis I psychiatric disorders, clinicians should be aware of the symptoms and adult manifestations of ADHD and include screening in every adult psychiatric evaluation. Rating scales can be helpful in complementing the clinical interview, quantifying target symptoms, and measuring treatment response.

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#### **COMPUTER-BASED TESTS IN ADHD DIAGNOSIS.**

**Ozkanoglu FK.**

Attention-deficit hyperactivity disorder (ADHD) is characterised by symptoms of inattention, hyperactivity, and impulsivity. It is an early onset, enduring heterogeneous neurodevelopmental deficit, with an estimated prevalence worldwide of 5-7%. Scientific publications show that the prevalence of ADHD is increasing year by year. Healthcare providers believe that still many ADHD patients are undiagnosed. ADHD has no definite biological, radiological, or genetic marker and the authors agree that ADHD is a clinical diagnosis. Therefore, the diagnosis is mainly based on clinical observations and questionnaires, which are arranged according to DSM criteria and if needed, neuropsychological or other testing are performed. It means that the diagnosis is influenced by perceptions of many different members of a child's community. Parents and teachers (according to their ethnic and cultural background) may have different views and perceptions of behavioural norms. In the absence of an objective gold standard, computerized continuous performance tests have been developed to help in the diagnosis of ADHD as objective measurements. The CPT test is a computer-based test that involves the rapid presentation of a series of visual or auditory stimuli over a period of time (typically numbers, letters, number/letter sequences, or geometric figures). Subjects taking the CPT tests are instructed to respond to the target stimulus by pressing a button and to refrain from responding to non-target stimuli. Responding to the designated target is referred to as a correct response, while missing a target is referred to as an omission error. Response to any stimulus other than the target is referred to as a commission error. Other measures of CPT responses include the number of correct responses, reaction time, and variability in reaction time. Although CPTs have been used for many years, they are often criticized for their test-retest reliability, low sensitivity, and specificity rates. But over time, CPTs are developed. A good example is MOXO d-CPT which includes visual and auditory stimuli serving as distractors. This feature increased the sensitivity and specificity rates. And today we are talking to use d-CPT with EEG (electroencephalography) together to help ADHD diagnosis. Healthcare providers should be innovative, suspicious, objective, and most importantly evaluate all data together with clinical findings.

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#### **METHYLPHENIDATE EFFECTS ON EEG CHARACTERISTICS IN SCHOOL AGE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Karaer Y.**

Attention-Deficit/ Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by inattentiveness and / or hyperactivity-impulsivity that disturbs the functioning or development of the individual. It is known that ADHD is accompanied by a number of electroencephalography (EEG) changes. Typically, ADHD children have increased theta activity which occurs primarily in the frontal regions, increased posterior delta and decreased alpha and beta activity, also most apparent in the posterior regions, compared to children without ADHD. Calculations of ratios of EEG activity between frequency bands have also been used to assess differences between clinical groups, with ADHD children having an increase in the theta/alpha and theta/beta ratios compared to normal children. These results have been shown as indicating that ADHD children have a maturational lag in central nervous system development or are cortically hypoaroused. In addition, the effects of drugs used in the treatment of ADHD on EEG have been investigated for a long time. Psychostimulants are the first choice drugs in the treatment of ADHD for many years. Psychostimulants have been shown to improve, but not normalize, many ADHD-associated abnormal EEG activities. methylphenidate (MPH) has a tendency to decrease the theta band and increase the beta band power, particularly when associated with medication-related improvements in cognition. Studies have shown that regular use of MPH in ADHD increases beta power on EEG. Several researchers have reported that EEG measures discriminate well between children with and without ADHD and others have asserted that the EEG works well in determining medication responders from non- responders. In this study, we tried to evaluate the effects of methylphenidate on EEG in children with ADHD during school age. In our current study 80 right handed, psychotropic medication naïve, 6-10 years old boys with a total IQ score of 75 or more and newly diagnosed with ADHD according to DSM-5 criteria were recruited. Detailed psychiatric evaluation, clinician and parent rated scales, along with WISC-IV and Bruininks-Oseretsky Test of Motor Proficiency was

administered and eyes open and closed resting state Electroencephalography (EEG) recordings were taken. In this study, it was observed that there was a decrease in theta/beta ratios in the frontal and parietal areas with MPH. This is dominant on the left but not statistically significant.

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**ACUTE DYSTONIA DUE TO DISCONTINUING OF METHYLPHENIDATE TREATMENT: A CASE.**

***Dogan Y, et al.***

The acute dystonic reaction is usually a side effect of an extrapyramidal system, which usually occurs suddenly due to antipsychotic and antiemetic drugs. Acute dystonia is described as sustained abnormal postures or muscle spasms that is observed mainly in the head and neck area. In this poster, we want to present a case with acute dystonic reaction in the head and neck area due to discontinuation of methylphenidate. Case presentation: A 6-year-old girl was referred to our outpatient clinic by her parents who complained of her excessive and inappropriate hyperactivity, failure to fulfil assigned duties and responsibilities, not obeying the class rules, having difficulty listening to her teacher. The girl was diagnosed as suffering from attention-deficit/hyperactivity disorder (ADHD) according to DSM-5 criteria. The patient was prescribed methylphenidate 10 mg/day. After one month of medication, the methylphenidate dosage was increased to 20 mg/day. Approximately 10 days after the increasing dose, a significant decrease in appetite was delayed and stopped the medication by the family. Her family noticed on the 2nd day of drug withdrawal that her speech was impairing and could not speak after a while, and chewing and swallowing functions was disappeared. Her parents also complained about episodes suggestive of dystonia in the form of torticollis, facial muscle spasm, and oculogyric crisis. The drug was given to the patient again because of the story of symptoms suspected when methylphenidate was discontinued. Her symptoms reduced again after methylphenidate treatment. Long-acting methylphenidate was started at a dose of 20 mg/day and her family reported that her ADHD symptoms reduced and there have been no signs of dystonia. A large number of drugs can cause acute dystonic reactions at the treatment dose. It is most commonly caused by antipsychotic and antiemetic drugs. In the literature, there were 3 rebound dystonia cases when methylphenidate treatment was discontinued during the use of antipsychotic and methylphenidate. In our case, an acute dystonia was detected when methylphenidate treatment was discontinued, although there was no use of antipsychotics. There was a dramatic improvement when the treatment was restarted

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Psychiatry and Clinical Psychopharmacology. 2018;28:352.

**THE IMPORTANCE OF RESTING STATE QUANTITATIVE EEG ANALYSIS IN ADHD.**

***Erbil N.***

EEG is defined as the summation of postsynaptic activation of synchronously firing neurons and accepted as a direct measure of neuronal activity. Neuronal oscillations are representations of spontaneous, continuous activity of central nervous system (CNS) and are different from autonomous, continuous typical pacemaker rhythms. Because its frequency is related to membrane potential and interaction among neuronal networks alters intrinsic properties of neurons such that fast rhythmic bursting cortical neurons may behave as fast-spiking neurons as a result of thalamic interactions. Resting state EEG records represents spontaneous activity and changes in response to stimuli. During resting state acquisitions, subjects are asked to stay eyes close/open and not to focus on any thoughts, i.e. wander Random Episodic Spontaneous Thoughts. It was estimated that 60-80% of the energy is consumed during the resting state activity of the CNS. The additional energy burden related to tasks was expected to be as little as 0.5-1%. It can be seen that the resting state does not mean inactive state, in fact it is the dynamic substrate of the present, momentary state of the brain, and determines the fate of incoming information. By examining ongoing activity on the basis of dynamical changes and network structures which is called as quantitative EEG analysis, it is possible to get more comprehensive information about the activity of CNS and the shifts from resting state to response and also understanding changes related to different diseases and/or disorders. In recent years, on the basis of the results of quantitative EEG analysis, it was shown that the increases in theta band activity

and in theta/beta power (+@/+!) ratio are two of the most reliable EEG findings in ADHD to date. The increase in theta band activity is concluded as the signatures of underarousal and maturational delay. It was also shown that children with ADHD having higher theta band activity power are more likely to show a positive response to medication. Results related to +@/+! ratio indicated that it was related to faster reaction times and increased omission errors and concluded by increased impulsivity, i.e. an increase in the speed with a decrease in the performance. As a result, examination of resting state rhythmical activity of CNS provides tools for getting more comprehensive information about CNS activity and finding signatures to identify different diseases/disorders. In the case ADHD, in addition to defining disorder-specific frequency bands, it is important to define topographical and dynamical shifts/changes during resting state.

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Psychiatry and Clinical Psychopharmacology. 2018;28:345.

**QUANTITATIVE EEG FINDINGS IN THE PSYCHOPHARMACOLOGICAL TREATMENT OF ADHD: STUDY PROTOCOL.**

***Cultura SEC.***

EEG provides information about the electrical activity of the brain. The scalp-recorded signal provides a diffuse picture of that underlying activity and that record can provide valuable information on the brain, with high temporal but poor spatial resolution. Recently, a number of studies have examined qEEG differences in children, adolescents, and adults with and without ADHD and a number of researchers have investigated the utility of EEG measures as a biomarker for ADHD. Briefly, a biomarker is an objectively measured index of pharmacological response or biological process that is quantifiable, precise, and reproducible. This biomarker may be used to diagnose or stage a disease process or predict a clinical response to treatment. Preliminary findings of our recently completed research, which was conducted collaboratively at Hacettepe University Child and Adolescent Psychiatry and Biophysics Departments, entitled Quantitative EEG findings in the psychopharmacological treatment of ADHD: Possible markers and the relations between these markers and motor competence, cognitive skills and treatment response will be presented along with a literature review within the scope of variables related to psychopharmacological treatment of ADHD. Our research protocol for review is outlined below: Eighty right-handed, psychotropic medication na+»ve, 6-10 years old children with a total IQ score of 75 or more on Wechsler Intelligence Scale for Children IV (WISC-IV), diagnosed with ADHD according to DSM-5 criteria without comorbid clinical learning disorders, conduct disorder, developmental coordination disorder, tic disorders, autism spectrum disorder, psychotic or affective disorders, anxiety disorders, obsessive-compulsive disorder, head trauma and chronic neurological disorders were enrolled. The control group consisted of 20 right-handed, psychotropic medication na+»ve, 6-10 years old children with a total IQ score of 75 and above on WISC-IV, who had no psychiatric disorders and neurological or long-term chronic diseases, and no history of head trauma, who were admitted to the General Paediatrics outpatient clinic of Hacettepe University Department of Pediatrics. All the children and their families gave informed consent to participate in the study. The study group was assessed immediately before the onset of psychopharmacological treatment and the control group after the acute complaints had been rectified and their physical health had been achieved. They were evaluated with a semi-structured diagnostic interview and different scales filled by the parents. Additionally, Bruininks-Oseretsky Test of Motor Proficiency (BOT) was administered and eyes open and closed resting state Electroencephalography (EEG) recordings were taken. Children in the study group were put on methylphenidate/atomoxetine treatment and the treatment response was evaluated along with all the other clinical and parent reported scales and eyes open and closed resting state EEG recordings were repeated in the 8-12th weeks of treatment. Patients who did not meet the widely accepted dosing and treatment algorithm of methylphenidate or atomoxetine (AACAP 2007), who did not have treatment compliance, and who did not tolerate treatment due to side effects, switching to/augmented with another psychopharmacological agent were excluded from the study. As a result, approximately 63 patients completed the study.

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Psychiatry and Clinical Psychopharmacology. 2018;28:182-83.

**SIDE EFFECT OF METHYLPHENIDATE IN CHILDREN WITH WILLIAMS SYNDROME: SYSTEMIC HYPERTENSION.**

**Eynalli E, Ray PC, Tahiroglu AY, et al.**

Williams syndrome (WS) caused by deletion at the chromosome 7q11.23 is a complex genetic condition characterized by cardiovascular disorders, mental retardation, friendly personality, dysmorphic face, and body features. The most common psychiatric disorders found in WS are attention-deficit/hyperactivity disorder (ADHD), specific phobia, and generalized anxiety disorder. Approximately 64% of individuals with WS meet criteria for ADHD and there have been studies on effectiveness of stimulants in WS. It has been reported that methylphenidate (MPH) is the first choice for ADHD treatment in WS, and common side effects are appetite reduction irritability, sleep problems, and headache. Increasing heart rate and high blood pressure have been reported during MPH treatment but not seen commonly. In this report, we presented a 6-year-old girl with WS who experienced high blood pressure after taking the long-acting MPH. Case presentation: A 6-year-old girl was referred to our outpatient clinic with complaints of hyperactivity, learning difficulties, muscle weakness and inattention. According to her family, he had developmental delay. She has been using 5 mg/d aripiprazole for behavioural problems and also 300 mg/d valproic acid for epilepsy. Aripiprazole treatment was stopped because she did not see any benefit. She was referred to genetic outpatient clinic because of her dysmorphic appearance and developmental delay and she was diagnosed with WS. According to her psychiatric assessment, she was diagnosed with ADHD and mental retardation-mild type. After the evaluation of paediatric nephrology and paediatric cardiology clinics 10 mg/d long-acting MPH was started. After 3 hours from the first dose, systolic blood pressure increased to 200 mm/Hg and diastolic blood pressure increased to 100 mm/Hg. Then, she was monitored in the intensive care unit and discharged after she recovered. ADHD are often seen in individuals with WS. It has been observed that MPH is often well tolerated in individuals with WS. But in our case, after the first dose of 10 mg long-acting MPH, intensive care was required for a life-threatening high blood pressure. Improvement of symptoms after termination of drug effect supports drug-related side effect in this case. The mechanisms explaining the relationship between psychostimulants and raised blood pressure is incompletely understood. Similarly, the etiopathogenesis underlying the WS vasculopathy is not yet understood. Further study is needed for enlightening this adverse effect. When physicians prescribe psychostimulants in children with WS, regular electrocardiography and blood pressure monitoring is important because psychostimulants may raise heart rate and blood pressure

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**SUICIDE ATTEMPT AFTER ATOMOXETINE USE IN A PATIENT WITH AUTISM.**

**Dogan O, Ozcan O.**

Studies which examine the frequency of ASD and ADHD comorbidity have found ADHD comorbidity in 28-83% of ASDs. In the ASD group, ATX has been reported to have moderate effects in decreasing ADHD symptoms, decrease irritability, stereotype, and social withdrawal; it has also been reported to have tolerable side effects, cause more progress in the longterm use, and have decreased adverse effects in time. Risk of suicidality with ATX has been reported in Europe since 2004 and in America since 2005. There is a warning label of suicide risk in the U.S.A. for Strattera. In the literature, studies conducted with suicidal risk and selfharm in typically developing, it has been associated with increases in suicidal risk, and comorbid situations such as depression and antisocial behaviour. In individuals with neurodevelopmental disorder, ADHD is more frequent when compared with typically developing. Although there is a wide literature on the efficacy of ATX on typically developing children and adolescents, there are few studies on individuals with neurodevelopmental disorder. Case presentation: A 12-year-old male patient had been followed since he was 2 years old with a diagnosis of autism and diagnosis of ADHD for 6 years old. For his irritability, treatment was initiated with risperidone and haloperidol. Since these drugs caused increases in cholesterol and triglyceride, the drugs were discontinued. Later, olanzapine 5 mg was used in case of need; however, due to elevated liver enzymes in liver function tests, it was discontinued. When the patient was referred again with complaints of taking off clothes, banging doors, and extreme irritability, he was started aripiprazole 5 mg/g; due to the continuation of irritability and burst of anger in follow-ups, aripiprazole dose was increased to 10 mg/g gradually, risperidone 1.5 mg/g was added, atomoxetine 50 mg/g was added for the ADHD

treatment. In this period, the parents were divorced and the patient's mother moved. During this period, there was an increase in bursts of anger, self-destructive behaviours, attempts for self-destruction with a knife, and upon his attempt to throw himself out from the window. He was treated in the paediatric psychiatry service. Strattera was cut down on and completely discontinued; in follow-ups decrease was observed in his self-destructive behaviours; however, his bursts of anger were continuing. In the follow-ups, a partial decrease in bursts of rage continued and no self-destructive behaviour was observed. As far as we know, this case is the only autism case reported in the literature that started to have suicidal and self-destructive behaviours after atomoxetine. The patient's self-destructive behaviours and suicidal thoughts started after Strattera and decreased after the drug was stopped; however, this situation can also be associated with the presence of domestic stressor, depression which may have developed with stress in the autistic patient caused by changes in routines due to moving or previous comorbid behaviour problems of the patient. We think that the close follow-up of selfmutilative and suicidal considerations in ASD patients with atomoxetine use as authors and the work to be done in this regard will have beneficial results

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Psychiatry and Clinical Psychopharmacology. 2018;28:377.

**ADULT ATTENTION-DEFICIENT/HYPERACTIVITY DISORDER AND CLASSICAL CYST APPLICATIONS.**

**Ogus, G.**

ADHD is a problem diagnosed in childhood and continues in adulthood. In follow-up studies, 80% of children with ADHD have been shown to be adolescent and 50-70% continue in adulthood. Adult ADHD in our country has become more and more recognized in recent years, and ADHD findings were seen in childhood with a majority of patients diagnosed with Anxiety Disorder, SAB, or BAB in these developments. Despite the use of medication in the treatment of ADHD, especially during childhood, medication is used in some special cases (academic exams or family crises) in adults and these medicines are not paid for in adults over 25 years of age. Cognitive Behavioural Therapy (CBT) is the most commonly applied treatment for children and adolescents besides taking medication. Children with this diagnosis met with better results when they were receiving skills training with the CBT as well as drug therapy. In adults, academic performance and self-esteem are negatively influenced by reasons such as not being able to finish work and dependency tendencies. Due to the fact that executive functions are impaired, these patients are negatively affected by their care and organizational and planning skills, and their work and family lives are negatively affected. For this reason, the panel will focus on the importance of using ADHD and individual BDT and the techniques used. BDT treatment protocol steps: (1) Psychoeducation: Disease and CBT education (2) Identification of problem areas: Problems such as not focusing attention, deferring, being unable to organize, taking responsibility, impulse control problems are common. (3) Skill development; Organization and planning skills, attention training, problem-solving skills development, the ability to control the prosperity is studied. (4) Cognitive configuration: It allows patients to develop new ability to cope and to create new experiences in life-threatening areas that are difficult to manage up to now. With these new experiences, it can be ensured that the belief system is rearranged, the impulse control, the longer thinking action and the motor action are performed properly. (5) Working with Secondary Psychiatric Problems: Negative events and criticism since childhood hurt self-confidence and often confront comorbid diagnoses such as depression and SAB. In recent years, studies on ADHD and CBT have increased. The Drug + CBT group was more effective in the single-blind study conducted by Safren et al. Significant improvements were observed in the symptoms of the patients in the 10 CBT patients, 10 in the cognitive training, and 10 in the pilot study (Virta et al. 2010). Another study in which Dialectical Behavioural Therapy (DBT) was reconstructed for ADHD based on the prediction that ADHD is a self-monitoring problem showed improvement in ADHD symptoms and depressive symptoms compared with patients on the waiting list (Hesslinger et al., 2002). The most important shortcoming of these studies is the inadequacy of the number of patients and there is a need for studies with a larger number of patients.

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Psychiatry and Clinical Psychopharmacology. 2018;28:87.

#### **THE RELATIONSHIP OF PLATELET ACTIVATION MARKERS WITH OBSESSIVE-COMPULSIVE SYMPTOMS IN ADOLESCENTS WITH ADHD.**

**Metin O, Ray PC, Kaypakli GY, et al.**

**Objective:** Structural and functional imaging findings have shown common abnormalities in ADHD and OCD. However, neurochemically they are varied, in particular, the involvement of dopamine (ADHD) and serotonin (OCD) systems. Platelets have been widely used as a peripheral model of the serotonergic system. Mean platelet volume (MPV) can be accepted as the marker of the platelet activation, and is also involved in the inflammatory processes. Limited studies have focused on MPV in ADHD, and results are controversial. In the present study, we aimed to assess the relationship between the PLT, MPV, and PDW as platelet activation markers and obsessive-compulsive symptoms (OCS) in ADHD.

**Methods:** The retrospective study included 147 stimulant-free adolescents aged 12-17 years who had been diagnosed with ADHD in the period between 2015 and 2017. Exclusion criteria included the presence of the OCD, psychotic disorder, substance abuse/dependence, and coagulation disorders. OCS was assessed by Maudsley-Obsessive-Compulsive Inventory (MOCI). Platelet count (PLT), MPV, and PDW values were obtained from CBC results that were concurrent with psychiatric measurement filling date.

**Results:** The study included a total of 147 adolescents aged 12-17 years (68 females (46.3%) and 79 males (53.7%)). Of these subjects, 81 (55.1%) were ADHD-C, 66 (44.9%) were ADHD-I. There were no significant differences in PLT, MPV, and PDW values between the ADHD subtypes ( $p > 0.05$ ). Control, cleanliness, doubt, and total scores of MOCI negatively correlated with MPV, and PDW values in all patients ( $p < 0.05$ ). In ADHD-I group, control, cleanliness, and total scores of MOCI negatively correlated with MPV. In ADHD-C group, only control subscale scores negatively correlated with MPV and PDW. In ADHD-I group, PDW values negatively correlated with the control, cleanliness, doubt, and total scores of MOCI.

**Conclusions:** The findings of the present study indicated that increasing OCS severity was related to decreasing MPV and PDW levels in adolescents with ADHD. Our findings might reflect that the decreasing platelet activation can be related to abnormal platelet functions rather than platelet counts. Indirectly, increased MPV values accepted as the predictor for inflammatory process. Although there is preliminary evidence for elevated markers of inflammation in children with neuropsychiatric disorders, the data are inconsistent. Our findings supported this inconsistency with the findings showed negative correlation OCS severity and platelet activation. It could reflect the decreased platelet activity, and serotonergic dysfunctions may be the shared pathophysiological mechanism for OCS. There are a few studies that have focused on MPV in ADHD populations. Firstly, increased levels of MPV in ADHD were reported. Another study has failed significant differences in MPV values between ASD, ADHD and the control groups. We found that control, cleanliness, and doubt scores negatively correlated with MPV and PDW. Rumination and slowness scores were unrelated to platelet markers. Different neurotransmitters may contribute to these OCS clusters. To the best of our knowledge, this is the first study which examined the platelet activation markers and OCS in patients with ADHD. Controlled studies are needed to evaluate platelet activation markers between the ADHD and OCD

Psychiatry and Clinical Psychopharmacology. 2018;28:31.

#### **EMOTIONAL INTELLIGENCE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Kaypakli GY, Metin O, Ray PC, et al.**

**Objective:** Emotional intelligence (EI) comprises emotional and social competencies, skills, and behaviours that determine how effectively we understand and express ourselves, understand others and relate with them, and cope with daily demands, problems, and pressure. In this study, we aimed to examine the socio-demographic and clinical characteristics related to EI in adolescents with attention-deficit/hyperactivity disorder (ADHD).

**Methods:** The prospective study included 150 adolescents aged 12-18 years who were diagnosed with ADHD. Study sample consisted of sixty-nine (46%) girls and eighty-one (54%) boys. The sociodemographic data form, K-SADS, Conners' Parent Rating Scale, DSM-IV-Based Screening and Rating Scale for Disruptive Behaviour Disorders, and Emotional Quotient (EQ) were used.

**Results:** Of all patients, 41.3% (n = 62) were ADHD-I, 58.7% (n = 88) were ADHD-C according to DSM-5 criteria. Gender and ADHD type were not related to total EI scores. ADHD-C type (27.8 -1 7.2 & 31.3 -1 7.2) and female patients (27.7 -1 6.8 & 30.6 -1 7.6) have lower mean EI-stress management score than others (p < 0.05). EI scores were higher in patients who exercise regularly and those who did not consume food additives. The difficulty in making friendships was related lower EI scores. EI and academic achievement were positively correlated (p < 0.05). There was a negative correlation between total EI scores and the symptom severity of ODD, CD, and social problems (p < 0.05). Patients whose parents reported spending special time with their child were found to have higher EI scores (107.9 -1 15.2 and 103.7 -1 17.7), but it was not statistically significant.

**Conclusions:** Limited studies evaluated the EI in ADHD population. Individuals with ADHD in a sample of primary school children were found to have a lower overall EI score and sub-test scores than non-ADHD subjects. Low EI has been shown to indicate increased ADHD symptom severity in a population of university students. Our findings showed that high EI scores in patients with ADHD were thought to be associated with lower symptom severity, better attention, less learning problem, better academic achievement, and better social relationships. The conceptualization of EI as a group of learnable talent suggests that EI education may have a therapeutic value. In this context, the results we have obtained suggest that EI education may be useful in adolescents with ADHD

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#### **CLINICAL PRESENTATION, PSYCHIATRIC COMORBIDITY, AND TREATMENT CHARACTERISTICS OF ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Erdogan E, Delibas DH.**

**Objective:** The aim of this study was to evaluate the clinical features, comorbidity, and treatment characteristics of adults with attention-deficit/ hyperactivity disorder (ADHD) in psychiatry outpatient clinic.

**Methods:** Adults diagnosed with ADHD between 2015 and 2017 were included in the study. Clinical interview based on DSM-IV was performed. Socio-demographic data form, Wender Utah Rating Scale, Adult ADD/ADHD DSM-IV Based Diagnostic Screening and Rating Scale, Adult ADHD Self-Report Scale (ASRS) and Personal and Social Performance Scale (PSP) were filled out. The detailed laboratory parameters were evaluated during the study.

**Results:** Ninety-one cases were included in the study. The mean age of the patients was 28.5 -1 10.4. A total of 50 patients were female (54.9%) and mean duration of education was 13,05 -1 2,19. Mean duration of ADHD treatment was 22.8 -1 24.46 months. ADHD was diagnosed in 7.7% of the cases before 12 years, 14,3% between 12 and 18 years and 71% after 18 years of age. When the ADHD subtypes were evaluated, 51.6% (n = 47) showed combined type, 42.9% (n = 39) showed attention deficit, and 5.5% (n = 5) showed hyperactive/ impulsive subtype. The rate of family history of ADHD was 50.5% (n = 46). The compliance rate of treatment in the first year was 85.7%; 20.9% (n = 19) of cases attempted suicide. The rate of medical illness was 28.6% (n = 26); 17.6% (n = 16) of the cases had drug side effects. The most frequent side effects were insomnia with 4.4% and anorexia with 2.2%. D vitamin level was low (mean = 19.42 -1 9.25%). In 44.8% of cases, the level of ferritin was low (mean: = 39.55 -1 41.2). Hyperlipidaemia was present in 32.6% of the sample. The first mean ASRS score was 49.08 -1 9.53, while the last mean ASRS score was 21.32 -1 8.38. The first mean PSP score was 60.6 -1 9.59, the last mean PSP score was 83.53 -1 6.92. 81.3% (n = 74) of the cases had comorbid diagnosis. Depression was the most common comorbidity with rate of 33% (n = 30). The most commonly used psychostimulant was methylphenidate, with an average dose of 26.18 -1 6.03 mg / day; 15.4% of the cases were using dual psychostimulants. When treatment response were evaluated, there was a significant difference between ADHD subtypes (p = 0.045). When the group with psychiatric comorbidity was compared with those who did not have comorbidity, severity of illness was higher and level of functioning was lower (p = 0.041).

**Conclusions:** ADHD is a neurodevelopmental disorder that can persist throughout life. ADHD is a risk factor for other psychiatric comorbidities if it continues in adulthood. In our study, the treatment response of the combined subtype emerged later, indicating that the use of psychotropic drug was higher in this group. ADHD comorbidity alters the appearance of other clinical conditions, increasing the negative effects of both diseases on severity and functioning. Systematic evaluation of cases and comorbidities in clinical practice will help to understand and manage the prognostic determinants of adult ADHD

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Psychiatry and Clinical Psychopharmacology. 2018;28:113.

**THE RELATIONSHIP BETWEEN PLATELET ACTIVATION MARKERS AND ANXIETY SYMPTOMS IN ADHD.**

**Metin O, Ray PC, Shamkhalova U, et al.**

**Objective:** Limited studies have focused on MPV in ADHD, and results are controversial. In the present study, we aimed to assess the relationship between the PLT, MPV, and PDW as platelet activation markers and anxiety symptoms in adolescents with ADHD.

**Methods:** The retrospective study included 138 stimulant-free adolescents aged 12-17 years who had diagnosed with ADHD in the period between 2015 and 2017. Exclusion criteria included the presence of the anxiety disorders, OCD, tic disorders, psychotic disorder, substance abuse/dependence, and coagulation disorders. Anxiety was assessed by STAI-2 (trait anxiety). Conners Parent Rating Scale and Stroop Test (card four and five scores) were used. Platelet count (PLT), MPV and PDW values were obtained from CBC results that were contemporaneous with psychiatric measurement filling date.

**Results:** The study included a total of 138 adolescents aged 12-17 years (62 females (44.9%) and 76 males (55.1%)). Of these subjects, 77 (55.8%) were ADHD-C, 61 (44.2%) were ADHD-I. There were no significant differences in mean PLT, MPV, and PDW values between the ADHD subtypes and genders. Total ADHD and STAI-II scores did not correlate with any platelet markers. DSM-IV-inattention subscale scores were negatively correlated with MPV values ( $r = -0.198$ ,  $p = 0.02$ ). In ADHD-C group, CPRS-anxiety subscale scores were positively correlated with PLT ( $r = 0.232$ ,  $p = 0.04$ ). STAI-II scores were negatively correlated with MPV values for the only ADHD-C group ( $r = -0.297$ ,  $p = 0.04$ ). PLT and Stroop-IV completing time were positively correlated in both for whole sample and ADHD-I group ( $p < 0.05$ ). In ADHD-C group, MPV levels were positively correlated with correction scores in Stroop-IV, and completion time on Stroop-V ( $< .05$ ) PDW levels were positively correlated with the correction scores on Stroop-IV in ADHD-C group ( $r = 0.327$ ,  $p = 0.004$ ).

**Conclusions:** Current literature on platelet markers and psychiatric disorders mainly focused on anxiety disorder, in particular panic. In these studies, the levels of platelet markers were assessed relative to healthy controls, but the relationship with symptomatology was not examined. Investigation of this relationship in ADHD groups has been moved a step further. The findings of the present study indicate that elevated MPV is related to increased inattention symptoms in all sample, and anxiety symptoms for males with ADHD-C. In the point of anxiety, STAI-II and anxiety subscale of CPRS can be conceptualized as different measurements from each other. Eventually, it is understandable that MPV was related to STAI-II total score, but PLT was related to CPRS-anxiety score. PLT might be involved in ADHD-related anxiety; on the other hand, MPV might seem to be related to trait anxiety. Both of MPV and PDW values were related the correction scores on ST-IV might be interpreted as the possible distractor effect of increased levels of these markers. Elevated MPV level was related to increased completion time on ST-V, which may suggest the possible interaction between the MPV and reaction time when distractor-related conditions occur. However, this last two findings have not been replicated for ADHD-I group. Next studies should be aimed to examine the possible relationship of different anxiety domains and platelet markers in ADHD patients

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**CASE REPORT: EFFECTS OF OSMOTIC-RELEASE ORAL SYSTEM AND MODIFIED-RELEASE METHYLPHENIDATE AGENTS ON ENURESIS AND ENCOPRESIS IN A CHILD WITH ADHD.**

**Sarigedik E, Cetin NY.**

Enuresis and encopresis can be comorbid to Attention-deficit/hyperactivity disorder (ADHD) with a percentage as high as 17-19.1% and 8-9.0% respectively. Drugs which contain methylphenidate and atomoxetine are reported to be effective in treating comorbid enuresis and encopresis. A case of a 6 years 10 months old boy is presented in this paper, who was diagnosed with ADHD, enuresis and encopresis all at once and experienced a decline of frequency in enuresis and encopresis episodes during modified-release methylphenidate treatment, and when switched to osmotic-release oral system methylphenidate the frequency of enuresis and encopresis increased again, and when the treatment was switched back to modified-release methylphenidate treatment, frequency of enuresis and encopresis is decreased back and ultimately disappeared. Case presentation: No organic pathology was identified during paediatric assessment of the child and his psychomotor development was found to be normal according to his age. Modified-release methylphenidate treatment was used to treat ADHD and behavioural approach was used to treat enuresis and encopresis. After medical treatment was started, there was a significant decline in the frequency of enuresis and encopresis episodes, but due to limited improvement in ADHD symptoms the treatment was switched to osmotic-release oral system methylphenidate. There was a notable increase in the frequency of enuresis and encopresis episodes. And after the treatment was switched back to modified-release methylphenidate, the enuresis and encopresis frequency decreased again and eventually disappeared. No similar case was found to be reported in the literature. Yet there are studies which states that cases whose encopresis cannot be reduced with immediate-release methylphenidate can benefit, even be cured with osmotic-release oral system methylphenidate. In conclusion, it should be noted that treatment response to different acting methylphenidate agents can differ between individuals

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**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND WORK .**

**Semerci B.**

One of the areas in which people with ADHD are affected is work. Workplace is a social construct other than performance and includes many relationships. Because of low performance and losing jobs of people with ADHD, they might be a big burden to the economy [4]. In a study of World Health Organization, which has been conducted in 10 countries, it was shown that 3.5% of workers have ADHD and they caused decreased workforce due to they not showing up for work and low performance [3]. The percentage of leaving school, frequently changing jobs and being unhappy in their work life is higher in people with ADHD when compared to others. Problems of people with ADHD start when applying for a job. Due to their attention deficits, they have problems filling out their forms and cooperation problems with the interviewers. The problems continue in job interviews. If the workplace is not suitable for them such as a creative job or a job with mobility, problems increase. Usually, changing jobs often without thinking through, incomplete projects due to time management issues or skipped meetings, lost paperwork due to organizational issues, cause the person's capacity to work efficiently to decrease. Also, the conflicts with the other employees due to being easily triggered cause problems for the workplace [1]. Symptoms, such as not being able to manage time, being distracted easily, not being able to listen through meetings caused by not being able to stay still, being late, not being able to get organized and regulate feelings, interfering people's words before they finish what they have to say shows these are not character but ADHD. Because they cannot control this situation, people with ADHD have to work harder and spend more time than others. Their bright ideas and creativity could be pushed aside due to their time management issues, being easily distracted or organizational difficulties. When anger and not being able to postpone desires add to all of this, problems grow bigger. Also, substance abuse, anxiety, depression, low self-esteem added to ADHD might make the process even harder [4]. The diagnosis and treatment of ADHD during childhood will recover functionality. The continuity of treatment in adulthood, use of medication, psychological and work support is important [2]. Before solving the problem, it should be assessed if the person's job is appropriate. The chosen job should be where passions can be addressed and the qualities which are problems can be controlled. People with ADHD can work very hard,

especially when motivated. Because of this, the employer and the employee should use positive aspects of ADHD when choosing and delegating jobs to prevent burnout [1]. Besides these fundamental symptoms, forgetting, time management issues, postponing, getting bored quickly, relationships with people should also be managed. Taking notes to control, keeping records, setting alarms for time, setting alarms to remind meetings, taking small breaks between jobs, making daily plans, and trying to stay on it, dividing jobs which are long and hard to track to pieces, getting help for the organization of the paperwork and making systems get the jobs easier. Setting deadlines on jobs or getting help from a person who is good at time management might solve postponing issues. If relationships with people cannot be managed, not only working alone can help but trying to learn to assess people's feelings and behaviours might also help to work together [5]. ADHD might cause problems in the workplace. But, if the solutions are searched with both employer and employee, it would help an employee to be gained who can manage very efficient and creative work.

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Psychiatry and Clinical Psychopharmacology. 2018;28:17.

**THE RELATIONSHIP OF SUICIDE IDEATION WITH EMOTIONAL REGULATION AND EXECUTIVE FUNCTIONS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Ugur O, Ozcan O.**

**Objective:** It has been reported that attention deficit, hyperactivity, and impulsivity in attention-deficit/hyperactivity disorder (ADHD) may lead to more frequent suicidal ideation and/or attempts. However, research on cases of ADHD with suicidal ideation and/or attempts is limited in children. We aimed to examine the relationship between the executive function deficits and emotional regulation difficulties of ADHD and suicidal ideation in children.

**Methods:** This study was performed between January and June of 2017 with patients between the ages of 8 and 12 years with diagnoses of ADHD presented to the outpatient clinics of the Child and Adolescent Psychiatry Department at the Turgut Ozal Medical Center at Inonu University. All participants met DSM-5 diagnostic criteria for ADHD according to clinical psychiatric and psychometric examinations. The K-SADS-PL questionnaire was used to determine suicidal ideation. Parents were assessed using behavioural-rating inventory of executive function (BRIEF) scale and emotion regulation checklist (ERC), while children were evaluated using the children depression inventory (CDI) and screen for child anxiety and related emotional disorders (SCARED) scale. Thirtyeight cases (ADHD + SI) describing suicidal ideation and 41 cases (ADHD) with no suicidal ideation were included in the study. Thirty-three healthy individuals were selected for the control group at similar ages. IBM SPSS Statistics 22.0 was used for statistical analysis of the data.

**Results:** Significant differences were found between the ADHD + SI, ADHD and the control group in terms of maternal and paternal psychiatric disorder, maternal suicidal behaviour, paternal drug use, and home violence. According to the DSM-5 ADHD severity rating, moderate and severe ADHD scores were significantly higher in the ADHD + SI group. Additionally, comorbid depressive disorder and conduct disorder were significantly more frequent in the ADHD + SI group. Significantly higher scores were also obtained in the ADHD + SI group in the subscale inhibit, emotion control, monitor, behavioural regulation index, and total scores, and the ERC lability\negativity subscale scores. Finally, significantly higher scores were obtained in the CDI and SCARED general anxiety, separation anxiety, and total test scores in the ADHD + SI group.

**Conclusions:** Executive function deficits associated with ADHD and difficulties in regulating emotions may lead to suicidal ideation. It is possible for suicidal thinking to proceed to suicide attempts and/or completed suicide. Recognition and treatment of executive functioning problems and difficulties in emotional management in children with ADHD may prevent the development of possible suicidal behaviour. Our results suggest the need for further and larger scale research to be conducted to better understand the relationship between ADHD and suicidal ideation

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Psychiatry and Clinical Psychopharmacology. 2018;28:52.

**ASSESSMENT OF SMOKELESS TOBACCO (MARAS POWDER) USE AND ITS RELATION TO THE EMOTIONAL BEHAVIOURAL PROBLEMS IN CHILDREN AND ADOLESCENTS WITH ATTENTIONDEFICIT/ HYPERACTIVITY DISORDER.**

**Altun H.**

**Objective:** Maras powder, a kind of smokeless tobacco, is commonly used in the South and Southeastern regions of Turkey, especially around Kahramanmaras and Gaziantep cities. In Kahramanmaras city, 16.8% of total population (25.1% males and 1.4% females) and 9.4% of the individuals with chronic diseases (16.0% males and 1.1% females) consume Maras powder. There are only a few studies investigating the association between smokeless tobacco use and psychiatric disorders. Only one study reported that the symptoms of adult attention-deficit/ hyperactivity disorder (ADHD) were higher in Maras powder and smoking users. However, to our knowledge, no studies have been conducted regarding Maras powder use in children and adolescent with ADHD. The aim of this study was to determine the use of Maras powder among children and adolescents with ADHD and healthy controls and its relationship to the emotional behavioural problems.

**Methods:** The study group consisted of 40 adolescent with ADHD aged 12-17 years according to DSM-5 and 40 healthy children as controls. A socio-demographic form, questionnaire form evaluating the frequency of use of Maras powder, its cause of use and the level of knowledge about Maras powder, Disruptive Behaviour Disorders Symptom Screening Scale and the Strengths and Difficulties Questionnaire (SDQ) were administered to the participants.

**Results:** There were no statistically significant differences between the two groups in terms of age and gender ( $p > 0.05$ ). The rates of Maras powder use in the patient group were higher than those in the control group. The rates of cigarette use in the patient group were also higher than those in the control group; 16 years and above males were found to use Maras powder at a higher rate in both groups. It was determined that compared to healthy controls, the emotional symptoms, conduct problem, hyperactivity scale, peer problem, and total difficulties scores were statistically significantly higher and prosocial scale scores were lower in children and adolescents with ADHD ( $p < 0.05$ ). Also the conduct problem and hyperactivity subscale scores of SDQ were statistically significantly higher and prosocial scale scores were lower in Maras powder use group.

**Results:** The results of this study showed that Maras powder use in ADHD group was higher than those in the controls and that the children and adolescents with the use of Maras powder had higher level of the conduct problem and hyperactivity subscale scores of SDQ and less prosocial subscale scores. Unfortunately, the sale of Maras powder in our region is not supervised. Easy access to Maras powder is a risk for all adolescents, especially those with ADHD, in terms of substance use. Especially children with ADHD and their families should be informed about the use of Maras powder and its risks and damages. Further investigations are needed with a large sample size on Maras powder usage in ADHD

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Psychiatry and Clinical Psychopharmacology. 2018;28:178-79.

**EXTENDED RELEASE METHYLPHENIDATE TREATMENT OF PRIMER ENURESIS NOCTURNA IN AN ADOLESCENT WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.**

**Sivri R.**

Enuresis is defined as the failure of urethral sphincter control involuntary. The term primary enuresis is used to describe those individuals who have never achieved continence [1]. The prevalence of enuresis is %15-20 in the child population but it is a self limited disorder with a substantial rate of spontaneous remission. Enuresis nocturna (EN) can cause loss of selfesteem and other psychological disorder and as the age progresses, the problem becomes more stressful. Attention Deficit Hyperactivity Disorder (ADHD) is a common heterogenous condition that impairs academic, social, and family function. An epidemiologic study shows that the most common comorbidity of ADHD is enuresis [2]. Children with ADHD had a 2.7 times higher incidence of enuresis than general population. ADHD and enuresis comorbidity studies show that ethiopathogenesis is associated with generalized developmental delay in maturation [3]. We report a case after initiating a treatment of extended release methylphenidate (ER-MPH) for ADHD that cessation of enuresis which wasn't reported in the first visit by the 17-year-old adolescent boy. Case presentation: C. was a 17 year-old male adolescent who was brought to our outpatient clinic by his parents due to carelessness, forgetfulness, unable to concentrate and work for exams. He was hyperactive since his primary school ages,

and he showed a significant decline in academic performance, especially in recent years. As a result of clinical evaluation and the information obtained from family, he was diagnosed with ADHD combined subtype according to the criteria of the DSM-5 (American Psychiatric Association 2013). No additional psychiatric illness was detected. He was started on ER-MPH (Medikinet Retard -«) and the dosage was adjusted to 20 mg/day. At 1-month follow up, his carelessness and forgetfulness symptoms were decreased and he had experienced significant improvement in academic performance. There was not any side effects. He also reported that he did not talk about the problem of urinary incontinence in the first visit despite being asked. He has never achieved continence before. He has always avoided certain social situations, like overnight camps and slumber parties. He reported that enuresis ceased rapidly during the first week of treatment and no more seen again for a month. In conclusion, this report suggest that clinician should be aware that the ER-MPH can cease enuresis in an adolescent. The precise mechanism of how ER-MPH stops enuresis remains to be elucidated. A high sleep arousal threshold was one of the hypothesis of enuresis nocturna. Stimulants decreasing sleep arousal threshold that results have their effects on enuresis. ER-MPH treatment can be alteratively used enuresis, especially in the presence of ADHD. And also clinicians should be aware under reported enuresis problems assessing adolescent for reasons such as stigmatization

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Psychiatry and Clinical Psychopharmacology. 2018;28:236-37.

**THE EFFICACY OF METHYLPHENIDATE TREATMENT IN AN ADOLESCENT PATIENT WITH ESSENTIAL TREMOR.**

**Uzun N, Ahmet BE.**

Essential tremor is a syndrome which characterized by postural or kinetic tremor, usually affecting the hands and forearms. The underlying cause of essential tremor is unknown. Epidemiological studies indicate that up to 5% of the adults have essential tremor, and 5- 30% of adults with essential tremor report tremor onset during childhood. However, no prospective studies targeted specifically to children about essential tremor. Some factors such as emotional stress, fatigue, hunger, caffeinated drinks, and smoking cigarettes can be worsening the severity of essential tremor. Also, some drugs such as lithium, antidepressants, antipsychotics, and methylphenidate can exacerbate tremor. Propranolol and primidone usually can be beneficial in the treatment of essential tremor. Case presentation: A 17-year-old boy consulted neurology clinic with complaints of hand tremor. In neurological examination, no pathology was obtained except tremor in both hands. Magnetic resonance imaging (MRI) was performed to the patient and MRI revealed no pathology. There was no problem in biochemical and hormone tests. The patient was diagnosed essential tremor and propranolol 60 mg/day was started. After one month, at the second visit propranolol was elevated to 120 mg/day because of continuation of the essential tremor. Meanwhile, the patient who had been followed up and treated with attention-deficit/hyperactivity disorder (ADHD) diagnosis in the last year, consulted again to the child and adolescent psychiatry clinic for ADHD treatment. Methylphenidate 27 mg/day treatment for ADHD treatment was initiated who has been used before for the treatment of ADHD. Essential tremor completely disappeared after one week after the patient started treatment with methylphenidate 27 mg/day. At this time, the patient stopped the treatment of propranolol by himself and essential tremor symptoms never recurred over 2 months of follow-up. Propranolol is frequently used in the treatment of essential tremor. Patients who do not benefit from treatment with propranolol may benefit from agents such as benzodiazepines, botulinum toxin, and gabapentin. However, antidepressants, antipsychotics, and stimulants used in psychiatric disorders often increase the severity of essential tremor. A recent study suggested that striatal dopamine transporter abnormalities can be seen in the patients with essential tremor. Our case has shown that methylphenidate may be useful in essential tremor treatment differently from the current literature. This may be related to striatal dopamine transporter abnormalities that occur in essential tremor cases. Future studies investigating the stimulants and essential tremor will improve our knowledge of this topic

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Psychiatry and Clinical Psychopharmacology. 2018;28:209-10.

**MYDRIASIS ASSOCIATED WITH ATOMOXETINE TREATMENT.**

**Yalvag O, et al.**

Atomoxetine is the first non-stimulant medication for the treatment of attention-deficit/ hyperactivity disorder (ADHD). Atomoxetine is generally safe and well tolerated for the treatment of ADHD in the paediatric population. Headaches, upper abdominal pain, decreased appetite, vomiting, nausea, irritability, dizziness, and somnolence are among the most common side effects. In addition to these common side effects, it has been reported that the use of atomoxetine can be associated with an increased risk of mydriasis (Alhatem and Decker 2008; Bahali et al. 2014). Herein, we report a case of mydriasis associated with atomoxetine in a child with ADHD and dyslexia. Case presentation: A 13-year-old boy, who had no significant medical history, presented with ADHD and dyslexia. The patient was started on 25 mg of atomoxetine orally once daily for 7 days. The dose was then increased gradually to 60 mg orally once daily. After three weeks of atomoxetine treatment pupil dilatation was noticed by him and his mother. The patient denied any blurred vision, headaches, nausea, vomiting, or pain in his eyes. The patient was notified about his dilated pupils as being a possible side effect of atomoxetine. The patient was consulted to the ophthalmology department two days after atomoxetine cessation for differential diagnosis and detecting possible effects of atomoxetine on visual functions. In his ophthalmologic examination, his visual acuity was 20/20 in both eyes without any correction. Direct and indirect light reflexes were normal. His intraocular pressures were both within the normal range. Other than mydriasis in his both eyes biomicroscopic and fundus examination revealed normal signs bilaterally. Pupil sizes were measured using a millimeter ruler while the patient was fixating on a distant, non-accommodative target. Under scotopic, mesopic, and photopic conditions, his pupil sizes of his right and left eye were 8.1 mm and 8.2 mm; 6.6 mm and 7 mm; 3 mm and 3.8 mm, respectively. Atomoxetine was stopped, and mydriasis resolved within five days. Atomoxetine is a highly selective and potent inhibitor of the presynaptic noradrenaline transporter, acting both centrally and peripherally. Atomoxetine increases both norepinephrine (NE) and dopamine (DA) levels, especially in the prefrontal cortex. Atomoxetine also increases the effect of norepinephrine in various regions (Dadashova and Silverstone 2012). Mydriasis results when stimulation of the sympathetic nerves excites the radial fibres of the iris causing dilation of the pupils. An increase in NE caused by NE reuptake transporter inhibition has been shown to induce mydriasis in healthy volunteers. It is possible that atomoxetine may induce mydriasis via indirect  $\alpha$ -1 adrenoceptor activation, mediated in turn via NE reuptake inhibitor effects (Dadashova and Silverstone 2012; Yu and Koss 2003). The clinical importance of mydriasis in patients using atomoxetine increases in the presence of shallow anterior chamber or angle abnormalities predisposing to acute angle closure. Acute angle closure glaucoma is an ophthalmic emergency and can cause blindness if left untreated. Although it is uncommon, clinicians should be aware of the possibility of atomoxetine-induced acute angle closure due to devastating outcomes

Psychiatry and Clinical Psychopharmacology. 2018;28:60-61.

**RIBOSOMAL DNA TRANSCRIPTION IN BUCCAL EPITHELIAL CELLS OF CHILDREN DIAGNOSED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): A PRELIMINARY STUDY.**

**Yektaf C, Eroz R.**

**Objective:** The nucleolar organizer regions (NORs) are functional subunits of the nucleolus and composed of ribosomal DNA and proteins. We aimed to examine the AgNOR protein levels in buccal epithelial tissue of ADHD children compared to the healthy controls.

**Study Design:** Buccal epithelial samples were collected from twelve male patients, diagnosed with ADHD-combined type. Ten age- and gender-matched patients without any psychiatric or chronic disease were included as control group. The captured images were transferred to image processing software and one hundred nuclei have been evaluated for each, and mean Total AgNOR number/Total nuclear number (TAN/TNN), and Total AgNOR area/Total nuclear area (TAA/TNA) ratios were calculated.

**Results:** TAA/TNA and TAN/TNN of ADHD patients was significantly lower than healthy controls ( $p < 0.05$ ). In polynomial regression analysis, there was a statistically negative relation between inattention subscale scores and TAA/TNA in ADHD patients ( $R^2: 0.72$ ;  $p = 0.014$ ). There was also statistically negative relation between hyperactivity-impulsivity scores and TAA/TNA in ADHD children ( $R^2: 0.59$ ;  $p = 0.05$ ).

**Conclusions:** There is no diagnostic or follow-up parameter for ADHD. AgNOR staining method from buccal epithelial cells is a conventional, karyometric, and non-invasive method which would be helpful to enhance the diagnostic accuracy of ADHD. Additional studies should be conducted to obtain more certain knowledge about this topic

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Psychiatry and Clinical Psychopharmacology. 2018;28:64.

**NEUROPSYCHIATRIC COMORBIDITIES IN CHILDREN WITH TUBEROUS SCLEROSIS: A RETROSPECTIVE COHORT STUDY.**

**Ugur C.**

**Objective:** Tuberous sclerosis complex (TSC) is an autosomal dominant condition, caused by mutations in either the TSC1 or TSC2 gene. It has widespread systemic manifestations and is associated with significant neurological morbidity. The most frequent neurologic symptoms are seizures, which occur in up to 90% of patients and are often intractable, followed by autism spectrum disorders (ASD), intellectual disability (ID), attention-deficit/ hyperactivity disorder (ADHD), and sleep problems. ADHD is frequently present in patients with TSC, with a rate of 50%, comparable to the prevalence of ASD in TSC. In this study, we aimed to examine the frequency of neuropsychiatric comorbidities like ASD, ADHD, and OCD in patients with TS.

**Methods:** We reviewed retrospectively the patient charts and medical reports of 67 patients with TS diagnosis between the ages of 2 and 16 years registered between 2014 and 2018 in our clinic. Psychiatric interviews based on DSM-5 for neuropsychiatric diseases were evaluated during the health report procedures of patients with TS, and each case was filled with an autism behaviour checklist and Conners' Parent and Teacher Rating Scales.

**Results:** The average age of the group was found to be 113.7 -1 56.7 months. Of the cases, 32 (47.8%) were female and 35 (52.2%) were male. ASD was detected 19.4% (n = 13) of the TS cases, 49.3% (n = 33) of intellectual disabilities, 28.4% (n = 19) of ADHD, 6.0% (n = 4) of OCD, and 7.5% (n = 5) of specific learning disorder were detected.

**Conclusions:** Neuropsychiatric disorders are present in up to 90% of patients with TSC and represent an important issue for families. In our study, the prevalence of neuropsychiatric disorders was found to be quite high in patients with TS. Our work was found to be consistent with the results of the few studies conducted in this area. TSC is one of the most frequently identified monogenic causes of autism and a promising model to study its pathogenetic mechanism. However, the neurobiological pathway remains unclear and severity seems to have a notable variability in TSC patients. This cohort report is important because of its potential to give a new direction to studies that aim at the importance of early ASD screening and intervention for infants with TSC. Early recognition of patients developing neuropsychiatric disorders such as ASD symptomatology can bring them to early behavioural intervention focused on specific signs, and can address the need of global care requested by the families

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Psychiatry and Clinical Psychopharmacology. 2018;28:328-29.

**EEG CHANGES IN ADHD AND EEG AS A DIAGNOSTIC TOOL.**

**Yavral F.**

Attention-deficit hyperactivity disorder (ADHD) is a common psychiatric disorder affecting children, adolescents, and adults. The prevalence of ADHD in children is around 5% and varies from 3% to 16% in adults depending on the diagnostic criteria. Despite the debate on the significance of EEG on cognitive and behavioural development, it is commonly accepted that EEG discharges have a high incidence in several neurodevelopmental disorders, including ADHD. Although various EEG alterations have been described in patients with ADHD, their pathological significance has not been determined. It has been suggested that there is a close relationship between ADHD and epilepsy. A recent large-scale study revealed that ADHD in children is often accompanied by epilepsy. Based on this background, reappraisal of EEG findings in children with ADHD is important in order to detect indications of potential comorbid epilepsy and to investigate the developmental mechanisms of the neurophysiological manifestations in patients with ADHD. Several studies have estimated increasing and, particularly, high rates of ADHD in childhood in contrast to the constant

comorbidity rate of epilepsy in childhood. About 70% of patients with frontal lobe epilepsy (FLE) have ADHD and there is an especially high affinity between ADHD and FLE. Children with childhood absence epilepsy (CAE) are prone to the comorbidity of inattentive-type ADHD. Moreover, it has been reported that symptoms of ADHD have a close relationship with benign epilepsy of childhood with centrotemporal spikes (BECT), rolandic discharges (RD), or Panayiotopoulos syndrome. EEG is a useful noninvasive screening tool for brain function and seizure susceptibility. Several reports showed a high incidence of interictal epileptiform abnormalities in children with ADHD. Frequency of rolandic spike is higher in children with ADHD, and frontal lobe dysfunction is well known to be associated with ADHD. Thus, it is hypothesized that the localization of epileptiform discharges in ADHD might reflect regional neuropathologic mechanism of ADHD. Increased slow wave activity and decreased beta activity, predominantly in posterior regions, have been reported in ADHD.

Psychiatry and Clinical Psychopharmacology. 2018;28:347-48.

#### **EFFECTS OF ADHD REGARDING SELF-CONCEPT ON HEALTH-RELATED QUALITY OF LIFE IN CHILDREN.**

**Arman AR.**

**Objective:** Attention-deficit/hyperactivity disorder (ADHD) in children is associated with deterioration of health-related quality of life (HRQoL) in several dimensions. Fluctuations of self-concept during the developmental course of illness may have an impact on the clinical presentation of ADHD as well as on HRQoL in children diagnosed with ADHD. The objective of the present study is to evaluate the burden of ADHD on HRQoL with respect to self-concept in children.

**Methods:** Eighty primary school children were diagnosed as ADHD in Marmara University Hospital Child Psychiatry Clinic, who were compared with 74 healthy controls. The children were newly diagnosed ADHD cases based on Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children-Present and Lifetime Version. The children completed the Piers-Harris Self Concept Scale (PHSCS) for the evaluation of their self-concept. Mothers completed the Conners Parent Rating Scale-Revised for ADHD and the Child Health Questionnaire-Parent Form 50(CHQ-PF50) for evaluating HRQoL in children. The Child Behavior Checklist and Negative Life Events Scale were also administered.

**Results:** ADHD and the control group did not differ in age (mean age: 10.4 -| 2.4 vs. 10.7 -| 2.4) and sex distribution (56 vs. 42 boys). Being female and parental separation is related to lower HRQoL in the ADHD group ( $p < 0.05$  for both). Children with ADHD had worse psychosocial and physical HRQoL than healthy controls ( $p < 0.05$ ). No relationship was found between academic achievement and physical or psychosocial scores of CHQ-PF50. Psychosocial QoL scores were found significantly higher in children with ADHD-hyperactive type ( $p < 0.05$ ). Children with ADHD reported lower self-concept than controls ( $p < 0.01$ ) and the decreasing tendency of self-concept scores in older ages was not observed, which was seen in healthy controls. Positive judgement on Happiness/satisfaction and Behavioural adjustment subscales of PHSCS appeared to affect the HRQoL positively ( $p < 0.01$ ). In contrast, adverse life events had a negative impact on HRQoL measures ( $p < 0.05$ ) in the ADHD group.

**Conclusions:** Low self-esteem in the presence of worse HRQoL measures may create difficulties in the adjustment processes of ADHD children. Families with ADHD children may be more prone to perceive HRQoL much worse when there is a history of adverse life event. Positive self-concept of children with ADHD may affect parents' perception of HRQoL.

Psychiatry and Clinical Psychopharmacology. 2018;28:75.

#### **THE QUALITY OF LIFE OF CHILDREN AGED 7-17 YEARS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.**

**Bilag O, Kavurma C, et al.**

**Objective:** The aim of this study was to evaluate quality of life in children and adolescents aged 7-17 years with attention-deficit hyperactivity disorder (ADHD) who were not in treatment, to compare the results with those in healthy control group.

**Methods:** The study sample consisted of 41 patients diagnosed with ADHD and 33 healthy controls. The quality of life in all children was evaluated by the Pediatric Quality of Life Inventory (PedsQL). The healthy control group consists of healthy trials without any psychiatric disease.

**Results:** The quality of life based on subscale scores and total scale scores was found significantly lower in parents of children with ADHD than in parents of healthy children. It was observed that children with ADHD had significantly lower Psychosocial Health Total subscale scores for PedsQL filled out by children compared to healthy control group.

**Conclusions:** The quality of life of children with ADHD is impaired during observation and plays an important role at the beginning of treatment. The results of the study showed that ADHD was observed to be affecting the quality of life negatively in every aspect of children's lives. When evaluation during observation and treatment of ADHD, care should cover all living areas, not just academic activities at school

Psychiatry and Clinical Psychopharmacology. 2018;28:37-38.

**BRUXISM PREVALENCE IN NON-MEDICATED CHILDREN WITH ADHD: PRELIMINARY RESULTS OF 34 CHILDREN IN A CLINICAL SAMPLE.**

**Ayutlu HC, Garker I.**

**Objective:** Bruxism is defined as a diurnal or nocturnal involuntary, non-functional, spasmodic gnashing, grinding, and clenching of teeth by the American Academy of Orofacial Pain. It is also defined as a sleep-related movement disorder by the International Classification of Sleep Disorders. Bruxism in children with ADHD has gained attention of researchers because of the reports of bruxism as a stimulant side effect. In some studies, it is reported that bruxism prevalence is higher in children with ADHD than healthy controls but the prevalence and effects of bruxism is mostly studied on medicated children with ADHD. With regard to the clinical evidence of ADHD and sleep problems association, it is aimed to present the preliminary results of prevalence of bruxism and discuss the related factors in non-medicated children with ADHD with this study.

**Methods:** Thirty-four cases of newly diagnosed ADHD without medical treatment and chronic medical disease were obtained as the study group. The Schedule for Affective Disorders and Schizophrenia for School Age Children was used to diagnose ADHD and comorbidities. The Children's Sleep Habits Questionnaire was used to detect sleep bruxism and provide information of sleep habits. Parents were asked for signs and symptoms related to bruxism in their children using a questionnaire.

**Results:** Prevalence of sleep bruxism was found in 23.5% (n = 8) in the study group; 50% of children with sleep bruxism (n = 4) also had awake bruxism and 62.5% (n = 5) described symptoms related to bruxism (tooth wear, jaw clicking, facial pain). ADHD combined type was found as the most common type (62.5%, n = 5) and ODD as the most common comorbidity (62.5%, n = 5) in children with sleep bruxism.

**Conclusions:** Although the number of cases is limited, our prevalence rate is similar with the previous studies. We may suggest that bruxism and related symptoms can be found frequently in non-medicated children with ADHD. Further studies especially focused on non-medicated children with ADHD may contribute to the clarification of the relationship between bruxism and ADHD

Psychiatry and Clinical Psychopharmacology. 2018;28:55.

**SOCIAL COGNITION IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER, SPECIFIC LEARNING DISORDER, OR AUTISM SPECTRUM DISORDER: RELATIONSHIP BETWEEN CLINICAL SIGNS.**

**Xahina B, et al.**

**Objective:** Autism Spectrum Disorder (ASD), Attention-deficit/ hyperactivity disorder (ADHD), and Special Learning Disorder (SLD) are neurodevelopmental disorders characterized by social impairments that are common in childhood. The relationship between social impairment and social cognition skills is first demonstrated in patients with ASD and there are many studies evaluating ASD and ADHD subjects. There are no social cognitive studies evaluating these three diagnostic groups which are the most common neurodevelopmental disorders in childhood. The aim of this study was to describe the social cognitive skills

of pre-adolescent ADHD, SLD, and ASD children and to compare these skills with typically developing children.

**Methods:** Twenty-four children with ADHD, 24 children with SLD, 26 children with ASD, and 24 children with no psychiatric diagnoses were included in the study. The Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADSPL), Peabody Picture Vocabulary Test, First and Second Order False Belief Task, Hinting Task, Faux Pas Task, and the Reading the Mind in the Eyes Task (RMET) were administered by the investigator, WISC-R was administered by the psychologist, and the parents and teachers filled out the Aberrant Behavior Checklist, Social Responsiveness Scale, Disruptive Behavior Disorder Rating Scale, Learning Disorders Symptom Scale, Autism Behavior Checklist, and Childhood Autism Rating Scale.

**Results:** It was found that in all the tests in which we evaluated the Theory of Mind (ToM) skills, the SLD, ADHD, and ASD groups showed low performance compared to the control group, and that the performance of all three patient groups did not differ significantly. Intelligence and language development showed a positive correlation with ToM performance and after these two covariates were controlled, there was a significant effect on RMET performance. There was a significant negative correlation between scale scores evaluating problems in social reciprocity, problem behaviour, attention and learning areas, and ToM skills. There was a relationship between disease severity and simple ToM skills in ASD subjects, but no correlations between advanced ToM skills were found. ODD comorbidities were found higher in ADHD patients. The presence of ODD comorbidity has an impact on the basic ToM skills but not on the advanced ToM skills. SLD subjects who have no ADHD comorbidity were found to be similar to the control group in terms of simple ToM skills but showed poor performance in advanced ToM skills.

**Conclusions:** The results of this study showed that the social cognition skills of the ASD, ADHD, and SLD were poorer than those of typically developed children. The children in the patient group have more social and academic problems and that there is a relationship between these problems and the ToM skills. There are many parameters that affect ToM skills. However, it is important to determine the social cognitive characteristics of the patients, to identify areas of difficulty, and to apply patient-tailored treatment approaches

Psychiatry and Clinical Psychopharmacology. 2018;28:230-31.

#### **ARIPRAZOLE-INDUCED STUTTERING IN AN 8 YEAR-OLD BOY WITH ADHD.**

***Lnay M, Adanir AS, +üzatalay E.***

Stuttering is defined as a disturbance in the normal fluency and pattern of speech in which a person tends to repeat sounds and syllables or whose speech includes sound prolongations and broken words. Two types of stuttering have been described: Iatrogenic and developmental. Iatrogenic stuttering is caused by drugs, as a side effect, generally in patients who have a developmental disorder or have a family history of stuttering. Stuttering associated with antipsychotics is a rarely encountered side effect. A number of studies have indicated that stuttering may occur as a side effect of antipsychotic drugs, such as chlorpromazine, trifluoperazine, fluphenazine, levomepromazine, olanzapine, risperidone, and clozapine. We found only two case reports of aripiprazole-induced stuttering. However, there are also case reports of the use of aripiprazole in the treatment of stuttering in the literature. Here, we present a case of exacerbation of stuttering in an ADHD patient which is thought to be related to a relatively lower dosage of aripiprazole. Case presentation: An 8-year-old boy was presented to our clinic with the complaints of lack of concentration, overactivity and getting bored easily, bothering his classmates during lectures, difficulty in completing his homework and tasks, and stuttering. His symptoms started at preschool period and increased by the time, especially during school time. The boy was the second of the three siblings with a non-specific past medical history but family history revealed that father had ADHD and stuttering. After a comprehensive psychiatric and psychometric evaluation, a diagnosis of ADHD combined-type was diagnosed according to DSM-5 criteria and 18 mg/day oros-methylphenidate (LA-MPH) was prescribed. Two days later, the patient was presented to our clinic with a complaint of widespread body rash and the drug was discontinued because of drug intolerance. 10 mg/day atomoxetine was initiated for the first week and increased to 25 mg/day during the second week by considering his body weight (21 kg). Despite the use of atomoxetine, the impulsivity symptoms persisted, so aripiprazole 2 mg/day was added to the treatment. After 10 days of aripiprazole usage, the family presented

the boy again and reported a severe exacerbation of his stuttering. The increase in stuttering was attributed to aripiprazole and he showed recovery after the cessation of the drug. Aripiprazole is an atypical antipsychotic with a distinct way of action from all currently available antipsychotic drugs. It acts on both postsynaptic dopamine D2 receptors and presynaptic autoreceptors, and is considered as a partial dopaminergic agonist. Although stuttering is mentioned as a rare side effect of antipsychotics, the possible mechanisms causing the occurrence of stuttering in this situation are not known. Analogous to the production of extrapyramidal side effects, dopamine/acetylcholine balance may be relevant to the suppression or aggravation of stuttering in susceptible persons. This hypothesis is relevant to the observation that neuroleptics have been reported to both provoke and suppress stuttering. In this case, aripiprazole treatment resulted in exacerbation of stuttering and discontinuation of aripiprazole abolished that effect. We believe that exacerbation of stuttering was triggered by aripiprazole

Psychiatry and Clinical Psychopharmacology. 2018;28:378.

#### **MINDFULNESS IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) THERAPY.**

**Xenyuva G.**

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental condition that is manifested in childhood with attention deficit, hyperactivity, and impulsivity. In the emergence of ADHD according to the results of the research, biological, genetic, psychosocial, and familial factors play a role. The prevalence of ADHD in the community is reported to be approximately 8% in childhood, 6% in adolescence, and 4% in adulthood. The inability to start a job in adult ADHD, the inefficiency and bad time management at work, the start of a large number of jobs, but not a majority, a meeting during a meeting, an inability to cope with stress and anger control problems, a tendency to tell the first thing that comes to mind and to fulfil marriage and responsibilities intensive problems often arise. Awareness is based on being able to pay attention to the present moment in a nonjudgmental way, and accepting whatever it is experiencing. In this approach awareness and consciousness, acceptance, judgment, self-observation, and focus are the main components. Certain regions of our brain have the ability to control self, the ability to manage emotions, and to make healthy decisions. The aim of the awareness therapy in ADHD individuals is to teach them to be aware of their mind and body, to be able to control their own behaviours, to increase their attention skills, self-confidence level, anger control skills, to adapt to social environments, and to make inter-person relations more healthy.

Psychiatry and Clinical Psychopharmacology. 2018;28:313-14.

#### **WHAT DOES CURRENT LITERATURE TELL US FOR THE AETIOLOGY OF ADHD?**

**Aksoy UM.**

Attention-deficit hyperactivity disorder (ADHD) is one the most common psychiatric disorder with pervasive effects. Epidemiological data represent a prevalence rate of % 4 in adults %6- 8 in children. ADHD arises on a polygenetic base with multiple heterogenous factors. Genetic Factors: ADHD is one of the most heritable disorder wit a mean 0.76 heritability surpassing schizophrenia and bipolar disorder. ADHD is a familial disorder with a relative risk about 5-9 in first-degree relatives of individulas with ADHD. Various different genomic variants have been associated with ADHD risk These variants include common DNA sequence variants - single nucleotide polymorphisms (SNPs)- Although many studies have been conducted, there is no precise single nucleotide polymorphism mainly associated with ADHD rather a a composite risk based upon these nucleotide polymorphisms could be discussed. Whole-genome investigations represent specific single dopaminergic, serotonergic, and noradrenergic candidate genes. Each of these genes were assumed to be associated with ADHD.However according to current knowledge, variants in single genes associated with ADHD should be investigated with caution as some of these variants reveale false positive results. Various nutritional factors, toxins, diateary factors and exposures to stressful life events in childhood and poor attachment with parents are also blamed for development of ADHD Low birth weight and maternal smoking during prgenancy are two major prenatal factors in pathogenesis of ADHD.in-utero exposure to

maternal stress, cigarette smoking, alcohol, prescribed drugs (eg, paracetamol), illicit substances are also other factors. Environmental toxins, especially in-utero exposure to lead, organophosphate pesticides, and polychlorinated biphenyls, are other factors for ADHD. Nutritional deficiencies (eg, zinc, magnesium, and polyunsaturated fatty acids) could not be shown systematically to cause ADHD evidence based. Sugars and artificial food additives and food colourings were also blamed and discussed further Feingold Diet with restriction of sugar and artificial additives and food colourings yielded negative results. Psychosocial risk factors low socioeconomic status, parental conflict have been found not casual rather correlated with ADHD. Studies regarding mother-child relation and attachment showed that the problems regarding child and parent relation is not a cause rather a result of ADHD. Whereas early parental and social deprivation has been shown for a casual relationship with ADHD. Animal studies also interestingly showed that some environmental factors could interact with genetic material and even change the genetic through methylation of DNA - epigenetic factors. These show that there is complex and intricate environmental and genetic factors which interact each other in each level.

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Psychiatry and Clinical Psychopharmacology. 2018;28:299-300.

**AN UPDATE ON AETIOLOGY OF ADHD.**

**Aksoy UM.**

Attention-deficit hyperactivity disorder (ADHD) is one of the most common psychiatric disorders with pervasive effects. Epidemiological data represent a prevalence rate of 4% in adults 6-8% in children. ADHD arises on a polygenic base with multiple heterogeneous factors. Genetic factors: ADHD is one of the most heritable disorders with a mean of 0.76 heritability surpassing schizophrenia and bipolar disorder. ADHD is a familial disorder with a relative risk of about 5-9 in first-degree relatives of individuals with ADHD. Various different genomic variants have been associated with ADHD risk. These variants include common DNA sequence variants - single nucleotide polymorphisms (SNPs). Although many studies have been conducted, there is no precise single-nucleotide polymorphism mainly associated with ADHD, rather a composite risk based upon these nucleotide polymorphisms could be discussed. Whole-genome investigations represent specific single dopaminergic, serotonergic, and noradrenergic candidate genes. Each of these genes was assumed to be associated with ADHD. However, according to current knowledge, variants in single genes associated with ADHD should be investigated with caution as some of these variants reveal false-positive results. Various nutritional factors, toxins, dietary factors, and exposures to stressful life events in childhood and poor attachment with parents, are also blamed for the development of ADHD. Low birthweight and maternal smoking during pregnancy are the two major prenatal factors in pathogenesis of ADHD. In utero exposure to maternal stress, cigarette smoking, alcohol, prescribed drugs (e.g. paracetamol), and illicit substances are also other factors. Environmental toxins, especially in utero exposure to lead, organophosphate pesticides, and polychlorinated biphenyls, are other factors for ADHD. Nutritional deficiencies (e.g. zinc, magnesium, and polyunsaturated fatty acids) could not be shown systematically to cause ADHD evidence based. Sugars and artificial food additives and food colourings were also blamed and discussed further Feingold Diet with restriction of sugar and artificial additives and food colourings yielded negative results. Psychosocial risk factors, low socioeconomic status, and parental conflict have been found not casual rather correlated with ADHD. Studies regarding mother-child relation and attachment showed that the problems regarding child and parent relation is not a cause rather a result of ADHD. Whereas early parental and social deprivation have been shown for a causal relationship with ADHD. Animal studies also interestingly showed that some environmental factors could interact with genetic material and even change the genetics through methylation of DNA-epigenetic factors. These show that there is complex and intricate environmental and genetic factors which interact each other at each level.

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Psychiatry and Clinical Psychopharmacology. 2018;28:51-52.

**HEAVY METAL LEVELS AND INVESTIGATIONS OF THEIR EFFECTS ON THIOL/DISULPHIDE STATUS IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.**

**Aydin DB, Elmas B, Nasiroğlu S, et al.**

**Objective:** Attention-Deficit/ Hyperactivity Disorder (ADHD) is one of the most common childhood psychiatric disorders. The aetiology of ADHD is multifactorial. Some heavy metals and oxidant/antioxidant imbalance are some of the controversial factors in aetiology. In this present study, we aimed to examine the heavy metal levels and thiol/disulphide status and the effect of heavy metals on thiol/disulphide homeostasis in children and adolescents with ADHD.

**Methods:** This study included a total of 35 children aged 6-18 years who were newly diagnosed with ADHD and age- and gender-matched 31 healthy children. Parents or guardians were administered a semi-structured questionnaire including demographic data, pre-postnatal smoking exposure, and breastfeeding history. Heavy metals including lead (Pb), mercury (Hg), and cadmium (Cd) levels were analysed. Serum total thiol, native thiol, disulphide levels, and their ratios were analysed with a newly developed automated spectrophotometric method.

**Results:** This study included 9 girls and 57 boys, total of 66 participants, mean age was 10.8 ± 2.8 years. Cigarette smoking during pregnancy was significantly higher in the ADHD group ( $p = 0.030$ ). The native and total thiol levels of the patients with ADHD were significantly higher than the control group ( $p < 0.001$ ). The Hg levels of the patients were significantly higher than the control group ( $p = 0.002$ ). Pb levels were not different between ADHD and control groups while Cd levels were significantly higher in the control group ( $p < 0.001$ ).

**Conclusions:** Maternal smoking during pregnancy and increase in blood Hg levels might be risk factors for ADHD. In ADHD patients in response to oxidation, antioxidant levels might increase. We could not find any relationship between thiol/disulphide levels and heavy metal levels in patients with ADHD

Psychiatry and Clinical Psychopharmacology. 2018;28:382-83.

**PSYCHOPHARMACOLOGICAL TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER COMORBIDITY IN ASD.**

**Ding GS.**

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are neurodevelopmental disorders. ASD is characterized by impairments in communication and social reciprocity and stereotypic and/or repetitive behaviours. ADHD, the most common psychiatric disorder diagnosed in childhood, is characterized by symptoms of inattention, impulsivity, and/or hyperactivity beyond what would be expected for the developmental level. Despite these main symptom differences, between 30% and 50% of individuals diagnosed with ASD also exhibit elevated levels of ADHD symptoms. These behaviours may be related to comorbid attention-deficit/hyperactivity disorder (ADHD) or to other factors that affect function in children with ASD (e.g. overarousal, anxiety). If the behaviours do not improve with environmental or behavioural interventions, they may respond to pharmacotherapy [1]. Psychostimulant medications: Methylphenidate appears to improve symptoms of hyperactivity and inattention in children with ASD, but the response to methylphenidate is lower in children with ASD than it is in children with isolated ADHD. In the largest crossover trial, approximately 50% of children with ASD responded to methylphenidate; the effect size ranged from 0.20 to 0.54, depending upon dose and rater, with greater improvement at higher doses [1,2]. Studies of amphetamines in the treatment of attentional symptoms in children with ASD are lacking. It is not clear that the results from trials of methylphenidate can be generalized to amphetamines [2]. Non-psychostimulant medications: Studies of atomoxetine for symptoms of hyperactivity and inattention in children with ASD are limited. Randomized crossover trials suggested some improvement in hyperactivity-impulsivity symptoms compared with placebo. However, as with methylphenidate, the overall effect size for atomoxetine in children with ASD and symptoms of ADHD is smaller than for children with ADHD without ASD [2,3]. Studies of alpha-2-adrenergic agonists are limited, and sample sizes are small. Some studies show that guanfacine and clonidine are effective in reducing hyperactivity, inattention, and irritability symptoms [1,2]. Other drugs that may be beneficial for symptoms of hyperactivity and inattention in children with ASD include risperidone and antiseizure drugs. The use of risperidone for symptoms of hyperactivity in children with ASD is supported by open-label and randomized controlled trials. The evidence for antiseizure agents is limited to small, open-

label, or observational studies [2]. In conclusion, researches generally support the use of psychopharmacological treatments for reducing impairing ADHD symptoms in individuals with ASD. But further studies are needed to increase understanding of the effectiveness and about clinical practice.

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Psychiatry and Clinical Psychopharmacology. 2018;28:36-37.

#### **INVESTIGATION OF IMPULSIVITY AND ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER IN EPILEPTIC PATIENTS.**

**Ceyhun HA, Aydin EF, et al.**

**Objective:** A number of conditions have been reported to be comorbid with epilepsy, including psychiatric disorders. Epileptic activity in both frontal and temporal lobes can cause impulsivity, attention problems and behavioural changes associated with orbitofrontal dysfunction. Attention Deficit Hyperactivity Disorder (ADHD) and impulsivity problems in childhood-onset epilepsies are monitored in almost one-third of cases. Approximately half of ADHD in childhood persists into adulthood. Besides this, symptoms of ADHD (such as inattention, hyperactivity, behavioural disorders) are often side effects of antiepileptic drugs. There are limited data on the frequency of ADHD symptoms in adult epilepsy patients. Here, we aimed to examine the relationship between impulsivity, ADHD symptoms, and life quality in epilepsy patients.

**Methods:** The study included 30 epilepsy patients aged 18-65 years followed by Atatürk University Hospital Neurology outpatient clinic and 30 healthy controls. Participants were assessed by the Sociodemographic Clinical Data Form, the Adult Attention-deficit/ hyperactivity disorder DSM-IV-based diagnostic screening scale (adult ADD), the Psychological Symptom Check List (SCL-90-R), the Barratt Impulsivity Questionnaire-11 (BIQ-11), and the Quality of Life Scale (WHOQOL-Brief).

**Results:** Epilepsy patients and control group were similar in terms of age, gender, education level, and presence of psychiatric family history. There were significant differences between groups in marital status, presence of children, and smoking. The number of marriages was higher in the control group but the number of grade repetitions, disciplinary punishments, physical traumas, job changes, forensic events, traffic accidents, and traffic fines were similar. The paranoid ideation subscale scores of SCL-90-R were not statistically different besides somatization, anxiety, obsessive-compulsiveness, depression, interpersonal sensitivity, psychoticism, hostility, phobic anxiety subscales, and total scores were significantly higher in epilepsy patients ( $p < 0.05$ ). There were significant differences between the plan subscale scores of the BIQ-11 ( $p < 0.05$ ), while motor, attention, and total scores were similar ( $p > 0.05$ ). According to adult ADD attention subscale, scores were statistically higher in epilepsy patients ( $p < 0.05$ ) but hyperactivity and impulsivity-related features were similar ( $p > 0.05$ ). We did not find any significant differences in life quality between the groups.

**Conclusions:** Our findings indicated that inattentiveness symptoms in epilepsy patients significantly higher than controls. Most of the previous studies have shown similar to our findings indicating the predominance of inattentiveness subtype in epilepsy patients comorbid with ADHD. The high occurrence of ADHD inattentiveness subtype in epilepsy provides insight into pathogenesis by revealing shared neurobiological mechanisms underlying multiple disorders. It has been suggested that specific neuropsychological impairments both in epilepsy and in ADHD like attention and working memory deficits can be responsible for the increased prevalence of inattentiveness symptoms. Alternatively, ADHD, like epilepsy, is a manifestation of underlying neurodevelopmental vulnerability or it may be the presence of ADHD that predisposes to a seizure disorder. Finally, treatment options for neuro-behavioural comorbidities remain to be developed. Treating physicians should be vigilant to the possibility of these comorbidities in epilepsy patients and future research should examine the impact of comorbidities on treatment outcomes in epilepsy

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Sleep: Journal of Sleep and Sleep Disorders Research. 2022 Sep;45:1-10.

**SLEEP ELECTROENCEPHALOGRAPH EVIDENCE OF DELAYED BRAIN MATURATION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: A LONGITUDINAL STUDY.**

**Darchia N, Campbell IG, Basishvili T, et al.**

**Study Objectives:** This study investigates whether longitudinally measured changes in adolescent brain electrophysiology corroborate the maturational lag associated with attention deficit hyperactivity disorder (ADHD) reported in magnetic resonance imaging (MRI) studies and cross-sectional sleep electroencephalogram (EEG) data.

**Methods:** Semiannually nine adolescents diagnosed with ADHD (combined presentation, DSM-V criteria, mean age  $12.39 \pm 0.61$  years at first time-point, two females) and nine typically developing controls ( $12.08 \pm 0.35$  years, four females) underwent all-night laboratory polysomnography, yielding four recordings.

**Results:** Sleep macrostructure was similar between groups. A quadratic model of the age change in non-rapid eye movement (NREM) delta (1.07–4 Hz) power, with sex effects accounted for, found that delta power peaked  $0.92 \pm 0.37$  years later in the ADHD group. A Gompertz function fit to the same data showed that the age of most rapid delta power decline occurred  $0.93 \pm 0.41$  years later in the ADHD group ( $p = 0.037$ ), but this group difference was not significant ( $p = 0.38$ ) with sex effects accounted for. For very low frequency (0.29–1.07 Hz) EEG, the ADHD lag ( $1.07 \pm 0.42$  years later,  $p = 0.019$ ) was significant for a Gompertz model with sex effects accounted for ( $p = 0.044$ ). Theta (4–7.91 Hz) showed a trend ( $p = 0.064$ ) toward higher power in the ADHD group. Analysis of the EEG decline across the night found that standardized delta and theta power in NREMP1 were significantly ( $p < 0.05$  for both) lower in adolescents with ADHD.

**Conclusions:** This is the first longitudinal study to reveal electrophysiological evidence of a maturational lag associated with ADHD. In addition, our findings revealed basically unaltered sleep macrostructure but altered sleep homeostasis associated with ADHD.

Our findings provide the first electrophysiological evidence that, compared to typically developing peers, adolescents diagnosed with attention deficit hyperactivity disorder (ADHD) have similar but delayed brain development trajectories. The study also demonstrates that homeostatic recovery occurs more slowly in adolescents with ADHD and that sleep macrostructure is basically normal in ADHD. These findings hold implications for fundamental and clinical research issues to further our understanding of this prevalent disorder and to reveal critical developmental periods of the underlying processes

Transl Psychiatry. 2022;12.

**ASSOCIATION BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOM SEVERITY AND WHITE MATTER INTEGRITY MODERATED BY IN-SCANNER HEAD MOTION.**

**Dziemian S, Barańczuk-Turska Z, Langer N.**

Attention-deficit/hyperactivity disorder (ADHD) is a common and debilitating neurodevelopmental disorder associated with various negative life impacts. The manifestation of ADHD is very heterogeneous, and previous investigations on neuroanatomical alterations in ADHD have yielded inconsistent results. We investigated the mediating effect of in-scanner head motion and ADHD hyperactivity severity on motion-corrected fractional anisotropy (FA) using diffusion tensor imaging in the currently largest sample ( $n = 739$ ) of medication-naïve children and adolescents (age range 5–22 years). We used automated tractography to examine whole-brain and mean FA of the tracts most frequently reported in ADHD; corpus callosum forceps major and forceps minor, left and right superior-longitudinal fasciculus, and left and right corticospinal tract (CST). Associations between FA and hyperactivity severity appeared when in-scanner head motion was not accounted for as mediator. However, causal mediation analysis revealed that these effects are fully mediated through in-scanner head motion for whole-brain FA, the corpus callosum forceps minor, and left superior-longitudinal fasciculus. Direct effect of hyperactivity severity on FA was only found for the left CST. This study illustrates the crucial role of in-scanner head motion in the identification of white matter integrity alterations in ADHD and shows how neglecting irremediable motion artifacts causes spurious findings.

When the mediating effect of in-scanner head motion on FA is accounted for, an association between hyperactivity severity and FA is only present for the left CST; this may play a crucial role in the manifestation of hyperactivity and impulsivity symptoms in ADHD

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Transl Psychiatry. 2022;12.

**TREATMENT BIOMARKERS FOR ADHD: TAKING STOCK AND MOVING FORWARD.**

**Michelini G, Norman LJ, Shaw P, et al.**

The development of treatment biomarkers for psychiatric disorders has been challenging, particularly for heterogeneous neurodevelopmental conditions such as attention-deficit/hyperactivity disorder (ADHD). Promising findings are also rarely translated into clinical practice, especially with regard to treatment decisions and development of novel treatments. Despite this slow progress, the available neuroimaging, electrophysiological (EEG) and genetic literature provides a solid foundation for biomarker discovery. This article gives an updated review of promising treatment biomarkers for ADHD which may enhance personalized medicine and novel treatment development. The available literature points to promising pre-treatment profiles predicting efficacy of various pharmacological and non-pharmacological treatments for ADHD. These candidate predictive biomarkers, particularly those based on low-cost and non-invasive EEG assessments, show promise for the future stratification of patients to specific treatments. Studies with repeated biomarker assessments further show that different treatments produce distinct changes in brain profiles, which track treatment-related clinical improvements. These candidate monitoring/response biomarkers may aid future monitoring of treatment effects and point to mechanistic targets for novel treatments, such as neurotherapies. Nevertheless, existing research does not support any immediate clinical applications of treatment biomarkers for ADHD. Key barriers are the paucity of replications and external validations, the use of small and homogeneous samples of predominantly White children, and practical limitations, including the cost and technical requirements of biomarker assessments and their unknown feasibility and acceptability for people with ADHD. We conclude with a discussion of future directions and methodological changes to promote clinical translation and enhance personalized treatment decisions for diverse groups of individuals with ADHD

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Trials. 2022;23.

**EFFECT OF VITAMIN D SUPPLEMENTATION ON BRAIN WAVES, BEHAVIORAL PERFORMANCE, NITRIC OXIDE, MALONDIALDEHYDE, AND HIGH-SENSITIVITY C-REACTIVE PROTEIN IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: STUDY PROTOCOL FOR A RANDOMIZED CLINICAL TRIAL.**

**Sangouni AA, Mirhosseini H, Hosseinzadeh M.**

**Background:** Attention deficit/hyperactivity disorder (ADHD) is the most common chronic mental and behavioral disorder among children. Some studies showed the lower levels of vitamin D in patients with ADHD compared with the healthy people. Few clinical trials were conducted in this field. The present study will be performed to examine the effect of vitamin D supplementation in children with ADHD.

**Methods:** We will conduct a double-blind, randomized controlled clinical trial to investigate the effect of vitamin D supplementation on brain waves, behavioral performance, serum nitric oxide, malondialdehyde, and high-sensitivity C-reactive protein in 50 patients with ADHD. The intervention group will receive one capsule 50,000 IU vitamin D every week, for 8 weeks. The control group will receive one placebo capsule containing 1000 mg olive oil every week. Electroencephalography will be performed for 10 min using Brain Master Discovery from 19 scalp sites both before the first intervention and the 10 sessions of the therapy. The artifact-free periods of 1-min electroencephalography data will be analyzed for quantitative electroencephalography measures.

**Discussion:** For the first time, this clinical trial will evaluate the effect of vitamin D supplementation on brain waves, serum nitric oxide, malondialdehyde, and high-sensitivity C-reactive protein in patients with ADHD. The results of the present clinical trial will provide a better vision about the vitamin D efficacy in patients with ADHD.

**Trial registration:** Registered on 5 November 2020 at Iranian Registry of Clinical Trials with code number IRCT20200922048802N1 (<https://www.irct.ir/trial/51410>)

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Z Kinder- Jugendpsychiatr Psychother. 2022.

**SOZIALE NETZWERKE VON KINDERN MIT PSYCHISCHEN STÖRUNGEN.**

**Titze K, Jaite C, Winter SM.**

The study compares the social networks of children with mental disorders with a matched control group (n = 75/75, male 69%/69%, age: 9.4/9.0 years). In addition, we examined the quantity and structure of social networks as well as the stresses and resources in the respective patient group in general and regarding specific disorders (hyperkinetic disorder, HKS, and childhood emotional disorder). We assessed their use of social networks with a revision of the Social Relationship Test for Children (SoBeKi-R) and their mental disorders via clinical diagnoses, CBCL, and SDQ. The patients reported significantly smaller networks overall and fewer social resources, particularly in the nonfamily domains. While children with emotional disorders were found to have fewer social strains than the comparison group, children with ADHD tended to have higher strain scores per network person, and externalizing symptoms were significantly associated with higher network strains. The results, which vary by disorder, suggest complex disorder-specific associations between the syndromes and the reported social network resources and strains

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## REVIEW ARTICLE

WILEY

# Transition care for adolescents and young adults with attention-deficit hyperactivity disorder (ADHD): A descriptive summary of qualitative evidence

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## Funding information

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## Abstract

The review presents a summary of available evidence about transition care of ADHD patients from all service users' perspectives. Common barriers, and suggestions for improvement ADHD of transition care, were extrapolated from qualitative research, including case notes studies, and were exposed. A comprehensive search of the PubMed, Embase, PsychInfo and Web of Science databases for articles published up to October 2021 was conducted to summarize recent evidence on the experiences of all stakeholders involved in the transition process. Reviews, other chronic conditions and different meaning of transition were excluded. Authors extracted data and assessed study quality independently. Findings were discussed taking into consideration barriers and suggestions from all service users' perspectives. Findings from 23 studies with different context and methods were collected and summarized. Most of the studies were conducted in UK, using interviews and questionnaires, and addressed to the physicians. The lack of information about ADHD as a condition and about transition process were the barriers most reported, while joint working and sharing transition protocols were the suggestions pointed out by all stakeholders. Despite different perspectives, all stakeholders exposed similar needs. The review reveals an evident need for defining and evaluating the effectiveness of transition programmes from child to adult ADHD services.

## KEYWORDS

attention-deficit hyperactivity disorder, descriptive summary, experiences, review, transition to adult care

## 1 | INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is a life span disorder that affects between 2% and 3% of the adult population (Agnew-Blais et al., 2016), starting in childhood and continuing in more than a half through adolescence, into adulthood, leading to a range of clinical signs and to great difficulties in different fields (e.g., school

achievement, in reaching employment and in maintaining relationships) (Baric et al., 2017; Coghill, 2017; DuPaul et al., 2017). The persistence of the disorder is frequently associated with other psychiatric comorbidities, such as mood and personality disorders (Biederman et al., 2010; Cadman et al., 2016; Copeland et al., 2013; Hennig et al., 2017; Kawatkar et al., 2014) and substance use disorder (Sihvola et al., 2011). Like other neurodevelopmental disorders as

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autism and dyslexia, ADHD is a chronic condition that starts in early childhood and often persists during adulthood (Van Cleave & Leslie, 2008; Wolraich et al., 2019), and as such, adolescence is a sensitive phase of the development that requires special attention from healthcare providers in order to support the adolescents in the passage from child to adult services (Caye et al., 2016; Meaux et al., 2009; Murphy et al., 2018; Saqr et al., 2018; Schaefer et al., 2017; Wilens et al., 2018). The transfer from child to adult care is called transition, which includes a series of steps to follow and whose main objective is to ensure the continuity of care (Schor, 2015). Over the last two decades, the importance of transition care has been increasingly recognized within both paediatric and adult sectors, also for other chronic disorders (Davignon et al., 2018; Elias & White, 2018; Levy et al., 2020; Merrick et al., 2020; Paton & Hiscock, 2019; Sezgin et al., 2020). In Europe, many projects (Janssens et al., 2020; Lepiece et al., 2020; Paul et al., 2013; Singh et al., 2008, 2010, 2017), programmes and register networks (Bonati et al., 2018; Jonsson et al., 2021; Poulton, 2017) concerning transition were created; also in Italy, a scoping review was conducted (Reale & Bonati, 2015); all these actions have highlighted the needing of a standard transition protocol with shared guidelines, formal policies and more investments in healthcare service delivery. Although abundant literature outlining agreed principles of good transitional care exists (Fournier et al., 2020; Kooij et al., 2019; Young et al., 2011, 2016), they have been criticized for poor feasibility, effectiveness and practicality (Gatej et al., 2019). Experiences of ADHD service users have been explored, but these studies were based on one stakeholder's perspective at a time or focused mainly on the barriers of transition care from child to adult services (Hovish et al., 2012; Jivanjee et al., 2009; Jivanjee & Kruzich, 2011; Reale et al., 2018). An updating of the evidence on ADHD transition care from child to adult services was the scope of this review, with emphasis on the experiences of all stakeholders involved: clinicians from primary and secondary care, patients and their parents/carers. Information on barriers and suggestions were collected and synthesized in order to identify the common needs for improving transition care.

## 2 | METHODS

### 2.1 | Definition and inclusion/exclusion criteria

The review was restricted to studies evaluating the transition experience of young ADHD patients from child to adult mental health services, from the perspective of patients, parents/carers or clinicians. The search was limited to original articles. Studies were eligible if they analysed stakeholders' experiences and suggestions for an optimal transition with qualitative methods (for example, interviews and questionnaires), including case note studies. Articles were excluded if they were not specific to ADHD condition, if ADHD transition findings were not reported separately or if they referred to closed studies. Book chapters, editorials, comments or letters, congresses, reviews or published errata were excluded.

### Key Messages

- Our review may support the development of pragmatic consensual policy/statements for transition practice applicable to patients and health services from all stakeholders' perspectives.
- An effective transition programme for specific chronic diseases could contribute to reducing side events related to unplanned, not shared, and inappropriate programmes.
- Research on transition care to adult services is still limited. Future research should define and evaluate transition care programmes from adolescence into adulthood.

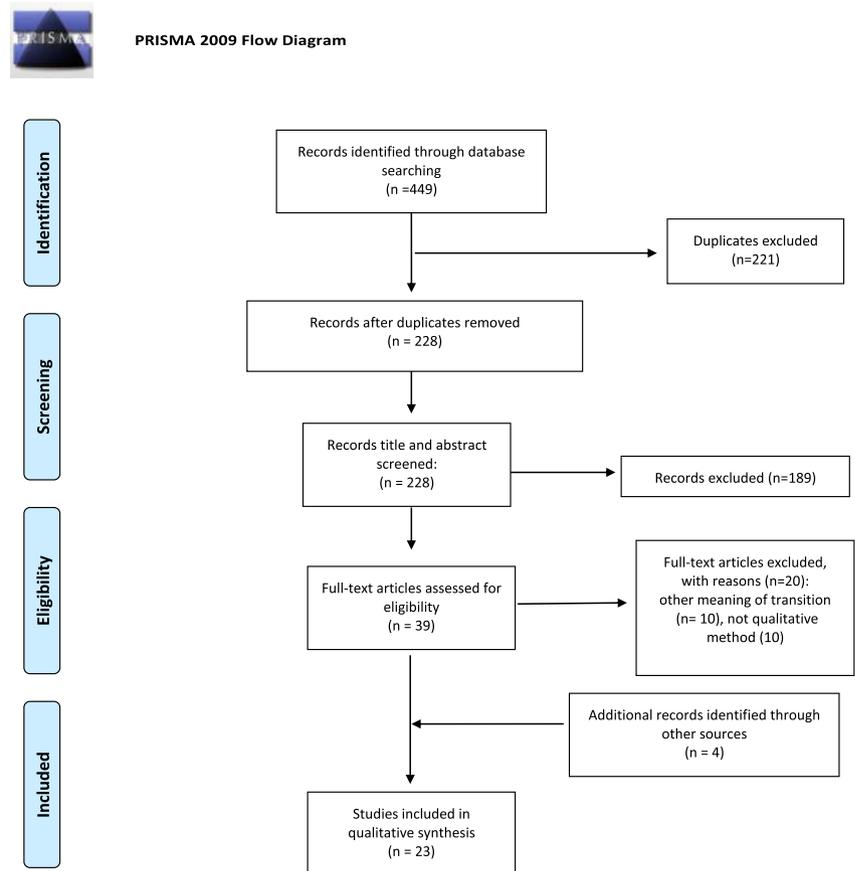
### 2.2 | Search strategy

The search was performed using the PubMed, Embase, PsycINFO and Web of Science databases, and all articles published up to 31 October 2021 were considered. For the present review, the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guidelines were followed (Figure 1) (Moher et al., 2015). The search strategy used, both, terms included in the title/abstract and in the subject headings, that is, Medical Subject Headings (MeSH) (Medline), Emtree (Embase) and thesaurus (PsycINFO). The search strategy used was ["transition\*" or "transfer\*" or "continuity of care" or "transition to adult care"] and ["attention deficit disorder with hyperactivity" or "ADHD"] and ["adolescent" or "young" or "young adult" or "youth\*"]. No date restrictions were applied. The titles and abstracts of each study were screened, and studies not pertinent to the target population or to transition within mental health services for patients with diagnosed ADHD were excluded. The full text of the remaining articles was obtained and evaluated by both authors independently to decide whether to include or exclude the studies. Disagreements on the eligibility of a study were resolved by discussion until consensus was reached. Moreover, a review of the references of the included studies was performed. Complete references were downloaded and stored using Reference Manager 2011.0.1 software (Thompson Research Soft, Carlsbad, CA, USA).

### 2.3 | Quality assessment

The quality of studies was assessed independently by the authors using the 'Quality assessment for the systematic review of qualitative evidence' checklist drawn directly from appendix D of Hawker et al. 2002 (Hawker et al., 2002). This tool contains nine questions, each of which can be answered with 'good', 'fair', 'poor' or 'very poor'. After applying the tool to the studies, it was converted into a numerical score by assigning points to the answers, from 1 point (*very poor*) to 4 points (*good*). This produced a score for each study, ranging from a minimum of 9 to a maximum of 36 points. To create the overall quality grades, we used the following definitions: high

**FIGURE 1** PRISMA flow diagram, from Moher et al. (2015). For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org). PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analysis



quality (A), 30–36 points; medium quality (B), 24–29 points; low quality (C), 9–24 points.

## 2.4 | Data analysis and synthesis

For each study, data concerning year, country, setting, population involved and data collection method were extracted following the methods used in one of our previous studies (Reale & Bonati, 2015). To summarize the findings, the results of all included studies were presented in tables according to three main aspects: experiences of the clinicians, experiences of the patients and experiences of the parents. Data were analysed in order to summarize findings and to provide an overview of the same results even if from different context, with the use of different methods and from different perspectives.

## 3 | RESULTS

### 3.1 | Search results

A total of 449 titles were retrieved: 237 in Pubmed, 81 in Embase, 46 in PsychInfo and 85 in Web of Science. A total of 221 studies were duplicates and were excluded. In all, 39 full-text articles were thus assessed for eligibility, and of these, 19 studies fit the selection

criteria. The references cited in the retrieved papers were checked to improve search outcomes and four additional, relevant publications were identified (Table 1). Data analysis and generalizability of the studies were the points of weakness for quality assessment (Appendix S1): 22 obtained a high score (A), and only 1 a medium score (B). The included studies were published in 20 journals, 4/23 on BMC Psychiatry, 2/23 on Child: Care, Health and Development and 2/23 on Early Intervention in Psychiatry. The studies were carried out between 1997 and 2019, and the papers published between 2000 and 2020. A total of 16 studies was performed in the United Kingdom, 3 in Ireland, 1 in Italy, 1 in USA, 1 in Turkey and 1 in Hong Kong. The participants in the studies were only clinicians in 11, only patients in 8, only parents in 1, both parents and patients in 2 and both parents and clinicians in 1 case. A total of 4705 participants (range 6–2186) was involved. Nine studies were conducted with the use of an interview, 9 with a questionnaire, 2 with both questionnaire and interview, and 3 were case note studies. The studies included youth aged 14–29 years, and most studies took place within the national mental health service. The majority of studies (12/23) were qualitative analyses performed as part of a larger project, such as the Catch Us (Children and Adolescents with ADHD in Transition between Children's and Adult Services), TRAMS (Transition to Adult Mental Health Services), iTRACK, TRACK (Transition from Child and Adolescent Mental Health Services to Adult Mental Health Services) and IMAGE projects (International Multi-centre ADHD Genetics).

TABLE 1 Study characteristics

Author	Country	Year of study	Project	Setting	Target population	Size of population	Data collection methods	Quality
Newlove-Delgado et al. (2019)	UK	Oct. 2017–Nov 2018	Catch Us	NMHS	C	14	I	B
Price, Newlove-Delgado, Eke, et al. (2019)	UK	2016–2017	Catch Us	NMHS	PT, P	64, 28	I	A
Eke, Janssens, et al. (2020)	UK	2016	Catch Us	NMHS	C	Baseline: 315 – Follow up: 247 Interview: 38	Q, I	A
Newlove-Delgado, Ford, Stein, and Garside (2018)	UK	Dec 2013–Sep 2015	Catch Us	NMHS	PT	7	I	A
Hall et al. (2015)	UK	May–Aug 2013	TRAMS	NMHS	C	37	Q	A
Hall et al. (2013)	UK	Aug–Dec 2012	TRAMS	NMHS	C	90	Q	A
Swift et al. (2013)	UK	Sep 2010–Sep 2011	TRAMS	Child and adolescent mental health service	PT	10	I	A
Tatlow-Golden et al. (2018)	Ireland	2010	iTRACK	NMHS	PT	20	CN	A
McNicholas et al. (2015)	Ireland	Jan–Dec 2010	iTRACK	NMHS	PT	19	CN	A
McNamara et al. (2014)	Ireland	2010	iTRACK	NMHS	C	57	I	A
Belling et al. (2014)	UK	2007–2008	TRACK	NMHS	C	34	I	A
Shanahan et al. (2021)	UK	Sep–Dec 2019	-	CHS	PT, P	6, 11	I	A
Heron et al. (2020)	USA	2016	-	HRSA, MCHB	P	2186	Q	A
Altın et al. (2016)	Turkey	May 2014	-	Institute of Psychiatry	C	124	Q	A
Cheung et al. (2015)	Hong Kong	Jun 2013–Jan 2014	-	Child and adolescent mental health service	PT	40	I	A
Eklund et al. (2016)	UK	Mar 2009–Jan 2013	IMAGE	Institute of Psychiatry	PT	91	Q, I	A
Reale et al. (2015)	Italy	2011	-	RAPC	C, P	27, 24	Q	A
Matheson et al. (2013)	UK	Dec 2010 Jun–2011	-	NMHS; ADDISS	PT	13	I	A
McCarthy et al. (2013)	UK	2010	-	NMHS	C	90	Q	A
Taylor et al. (2010)	UK	2007	-	Paediatric neurodevelopment service	PT	139	CN	A
Marcer et al. (2008)	UK	2007	-	Community paediatric services	C	78	Q	A
Edwin and McDonald (2007)	UK	May–Jun 2006	-	RCPsych	C	1030	Q	A
Keen et al. (2000)	UK	1997–1998	-	RCPsych, RCPCH	C	113	Q	A

Abbreviations: ADDIS, Attention Deficit Disorder Information and Support Service; C, clinicians; CHS, Community Healthcare Service; CN, case note; HRSA, Health Resources and Service Administration; I, interview; MCHB, Maternal and Child Health Bureau; NMHS, National Mental Health Service; P, parents; PT, patients; Q, questionnaire; RAPC, Regional ADHD Paediatric Centres; RCPCH, Royal College of Paediatrics and Child Health; RCPsych, Royal College of Psychiatrists.

### 3.2 | Clinicians' experience: Barriers and suggestions

About 2000 clinicians (range 14–1030) from four different countries were enrolled in 12 studies, 8/12 using questionnaires, 3/12 using interviews, 1/12 using both questionnaires and interviews (Table 2). Of these, 244 were child psychiatrists, 1254 were psychiatrists, 42 were psychologists, 41 were other professionals (i.e., nurses and social workers), 339 were paediatricians and 104 were general practitioners. Most studies (10/12) reported the lack of knowledge about ADHD in all professional groups (Altin et al., 2016; Edwin & McDonald, 2007; Eke, Janssens, et al., 2020; Hall et al., 2013, 2015; Keen et al., 2000; Marcer et al., 2008; McCarthy et al., 2013; Newlove-Delgado et al., 2019; Reale et al., 2015). In particular, psychiatrists felt ill-prepared to treat ADHD patients (Altin et al., 2016; Edwin & McDonald, 2007; Hall et al., 2015). More than half of the studies (7/12) reported scant coordination between services (Altin et al., 2016; Eke, Janssens, et al., 2020; Hall et al., 2013; McCarthy

et al., 2013; McNamara et al., 2014; Newlove-Delgado et al., 2019; Reale et al., 2015) and no transition protocols or formal policies (Eke, Janssens, et al., 2020; Hall et al., 2013, 2015; Keen et al., 2000; McCarthy et al., 2013; McNamara et al., 2014; Reale et al., 2015). Most psychiatrists (85%) had no information about clinical history of referred patients (Altin et al., 2016), and only 300/1030 consultant psychiatrists had been informed about the transfer of their child patients to adult services (Edwin & McDonald, 2007). Almost half of the studies (5/12) reported difficulties in identifying specific and available adult services (Belling et al., 2014; Keen et al., 2000; Marcer et al., 2008; Newlove-Delgado et al., 2019; Reale et al., 2015), scarce resources and high workload (Belling et al., 2014; Edwin & McDonald, 2007; Eke, Janssens, et al., 2020; Hall et al., 2013, 2015; Marcer et al., 2008). Cultural differences were reported in 2/12 studies (Belling et al., 2014; Eke, Janssens, et al., 2020). Concerning GPs, they reported low self-confidence and scarce information about patients' medical histories, impacting the risk and responsibility in prescribing medication (Newlove-Delgado et al., 2019). The pharmacological

**TABLE 2** Characteristics of studies involving physicians

References	Group of participants	Sample size	Data collection methods	Barriers (n = number of studies)	Suggestions
McNamara et al. (2014)	PS-C PS-A	32 25	I	<ol style="list-style-type: none"> <li>Lack of knowledge about ADHD (n = 10)</li> <li>No coordination between services (n = 7)</li> <li>No transition protocols and formal policies (n = 7)</li> <li>Service availability (n = 5)</li> <li>Access to services (n = 5)</li> <li>Workload and poor resources (n = 5)</li> <li>Cultural differences between services (n = 2)</li> <li>Risk and responsibility about prescribing medication (n = 1)</li> </ol>	<ol style="list-style-type: none"> <li>Joint working (n = 10)</li> <li>Investments in mental health (n = 8)</li> <li>Specialist ADHD adult service (n = 8)</li> <li>Sharing transition protocols (n = 8)</li> <li>ADHD specific training (n = 7)</li> <li>Mapping services (n = 4)</li> <li>Access continuity to drug therapy (n = 1)</li> <li>Primary care involvement (GP/PD) (n = 3)</li> </ol>
Belling et al. (2014)	PS-C PS-A PSY O	4 2 2 22	I		
Hall et al. (2013)	PS-C PS-A PSY O PD	25 22 6 15 22	Q		
Eke, Janssens, et al. (2020)	PS-C PD PS-C PS-A O PD	113 202 3 16 4 15	Q; I		
Reale et al. (2015)	PS-C	27	Q		
Keen et al. (2000)	PS-C PSY PD	43 33 37	Q		
Altin et al. (2016)	PS-A	124	Q		
Hall et al. (2015)	PS-A PSY	35 1	Q		
Edwin and McDonald (2007)	PS-A	1030	Q		
Marcer et al. (2008)	PD	78	Q		
Newlove-Delgado et al. (2019)	GP	14	I		
McCarthy et al. (2013)	GP	90	Q		

Abbreviations: CN, case note; GP, general practitioners; I, interview; O, others; PD, paediatricians; PSY, psychologists; PS-A, adult psychiatrists; PS-C, child psychiatrists; Q, questionnaire.

treatment was rarely discussed and provided under a shared care protocol with the previous physician (McCarthy et al., 2013). The suggestions most commonly reported (10/12) were the urgency of increasing joint working between services, and preparing transition in advance, with a period of parallel care (Altin et al., 2016; Edwin & McDonald, 2007; Eke, Janssens, et al., 2020; Hall et al., 2013, 2015; Keen et al., 2000; Marcer et al., 2008; McCarthy et al., 2013; Newlove-Delgado et al., 2019; Reale et al., 2015), followed by more investments in mental health care, with the creation of specialist ADHD adult services (8/12) for both medication and psychological treatment in order to provide adequate support (Belling et al., 2014; Edwin & McDonald, 2007; Eke, Janssens, et al., 2020; Hall et al., 2013, 2015; Keen et al., 2000; McCarthy et al., 2013; Newlove-Delgado et al., 2019), and sharing transition protocols (8/12) developing a formal policy (Belling et al., 2014; Eke, Janssens, et al., 2020; Hall et al., 2013, 2015; Keen et al., 2000; Marcer et al., 2008; McNamara et al., 2014; Reale et al., 2015). Introducing ADHD specific training for clinicians (Altin et al., 2016; Hall et al., 2015; Keen et al., 2000; Marcer et al., 2008; McCarthy et al., 2013; McNamara et al., 2014; Newlove-Delgado et al., 2019), in particular, for adult psychiatrists and GPs, were reported in 7 studies. The introduction of a website mapping service system was suggested in 4/12 studies to better identify the appropriate place to refer patients (Belling et al., 2014; Edwin & McDonald, 2007; Hall et al., 2013; Reale

et al., 2015). Only one study reported the need to have access to drug therapies (Reale et al., 2015). GPs and paediatricians requested to be more involved in the transition care and to increase collaboration and communication with secondary care (Hall et al., 2013; McCarthy et al., 2013; Newlove-Delgado et al., 2019).

### 3.3 | Patients' experience: Barriers and suggestions

More than 400 patients (range 6–139) from three different countries were enrolled in 10 studies, 6/10 using interviews, 1/10 using both interviews and questionnaires and 3/10 analysing their case notes. The age range of patients was between 14 and 29 years, and they enrolled at different stages of transition: 45 before transition, 247 during transition and 17 after transition, while 79 had been discharged from services and 21 had been disengaged and then had been re-inserted in adult services. (Table 3). Data from three case notes studies including responses of 178 patients (McNicholas et al., 2015; Tatlow-Golden et al., 2018; Taylor et al., 2010). Patients reported the same barriers of the clinicians; the most present default was the scant coordination and communication between services (8/10) (Cheung et al., 2015; Eklund et al., 2016; McNicholas et al., 2015;

**TABLE 3** Characteristics of studies involving patients

References	Group of participants	Sample size	Age range	Data collection methods	Barriers (n = number of studies)	Suggestions
Price, Newlove-Delgado, Eke, et al. (2019)	Pre	21	14–17	I	1. No coordination between services (n = 8) 2. Lack of knowledge about ADHD (n = 7) 3. Access to services (n = 7) 4. Lack of support (n = 7) 5. Lack of information about transition (n = 5) 6. Poor relationship with clinicians/GP (n = 5) 7. Cultural differences between services (n = 4)	1. Joint working (n = 8) 2. Parents involvement (n = 5) 3. Raise public awareness about ADHD (n = 5) 4. Increase age-threshold of child services (n = 4) 5. More patient-centred transition planning (n = 4) 6. Investment in mental health (n = 4) 7. Specialist ADHD adult service (n = 4) 8. Sharing transition protocols (n = 4) 9. ADHD specific training (n = 4) 10. More regular follow up (n = 3) 11. Primary care involvement (n = 2) 12. Access continuity to drug therapy (n = 1) 13. Service responsibility to provide care (n = 1)
	At	22	17–21			
	Re-entered	21	19–29			
Swift et al. (2013)	Pre	4	17–18	I		
	At	1				
	T	3				
	D	2				
Cheung et al. (2015)	Pre	20	16–17	I		
	At	20	18–23			
Eklund et al. (2016)	At	42	14–24	Q; I		
	T	8				
	D	41				
Newlove-Delgado, Ford, Stein, & Garside (2018)	At	2	17–18	I		
	T	5				
Shanahan et al. (2021)	At	6	18–25	I		
Matheson et al. (2013)	At	13	18–25	I		
Taylor et al. (2010)	At	128	14–19	CN		
	D	11				
Tatlow-Golden et al. (2018)	At	10		CN		
	D	10				
McNicholas et al. (2015)	At	3	17–19	CN		
	T	1				
	D	15				

Abbreviations: At, at transition; CN, case note; D, discharged from services; I, interview; Not, not transitioned (disengaged from child service for more than 1 year and then re-entered from adult service); Pre, pre transition; Q, questionnaire; T, transitioned.

Newlove-Delgado, Ford, Stein, & Garside, 2018; Price, Newlove-Delgado, Eke, et al., 2019; Swift et al., 2013; Tatlow-Golden et al., 2018; Taylor et al., 2010), followed by the lack of knowledge on ADHD (Cheung et al., 2015; Eklund et al., 2016; Matheson et al., 2013; Newlove-Delgado, Ford, Stein, & Garside, 2018; Price, Newlove-Delgado, Eke, et al., 2019; Shanahan et al., 2021; Swift et al., 2013), difficulties in accessing the services (Eklund et al., 2016; Matheson et al., 2013; McNicholas et al., 2015; Shanahan et al., 2021; Swift et al., 2013; Tatlow-Golden et al., 2018; Taylor et al., 2010) and lack of support (7/10) (Cheung et al., 2015; Eklund et al., 2016; Matheson et al., 2013; Newlove-Delgado, Ford, Stein, & Garside, 2018; Price, Newlove-Delgado, Eke, et al., 2019; Shanahan et al., 2021; Swift et al., 2013). In particular, adult services were hard to reach because of strict eligibility criteria to have access (i.e., age, symptoms severity and comorbidities), and many refused referral; more than a half of young patients refused by adult services remained in charge of child services or discharged from child services seeking help in private practice (Eklund et al., 2016; Tatlow-Golden et al., 2018). The lack of support made patients feeling less involved and abandoned. Half of the studies reported lack of knowledge about the transition process (Cheung et al., 2015; Eklund et al., 2016; Newlove-Delgado, Ford, Stein, & Garside, 2018; Price, Newlove-Delgado, Eke, et al., 2019; Shanahan et al., 2021; Swift et al., 2013) and a poor relationship with the clinician (e.g., spending 5 to 10 min asking routine questions), impeding the building-up of a relationship (Cheung et al., 2015; Eklund et al., 2016; Matheson et al., 2013; Newlove-Delgado, Ford, Stein, & Garside, 2018; Swift et al., 2013). In a few cases, child clinicians did not provide clear information about transition or introduce this theme with a brief conversation (Eklund et al., 2016), and patients perceiving them as not prepared and elicited patient disengagement from the service or the request for a new clinician. Patients who disengaged from child services for at least 1 year did not receive any information on how to re-enter the services as adults (Price, Newlove-Delgado, Eke, et al., 2019). Those who were discharged to the GPs reported communication problems due to the physicians' scepticism towards ADHD and low qualification in tailoring dosage and medication type, in coping with side effects, and in comprehensively answering patient doubts (Newlove-Delgado, Ford, Stein, & Garside, 2018). GPs were seen solely as medication prescription providers, with no opportunity to set up a good relationship (Matheson et al., 2013). Among half of the studies (4/10) reported large cultural differences between services (Eklund et al., 2016; Newlove-Delgado, Ford, Stein, & Garside, 2018; Price, Newlove-Delgado, Eke, et al., 2019; Swift et al., 2013).

The recommendation most suggested by patients (8/10) was the enhancement of joint working between services (Cheung et al., 2015; Eklund et al., 2016; McNicholas et al., 2015; Newlove-Delgado, Ford, Stein, & Garside, 2018; Price, Newlove-Delgado, Eke, et al., 2019; Swift et al., 2013; Tatlow-Golden et al., 2018; Taylor et al., 2010), in agreement with the clinicians' perspective. Half of the studies (5/10) reported the need for parental involvement, which is fundamental in delivering and translating medical information and in managing

administrative issues (i.e., making and getting to appointments and ordering prescriptions) (Price, Newlove-Delgado, Eke, et al., 2019) and raising clinicians' and teachers' awareness about ADHD with the use of psychoeducational materials, links, videos and websites as supportive tools (Cheung et al., 2015; Matheson et al., 2013; McNicholas et al., 2015; Tatlow-Golden et al., 2018).

Among half of the studies (4/10) suggested increasing the child service age threshold to 21 years (Eklund et al., 2016; Newlove-Delgado, Ford, Stein, & Garside, 2018; Tatlow-Golden et al., 2018; Taylor et al., 2010), and planning a more patient-centred transition process, with a pre-transition period, in which preparing them on what will happen (i.e., when and where the transition would take place), explaining the differences between services and providing a contact in the adult service, possibly introducing the child to the new clinician with a photograph or a written letter (Matheson et al., 2013; Newlove-Delgado, Ford, Stein, & Garside, 2018; Price, Newlove-Delgado, Eke, et al., 2019; Taylor et al., 2010). Once again in accordance with the clinicians, patients required more investments in mental health care (4/10), creating some specialist ADHD adult services, sharing transition protocols and introducing specific ADHD training for parents and teachers (Cheung et al., 2015; Eklund et al., 2016; Tatlow-Golden et al., 2018; Taylor et al., 2010). Providing more regular follow ups was suggested in order to monitor treatment and review medication dosage frequently (3/10) (Cheung et al., 2015; Matheson et al., 2013; Newlove-Delgado, Ford, Stein, & Garside, 2018). In line with GPs, patients suggested involving primary care in the process of transition (2/10) (Tatlow-Golden et al., 2018; Taylor et al., 2010). Having free access to drug therapy (Matheson et al., 2013) and increasing services responsibility in providing care continuity were less frequently reported (Swift et al., 2013).

### 3.4 | Parents' experience: Barriers and suggestions

Results from four studies examined the experiences of more than 2000 parents of ADHD patients in transition (range 11–2186) from three different countries using interviews (2/4) or questionnaires (Table 4).

All the studies (4/4) reported the lack of knowledge about ADHD and the transition process (Heron et al., 2020; Price, Newlove-Delgado, Eke, et al., 2019; Reale et al., 2015; Shanahan et al., 2021). In accordance with their children's views, most of parents (3/4) reported perceiving lack of support (Heron et al., 2020; Price, Newlove-Delgado, Eke, et al., 2019; Reale et al., 2015), and scant coordination between services (Price, Newlove-Delgado, Eke, et al., 2019; Reale et al., 2015; Shanahan et al., 2021) seeking help from private services, or choosing the service needed alone, on the basis of other parents' experiences. Lack of clear information about services available and the difficulties in accessing were reported in half of the studies (Heron et al., 2020; Reale et al., 2015). In order to optimize transition, parents suggested improving joint working between services (2/4) (Price, Newlove-Delgado, Eke, et al., 2019; Reale et al., 2015) and building a relationship with the clinician (2/4) who was asked to inform parents about the transition process

**TABLE 4** Characteristics of studies involving parents

References	Group of participants	Sample size	Data collection methods	Barriers (n = number of studies)	Suggestions
Reale et al. (2015)	P	24	Q	1. Lack of knowledge about ADHD (n = 4)	1. Joint working (n = 2)
Price, Newlove-Delgado, Eke, et al. (2019)	P PT	28 64	I	2. Lack of information about transition (n = 4)	2. Build a relationship with clinicians/GP (n = 2)
Heron et al. (2020)	P	2186	Q	3. Lack of support (n = 3)	3. Increase age-threshold of child services (n = 1)
Shanahan et al. (2021)	P PT	11 6	I	4. No coordination between services (n = 3)	4. More patient centred transition planning (n = 1)
				5. Service availability (n = 2)	5. Investment in mental health (n = 1)
				6. Access to services (n = 2)	6. Specialist ADHD adult service (n = 1)
					7. ADHD specific training (n = 1)
					8. Raise public awareness about ADHD (n = 1)
					9. Mapping services (n = 1)
					10. Access continuity to drug therapy (n = 1)
					11. Service responsibility to provide care (n = 1)

Abbreviations: CN, case note; I, interview; P, parents; PT, young patients; Q, questionnaire.

(Heron et al., 2020; Reale et al., 2015). Analogously to their children, parents requested more patient-centred transition planning, and increasing child service age-threshold to 21 years (Shanahan et al., 2021). In accordance with clinicians, parents also advocated more investments in mental health, with the creation of specialist ADHD adult services (Shanahan et al., 2021), and the introduction of ADHD specific training (Reale et al., 2015) both for them and for clinicians, in order to raise public awareness about ADHD (Reale et al., 2015). Parents suggested a mapping service system in order to identify those ADHD services available (Shanahan et al., 2021). Having free access to medication and psychological treatment (Reale et al., 2015), and increasing services' responsibility in providing continuity of care, were also reported (Reale et al., 2015). Seven common barriers were pointed out by the physicians, parents and patients as well as suggestions for overcoming them (Table 5). A detailed description of principle findings about barriers and suggestions reported by clinicians, patients and parents could be found in Supporting Information (Appendices S2–S3).

## 4 | DISCUSSION

The present update of the current literature, reporting the qualitative findings concerning clinicians', patients', and parents' experiences with ADHD transition, permitted the most frequent impediments associated with transition and commonly perceived suggestions to be defined.

The role of information seems to be the key component for an optimal transition for both clinicians and service users (Kooij et al., 2019; National Institute for Health and Care Excellence

[NICE], 2019). The clarity of information about transition is one of the priority; information should include clear indications about which adult service would be available, together with times and modalities of patient transfer (Price, Janssens, Woodley, et al., 2019). The lack of information together with scarce support, on the other hand, drives many young people to look for informal sources and promotes considerable anxiety, worrying and distress (Price, Newlove-Delgado, Eke, et al., 2019). As reported in our review, young patients frequently rely on their parents, who end up becoming 'the advocates of their child' (Shanahan et al., 2021). Our results should be interpreted taking into consideration some limitations. First, results are limited by the qualitative methodologies and instruments used to explore similar aims by studies. Second, the scarce generalizability of the results to a worldwide level due to the geographic location of the studies, which was limited mostly to Europe and a few non-European countries. Third, different perspectives are difficult to report in synthesis due to the wide range of instruments and study types, in particular, with case notes studies; comments left on an open question in a survey, or written by a clinician as a parts of case notes, compared with statements made in a semi-structured interview, are likely to be different. Nevertheless, this is the first review considering the common needs of a wide range of stakeholders' perspectives, that is, clinicians, parents and patients, in order to define a relevant, pragmatic consensual policy for transition practice. The results suggested some implications, such as the care gap between child and adult services could be solved by promoting a shared, structured and well-planned transitional pathway, scheduling meetings, monitoring the transfer process and evaluating the transition outcomes (dosReis et al., 2016; Moen et al., 2021; Reale et al., 2018). As reported in previous studies, transition care should be more patient oriented; adolescents should be guided in the

**TABLE 5** Common barriers identified and suggestions by clinicians, patients and parents

Barriers	Suggestions
Lack of knowledge about ADHD (onset, lifespan, implications)	Joint working between services (preparing transition in advance, improving communication, scheduling meetings or phone contacts, parallel care period)
Scant coordination between services (scant communication, no planned transition, no sharing transition protocols)	Involvement of all stakeholders (clinicians/patients/parents AND primary care)
Service available (lack of clarity about which services are available, how to reach, who to contact)	Accessing information about service available (website mapping services, links, telephone number)
Access to services (variability in child service cut off age, strict eligibility criteria, refused referral)	Sharing transition protocols and formal policies
Cultural differences between services (family-oriented VS individual-oriented)	Raising public awareness about ADHD (spreading psychoeducational materials, website, videos, books)
Workload and scarce resources (poor service structure, ill-equipped staff)	More investments in mental health (creating of a specialist adult ADHD services, ADHD specific trainings)
GP unprepared on ADHD (not involved in the process of transition, no self-confidence with ADHD, risk and responsibility in prescribing medication)	Access continuity to ADHD drug therapies

process of transition by the clinicians because they are not prepared to manage their chronic illness alone, in terms of taking medication or getting appointments (Schaefer et al., 2017). Previous studies have suggested the creation of a specific adolescent mental health service in order to reduce care gap in transition (Singh et al., 2017). The protracted transfer waiting times cause service discharge and/or medication interruption, with negative lifetime consequences such as symptom aggravation (Brinkman et al., 2012; Islam et al., 2016; Murphy et al., 2018). People who remain in the transition gap for a long time continue to suffer alone, seeking help in private care or requesting assistance in other parts of the health system, with significant costs for themselves and society (Bachmann et al., 2017; Libutzki et al., 2019; Maia et al., 2016; Price, Janssens, Dunn-Morua, et al., 2019). The large variation in medications prescribed between primary and secondary care, the scarce service utilization and the low medication adherence (Ames et al., 2021; Johansen et al., 2015) suggest that some patients may stop medications due to a change of services rather than to a decline in symptoms (Cortese, 2020; Eke, Ford, et al., 2020; Newlove-Delgado, Ford, Hamilton, et al., 2018).

A retrospective study found that slightly less than 20% of adult patients diagnosed during childhood and transferred to adult services were regularly followed up (Blasco-Fontecilla et al., 2012). A good relationship with the doctor is the first step to promoting care continuity (Davis et al., 2021). Clinicians' tenacity promoted optimal transitions, while clinicians' indifference led young patients to feel 'dumped' by the service (Swift et al., 2013). This specific difference in outcomes may be connected to the different cultural attitudes between child and adult services, with the first being more family-oriented and the second more focused exclusively on symptomatology. The findings of our review highlighted the importance of raising public awareness about ADHD, improving patient quality of care, promoting a standard pathway through different levels of care (Ford, 2020) and increasing investments in mental health care, as the creation of specialist ADHD adult services (Price, Ford, et al., 2020; Price, Janssens, et al., 2020; Singh et al., 2017) or transitional clinics (Verity & Coat, 2007). In Italy a national survey was launched (Zadra et al., 2020), but more is yet to be done in order to establish a consensus ADHD transition model.

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## CONFLICT OF INTEREST

The authors have no conflicts of interest relevant to this article to disclose.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available in the supporting information of this article.

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#### SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza  
(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)

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