

NEWSLETTER



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BIBLIOGRAFIA ADHD AGOSTO 2022

Acad Pediatr. 2022.

PEDIATRIC CAREGIVER VERSION OF THE SHARED DECISION MAKING PROCESS SCALE: VALIDITY AND RELIABILITY FOR ADHD TREATMENT DECISIONS.

Valentine KD, Lipstein EA, Vo H, et al.

Objective: Shared decision making (SDM) is recommended for common pediatric conditions; however, there are limited data on measures of SDM in pediatrics. This study adapted the SDM Process scale and examined validity and reliability of the scale for attention-deficit/hyperactivity disorder (ADHD) treatment decisions.

Methods: Cross-sectional survey of caregivers (n = 498) of children (aged 5-13) diagnosed with ADHD, who had made a decision about ADHD medication in the last 2 years. Surveys included the adapted SDM Process scale (scores range 0-4, higher scores indicate more SDM), decisional conflict, decision regret, and decision involvement. Validity was assessed by testing hypothesized relationships between these constructs. A subset of participants was surveyed a week later to assess retest reliability.

Results: Pediatric Caregiver version of the SDM Process scale (M = 2.8, SD = 1.05) showed no evidence of floor or ceiling effects. The scale was found to be acceptable (<1% missing data) and reliable (intraclass correlation coefficient = 0.74). Scores demonstrated convergent validity, as they were higher for those without decisional conflict than those with decisional conflict (2.93 vs 2.46, P <.001, d = 0.46), and higher for caregivers who stated they made the decision with the provider than those who made the decision themselves (3.0 vs 2.7; P =.003). Higher scores were related to less regret (r = 0.15, P <.001), though the magnitude of the relationship was small.

Conclusions: The adapted Pediatric Caregiver version of the SDM Process scale demonstrated acceptability, validity and reliability in the context of ADHD medication decisions made by caregivers of children 5-13. Scores indicate pediatricians generally involve caregivers in decision making about ADHD medication

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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.

Am J Intellect Dev Disabil. 2022 Jul;127:293-312.

THE QUALITY OF EVERYDAY EYE CONTACT IN WILLIAMS SYNDROME: INSIGHTS FROM CROSS-SYNDROME COMPARISONS.

Ridley E, Arnott B, Riby DM, et al.

Past research shows that individuals with Williams syndrome (WS) have heightened and prolonged eye contact. Using parent report measures, we examined not only the presence of eye contact but also its qualitative features. Study 1 included individuals with WS (n = 22, ages 6.0-36.3). Study 2 included children with different neurodevelopmental (ND) conditions (WS, autism spectrum condition, fragile X syndrome, attention-deficit/hyperactivity disorder) and children with neurotypical development (NT; n = 262, ages 4.0-17.11). Unusual eye contact features, including staring, were found in approximately half of the WS samples. However, other features such as brief glances were frequently found in WS and in all ND conditions, but not NT. Future research in ND conditions should focus on qualitative as well as quantitative features of eye contact

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Am J Obstet Gynecol. 2022.

LABOR EPIDURAL ANALGESIA AND SUBSEQUENT RISK OF OFFSPRING AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A CROSS-NATIONAL COHORT STUDY OF 4.5 MILLION INDIVIDUALS AND THEIR SIBLINGS.

Hegvik TA, et al.

Background: A recent study has suggested that labor epidural analgesia may be associated with increased rates of offspring autism spectrum disorder. Subsequent replication attempts have lacked sufficient power to confidently exclude the possibility of a small effect, and the causal nature of this association remains unknown.

Objective: This study aimed to investigate the extent to which exposure to labor epidural analgesia is associated with offspring autism spectrum disorder and attention-deficit/hyperactivity disorder following adjustments for unmeasured familial confounding.

Study Design: We identified 4,498,462 singletons and their parents using the Medical Birth Registers in Finland (cohorts born from 1987-2005), Norway (1999-2015), and Sweden (1987-2011) linked with population and patient registries. These cohorts were followed from birth until they either had the outcomes of interest, emigrated, died, or reached the end of the follow-up (at mean ages 13.6 16.8 years), whichever occurred first. Cox regression models were used to estimate country-specific associations between labor epidural analgesia recorded at birth and outcomes (eg, at least 1 secondary care diagnosis of autism spectrum disorder and attention-deficit/hyperactivity disorder or at least 1 dispensed prescription of medication used for the treatment of attention-deficit/hyperactivity disorder). The models were adjusted for sex, birth year, birth order, and unmeasured familial confounders via sibling comparisons. Pooled estimates across all the 3 countries were estimated using inverse variance weighted fixed-effects meta-analysis models.

Results: A total of 4,498,462 individuals (48.7% female) were included, 1,091,846 (24.3%) of which were exposed to labor epidural analgesia. Of these, 1.2% were diagnosed with autism spectrum disorder and 4.0% with attention-deficit/hyperactivity disorder. On the population level, pooled estimates showed that labor epidural analgesia was associated with increased risk of offspring autism spectrum disorder (adjusted hazard ratio, 1.12; 95% confidence interval, 1.10-1.14, absolute risks, 1.20% vs 1.07%) and attention-deficit/hyperactivity disorder (adjusted hazard ratio, 1.20; 95% confidence interval, 1.19-1.21; absolute risks, 3.95% vs 3.32%). However, when comparing full siblings who were differentially exposed to labor epidural analgesia, the associations were fully attenuated for both conditions with narrow confidence intervals (adjusted hazard ratio [autism spectrum disorder], 0.98; 95% confidence interval, 0.93-1.03; adjusted hazard ratio attention-deficit/hyperactivity disorder, 0.99; 95% confidence interval, 0.96-1.02).

Conclusion: In this large cross-national study, we found no support for the hypothesis that exposure to labor epidural analgesia causes either offspring autism spectrum disorder or attention-deficit/hyperactivity disorder

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Ann Med -Psychol. 2022.

INTEREST OF THE CONCEPT OF PSYCHOTIC EMERGENCES IN ADOLESCENCE: AROUND TWO CLINICAL SITUATIONS.

Meneveau M, Tandonnet L.

Objectives: Psychotic symptoms are common in the adolescent population and can occur even in those who have no underlying mental health disorders. For the practicing clinician, psychotic symptoms can represent a myriad of underlying pathologies that can be identified within a range of different circumstances. These include both organic (neurocognitive disorders, genetic disorders, brain lesions, etc.) and non-organic disorders (schizophrenia and bipolar). They can also represent non-pathological processes such as sensory deprivation. Regarding mental health, the positive symptoms of psychosis are associated with many disorders none of which are pathognomonic to any particular diagnosis. However, classically they are associated with the beginning of a schizophrenic disorder. Psychotic symptoms presenting during adolescence pose a unique diagnostic challenge. The emotional instability during this period proves to be an unsteady platform and the symptoms of psychosis are associated with a much broader differential diagnosis. Consequently, psychotic symptoms during this period can be misleading. Therefore, it remains very difficult to decide clinically between the onset of psychosis, an affective or thymic reaction, certain autistic spectrum disorders or the expression of neurocognitive particularities such as attention deficit disorder with or without hyperactivity. The objective of this article is to stress the difficulty of making a diagnosis in the adolescent population with regard to psychosis and to explore the concept of emergent psychosis applied to this age group. We have illustrated our propositions with two case reports.

Patients: The first patient is a 13-year-old teenager hospitalized for severe heteroaggressive behavior. We identified school bullying in his past medical history with a positive family history for ADHD. At first, he described having difficulties with his peers, moderate anxiety and a low-level mood. We observed hyperactivity and impulsivity in the service. The initial diagnosis suggested ADHD and social anxiety. Finally, without any clear positive symptomatology, the use of a screening scale (CAARMs) pointed out a disturbance in thought, which could correspond to a high risk of psychotic transition, which would require early treatment. The second patient is a 12-year-old teenager who presented with intense psychotic symptoms, suicidal tendencies and severe anxiety associated with a low-level mood. He described moments of experiencing a disassociation from reality, auditory hallucinations and interpretative delirious ideas. His mood seemed correlated to those psychotic symptoms. Our first hypothesis was a schizophrenic process. However, we found restricted interest and difficulties in social interaction. An ADOS-2 and an ADI suggested a high probability of autistic spectrum disorder. Finally, by effectively treating his anxiety, the patient showed great improvement with a dramatic reduction in the positive symptoms he had previously exhibited.

Discussion: In the first case report, we found no psychotic symptoms. The patient showed discrete symptoms of disorganization and discrete negative symptoms that suggested a very high risk of psychotic transition. In contrast, the second case report showed very severe positive symptoms. However, we did not find any disorganization or negative symptoms in his presentation. Finally, his anxiety seemed to exacerbate the psychotic symptoms in the context of autism.

Conclusions: The early detection of psychotic prodromes represents a major prognostic challenge in the functional disability that a low-grade psychotic process can generate. However, the appearance of the first positive symptoms does not presume an assured outcome. Thus, the notion of emergent psychosis in young adolescents has the advantage of not excluding the risks of future evolution towards a psychotic pathology, while keeping in mind other hypotheses

ANN CLIN PSYCHIATRY. 2022;34:1-2.

NONPHARMACOLOGIC OPTIONS FOR ADHD: ONLINE CME IMPROVES PSYCHIATRISTS' KNOWLEDGE AND CONFIDENCE.

Guevara N, Wright C, Chatterjee-Shin P.

BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD) is a heritable neurodevelopmental disorder, with onset predominantly in early childhood. Approximately 11% of children aged 4 to 17 years have a diagnosis of ADHD. (Treatment generally consists of age-appropriate stimulant medication for children as well as behavior therapy (CDC 2020b). In the past several years, new nonpharmacologic options for psychiatric disorders have become available, including digital therapeutic devices for ADHD. However, the

pace at which these new technologies are emerging makes it challenging for clinicians to remain abreast of the latest developments.

OBJECTIVES: This study examined whether online continuing medical education (CME) could improve the knowledge and confidence of psychiatrists regarding the available clinical data and evidence for nonpharmacologic therapeutic options in the management of ADHD.

METHODS: Psychiatrists participated in a 30-minute online video-based lecture presented by an expert faculty. Educational effect was assessed using a repeated-pair design with pre-/post-assessment. Three multiple choice questions assessed knowledge, and 1 question rated on a Likert-type scale assessed confidence. A paired samples t-test was conducted for significance testing on overall average number of correct responses and for confidence rating, and a McNemar's test was conducted at the learning objective level (5% significance level, $P < .05$). Cohen's d with correction for paired samples estimated the effect size of the education on number of correct responses (< 0.20 modest, 0.20 to 0.49 small, 0.59 to 0.79 moderate, ≥ 0.80 large). Data were collected from 11/24/2021 to 1/24/2022.

RESULTS: This analysis set consisted of responses from psychiatrists ($N=551$). Analysis demonstrated a significant improvement in knowledge ($P < .001$) and confidence related to understanding the role of nonpharmacologic interventions in ADHD management: 19% of psychiatrists significantly improved their knowledge related to how nonpharmacologic therapies function to impact ADHD symptoms ($P < .001$), showing a 31% relative increase in correct responses from pre- to post-CME (42% pre, 55% post). 34% of psychiatrists significantly improved their knowledge related to clinical data on the use of nonpharmacologic treatments for the management of ADHD symptoms ($P < .001$), showing a 30% relative increase in correct responses from pre- to post-CME (37% pre, 48% post). 83% of psychiatrists had a measurable increase in confidence ($P < .001$), resulting in 14% who were mostly or very confident in their knowledge of clinical data relating to the efficacy of digital and device-based treatment modalities for the management of ADHD (9% pre-CME).

CONCLUSIONS: This study demonstrated the success of online, video-based panel discussion CME on improving knowledge and confidence related to clinical data for nonpharmacologic interventions in the management of ADHD. These findings suggest the benefits of education that addresses clinicians' individual needs across the continuum of their professional development

ANN CLIN PSYCHIATRY. 2022;34:2.

STARS ADJUNCT TRIAL: EVIDENCE FOR THE EFFECTIVENESS OF A DIGITAL THERAPEUTIC AS ADJUNCT TO TREATMENT WITH MEDICATION IN PEDIATRIC ADHD.

Lisa P, Canadas E, Jina A.

BACKGROUND: Treatment of attention-deficit/ hyperactivity disorder (ADHD) includes pharmacologic and nonpharmacologic interventions, both of which have demonstrated short-term efficacy. While efficacious, there are limitations to both modalities of treatment. Due partly to these limitations, there has been considerable interest in additional approaches to augmenting ADHD management. Digital therapeutics may offer improved access, minimal adverse effects, and low potential for abuse while providing targeted treatment options for improving cognitive functions, such as attention. AKL-T01s the first and only FDA-approved nonpharmacologic prescription digital therapeutic delivered through a video game interface for the treatment of ADHD.

OBJECTIVE: The objective is to summarize the data from a clinical trial (Kollins et al 2021) in support of FDA clearance using AKL-T01 adjunctively in children currently taking stimulant medication for ADHD.

METHODS: The STARS-Adjunct Trial was a multicenter, 12-week, open-label study of AKLT01 in 206 children aged 8 to 14 years with a confirmed diagnosis of primarily inattentive or combined-type ADHD. The study included 2 cohorts: (1) patients currently treated with ADHD medication ($n=130$) and (2) patients not on any ADHD medication ($n=76$). Participants had an ADHD Impairment Rating Scale (IRS) score ≥ 3 at baseline, and both cohorts used AKL-T01 for approximately 25 minutes per day, 5 days per week, over two 4-week treatment periods separated by a 4-week treatment pause.

RESULTS: AKL-T01 significantly improved (lowered) ADHD-related impairment as measured by the IRS (clinician rated) after the first 4-week treatment in both cohorts ($P < .001$). Results show that effects persisted during a 4-week treatment pause and further improved with a second 4-week treatment period. A majority of parents and children indicated a perceived improvement in ability to pay attention after the trial. Most

common device-related adverse events were decreased frustration tolerance, headache, and irritability which ranged from mild to moderate. No serious adverse events were reported.

CONCLUSIONS: This study adds to and extends the clinical evidence base for AKL-T01, a video game-based treatment for improving attention in children aged 8 to 12 years with ADHD. Continued evaluation of the effects of AKL-T01 on other important aspects of functioning like academic and social functioning, health utilization, and health outcomes would continue to add to the evidence base that the effects observed in this and previous studies have substantial clinical and functional impact

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Aust New Zealand J Psychiatry. 2022.

PATTERNS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER MEDICINE USE IN THE ERA OF NEW NON-STIMULANT MEDICINES: A POPULATION-BASED STUDY AMONG AUSTRALIAN CHILDREN AND ADULTS (2013-2020).

Bruno C, Havard A, Gillies MB, et al.

Background and aims: New therapeutic options such as lisdexamfetamine and guanfacine have recently become available for the treatment of attention deficit hyperactivity disorder. We described contemporary patterns of attention deficit hyperactivity disorder medicine use among children, adolescents and adults in Australia.

Methods: This population-based study used dispensing data for a 10% random sample of Australian residents between July 2012 and December 2020. We estimated the annual prevalence and incidence of attention deficit hyperactivity disorder medicines, second-line guanfacine use and examined concurrent medicine use of both stimulants and non-stimulants. We followed incident users for up to 5 years and analysed treatment persistence using a novel proportion of people covered method. Analyses were stratified by attention deficit hyperactivity disorder medicine, sex and age group; young children (5 years), children (6-12 years), adolescents (13-17 years), young adults (18-24 years) and adults (25 years).

Results: We observed a twofold increase in the overall prevalence of attention deficit hyperactivity disorder medicine use between 2013 and 2020, from 4.9 to 9.7 per 1000 persons. Incident use also increased across all age groups and both sexes, with the most pronounced increases among adolescent females (from 1.4 to 5.3 per 1000 persons). Stimulant treatment persistence after 5 years was highest among those initiating treatment as young children (64%) and children (69%) and lowest among those initiating treatment in adolescence (19%). Concurrent use of stimulants and non-stimulants was more common among males and younger age groups. Most children (87%) initiating guanfacine had prior dispensings of attention deficit hyperactivity disorder medicines.

Conclusion: We observed increasing attention deficit hyperactivity disorder medicine use in Australia, especially among young females. Nevertheless, treatment rates remain lower than the estimated prevalence of attention deficit hyperactivity disorder across all subpopulations. Poor long-term treatment persistence in adolescence may warrant improved clinical monitoring of attention deficit hyperactivity disorder in patients transitioning from paediatric to adult care. Reassuringly, use of newly approved guanfacine appeared to be in accordance with guidelines among children

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Autism Res. 2022.

SENSORY PROCESSING IN 16P11.2 DELETION AND 16P11.2 DUPLICATION.

Smith H, Lane C, Al-Jawahiri R, et al.

Deletions and duplications at the chromosomal region of 16p11.2 have a broad range of phenotypic effects including increased likelihood of intellectual disability, autism, attention deficit hyperactivity disorder (ADHD), epilepsy, and language and motor delays. However, whether and how sensory processing is affected has not yet been considered in detail. Parents/caregivers of 38 children with a 16p11.2 deletion and 31 children with a 16p11.2 duplication completed the Sensory Behavior Questionnaire (SBQ) and the Child Sensory Profile 2 (CSP-2) along with other standardized questionnaires assessing autistic traits (SRS-2), ADHD traits (Conners 3), anxiety (SCAS-P) and adaptive behavior (VABS-3). SBQ and CSP-2 responses found that sensory processing differences were clearly evident in both 16p11.2 deletion and 16p11.2 duplication, though there was significant variation in both cohorts. SBQ data indicated the frequency and impact of sensory behavior were more severe when compared to neurotypical children, with levels being similar to autistic

children. CSP-2 data indicated over 70% of children displayed clear differences in sensory registration (missing sensory input). Seventy-one percent with 16p11.2 duplications were also unusually sensitive to sensory information and 57% with 16p11.2 duplications were unusually avoidant of sensory stimuli. This first detailed assessment of sensory processing, alongside other clinical features, in relatively large cohorts of children with a 16p11.2 deletion and 16p11.2 duplication demonstrates that sensory processing differences have a profound impact on their lives. Lay Summary: Responses to everyday sensory experiences in 38 16p11.2 deletion children and 31 16p11.2 duplication children were assessed. The frequency and impact of sensory behaviour differences was profound, though there was significant variation in both groups. Overall, sensory behaviour was found to be similar to autistic children. In both groups, over 70% failed to effectively register sensory information. 71% of 16p11.2 duplication children were very sensitive to sensory information and 57% of 16p11.2 duplication children were very avoidant of sensory stimuli

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Behav Ther. 2022.

MODIFIED COMPREHENSIVE BEHAVIORAL INTERVENTION FOR TICS: TREATING CHILDREN WITH TIC DISORDERS, CO-OCCURRING ADHD, AND PSYCHOSOCIAL IMPAIRMENT.

Greenberg E, Albright C, Hall M, et al.

Our objective was to evaluate the feasibility and acceptability, and preliminary efficacy of a modified comprehensive behavioral intervention for tics (MCBIT) therapy for youth with chronic tic disorders (CTDs), co-occurring attention-deficit hyperactivity disorder (ADHD), and associated psychosocial impairment. Seventeen youth ages 10-17 with CTD and co-occurring ADHD were randomly assigned to the MCBIT group (n = 9) or to a control group where they received traditional comprehensive behavioral intervention for tics (CBIT) therapy (n = 8). Both groups received ten 55-minute weekly treatment sessions, and two 55-minute biweekly relapse prevention sessions. Sixteen of the 17 participants completed the study, and acceptability ratings in both treatment groups were high with no significant differences in expectation of improvement. The MCBIT and CBIT groups in combination showed significant improvement in tic severity, ADHD symptom severity, and tic-related impairment. Group differences were not significant. The results indicate that MCBIT treatment is feasible and acceptable for youth with CTD and ADHD, and is similarly well tolerated relative to traditional CBIT. Results were not sufficiently superior to recommend MCBIT over CBIT for this population. However, given the demonstrated benefit of behavioral treatments that target co-occurring conditions concurrently, continuing to examine novel behavioral approaches that can target tics and related conditions simultaneously and successfully is recommended

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BMC Neurol. 2022;22.

KYNURENINE AND OXIDATIVE STRESS IN CHILDREN HAVING LEARNING DISORDER WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER: POSSIBLE ROLE AND INVOLVEMENT.

Kilany A, Nashaat NH, Zeidan HM, et al.

Background: The etiological and pathophysiological factors of learning disorder (LD) and attention deficit hyperactivity disorder (ADHD) are currently not well understood. These disorders disrupt some cognitive abilities. Identifying biomarkers for these disorders is a cornerstone to their proper management. Kynurenine (KYN) and oxidative stress markers have been reported to influence some cognitive abilities. Therefore, the aim was to measure the level of KYN and some oxidative stress indicators in children with LD with and without ADHD and to investigate their correlations with the abilities of children with LD.

Methods: The study included 154 participants who were divided into 3 groups: one for children who have LD (N = 69); another for children with LD and ADHD (N = 31); and a group for neurotypical (NT) children (N = 54). IQ testing, reading, writing, and other ability performance evaluation was performed for children with LD. Measuring plasma levels of KYN, malondialdehyde, glutathione peroxidase, and superoxide dismutase by enzyme-linked immunosorbent assay was performed for all participants.

Results: Some IQ measures and learning skills differed between the first two groups. The biochemical measures differed between children with LD (with and without ADHD) and NT children ($p < 0.001$). However, the biochemical measures did not show a significant statistical difference between the first two groups. KYN

and glutathione peroxidase levels were correlated with one-minute writing and at-risk quotient, respectively ($p = 0.03; 0.04$). KYN and malondialdehyde showed the highest sensitivity and specificity values.

Conclusion: These biochemical measures could be involved or have a role in the abilities performance of children with specific learning disorder

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BMC Psychiatry. 2022 Sep;22:596.

THE RELATIONSHIP MODEL AMONG PARENT-CHILD RELATIONSHIP, COPING RESPONSES AND BEHAVIORAL PROBLEMS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Taghizade S, Mahmoodi Z, Zandifar A, et al.

BACKGROUND: Attention Deficit Hyperactivity Disorder (ADHD) constitutes a prevalent behavioral problem. The present study examined the parent-child relationship model and investigated strategies to cope with behavioral problems in children with ADHD.

METHODS: This descriptive study selected 300 children with ADHD using convenience sampling. The data collected using the child behavior checklist, the parent-child relationship scale (PCRS), the Billings and Moos Coping Checklist, the socioeconomic status questionnaire, the general health questionnaire-28 (GHQ-28) and a demographic checklist were analyzed in SPSS-25 and LISREL 8.8.

RESULTS: According to the results of the path analysis on the relationship model among parent-child relationship domains, coping responses and children's behavioral problems, parent-child dependency domain ($B=0.22$) in the direct path, disease duration ($B=0.085$) in the indirect path, and conflicts in the domain of parent-child relationship ($B=0.366$) in both direct and indirect paths had the most positive causal effect on behavioral problems. Furthermore, intimacy in the said domain ($B=-0.42$) had the most negative causal effect in both direct and indirect paths. The extent to which parents used coping responses via the direct path had a positive causal effect on behavioral problems ($B=0.12$). Based on the path analysis test findings in the relationship model among positive parent-child relationship, coping responses and children's behavioral problems, the positive parent-child relationship score had the most negative causal effect via the direct path ($B=-0.56$). Conversely, the child's age had the highest positive causal effect via the indirect path ($B=0.1$) on behavioral problems in children.

CONCLUSION: Based on findings, there is a causal and significant relationship between the parent-child relationship and the extent to which coping responses are used. It is recommended that training programs be developed to strengthen communication skills, coping responses and problem-solving techniques in parents

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BMJ Open. 2022 Sep;12:e063874.

PREVALENCE OF NAIL BITING AND ITS CHRONOLOGICAL RELATIONSHIP WITH TICS IN CHILD AND ADOLESCENT OUTPATIENTS WITH TOURETTE SYNDROME: A SINGLE-CENTRE, RETROSPECTIVE OBSERVATIONAL STUDY.

Hsueh CW, Chen CW.

OBJECTIVE: To evaluate the prevalence of nail biting in child and adolescent outpatients at a single institution and the chronological relationship between nail biting and tics in patients with Tourette syndrome (TS) with or without attention-deficit hyperactivity disorder (ADHD).

DESIGN: Retrospective observational study.

SETTING: Teaching hospital in Taiwan.

PARTICIPANTS: All participants were aged 4-18 years, including 535 patients with TS, 230 patients with provisional tic disorder and 1460 patients without neurological or psychiatric disorders (controls).

OUTCOME MEASURES: Presence of nail biting, starting age for nail biting and starting age for motor and/or vocal tics. **RESULTS:** Nail biting was more commonly observed in patients with TS (56.6%) than in patients with provisional tic disorder (27.4%) or controls (15.0%), regardless of sex (all $p<0.020$). Nail biting was also more common in patients with TS with ADHD than in those without (75.0% vs 47.6%; $p<0.001$), but the starting age was significantly later in those with concomitant ADHD than without (5.3 vs 3.8 years; $p<0.001$). In patients with TS, the onset of nail biting occurred earlier than that of tics, regardless of ADHD status.

CONCLUSION: Nail biting was more prevalent and occurred earlier than tics in patients with TS, regardless of ADHD status, in the study population

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BMJ Open. 2022 Sep;12:e061626.

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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BMJ Paediatr Open. 2022 Jun;6.

PREDICTIVE VALIDITY OF THE INFANT TODDLER CHECKLIST IN PRIMARY CARE AT THE 18-MONTH VISIT AND DEVELOPMENTAL DIAGNOSIS AT 3-5 YEARS: A PROSPECTIVE COHORT STUDY.

Borkhoff CM, Atalla M, Bayoumi I, et al.

OBJECTIVE: There is international variation in recommendations regarding developmental screening and growing recognition of the low sensitivity of commonly used developmental screening tools. Our objective was to examine the predictive validity of the Infant Toddler Checklist (ITC) at 18 months to predict a developmental diagnosis at 3-5 years, in a primary care setting.

METHODS: We designed a prospective cohort study, recruiting in primary care in Toronto, Canada. Parents completed the ITC at the 18-month visit and reported developmental diagnosis at 3-5 years (developmental delay, autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), learning problem). We calculated screening test properties with 95% CIs. We used multivariable logistic regression analyses adjusted for important covariates.

RESULTS: In the final sample (n=488), mean age at screening was 18.5 (SD 1.1) months, and at follow-up was 46.6 (SD 10.0) months. At screening, 46 (9.4%) had a positive ITC. At follow-up, 26 (5.3%) had a developmental diagnosis, including: developmental delay (n=22), ASD (n=4), ADHD (n=1), learning problem (n=1); parents of two children each reported two diagnoses (total of 28 diagnoses). Of four children with a

diagnosis of ASD at follow-up, three had a positive ITC at 18 months. The ITC specificity (92%, 95% CI: 89% to 94%) and negative predictive value (96%, 95% CI: 95% to 97%) were high; false positive rate was low (8%, 95% CI: 6% to 11%); sensitivity was low (31%, 95% CI: 14% to 52%). There was a strong association between a positive ITC at 18 months and later developmental diagnosis (adjusted OR 4.48, 95% CI: 1.72 to 11.64; $p=0.002$).

CONCLUSION: The ITC had high specificity, high negative predictive value, low false positive rate, and identified children with later developmental delay and ASD. The ITC had low sensitivity, similar to other screening tools underscoring the importance of continuous developmental surveillance at all health supervision visits

Brain Behav. 2022.

ROLE OF SNAP-25 MNI I VARIANT IN IMPAIRED WORKING MEMORY AND BRAIN FUNCTIONS IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Fang D, Yang B, Wang P, et al.

Introduction: Attention deficit/hyperactivity disorder (ADHD) is a hereditary neurodevelopmental disorder characterized by working memory (WM) deficits. The MnlI variant (rs3746544) of the synaptosomal-associated protein 25 (SNAP-25) gene is associated with ADHD. In this study, we investigated the role and underlying mechanism of SNAP-25 MnlI variant in cognitive impairment and brain functions in boys with ADHD.

Method: We performed WM capacity tests using the fourth version of the Wechsler Intelligence Scale for Children (WISC-IV) and regional homogeneity (ReHo) analysis for the resting-state functional magnetic resonance imaging data of 56 boys with ADHD divided into two genotypic groups (TT homozygotes and G-allele carriers). Next, Spearman's rank correlation analysis between the obtained ReHo values and the WM index (WMI) calculated for each participant.

Results: Compared with G-allele carrier group, there were higher ReHo values for the left medial prefrontal cortex (mPFC) and higher WM capacity in TT homozygote group. Contrary to TT homozygote group, the WM capacity was negatively correlated with the peak ReHo value for the left mPFC in G-allele carrier group.

Conclusion: These findings suggest that SNAP-25 MnlI variant may underlie cognitive and brain function impairments in boys with ADHD, thus suggesting its potential as a new target for ADHD treatment

Brain Behav. 2022.

UNDERSTANDING THE ASSOCIATION BETWEEN ADVERSE CHILDHOOD EXPERIENCES AND SUBSEQUENT ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES.

Zhang N, Gao M, Yu J, et al.

Objectives: Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in childhood, which may be related to adverse childhood experiences (ACEs). Our study aims to explore the association between ACEs and subsequent ADHD, and analyze the potential moderators.

Methods: Literature search was conducted by a combined computer-assisted and manual method. Studies were included if they had reported the association between ACEs and subsequent ADHD. Overall estimates of odds ratios (ORs) were obtained using random-effects meta-analyses, meta-regressions and further stratified analyses were conducted to examine potential moderator variables.

Results: Totals of 70 studies involving nearly 4 million participants from among 6,452 unique articles were included. In the primary analyses, ACEs were found to be associated with subsequent ADHD (OR=1.68, 95% CI: 1.54-1.83), and the negative effects of different forms of ACEs for ADHD were nonequivalent. Such as lived in the stepfamily, been adopted or fostered, and experienced sexual abuse were more deleterious than others. It was found that individuals who had experienced multiple ACEs or who are female were more vulnerable to ADHD.

Conclusions: The findings provide critical evidence for understanding the association between ACEs and ADHD. ACEs could increase the susceptibility of ADHD, especially for individuals who ever experienced multiple ACEs and females

Brain Imaging Behav. 2022.

BEHAVIORAL AND BRAIN FUNCTIONAL CHARACTERISTICS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ANXIETY TRAIT.

Wu ZM, Wang P, Liu J, et al.

The current study aimed to explore the behavioral, daily-life executive functional, and brain functional connectivity patterns in children with attention-deficit/hyperactivity disorder (ADHD) and anxiety. A total of 246 children with non-comorbid ADHD and 91 healthy controls (HCs) participated in the current study, among whom 175 subjects went through resting-state functional magnetic resonance imaging (fMRI) scans. The ADHD participants were divided into two subgroups: ADHD with a high level of anxiety (ADHD + ANX) and ADHD with a low level of anxiety (ADHD-ANX). The Child Behavior Checklist (CBCL) and the Behavior Rating Inventory of Executive Function (BRIEF) were used to capture the behavioral and daily-life executive functional characteristics. Independent component analysis with dual regression models was applied to the fMRI data. All statistical models were estimated with age and sex as covariates. Compared with the ADHD-ANX group, the ADHD + ANX group showed more withdrawn, somatic, social, thought, attention, delinquent, and aggressive problems (all corrected $p < 0.05$). The ADHD + ANX group also displayed more impaired emotional control and working memory than the ADHD-ANX (all corrected $p < 0.05$). The ADHD-ANX group, but not the ADHD + ANX group, showed elevated functional connectivity within the default mode network compared with the HC group. The mean function connectivity within the default mode network significantly mediated the correlation between anxiety level and attention problems. In sum, anxiety in children with ADHD was associated with more social, emotional, and behavioral problems, more impaired daily-life executive function, and altered brain function. Our work provides important information on the heterogeneity of ADHD

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Brain Sciences. 2022;12.

AGE-RELATED VARIANCE IN PERFORMANCE VERSUS RATINGS OF ATTENTION AND IMPULSE REGULATION IN CHILDREN: IMPLICATIONS FOR THE ASSESSMENT OF ADHD.

Lyon RE, Rizeq J, Flora DB, et al.

Executive function task (EF) deficits are hypothesized to underlie difficulties with self-regulation. However, tasks assessing EF impairments have only been weakly correlated with rating scales that index self-regulation difficulties. A community sample of children and youth aged between 8 and 20 years old were assessed longitudinally. Growth curve analyses and correlations were conducted to better understand how these two types of measures relate to one another across development, as well as the impact of age-related variance. EF was assessed using the Stroop Task and Trail Making test and behavioral ratings of self-regulation were captured using the SWAN scale. EF task performance improved steeply until age 14-15, whereas the SWAN Scale showed small age-related decreases. EF task performance was moderately correlated with age among 8-13 year-olds and to a lesser extent among 14-20 year-olds. SWAN scores were not significantly related to age in either group. Correlations were similar in an ADHD at-risk subgroup. EF task performance and parent ratings of attention regulation have different developmental trajectories, which may partly explain why correlations are low to modest in these samples. In particular, age-related variance is an important methodological consideration with significant implications for the assessment of self-regulation in children and youth with ADHD

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Brain Sciences. 2022;12.

THE CONTRIBUTIONS OF COGNITIVE ABILITIES TO THE RELATIONSHIP BETWEEN ADHD SYMPTOMS AND ACADEMIC ACHIEVEMENT.

Tsantilas D, Ilie A, Waldon J, et al.

The main objective of this study was to examine whether increased levels of inattentive (INA) and hyperactive/impulsive (H/I) behaviours were associated with lower scores on standardized tests of achievement in basic reading, spelling, and math skills, after accounting for certain known background risk factors and cognitive processes. Clinical assessment data from a rigorously diagnosed, stimulant-medication-naïve sample of 354 elementary school-aged children experiencing academic difficulties and behavioural symptoms of inattention and/or hyperactivity/impulsivity were analyzed. Although higher scores

of INA were significantly associated with lower scores in reading, spelling, and math, these associations did not persist when cognitive variables were added to the models. H/I was associated with math achievement, along with cognitive and background variables. Overall, cognitive variables accounted for the majority of the variance across basic reading, spelling, and math skills. Additionally, the only background demographic variables associated with academic achievement were age and sex for spelling and math. This finding highlights the importance of looking beyond observable INA and H/I behaviours to determine the underlying factors influencing academic achievement. Accurate identification of deficits in specific academic skills and the underlying factors influencing achievement in these skills are essential components in determining appropriate recommendations and targeted interventions

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Brain Sciences. 2022;12.

THE IMPACT OF BILATERAL ANODAL TDCS OVER LEFT AND RIGHT DLPFC ON EXECUTIVE FUNCTIONS IN CHILDREN WITH ADHD.

Salehinejad MA, Vosough Y, Nejati V.

Transcranial direct current stimulation (tDCS) is increasingly used for therapeutic purposes in attention-deficit hyperactivity disorder (ADHD). The dorsolateral prefrontal cortex (DLPFC) is the most targeted region of tDCS studies in ADHD. There is limited knowledge and mixed results about the relevance of left or right DLPFCs in ADHD's cognitive deficits. No study so far has investigated the impact of the increased excitability of both left and right DLPFC with anodal tDCS on cognitive deficits in ADHD. Here, we explored the impact of online bilateral anodal left and right DLPFC tDCS on executive dysfunction in children with ADHD. Twenty-two children with ADHD (mean age \pm SD = 8.86 \pm 1.80) received bilateral anodal online tDCS over the left and right DLPFC (1.5 mA, 15 min) in two separate sessions in active and sham states. They underwent a battery of four neuropsychological tasks of executive functions during stimulation that measured working memory, cognitive flexibility, response inhibition, and executive control. Bilateral anodal left and right DLPFC tDCS did not improve performance on working memory, cognitive flexibility, and response inhibition. Executive control was, however, partially improved for those who received active tDCS first. The upregulation of bilateral DLPFC tDCS with anodal polarity does not improve executive dysfunction in children with ADHD. The unilateral modulation of DLPFC with anodal tDCS may be more beneficial to cognitive deficits in ADHD in light of previous works targeting only left and/or right DLPFC

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Brain Sciences. 2022;12.

A REVIEW OF CANADIAN DIAGNOSED ADHD PREVALENCE AND INCIDENCE ESTIMATES PUBLISHED IN THE PAST DECADE.

Espinete SD, Graziosi G, Toplak ME, et al.

(1) Background: ADHD is recognized as one of the most common neurodevelopmental disorders. The worldwide prevalence of ADHD is estimated at 5.3%; however, estimates vary as a function of a number of factors, including diagnostic methods, age, sex and geographical location. A review of studies is needed to clarify the epidemiology of ADHD in Canada.

(2) Methods: A search strategy was created in PubMed and adapted for MEDLINE and PsycINFO. Papers were included if they examined diagnosed ADHD prevalence and/or incidence rates in any region of Canada, age group and gender. A snowball technique was used to identify additional papers from reference lists, and experts in the field were consulted.

(3) Results: Ten papers included in this review reported on prevalence, and one reported on incidence. One study provided an overall prevalence estimate across provinces for adults of 2.9%, and one study provided an overall estimate across five provinces for children and youth of 8.6%. Across age groups (1 to 24 years), incidence estimates ranged from 0.4% to 1.2%, depending on province. Estimates varied by age, gender, province, region and time.

(4) Conclusions: The overall Canadian ADHD prevalence estimate is similar to worldwide estimates for adults. Most studies reported on prevalence rather than incidence. Differences in estimates across provinces may reflect the varying number of practitioners available to diagnose and prescribe medication for ADHD across provinces. To achieve a more comprehensive understanding of the epidemiology of ADHD in Canada,

a study is needed that includes all provinces and territories, and that considers estimates in relation to age, gender, ethnicity, geographical region, socioeconomic status and access to mental healthcare coverage. Incidence rates need further examination to be determined

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Brain Sciences. 2022;12.

SLEEP FOSTERS ODOR RECOGNITION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER BUT NOT IN TYPICALLY DEVELOPING CHILDREN.

Munz M, Wiesner CD, Vollersen-Krekieln M, et al.

Prior experience represents a prerequisite for memory consolidation across various memory systems. In the context of olfaction, sleep was found to enhance the consolidation of odors in adults but not in typically developing children (TDC), likely due to differences in pre-experience. Interestingly, unmedicated children with attention deficit hyperactivity disorder (ADHD), a neurodevelopmental condition related to dopamine dysfunction, showed lower perceptive thresholds for odors, potentially allowing for more odor experience compared to TDC. We investigated sleep-associated odor memory consolidation in ADHD. Twenty-eight children with ADHD and thirty age-matched TDC participated in an incidental odor recognition task. For the sleep groups (ADHD: n = 14, TDC: n = 15), the encoding of 10 target odorants took place in the evening, and the retention of odorants was tested with 10 target odorants and 10 distractor odorants the next morning. In the wake groups (ADHD: n = 14, TDC: n = 15), the time schedule was reversed. Odor memory consolidation was superior in the ADHD sleep group compared to the TDC sleep and the ADHD wake groups. Intensity and familiarity ratings during encoding were substantially higher in ADHD compared to TDC. Sleep-associated odor memory consolidation in ADHD is superior to TDC. Abundant pre-experience due to lower perceptive thresholds is suggested as a possible explanation. Olfaction might serve as a biomarker in ADHD

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Brain Sciences. 2022;12.

TOLERANCE TO STIMULANT MEDICATION FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER: LITERATURE REVIEW AND CASE REPORT.

Handelman K, Sumiya F.

Recommended treatment for attention deficit hyperactivity disorder (ADHD) includes stimulant medication. While these medicines are effective for most ADHD patients, benefits may wear off, suggesting tolerance. This paper reviews the published literature on tolerance to stimulant medication treatment for ADHD. As there are relatively few studies published, pivotal studies and ADHD treatment guidelines were also reviewed. Research demonstrates physiological changes related to continued stimulant usage in neurons and certain brain regions, suggesting a mechanism for tolerance development. One clinical study showed that 24.7% of patients developed tolerance to stimulants in the time of days to weeks; another showed 2.7% developed tolerance over 10 years. Long term follow-up studies demonstrate that medication response may lessen over longer durations of treatment in a high percentage of patients. Strategies to manage tolerance include switching stimulant medicines, drug holidays, or clinical reassessment. Three cases illustrate challenges with treating patients who develop tolerance to stimulant medication. The paucity of research and lack of guidance to clinicians may contribute to significant under recognition of tolerance to stimulant medication. Further research is required to define clinical tolerance for stimulants in ADHD and to provide guidance on identifying and managing tolerance in clinical practice

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Child Adolesc Ment Health. 2022.

SCHOOL CONNECTEDNESS MEDIATES THE ASSOCIATION OF SOCIAL FUNCTION WITH DEPRESSIVE SYMPTOMS IN TEENAGERS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Kappi A, Linares AM, Chung ML.

Background: Depressive symptoms commonly co-occur in teenagers with attention deficit hyperactivity disorder (ADHD), and poor social function is a known predictor of depressive symptoms. This study's purpose was to determine whether school connectedness mediates the association between social function and depressive symptoms in teenagers with ADHD.

Method: In this secondary analysis, we selected 313 (74%) of 425 teenagers with ADHD (male 72%, mean age = 15 years) who had completed data on depressive symptoms, social function, and school connectedness in the Fragile Families and Child Well-Being Study. The mediation effect of school connectedness was tested by multiple regression using SPSS PROCESS macro with 5000 bootstrap samples controlling covariates (teenagers' age, gender, and race, their relationship with primary caregivers, type of school teenager attends, time of living with primary caregivers, and primary caregivers' education).

Results: Social function predicted depressive symptoms (direct effect = 0.132, 95% CI = 0.218, 0.045). School connectedness mediated the relationship between social function and depressive symptoms (indirect effect = 0.084; 95% CI = 0.130, 0.045).

Conclusion: This study points to the importance of considering school factors in understanding depression symptoms in children with ADHD. Also, clinicians should consider asking teenagers about school-related factors such as school connectedness which is likely important in understanding the experience of depressive symptoms in this population. Identifying ways to help enhance school connectedness for young people with ADHD should be prioritized

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Child Care Pract. 2022;28:561-75.

RESILIENCE IN FAMILIES OF EARLY ADOLESCENTS WITH ADHD: IMPLICATIONS FOR PRACTICE.

McMenemy C, Nicholas D.

Although the families of adolescents with ADHD are at risk of various adverse outcomes, many experience resilience processes that support the adolescent and family members to thrive. This qualitative study explored the experience and perspectives of parents and caregivers of young adolescents in Canada with ADHD and professionals who support them regarding resilience-promoting factors. Participants identified a process of Journeying Together, which described the ways that families of young adolescents with ADHD face adversities like social stigma and limited ADHD-specific resources, navigating through them to experience positive outcomes and reinforce family relationships. The implications for social workers, mental health practitioners and other professionals who work with adolescents with ADHD and their families are discussed

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Child Neuropsychol. 2022.

ADHD AND ASD SYMPTOMS IN YOUNG MALES WITH FRAGILE X SYNDROME: ASSOCIATIONS WITH EARLY TRAJECTORIES OF INHIBITORY CONTROL.

Hunt E, Hogan A, Will EA, et al.

Inhibitory control (IC), the ability to suppress inappropriate responses, emerges late in the first year of life and improves across typical development, concurrent with brain maturation. The development of IC is critical to various social-emotional and behavioral functions, with IC difficulties being linked to numerous neurodevelopmental disorders, including attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD). Fragile X syndrome (FXS) is a single-gene disorder characterized by IC difficulties, and elevated rates of ADHD and ASD, making it a useful model for understanding the early development and consequences of IC. In this longitudinal study, we characterized IC trajectories across multiple time points between 16 and 71 months of age in young males with FXS (n = 79) relative to neurotypical (NT) controls (n=49). To explore the association between behavioral outcomes and IC, we identified a subsample of 50 children with longitudinal IC data and an outcome assessment for ADHD and ASD symptoms at age 5 (FXS: n = 26, NT: n = 24). Results indicated that, compared to their NT peers, young males with FXS exhibit differences in IC as early as 24 months, with group differences increasing through age 5. Additionally, we determined that lower IC levels at 24 months were associated with later ADHD symptoms and a decreasing slope in IC over time was associated with later ASD symptoms in male children with FXS. These findings help refine early developmental phenotypes of FXS and highlight IC as a potential target for early detection and intervention of ASD and ADHD symptoms in male children with FXS

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Child Youth Serv Rev. 2022 Sep;140:1-7.

TRAJECTORIES OF MENTAL HEALTH SERVICES FOR YOUTH IN FOSTER CARE WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Mowbray O, Probert K, Jaramillo J, et al.

Youth in foster care with Attention Deficit Hyperactivity Disorder (ADHD) often have significant needs for mental health services. The degree to which youth taking medication for ADHD use mental health services in relation to sibling co-placement and their level of need over time is unclear. To examine these issues, caregivers (N = 54) provided information on youth mental health service use across an 18-month study period. Results show that siblings living apart had a higher probability of mental health service use. For youth with higher CBCL scores, probability of mental health service use was both high and stable over time. However, youth with lower CBCL scores showed a decrease in probability of mental health service use over time. The sustained commitment to receipt of mental health services among youth with ADHD is something all behavioral health providers who work with foster care involved youth can benefit from, as well as the youth themselves.

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Chinese Traditional and Herbal Drugs. 2022;53:4447-64.

BAYESIAN NETWORK META-ANALYSIS OF CHINESE PATENT MEDICINES IN TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN.

Liu L, Zhou LA, Sun YL.

Objective The Bayesian network Meta-analysis method was used to compare the efficacy differences between Chinese patent medicines in the treatment of children with attention deficit hyperactivity disorder (ADHD).

Methods Randomized controlled trials on the treatment of children with ADHD with Chinese patent medicines were searched from PubMed, EMBase, Cochrane Library, China National Knowledge Infrastructure Database (CNKI), China Biology Medicine Database (CBM), Wanfang Database (Wanfang), and VIP Database (VIP) with the database establishment to July 1, 2021. The quality of the included literature was evaluated according to the strategy in the Cochrane systematic review manual, and the efficacy differences of different Chinese patent medicines was compared using Bayesian network Meta-analysis.

Results Finally, a total of 50 literatures were included, involving six kinds of Chinese patent medicines [Jingling Oral Liquid (静灵口服液), Xiaoer Zhili Syrup (小儿智力糖浆), Xiaoer Huanglong Granules (小儿黄龙颗粒), Duodongning Capsules (多动宁胶囊), Dimu Ningshen Oral Liquid (地牡宁神口服液), and Jiuwei Zhenxin Granules (九味镇心颗粒)], involving 4445 patients. The results of the network Meta-analysis showed that in terms of effective rate, Jingling Oral Liquid combined with western medicine, Jiuwei Zhenxin Granules combined with western medicine, Xiaoer Huanglong Granules, Xiaoer Huanglong Granules combined with western medicine, Xiaoer Zhili Syrup, and Xiaoer Zhili Syrup combined with western medicine were better than western medicine alone. The top three in terms of probability were Jiuwei Zhenxin Granules combined with western medicines, Xiaoer Huanglong Granules combined with western medicines, and Xiaoer Zhili Syrup combined with western medicines. In terms of Conners abbreviated symptom questionnaire (ASQ) score, Jingling Oral Liquid combined with western medicine was better than western medicine alone. The top three in terms of probability were Dimu Ningshen Oral Liquid combined with western medicine, Jingling Oral Liquid combined with western medicine, and Jiuwei Zhenxin Granules combined with western medicine. In terms of Conners symptom questionnaire score, the probability of each index ranked top three: hyperactivity index score was Xiaoer Huanglong Granules combined with western medicines, Xiaoer Zhili Syrup combined with western medicines, and Xiaoer Huanglong Granules; The hyperactivity impulse score was Xiaoer Zhili Syrup, Xiaoer Zhili Syrup combined with western medicines, and Duodongning Capsules combined with western medicines; The conduct problem score was Xiaoer Zhili Syrups combined with western medicines, Jingling Oral Liquid, and Duodongning Capsules combined with western medicines; The learning problem score was Duodongning Capsules combined with western medicines, Jingling Oral Liquid, and Xiaoer Zhili Syrup combined with western medicine; The physical and mental disability score, Jingling Oral Liquid, Xiaoer Zhili Syrup combined with western medicine, Duodongning Capsules combined with western medicine; The anxiety score was Duodongning Capsules combined with western medicine, Xiaoer

Zhili Syrup combined with western medicines, and Jingling Oral Liquid. In terms of safety, the six Chinese patent medicines had good safety, and did not increase the incidence of adverse reactions.

Conclusion Chinese patent medicine is effective in the treatment of children with ADHD. In terms of effective rate, Jiuwei Zhenxin Granules combined with western medicine, Xiaoer Huanglong Granules combined with western medicine, and Xiaoer Zhili Syrup combined with western medicine have better curative effects. Due to the low methodological quality of the included research, this result should be interpreted with caution, and the conclusion needs to be verified by more high-quality studies in the future

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Clin J Sport Med. 2022 Sep;32:e451-e456.

EXAMINATION OF NEAR POINT OF CONVERGENCE SCORES IN HIGH-SCHOOL ATHLETES: IMPLICATIONS FOR IDENTIFYING BINOCULAR VISION DYSFUNCTION AFTER CONCUSSION INJURY.

Del RG.

OBJECTIVE: To identify normative near point of convergence (NPC) data for healthy high-school-aged athletes (13-19 years old) and determine the percentage of individuals with NPC scores that fall outside the currently accepted clinical cutoff value of 5 cm. Another objective was to determine the relationship between sex, concussion history, and attention deficit disorder/attention deficit hyperactivity disorder (ADD/ADHD) with NPC scores, if any.

DESIGN: Case series.

SETTING: High-school sports medicine clinic.

PATIENTS OR PARTICIPANTS: Near point of convergence was assessed in 718 high-school student athletes (141 females and 577 males) with an average age of 15.96 ± 1.16 years.

INTERVENTIONS: None.

MAIN OUTCOME MEASURES: An accommodation convergence ruler was used to measure NPC. Near point of convergence scores were repeated a total of 3 times and the mean used for all statistical analyses.

RESULTS: The NPC scores for all participants averaged 3.58 cm, and the intraclass correlation coefficient for the 3 repeated measurements was 0.956. Approximately 20% of mean NPC scores were above the accepted upper limit of 5 cm. Although a statistically significant effect for sex was identified, the difference between them was considered clinically insignificant. No relationship between NPC and history of concussion or ADD/ADHD was identified.

CONCLUSIONS: Results indicate that in high-school-aged subjects, approximately 20% of individuals may have NPC values that fall outside the current critical cutoff value and may lead to incorrect diagnosis of ocular dysfunction. In addition, NPC does not seem to be affected by the history of concussion or a diagnosis of ADD/ADHD

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Clin EEG Neurosci. 2022.

A CLASS ACTIVATION MAP-BASED INTERPRETABLE TRANSFER LEARNING MODEL FOR AUTOMATED DETECTION OF ADHD FROM FMRI DATA.

Uyulan C, Erguzel TT, Turk O, et al.

Automatic detection of Attention Deficit Hyperactivity Disorder (ADHD) based on the functional Magnetic Resonance Imaging (fMRI) through Deep Learning (DL) is becoming a quite useful methodology due to the curse of-dimensionality problem of the data is solved. Also, this method proposes an invasive and robust solution to the variances in data acquisition and class distribution imbalances. In this paper, a transfer learning approach, specifically ResNet-50 type pre-trained 2D-Convolutional Neural Network (CNN) was used to automatically classify ADHD and healthy children. The results demonstrated that ResNet-50 architecture with 10-k cross-validation (CV) achieves an overall classification accuracy of 93.45%. The interpretation of the results was done via the Class Activation Map (CAM) analysis which showed that children with ADHD differed from controls in a wide range of brain areas including frontal, parietal and temporal lobes

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Cogn Neurodyn. 2022.

MULTISCALE ENTROPY OF ADHD CHILDREN DURING RESTING STATE CONDITION.

Angulo-Ruiz BY, Muñoz V, Rodríguez-Martínez EI, et al.

This present study aims to investigate neural mechanisms underlying ADHD compared to healthy children through the analysis of the complexity and the variability of the EEG brain signal using multiscale entropy (MSE), EEG signal standard deviation (SDs), as well as the mean, standard deviation (SDp) and coefficient of variation (CV) of absolute spectral power (PSD). For this purpose, a sample of children diagnosed with attention-deficit/hyperactivity disorder (ADHD) between 6 and 17 years old were selected based on the number of trials and diagnostic agreement, 32 for the open-eyes (OE) experimental condition and 25 children for the close-eyes (CE) experimental condition. Healthy control subjects were age- and gender-matched with the ADHD group. The MSE and SDs of resting-state EEG activity were calculated on 34 time scales using a coarse-grained procedure. In addition, the PSD was averaged in delta, theta, alpha, and beta frequency bands, and its mean, SDp, and CV were calculated. The results show that the MSE changes with age during development, increases as the number of scales increases and has a higher amplitude in controls than in ADHD. The absolute PSD results show CV differences between subjects in low and beta frequency bands, with higher variability values in the ADHD group. All these results suggest an increased EEG variability and reduced complexity in ADHD compared to controls

Cogn Neuropsychiatry. 2022.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER PERSISTENCE FROM CHILDHOOD INTO YOUNG ADULT AGE: A 10-YEAR LONGITUDINAL STUDY.

Skogli EW, Orm S, Fossum IN, et al.

Introduction: The aim of this study was to estimate ADHD persistence in a European clinical sample of children diagnosed with ADHD and followed prospectively for 10 years into young adulthood.

Methods: We assessed 85 children with ADHD at baseline (M age= 11.6, SD = 2.1, 54% male) and re-assessed 59 at 10-year follow-up (M age= 21.4, SD = 2.3, 54% male). ADHD symptoms at baseline were assessed with a semi-structured clinical interview (Kiddie-Schedule for Affective Disorders and Schizophrenia/Present and lifetime version) and parent rating scales (ADHD Rating Scale IV, Child Behavior Checklist). ADHD symptoms at 10-year follow-up were assessed with a semi-structured clinical interview (MINI-Plus) and self-report scales (ADHD Self-Report Scale version 1.1 screener, Adult Self Report). Functional impairment at 10-year follow-up was assessed with the Global Assessment of Functioning scale.

Results: At 10-year follow-up, 39% met ADHD symptom thresholds based on clinical evaluation using MINI-Plus or the ADHD Self-Report Scale version 1.1 screener or the Adult Self Report together with clinicians rating of functional impairment.

Conclusion: ADHD persistence rates in this European clinical sample match previous estimates and indicate that a significant proportion of those diagnosed with ADHD as children still exhibit clinical levels of ADHD symptoms in adulthood

Current Psychopharmacology. 2022;11:18-29.

RECENT ADVANCES OF ARTIFICIAL INTELLIGENCE TOOLS IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD).

Walvekar S, Thawkar B, Chintamaneni M, et al.

Attention deficit hyperactive disorder or ADHD is a common disorder among children, and if not identified early, it may affect the child's later life. Pharmacotherapy in ADHD has been linked to the emergence of other emotional disorders. Children who get pharmacological treatment are more likely to continue taking these medications until adulthood, increasing their risk of acquiring other psychological problems. As a result, the majority of ADHD patients are eventually prescribed numerous medicines to manage emotional difficulties as well. Thus, AI tools are seen to be a boon for ADHD patients and clinicians. There have been emerging approaches in using artificial intelligence tools to diagnose and treat ADHD in recent years. Different algorithms and medical devices are used for greater accuracy and precision. The various neural networks detect complex signals in the human brain and analyze them. As it is a neurodevelopmental disorder, AI

gives the best tools for proper diagnosis and treatment. Virtual and physical branches of AI are a great help to the patient. This review article focuses on the use of various AI models and tools that employ ADHD symptoms, MRI scans, and EEG signals, using electroencephalogram sensors to monitor brain activity, to help physicians better manage this prevalent neurodevelopmental disorder

Dev Med Child Neurol. 2022.

PRETERM POSTNATAL COMPLICATIONS AND RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Tso WWY, Ho FKW, Coghill D, et al.

Aims: To investigate the association between the risk of attention-deficit/hyperactivity disorder (ADHD) and preterm birth and determine how postnatal complications in children born preterm is associated with the risk of ADHD.

Method: This population-based cohort study used data from the Hong Kong electronic medical records. We followed 359 614 children (48% female; 6-17 years old, mean 11 years 7 months, SD 3 years 2 months) born in public hospitals in Hong Kong from 1st January 2004 to 31st December 2014 and collected medical records and demographic details for mothers and children until 11th November 2020.

Results: The risk of ADHD was 4.0% in children born at term and 5.1% in children born preterm. The odds ratio for ADHD was 2.08 (95% confidence interval [CI] 1.64-2.64) for children born extremely preterm, 1.64 (95% CI 1.46-1.85) for children born very preterm, and 1.15 (95% CI 1.08-1.23) for children born late preterm. Among preterm postnatal complications, only early respiratory disease, retinopathy of prematurity (ROP), and intraventricular haemorrhage were significant predictors of ADHD after controlling for preterm birth, other risk factors, and sociodemographic variables. The excess risk of ADHD among children born very preterm or late preterm could be partly explained by respiratory disease. ROP partially mediated the risk of ADHD in children born very preterm.

Interpretation: Children born preterm in all subcategories, from extremely preterm to late preterm, have increased risk of ADHD. Early respiratory infection partially mediates the risk of ADHD in children born preterm

Diabetologia. 2022;65:S68-S69.

MATERNAL DIABETES AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDHOOD.

Cesta CE, Man KKC, Kjerpeseth LJ, et al.

Background and aims: Recent studies suggest an increased risk of attention-deficit/hyperactivity disorder (ADHD) in the children born to mothers with diabetes mellitus during pregnancy, including pregestational diabetes (PGDM) and gestational diabetes mellitus (GDM). However, current evidence remains inconclusive. This study aims to assess the association between prenatal exposure to maternal diabetes mellitus (MDM) and the risk of ADHD in childhood.

Materials and methods: This is a multinational cohort study with linked mother-child pairs using healthcare databases from Asia (Hong Kong (HK), Taiwan) and Northern Europe (NorPreSS: Finland, Iceland, Norway, Sweden) including children born between 2001-2018 with follow-up through 2020 (subject to data availability). Cox proportional hazard regression models and propensity score fine stratification, including demographic, comorbidity, and comedication covariates, were used to calculate hazard ratios (HR) with a 95% confidence interval (CI) for each comparison.

Results: We included 4,554,325 million mother-child pairs (HK: 535,924; Taiwan: 887,120; NorPreSS: 3,131,281) in the analyses, of which 6.1% of children were prenatally exposed to MDM (71,232 to PGDM; 207,171 to GDM). A total of 158,154 children had ADHD (HK: 16,453; Taiwan: 85,471; NorPreSS: 56,230). Children born to mothers with MDM were at a higher risk of developing ADHD (HK: PS-weighted HR 1.18, 95%CI 1.11-1.26; Taiwan: 1.13, 1.09-1.18; NorPreSS: 1.22; 1.18-1.26). The elevated risk was present separately for PGDM (HK=1.20, 0.98-1.46; Taiwan=1.63, 1.45-1.83; NorPreSS=1.31, 1.24-1.38) and for GDM (HK=1.18, 1.10-1.25; Taiwan=1.11, 1.07-1.15; NorPreSS=1.17, 1.12-1.22). Study sized allowed for a sibling-matched GDM analysis, which showed no association between prenatal exposure to GDM and the risk of ADHD (HK: 1.00, 0.86-1.16; Taiwan: 0.96, 0.85-1.07).

Conclusion: Our findings suggest that children prenatally exposed to maternal diabetes in general, and specifically to PGDM and GDM, have an increased risk of ADHD in childhood. However, for at least GDM exposure the risk is largely due to unmeasured familial confounding. Further investigation will assess the role of pharmacological treatment of MDM during pregnancy and glycaemic control on the association between maternal diabetes and child ADHD

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Encephale. 2022 Sep;48 Suppl 1:S56-S60.

SHIATSU: A COMPLEMENTARY MEDICINE FOR THE RELIEF AND VERBALIZATION OF TRAUMA.

Zittoun C, Garbous W, Raffin H, et al.

OBJECTIVES: In child and adolescent psychiatry, symptoms such as aggressive behaviors directed against others or self, anxiety, impulsivity, oppositional behaviors, sleep disorders, and impairments in emotional regulation or social interaction can resist conventional therapies, particularly in children with autism spectrum disorder and/or intellectual disability, early childhood trauma, or attachment disorders. Among complementary medicine, yoga and mindfulness meditation, which are relatively well documented, provide interesting avenues especially for emotional control in adolescents or any individuals with oppositional behaviors, anxiety, impulsivity or hyperactivity in males with attention deficit/hyperactivity disorder. Less well known is shiatsu, a Japanese medicine based on traditional Chinese medicine using deep pressure on the paths of the acupuncture meridians. Clinical observations and rare studies on this topic were encouraging, especially for the treatment of sleep and conduct disorders, but there is a lack of empirical data. The objective of this study was to examine better the possible therapeutic effects of shiatsu in a clinical population of children treated in child and adolescent psychiatry.

METHODS: The present research, a qualitative descriptive and non-interventional study, was conducted on children treated in daycare hospital units and outpatient clinical settings. Shiatsu was administered, at least during 3 sessions, to children with autism spectrum disorder or other disorders according to ICD-11 criteria (such as conduct disorders with impulsivity or attention deficit). The evaluation was performed by two independent researchers (a child psychiatrist and a psychologist who were not the caregivers) based on a direct observation of children during the shiatsu sessions, combined with semi-structured non-inductive interviews with their parents, and data collected from focus groups conducted with the children's caregivers. A phenomenological interpretive analysis (IPA) approach with Nvivo coding software was used to analyze the data.

RESULTS: Based on semi-structured interviews with 13 parents cross-referenced with data from 2 focus groups and direct observations of 7 children during 2 full shiatsu sessions for each observation, the results show that shiatsu has positive effects on internal tension (a relief effect, notably on aggressive behaviors directed against others or self), sleep (including improvement of sleep quality), social interaction, attention, verbalization of affects and verbalization of traumatic memories of early childhood, as well as on the perception of bodily limits. As these children benefit from several treatments, it cannot be proved that the positive effects observed in this study are related specifically to shiatsu practice in a effect-cause relationship. Shiatsu may participate and facilitate the effects of other treatments. It is noteworthy that most of the children came willingly to the shiatsu sessions, ask their parents to repeat the shiatsu sessions at home, and indicate to the practitioner, from one session to the next, their elective body points where they wish to receive the application of shiatsu.

CONCLUSIONS: The findings suggest therapeutic benefits of shiatsu, especially on externalize violence with a relief of aggressive behavior directed against others or self (knowing, moreover, that internal tension, sleep disorders and non-verbalization of affects or traumatic memories, all improved by shiatsu, are also all risk factors for externalize violence). These results highlight, therefore, the need to develop a daily practice of shiatsu in child and adolescent psychiatry. Further research is required to clarify the effects of shiatsu and ascertain better its underlying mechanisms based on this exploratory pilot study

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Eur Child Adolesc Psychiatry. 2022.

TEMPERAMENTAL AND PSYCHOMOTOR PREDICTORS OF ADHD SYMPTOMS IN CHILDREN BORN AFTER A THREATENED PRETERM LABOUR: A 6-YEAR FOLLOW-UP STUDY.

Navalin P, Ghosn F, Ferrin M, et al.

Children born after threatened preterm labour (TPL), regardless of whether it ends in preterm birth, may represent an undescribed ADHD cluster. The aim of this cohort study is to identify early temperament and psychomotor manifestations and risk factors of TPL children who present ADHD symptoms. One hundred and seventeen mother-child pairs were followed from TPL diagnosis until the child's 6 years of life. TPL children were divided according to the prematurity status into three groups: full-term TPL (n = 26), late-preterm TPL (n = 53), and very-preterm TPL (n = 38). A non-TPL group (n = 50) served as control. Temperament and psychomotor development at age 6 months and ADHD symptoms at age 6 years were assessed. Perinatal and psychosocial factors were also recorded. All TPL groups showed higher severity of ADHD symptoms compared with non-TPL children (difference in means + 4.19 for the full-term group, + 3.64 for the late-preterm group, and + 4.99 for the very-preterm group, all ps < 0.021). Concretely, very-preterm and late-preterm TPL children showed higher restless/impulsive behaviours, whereas full-term TPL children showed higher emotional lability behaviours. Higher surgency/extraversion and delayed fine motor skills at age 6 months predicted ADHD symptoms at 6 years in TPL children. Male sex, maternal state anxiety symptoms at TPL diagnosis, low parental education, and past maternal experience of traumatic events predicted higher ADHD symptoms in TPL children. Therefore, TPL children may have a higher risk for developing ADHD symptoms, presenting a phenotype that depends on the prematurity status. Moreover, the specific combination of early manifestations and risk factors suggests that TPL children may conform an undescribed group at-risk of ADHD symptoms

Eur Child Adolesc Psychiatry. 2022.

FACIAL EMOTION RECOGNITION IN CHILDREN AND YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND IRRITABILITY.

Levy T, Dupuis A, Andrade BF, et al.

The ability to recognize emotions evident in people's faces contributes to social functioning and might be affected by ADHD and irritability. Given their high co-occurrence, we examined the relative contribution of ADHD and irritability to facial emotion recognition (FER). We hypothesized that irritability but not ADHD traits would predict increased likelihood of misrecognizing emotions as negative, and that FER performance would explain the association of ADHD and irritability traits with social skills. FER was measured using the Reading the Mind in the Eyes Test (RMET) in children (6-14 years old) referred for ADHD assessment (n = 304) and healthy controls (n = 128). ADHD, irritability, and social skills were measured using parent ratings. We used repeated measure logistics regression, comparing the effects across emotion valence of images (i.e., neutral/positive/negative). High irritability but not ADHD diagnosis predicted lower RMET accuracy. ADHD traits predicted lower RMET accuracy in younger but not older participants, whereas irritability predicted poorer accuracy at all ages. ADHD traits predicted lower RMET accuracy across all emotion valences, whereas irritability predicted increased probability of misrecognizing neutral and positive but not negative emotions. Irritability did not increase the probability for erroneously recognizing emotions as negative. ADHD and irritability traits fully explained the association between RMET and social skills. ADHD and irritability traits might impact the ability to identify emotions portrayed in faces. However, irritability traits appear to selectively impair recognition of neutral and positive but not negative emotions. ADHD and irritability are important when examining the link between FER and social difficulties

Europ J Spec Needs Educ. 2022.

Pharmacological treatment of children with ADHD: how educators persuade parents to use it.

Fleischmann A, Gavish B.

Educators are key in advising doctors and parents on whether to medicate pupils with attention deficit hyperactivity disorder (ADHD). Here, using a semi-structured in-depth interview and grounded theory, we ask how 138 Israeli teachers and headmasters perceive their role in parents decisions to medicate.

Generally, teachers refrain from persuading parents to use medication and some even talk them out of it. There is, however, a gradual escalation in educators attitudes towards persuading parents to medicate when educators consider the difficulties flowing from ADHD. When these difficulties find expression mainly in pupils achievements, persuasion is usually indirect, manifested in hints to parents about the need to medicate. When problematic if not violent behaviour manifests, stronger persuasive tactics are used, such as summoning parents to meetings and suspending pupils. Many educators do not regard these sanctions against parents who resist medicating their children as unfair pressure but do admit that they are meant to persuade parents to allow medication. Thus, Israeli educators send a bivalent message. The systemİÇÖs approach explicitly upholds parents right to decide on their own. The other voice is manifested in de facto policy, especially when the behaviour of the pupil with ADHD is improper

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Eur Neuropsychopharmacol. 2022;63:e4.

INTEGRATIVE MULTI-OMICS APPROACHES TO CHILDHOOD AGGRESSION AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Hagenbeek F, Hubers N, Van Dongen J, et al.

Childhood aggression and Attention-Deficit Hyperactivity Disorder (ADHD) are common and have a profound negative impact on children, their families, teachers, and their broader environment. Despite the high prevalence of these externalizing behaviors, there is considerable individual variation. As such, much research has been devoted to identifying biomarkers: measurable characteristics that can serve as individual indicators of the presence or absence of a trait or disorder. Biomarkers from multiple, integrated, omics types (e.g., genomics, or metabolomics) are hypothesized to result in better patient stratification for both diagnosis and treatment. Therefore, we explored genomic, epigenomic, and metabolomic data to identify potential multi-omics biomarkers for childhood aggression and ADHD and to investigate the connections among the different omics levels. We employed an integrated multi-omics approach comprising metabolomics, DNA methylation, and direct and indirect polygenic scores (PGSs) for childhood aggression, attention problems, and correlated traits in Dutch twins (Aggression: N = 645, age range: 6-13, %females = 49%; ADHD: N = 596, age range: 5-13, %females = 51%) and patients (Aggression: N = 142, age range: 6-13, %females = 28%; ADHD: N = 145, age range: 6-13, %females = 26%). We obtained aggression- or ADHD-associated omics traits for each omics level with sparse Partial Least Squares Discriminant Analysis (sPLS-DA) and then investigated the pairwise cross-omics correlations among the loading scores of the PLS components for the selected omics traits. Next, we employed integrative multi-omics analyses (multi-block sPLS-DA) to investigate patterns of high correlations among the loading scores of the PLS components for the selected omics traits for aggression and ADHD. The single-omics models selected 31 PGSs, 1614 DNA methylation probes, and 90 metabolites for childhood aggression and 17 PGSs, 486 CpGs, and 90 metabolites for ADHD. The average correlations across these omics PLS loading scores ranged from 0.18 to 0.28 for childhood aggression and from 0.23 to 0.29 for ADHD. For childhood aggression, the multi-omics model comprised 44 PGSs, 746 CpGs, and 90 metabolites and was summarized into 5 sets of correlation patterns with high correlations among the loading scores of the aggression-related omics traits. These patterns associate with traits that link the phenotype-associated omics traits to biological processes related to inflammation, carcinogens, aging, sex differentiation, IQ, and smoking. For ADHD, the multi-omics model selected 30 PGSs, 143 CpGs, and 90 metabolites and highlighted potential novel findings, including indirect genetic effects and CpGs of the STAP2 gene, while also confirming known associations with ADHD such as MAD1L1 and glucocorticoid exposure. Our study shows that considering interrelated omics layers within multi-omics designs can help unravel the complex biology underlying behavioral problems. Disclosure: Nothing to disclose

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Eur Neuropsychopharmacol. 2022;63:e307.

GENETIC ARCHITECTURE OF TREATMENT DISCONTINUATION IN CHILDREN AND ADULTS WITH ADHD.

Thirstrup J, Brikell I, Agerbo E, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is a childhood onset neurodevelopmental disorder that often persist into adulthood. Stimulant medications are the first-line recommended

pharmacotherapy for ADHD and have proven effective in reducing ADHD symptoms. Despite the high efficacy of stimulants, many patients discontinue stimulant treatment, with poor response or side effects being common reasons. However, the role of common variants in medication discontinuation is not yet well established and it is not known if the genetic architecture influencing discontinuation of medication treatment differs between children and adults with ADHD. We aim to characterize the genetic architecture of discontinuation of stimulant medication in 1) all ADHD cases (DISCall) 2) in children i.e., ADHD cases below 18 years of age at first prescription (DISCch), and 3) in adults i.e., ADHD cases above 18 years of age at first prescription (DISCad).

Methods: We analyzed GWAS data and prescription data in the Danish iPSYCH2015 cohort. Medication discontinuation cases were defined as ADHD cases initiating stimulant medication treatment and discontinued the treatment for a period longer than 180 days within two years of initiation. Controls were defined as ADHD cases initiating treatment without discontinuation. In total, 18,774 ADHD cases started stimulant treatment (13,839 DISCch and 4,935 DISCad) and 9,109 discontinued (5,759 DISCch and 3,340 DISCad). To evaluate the contribution of common variants to stimulant discontinuation, SNP heritabilities (h^2_{SNP}) were estimated and GWASs were performed.

Results: h^2_{SNP} for DISCall was 0.042 (se = 0.021, $P = 0.042$). For DISCch the h^2_{SNP} was 0.046 (se = 0.03, $P = 0.13$) and h^2_{SNP} for DISCad was 0.09 (se = 0.08, $P = 0.26$), and the two estimates were not significantly different from zero. The genetic correlation (r_g) between DISCch and DISCad was 0.47 (se = 0.6) and not significantly different from 1 ($P = 0.58$). No genome-wide significant loci were identified in any of the GWASs. There was no concordance between the most strongly associated loci ($P = 10^{-5}$) for DISCch and DISCad.

Discussion: We found that common genetic variants explain a small significant proportion of the risk for stimulant discontinuation in the full sample. The genetic correlation for medication discontinuation in children and adults indicated a partial overlap in the polygenic impact on discontinuation in the two groups. Additionally, our results indicated that the contribution from common variants might explain more of medication discontinuation in adults compared to children. It should be stressed that the potential differences between children and adults are not significant and could be driven by noise in the phenotype definition rather than differences in true underlying biological causes. The results need to be verified in larger studies.

Disclosure: Nothing to disclose

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Eur Neuropsychopharmacol. 2022;63:e61.

29. EPIGENOME-WIDE ASSOCIATION META-ANALYSIS OF ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Meijer M, Zayats T, Starnawska A, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder with a prevalence of 5% in children, but 65% of these children persistently meet diagnostic criteria in adulthood (aADHD). Both genetics and environmental adversities play a role in the onset, and possibly the persistence of ADHD. Epigenome-wide association studies (EWAS) provide us with the possibility to study DNA methylation (DNAm) as marker of the interplay between genome and environment. Robustly identified DNAm biomarkers for ADHD are still lacking, possibly due to small samples sizes, and phenotypical and methodological heterogeneities. To date, most EWAS of ADHD focused on children or ADHD symptoms. EWAS in adults with a clinical ADHD diagnosis are scarce. Furthermore, association studies do not necessarily reflect whether the epigenetic patterns observed are causal or consequential of the studied phenotype. Therefore, to identify DNAm patterns associated with aADHD, we designed the largest EWAS meta-analysis to date for well-defined aADHD case-control cohorts. On top of that, we build methylation risk scores (MRS) for aADHD both based on birth blood samples and samples taken during adulthood to gain more insights into the possible causes and consequences of DNAm in aADHD.

Methods: We collected data on aADHD in four cohorts from the International Multicenter persistent ADHD CollaboraTion (IMpACT; total N cases=1016; total N controls=992, mean age DNAm assessment=30 years), and iSPYCH (N cases=854; N controls=688). ADHD status was assessed according to DSM-IV criteria. Whole blood DNAm was measured with the Infinium-« MethylationEPIC BeadChip (Illumina, San Diego, CA, USA). To minimize heterogeneity, all samples were processed using the same centralized protocols and cases and controls were sex- and age-matched. Quality control and normalization of DNAm data in the individual cohorts was harmonized across the cohorts. Differential DNAm between participants

with aADHD and healthy controls was assessed per cohort with a linear regression model, covarying for age, sex, a smoking score based on DNAm data, principal components that reflected technical variation, and surrogate variables that reflected unmeasured variation in the data. Results of the EWAS performed in the individual IMpACT cohorts were meta-analyzed with an inverse variance weighted fixed effect model with METAL. Next, an EWAS for lifetime clinical ADHD diagnosis was performed in whole blood collected around birth in the iPSYCH cohort. Results of IMpACT and iPSYCH were also compared and meta-analyzed.

Results: Preliminary results of the IMpACT meta-analysis showed six λ -corrected significant differentially methylated regions to be associated with aADHD. These regions were located in CIDEB and LRB4R2, CORO1B, TNF, upstream of PLXNB1, SIT1, AX748309, and LINC02226 (corrected p-value range: 1.67×10^{-11} - 7.74×10^{-3}). Interestingly, these genes are involved in immune and semaphoring signaling, which have been linked ADHD (symptoms) in previous EWAS.

Discussion: In conclusion, most case-control designs for ADHD focused on childhood and adolescent ADHD, but little is known about DNAm in aADHD. Therefore, the first epigenome-wide significant associations resulting of the largest EWAS of aADHD with >2000 participants are a valuable addition to the research field. The demonstrated ability to screen the epigenome in aADHD opens a new perspective for our understanding of this disorder.

Disclosure: Nothing to disclose

Eur Neuropsychopharmacol. 2022;63:e58-e59.

26. GENOME-WIDE ANALYSES OF VOCABULARY SIZE IN INFANCY AND TODDLERHOOD: LINKS WITH ADHD AND COGNITIVE TRAITS.

Verhoef E, Allegrini A, Jansen P, et al.

Background: The number of words a child produces (expressive vocabulary) and/or understands (receptive vocabulary) are widely used measures to assess language development in infancy and toddlerhood. Our understanding of the underlying genetic architectures, including its links with later-life behavioural, cognitive and health measures, is, however, limited for these traits. Here, we performed a meta- genome-wide association study (meta-GWAS) of early expressive and receptive vocabulary (age: 15-38 months), based on 37,913 observations and 17,298 individuals, within the Early Genetics and Life Course Epidemiology (EAGLE) Consortium. We (i) investigated the multivariate genetic architecture underlying vocabulary size during infancy and toddlerhood, and (ii) characterised polygenic links with later-life cognitive, behavioural and health outcomes, including Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD).

Methods: We studied data on expressive and/or receptive vocabulary assessed using parent questionnaires in 15 to 38 month-old children of European descent from seven independent population-based or community-based cohorts. meta-GWAS was performed for early-phase expressive vocabulary (15-18 months, N=8,799), late-phase expressive vocabulary (24-38 months, N=16,615), late-phase receptive vocabulary (24-38 months, N=6,291), and combinations thereof. SNP-heritability (SNP-h²) and genetic correlations (rg) between vocabulary traits and cognition-related traits (mid-childhood/early-adulthood reading skills, intelligence across the lifespan, adult educational attainment), growth (infant/childhood head circumference), childhood behaviour (aggression, internalising symptoms), childhood-onset neurodevelopmental disorder (ADHD and ASD) and exposure to childhood maltreatment were estimated with high-definition likelihood. Multivariate genetic architectures were modelled with structural equation modelling (SEM) techniques (GenomicSEM, GRM-SEM).

Results: SNP-h² was modest for all vocabulary traits (early-phase expressive vocabulary: 0.24(SE=0.03), late-phase expressive vocabulary: 0.08(SE=0.01), late-phase receptive vocabulary: 0.20(SE=0.04)). Late-phase expressive vocabulary shared, to a large extent, genetic influences with both early-phase expressive (rg=0.69(SE=0.14)) and late-phase receptive vocabulary (rg=0.67(SE=0.16)). However, latter measures were genetically unrelated (rg=0.07(SE=0.10)), suggesting at least two distinct underlying genetic factors. Consistently, we observed different polygenic association patterns: larger early-phase expressive vocabulary size was genetically correlated to higher ADHD risk (rg=0.23(SE=0.08)) and more exposure to childhood maltreatment (rg=0.19(SE=0.07)), while larger late-phase receptive vocabulary size was genetically associated with less exposure to childhood maltreatment (rg=-0.33(SE=0.08)). Genetic links with cognitive

outcomes were positive, but detectable in toddlerhood only (e.g. larger late-phase expressive vocabulary and higher intelligence: $rg=0.32(SE=0.08)$).

Discussion: Our findings provide evidence for at least two different genetic factors that capture the genetic architecture underlying early vocabulary development and shape polygenic associations with several later-life outcomes, especially ADHD and cognitive traits. Disclosure: Nothing to disclose

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Front Public Health. 2022;10:876769.

USING IMPLEMENTATION MAPPING TO DEVELOP PROTOCOLS SUPPORTING THE IMPLEMENTATION OF A STATE POLICY ON SCREENING CHILDREN FOR ADVERSE CHILDHOOD EXPERIENCES IN A SYSTEM OF HEALTH CENTERS IN INLAND SOUTHERN CALIFORNIA.

Pèrez JM, et al.

Adverse Childhood Experiences (ACEs) are defined as traumatic events occurring before age 18, such as maltreatment, life-threatening accidents, harsh migration experiences, or violence. Screening for ACEs includes asking questions about an individual's early exposure to these types of events. ACEs screenings have potential value in identifying children exposed to chronic and significant stress that produces elevated cortisol levels (i.e., toxic stress), and its associated physical and mental health conditions, such as heart disease, diabetes, depression, asthma, ADHD, anxiety, and substance dependence. However, ACEs screenings are seldom used in primary care settings. The Surgeon General of California has addressed this care gap by introducing ACEs Aware, an ACEs screening fee-for-service healthcare policy signed into law by Gov. Gavin Newsom. Since January 2020, Medi-Cal, California's Medicaid health care program, has reimbursed primary care providers for using the Pediatric ACEs and Related Life-events Screener (PEARLS) tool to screen children and adults for ACEs during wellness visits. To achieve the goals set by the ACEs Aware state policy, it is essential to develop and test implementation strategies that are informed by the values, priorities, and resources of clinical settings, healthcare professionals, and end-users. To address this need, we partnered with a system of federally qualified health centers in Southern California on a pilot study to facilitate the implementation of ACEs screenings in five community-based clinics. The health centers had broad ideas for an implementation strategy, as well as best practices to improve adoption of screenings, such as focusing on staff training to improve clinic workflow. This knowledge was incorporated into the development of an implementation strategy template, used at the outset of this study. We used the Exploration, Preparation, Implementation and Sustainment (EPIS) framework to guide the study and inform a participatory planning process called Implementation Mapping. In this paper, we describe how Implementation Mapping was used to engage diverse stakeholders and guide them through a systematic process that resulted in the development of the implementation strategy. We also detail how the EPIS framework informed each Implementation Mapping Task and provide recommendations for developing implementation strategies using EPIS and Implementation Mapping in health-care settings

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Front Human Neurosci. 2022;16.

EVALUATING ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS IN CHILDREN AND ADOLESCENTS THROUGH TRACKED HEAD MOVEMENTS IN A VIRTUAL REALITY CLASSROOM: THE EFFECT OF SOCIAL CUES WITH DIFFERENT SENSORY MODALITIES.

Cho YJ, Yum JY, Kim K, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is clinically diagnosed; however, quantitative analysis to statistically analyze the symptom severity of children with ADHD via the measurement of head movement is still in progress. Studies focusing on the cues that may influence the attention of children with ADHD in classroom settings, where children spend a considerable amount of time, are relatively scarce. Virtual reality allows real-life simulation of classroom environments and thus provides an opportunity to test a range of theories in a naturalistic and controlled manner. The objective of this study was to investigate the correlation between participants head movements and their reports of inattention and hyperactivity, and to investigate how their head movements are affected by different social cues of different sensory modalities.

Methods: Thirty-seven children and adolescents with ($n = 20$) and without ($n = 17$) ADHD were recruited for this study. All participants were assessed for diagnoses, clinical symptoms, and self-reported symptoms. A

virtual reality-continuous performance test (VR-CPT) was conducted under four conditions: (1) control, (2) no-cue, (3) visual cue, and (4) visual/audio cue. A quantitative comparison of the participants head movements was conducted in three dimensions (pitch [head nods], yaw [head turns], and roll [lateral head inclinations]) using a head-mounted display (HMD) in a VR classroom environment. Task-irrelevant head movements were analyzed separately, considering the dimension of movement needed to perform the VR-CPT.

Results: The magnitude of head movement, especially task-irrelevant head movement, significantly correlated with the current standard of clinical assessment in the ADHD group. Regarding the four conditions, head movement showed changes according to the complexity of social cues in both the ADHD and healthy control (HC) groups.

Conclusion: Children and adolescents with ADHD showed decreasing task-irrelevant movements in the presence of social stimuli toward the intended orientation. As a proof-of-concept study, this study preliminarily identifies the potential of VR as a tool to understand and investigate the classroom behavior of children with ADHD in a controlled, systematic manner

Front Human Neurosci. 2022;16.

CLASSIFICATION OF DRUG-NAIVE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER FROM TYPICAL DEVELOPMENT CONTROLS USING RESTING-STATE FMRI AND GRAPH THEORETICAL APPROACH.

Rezaei M, Zare H, Hakimdavoodi H, et al.

Background and objectives: The study of brain functional connectivity alterations in children with Attention-Deficit/Hyperactivity Disorder (ADHD) has been the subject of considerable investigation, but the biological mechanisms underlying these changes remain poorly understood. Here, we aim to investigate the brain alterations in patients with ADHD and Typical Development (TD) children and accurately classify ADHD children from TD controls using the graph-theoretical measures obtained from resting-state fMRI (rs-fMRI).

Materials and methods: We investigated the performances of rs-fMRI data for classifying drug-naive children with ADHD from TD controls. Fifty six drug-naive ADHD children (average age 11.86 ± 2.21 years; 49 male) and 56 age matched TD controls (average age 11.51 ± 1.77 years, 44 male) were included in this study. The graph measures extracted from rs-fMRI functional connectivity were used as features. Extracted network-based features were fed to the RFE feature selection algorithm to select the most discriminating subset of features. We trained and tested Support Vector Machine (SVM), Random Forest (RF), and Gradient Boosting (GB) using Peking center data from ADHD-200 database to classify ADHD and TD children using discriminative features. In addition to the machine learning approach, the statistical analysis was conducted on graph measures to discover the differences in the brain network of patients with ADHD.

Results: An accuracy of 78.2% was achieved for classifying drug-naive children with ADHD from TD controls employing the optimal features and the GB classifier. We also performed a hub node analysis and found that the number of hubs in TD controls and ADHD children were 8 and 5, respectively, indicating that children with ADHD have disturbance of critical communication regions in their brain network. The findings of this study provide insight into the neurophysiological mechanisms underlying ADHD.

Conclusion: Pattern recognition and graph measures of the brain networks, based on the rs-fMRI data, can efficiently assist in the classification of ADHD children from TD controls

Frontiers in Neuroscience. 2022;16.

TWO NOVEL HETEROZYGOUS TRUNCATING VARIANTS IN NR4A2 IDENTIFIED IN PATIENTS WITH NEURODEVELOPMENTAL DISORDER AND BRIEF LITERATURE REVIEW.

Song X, Xu W, Xiao M, et al.

Pathogenic variants in the nuclear receptor superfamily 4 group A member 2 (NR4A2) cause an autosomal dominant neurodevelopmental disorder with or without seizures. Here, we described two patients presenting with developmental delay, language impairment, and attention-deficit hyperactivity disorder. Trio-based whole exome sequencing revealed two novel heterozygous variants, c.1541-2A > C and c.915C > A, in NR4A2. Both variants were identified as de novo and confirmed by Sanger sequencing. In vitro functional analyses were performed to assess their effects on expression of mRNA or protein. The canonical splicing

variant c.1541-2A > C caused aberrant splicing, leading to the retention of intron 7 and a truncated protein due to an early termination codon within intron 7 with decreased protein expression, while the variant c.915C > A was shown to result in a shorter protein with increased expression level unexpectedly. The clinical and genetic characteristics of the previously published patients were briefly reviewed for highlighting the potential link between mutations and phenotypes. Our research further confirms that NR4A2 is a disease-causing gene of neurodevelopmental disorders and suggests alterations in different domains of NR4A2 cause various severity of symptoms

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Frontiers in Neuroscience. 2022;16.

ABNORMAL PHYSIOLOGICAL RESPONSES TOWARD SENSORY STIMULUS ARE RELATED TO THE ATTENTION DEFICITS IN CHILDREN WITH SLUGGISH COGNITIVE TEMPO.

Yung TWK, Lai CYY, Chan CCH.

Previous studies have found that sluggish cognitive tempo (SCT) is often associated with difficulties in real-life functioning, such as social problems, emotional difficulties, and academic learning difficulties. However, the underlying mechanisms contributing to the SCT symptoms and its associated real-life difficulties have still not been clearly understood. A previous study has found that SCT symptoms were associated with hypoarousal and hyperarousal toward the sensory stimulus. However, it is still unclear whether such abnormal arousal regulation is related to sustained attention difficulties that have been found to be related to social difficulties and withdrawn behavior in children with SCT. In this study, arousal regulation deficit in SCT is examined by the physiological responses quantified by HRV and EEG in the sensory challenge paradigm. This study aimed to establish a linkage between arousal regulation reflected by HRV and EEG and attention difficulties in children with SCT. The results of this study showed that higher theta power in the auditory stimulation condition than in the resting condition was associated with higher omission errors in sustained attention tasks in the SCT group. It was also found that higher parasympathetic activities during sensory stimulation conditions were associated with higher commission errors in the SCT group. These results reflected that hypersensitivity toward stressful sensitivity toward a stressful sensory stimulus is associated with attention difficulties in children with SCT. This further supported the notion that SCT should be conceptualized as a condition characterized by multiple deficits in different biological systems, such as the cognitive system, the negative valence system, and the arousal regulatory system

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Frontiers in Pediatrics. 2022;10.

SLEEP DISTURBANCES AND SLEEP PATTERNS IN CHILDREN WITH TIC DISORDER: A CASE-CONTROL STUDY.

Mi Y, Zhao R, Sun X, et al.

Study objectives: To characterize sleep disturbances and sleep patterns in children with Tic disorder (TD), and explore their association with TD severity and types.

Methods: A case-control study was conducted in 271 children with TD recruited from a clinical setting and 271 non-TD children recruited from a primary school, matched by age (mean = 8.47 years, SD = 1.53 years) and gender (15.1% female). The Children's Sleep Habits Questionnaire (CSHQ) was used to assess sleep patterns and sleep disturbances. The TD types and severity were assessed with the Yale Global Tic Severity Scale (YGTSS).

Results: The TD children scored higher on CSHQ total score than non-TD group ($t = 29.50$, $p < 0.001$) and demonstrated severer global sleep disturbance. Compared to non-TD children, TD children presented with increased risks for global sleep disturbance (aOR: 1.95; 95% CI = 1.20-3.06), and most specific sleep disturbances, including bedtime resistance (aOR: 3.15; 95% CI = 1.96-5.06), sleep onset delay (aOR: 3.43; 95% CI = 1.58-7.46), sleep anxiety (aOR: 2.83; 95% CI = 1.83-4.38), parasomnias (aOR: 3.68; 95% CI = 2.02-6.62), night waking (aOR: 9.29; 95% CI = 2.64-32.65), sleep disordered breathing (aOR: 1.72; 95% CI = 1.03-2.90) and daytime sleepiness (aOR: 1.72; 95% CI = 1.09-2.74). Children with mild and moderate tics, Provisional Tic Disorder (PTD), Chronic Tic Disorder (CTD) and Tourette Syndrome (TS) presented with more global and more specific sleep disturbances. In addition, combined ADHD, etc.

Conclusion: Children with TD are major risks for increased sleep disturbances, especially for those with severe and chronic symptoms. Furthermore, comorbid ADHD increases risk in certain areas of sleep. These findings highlight the importance to consider sleep outcomes in the assessment and treatment for children with TD

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Front Psychiatry. 2022;13.

SELF-MANAGEMENT TRAINING VS. NEUROFEEDBACK INTERVENTIONS FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER: RESULTS OF A RANDOMIZED CONTROLLED TREATMENT STUDY.

Korfmacher AK, Hirsch O, Chavanon ML, et al.

Objectives: Neurofeedback (NF) and self-management training (SMT) may be viable treatment options for patients with attention deficit hyperactivity disorder (ADHD) if they alleviate core symptoms, enhance the patients self-concept and improve their quality of life (QoL). Aim of the current study is evaluating both interventions accordingly and to test whether specific improvements in core symptoms lead to more general improvements in self-concept and QoL.

Methods: In a psychotherapeutic outpatient clinic in Germany, a total of N = 139 children with ADHD were screened for eligibility, of which 111 fulfilled inclusion criteria and participated in the study in accordance with the CONSORT 2010 statement. These were randomly assigned to NF vs. SMT interventions. Changes from pre- to post-intervention in core ADHD symptoms relying on parent and teacher reports (CONNERS 3) and objective tests (Qb-Test) as well as self-concept (interview with the children) and QoL assessments (using the KINDL-R self-report) were compared between patients receiving NF or SMT.

Results: Significant improvements in ADHD symptoms were achieved similarly in both treatment groups, whilst QoL and self-concept improved after SMT only.

Conclusion: This treatment study provides further evidence that SMT and NF may reduce core symptoms, but SMT may also improve patients' self-concept and QoL and may thus in its current form be the favorable treatment option in naturalistic settings. However, several limitations of the current study implicate that further research is required before definitive conclusions and recommendations for clinical practice can be given. Clinical trial registration: [www.clinicaltrials.gov], identifier [NCT01879644]

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Front Psychiatry. 2022;13.

FACTORS INFLUENCING RESILIENCE OF PARENTS WITH CHILDREN WITH NEURODEVELOPMENTAL DISORDERS: THE ROLE OF STRUCTURAL LANGUAGE, SOCIAL COGNITION, AND SOCIAL SUPPORT.

Flores-Buils R, Andr s-Roqueta C.

Background: Resilience allows a more positive coping and improves parents' wellbeing when they face a difficult situation like having a child with a neurodevelopmental disorder (NDD). We aim to analyze the development of resilience in parents of children with different NDD (ASD, DLD and ADHD) with different levels of structural language and social cognition, as well as the social support available for their families, and compare it to children with typical development (TD).

Method: We analyzed the level of resilience of 156 parents, 73 with children with TD and 73 with three different NDD, taking into account variables such as age, structural language (receptive grammar) and social cognition (emotional understanding) of the children, and also the type of social support available to them.

Results: Children with DLD and ASD showed lower receptive grammar and emotional comprehension skills, although only parents of children with ASD obtained better resilience scores. Moreover, age of children and formal support variables predicted the resilience of the parents according to the type of NDD.

Discussion: The severity of social cognition and structural language difficulties of children with NDD and the fact of having support from professionals and family associations have a significant influence on the development of parental resilience

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Gait Posture. 2022;98:96-100.

FACTORS ASSOCIATED WITH TEXTING AND WALKING PERFORMANCE IN CHILDREN WITH ADHD: THE ROLE OF AGE, ENVIRONMENT, AND SYMPTOM SEVERITY.

Krasovsky T, Korytny T, Hamady H, et al.

Background: Children with ADHD show deficits in executive function, as well as motor symptoms such as difficulties in gross and fine motor skills and gait stability. Texting while walking is becoming increasingly common and is a significant health risk among people of all ages.

Research question: The objective of this work was to compare texting and walking performance between children with ADHD and controls and between two environments (indoors and outdoors), and evaluate the role of age and symptom severity in dual-task performance.

Methods: Nineteen children with ADHD and 30 healthy children walked across an indoors corridor and an outdoors street, with and without texting on a mobile phone. Walking and texting performance were measured using inertial measurement units and a custom-made mobile app.

Results: No between-group differences were found in texting or walking performance. Walking and texting were similar across environments. In both groups, older children had smaller dual-task performance deficits for both gait and texting speed. Children with ADHD who had more severe symptoms of hyperactivity had larger dual task costs for gait speed outdoors ($r = 0.69$, $p = 0.002$), and those with more motor symptoms typed faster under dual-task conditions indoors ($r = 0.6$, $p = 0.007$) but were less accurate ($r = 0.60$, $p = 0.009$).

Significance: Children with ADHD do not demonstrate deficits in dual-task performance of a texting and walking task indoors or outdoors. The relationship of age, hyperactivity and motor symptoms with texting and walking performance supports a more personalized approach for examination of dual-task performance in children with ADHD

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Haemophilia. 2022.

SCREENING FOR INATTENTION, HYPERACTIVITY AND IMPULSIVITY IN CHILDREN WITH HAEMOPHILIA: A QUALITY IMPROVEMENT INTERVENTION.

Boggs JE, Pullen A, Molnar AE, et al.

Introduction: Children with haemophilia have been reported with increased rates of inattention (IN) and hyperactivity/impulsivity (HI) and, therefore, are particularly vulnerable to poor social and academic outcomes. Aim: To examine the benefit of utilizing a formal screening process for IN/HI in children with haemophilia during comprehensive clinic visits using a quality improvement approach.

Methods: At a single haemophilia treatment centre, screening for psychosocial issues was expanded and formalised to include (1) the Conners 3rd Edition (Conners3) screening tool for IN/HI symptoms administered during the standard psychosocial assessment (SPA) by the social worker and school advocacy coordinator, (2) formal pathways to diagnosis and intervention as indicated including psychology consultation, psychological testing, or referral to community-based mental health professionals, and in-person advocacy assistance in the patient's community school.

Results: Forty-four patients, age 9.9-á-l-á4.8 years (range 3ΓÇô16) were targeted. The initial screening approach was modified to improve the communication with caretakers during assessments and streamline diagnostic pathways if no, moderate or significant behavioural concerns were identified. Eleven patients had pre-existing mental health diagnoses. Thirteen of the remaining 33 patients (39.4%) received a new mental health diagnosis, ADHD in 8/33 (24.2%). Of the total cohort, 54.5% were found to have a mental health diagnosis. The rate of ADHD (29.5%) was significantly higher than reported in the general population.

Conclusion: The described process, developed through a QI approach, allowed formal and objective screening for IN/HI, streamlined a pathway to diagnosis and intervention, and identified undiagnosed disabilities in children with haemophilia improving their access to services

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Health Promot Chronic Dis Prev Can. 2022 Sep;42:355-83.

ACCURACY OF ADMINISTRATIVE DATABASE ALGORITHMS FOR AUTISM SPECTRUM DISORDER, ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND FETAL ALCOHOL SPECTRUM DISORDER CASE ASCERTAINMENT: A SYSTEMATIC REVIEW.

O'Donnell S, Palmetter S, Lavery M, et al.

INTRODUCTION: The purpose of this study was to perform a systematic review to assess the validity of administrative database algorithms used to identify cases of autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD) and fetal alcohol spectrum disorder (FASD).

METHODS: MEDLINE, Embase, Global Health and PsycInfo were searched for studies that validated algorithms for the identification of ASD, ADHD and FASD in administrative databases published between 1995 and 2021 in English or French. The grey literature and reference lists of included studies were also searched. Two reviewers independently screened the literature, extracted relevant information, conducted reporting quality, risk of bias and applicability assessments, and synthesized the evidence qualitatively. PROSPERO CRD42019146941.

RESULTS: Out of 48 articles assessed at full-text level, 14 were included in the review. No studies were found for FASD. Despite potential sources of bias and significant between-study heterogeneity, results suggested that increasing the number of ASD diagnostic codes required from a single data source increased specificity and positive predictive value at the expense of sensitivity. The best-performing algorithms for the identification of ASD were based on a combination of data sources, with physician claims database being the single best source. One study found that education data might improve the identification of ASD (i.e. higher sensitivity) in school-aged children when combined with physician claims data; however, additional studies including cases without ASD are required to fully evaluate the diagnostic accuracy of such algorithms. For ADHD, there was not enough information to assess the impact of number of diagnostic codes or additional data sources on algorithm accuracy.

CONCLUSION: There is some evidence to suggest that cases of ASD and ADHD can be identified using administrative data; however, studies that assessed the ability of algorithms to discriminate reliably between cases with and without the condition of interest were lacking. No evidence exists for FASD. Methodologically higher-quality studies are needed to understand the full potential of using administrative data for the identification of these conditions

Human Gene. 2022;34.

DIFFERENTIAL EFFECT OF FOLATE METABOLIC SYSTEM GENETIC VARIANTS ON ATTENTION DEFICIT HYPERACTIVITY DISORDER SEVERITY.

Saha T, Saha S, Karmakar A, et al.

Background: Adequate folate level is vital for the synthesis of neurotransmitters, and hence, folate deficiency was related to neurobehavioral disorders like depression, Autism spectrum disorders, and Attention Deficit Hyperactivity Disorder (ADHD). Genetic variants involved in folate metabolism were also reported to affect ADHD traits. We have analyzed the contribution of FOLR1 rs2071010, FOLR2 rs2298444, TCN2 rs1801198, and SHMT1 rs1979277 in the etiology of Indian ADHD probands.

Methods: Ethnically matched controls (N = 286) and unrelated nuclear families with ADHD probands (N = 221) were recruited following the Diagnostic and Statistical Manual for Mental Disorders (DSM). Traits were assessed using the Conners' Parent Rating Scale-Revised, DSM, and Parental Account of Children's Symptoms criteria. Genetic variants were analyzed by PCR-based methods/TaqMan assay. Genetic association analyses were performed using the UNPHASED. Linkage disequilibrium was calculated using Haploview. Quantitative Trait Analysis was performed to identify the association between genetic variants and trait scores.

Results: Parental bias in the transmission of rs1979277 C to the ADHD probands was detected. Maternally biased transmission of rs2298444 G was also observed. LD between rs2071010-rs2298444 was strong in the control population. Trait scores of the male ADHD probands were higher in the presence of rs2298444 A while the behavioral problem was less in the presence of rs1801198 CC. In the male probands, studied sites exhibited stronger independent effects, while in the female probands, additive effects between rs2298444-rs1801198 and rs2298444-rs1979277 were observed.

Conclusion: We infer that ADHD severity is differentially influenced by genetic variants regulating folate metabolism

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Indian J Physiol Pharmacol. 2018;62:76.

SLOW BUT STEADY WINS THE RACE? - BEHAVIOURAL MANIFESTATION OF ADHD DURING AN N BACK VISUOSPATIAL WORKING MEMORY TASK.

Batabyal T, Sharma R, Sagar R, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood. Impairments in working memory create difficulties for children with ADHD in their cognitive, academic and social activities, thereby affecting their quality of life.

Objectives: To assess Visuospatial working memory (VSWM) in children with ADHD compared to age matched controls.

Methods: 15 ADHD children diagnosed using DSM V and 15 age matched controls, performed 40 trials of 1N back VSWM task wherein subject had to remember the position of the box and respond by matching the position of the current stimulus with the 1-back position. Response was made by pressing key 1 for match and key 2 for Not a match in response pad. Reaction time and accuracy percentage of each subject were logged and statistically compared.

Results: Fifteen ADHD children (11.73 \pm 0.7713 yr, 13 males) and 15 age matched control (11.60 \pm 0.7224 yr, 10 males) each performed 1nback VSWM. Interestingly, there was a significant difference ($p < 0.0001$) in reaction time (889.8 \pm 16.16 vs 753.9 \pm 13.60), however, there was no significant difference ($p = 0.9005$) in accuracy percentage (77 \pm 3.030 vs 83 \pm 1.985, $t = 1.657$, $df = 24$) between ADHD and controls respectively.

Conclusion: ADHD subjects take longer time to perform a visuospatial working memory task but doesn't compromise on accuracy percentage. The neural compensatory mechanism associated with such a behavioural manifestation can be further explored using EEG connectivity and time frequency analysis on task data

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Indian J Physiol Pharmacol. 2018;62:76-77.

EXPLORING EMOTIONAL AND COGNITIVE INTERFERENCE CONDUCT IN ADHD CHILDREN.

Leon C, Tayade PT, Sagar R, et al.

Background: Attention Deficit Hyperactive Disorder (ADHD) children have deficits in cognitive interference, thereby affecting goal directed 'executive functions. Whether deficit in interference control is due to suppression in motor responses or due to cognitive suppression is controversial. Further, limited literature is present to demonstrate the effect of interference in emotional domain in ADHD.

Objectives: To assess the reaction time and accuracy in ADHD subjects compared to age matched healthy controls in emotional and non-emotional stroop interference task.

Methods: A paradigm with blocks of 20 trial consisting of color-word stimuli (non emotional task) of stroop neutral(SN), stroop facilitation(SF) and stroop interference(SI) and 60 trials consisting of emotional stroop(ES) of word face(WF) and face word(FW) was performed. The response, accuracy and reaction time were logged.

Results: DSM-V diagnosed 15 ADHD children (11.73 \pm 0.7 yr) and age matched control (11.60 \pm 0.7 yr) each performed both the task. There was a significant difference ($p < 0.0001$) in reaction time between ADHD and controls in all the tasks. Mean reaction time were FW (1126 \pm 15.05 vs 1076 \pm 13.81), WF (911.9 \pm 12.16 vs 941.5 \pm 11.25), SN (994.6 \pm 24.55 vs 804.4 \pm 14.11), SF (815.2 \pm 17.61 vs 747.1 \pm 17.54) SI (1105 \pm 30.63 vs 815.0 \pm 17.91). However, significant difference ($p < 0.01$) in accuracy percentage between ADHD and Controls (93.23 \pm 1.284 vs 87.09 \pm 5.424) was only found in WF.

Conclusion: Increased reaction time is a suggestive of executive function (EF) deficit. Behaviorally, all tasks elicited interference effect, with significantly slower RTs in ADHD. Accurate performance in each task reflects two different pathways for RT and accuracy thereby reflecting that ADHD kids take time in processing information but decodes the information correctly

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Int J Environ Res Public Health. 2022 Sep;19.

VALIDATING THE FIVE-ITEM WORLD HEALTH ORGANIZATION WELL-BEING INDEX.

Nylan-Eriksen M, et al.

Purpose: Research on the psychological well-being of caregivers of children diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD) suggests that the well-being of parents and caregivers has been negatively affected by the COVID-19 pandemic. Although the psychological well-being of caregivers is a major concern, few validated well-being measures exist for caregivers of children diagnosed with ADHD. Therefore, a valid self-report scale is needed to assess well-being during the pandemic. The brief Five-Item World Health Organization Well-Being Index (WHO-5) has previously been used in studies on caregivers. However, its validity in this population remains unknown. This study aimed to evaluate the reliability and construct validity of the WHO-5 with caregivers of children with ADHD.

Methods: A cross-sectional anonymous online survey was conducted in Norway. The study recruited caregivers from a community sample during the COVID-19 pandemic. This was carried out to investigate the construct validity by exploring the relationship between well-being, quality of life, social support, self-reported psychological distress, and perceived stress.

Results: The findings of unidimensionality and high internal consistency, together with the results from the hypothesis testing, demonstrate the reliability and construct validity of the Norwegian version of the WHO-5 in this population.

Conclusions: This study provides the first empirical evidence of the validity and reliability of the WHO-5 from a sample of Norwegian caregivers of children diagnosed with ADHD, with excellent reliability and construct validity. The scale can be used to systematize the measurement of well-being in caregivers because of its brevity and good psychometric properties, making it a valuable resource in research settings and assisting healthcare professionals in their crucial work of caring for caregivers

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Int J Environ Res Public Health. 2022 Sep;19.

Family Socioeconomic Status and Attention Deficit/Hyperactivity Disorder in Preschool Children: The Mediating Role of Executive Function.

Fan L, Qing W, Wang Y, et al.

This study aimed to explore the relationship between family socioeconomic status (SES) and attention deficit/hyperactivity disorder (ADHD) symptoms in preschool children and the mediating role of executive function (EF). A total of 361 parents of preschool children were surveyed using the self-reported Family Situation Questionnaire, the Child Executive Functioning Inventory, and the Child Strengths and Difficulties Questionnaire. The results revealed that (1) there were significant pairwise correlations between SES, EF and its dimensions, and ADHD, except for a non-significant correlation between SES and regulation ability; (2) after controlling for preschool children's age and sex, SES directly predicted preschoolers' ADHD and EF partially mediated the association between SES and ADHD; and (3) among the EF dimensions, working memory and inhibitory ability significantly mediated the association between SES and ADHD, whereas the mediating effect of regulatory ability was not significant. These results suggest that SES can affect the ADHD of preschoolers both directly and through EF, especially through working memory and inhibitory ability. This supports the family stress model and family investment model of the relationship between SES and the development of children to some extent, and provides a reference for the early prevention of ADHD in children with low SES

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Int J Mol Sci. 2022 Sep;23.

PSYCHOSTIMULANTS MODAFINIL, ATOMOXETINE AND GUANFACINE IMPAIR BONE CELL DIFFERENTIATION AND MSC MIGRATION.

Wagener N, Lehmann W, Weiser L, et al.

Attention deficit hyperactivity disorder (ADHD) is one of the most common worldwide mental disorders in children, young and adults. If left untreated, the disorder can continue into adulthood. The abuse of ADHD-related drugs to improve mental performance for studying, working and everyday life is also rising. The potentially high number of subjects with controlled or uncontrolled use of such substances increases the

impact of possible side effects. It has been shown before that the early ADHD drug methylphenidate influences bone metabolism negatively. This study focused on the influence of three more recent cognitive enhancers, modafinil, atomoxetine and guanfacine, on the differentiation of mesenchymal stem cells to osteoblasts and on their cell functions, including migration. Human mesenchymal stem cells (hMSCs) were incubated with a therapeutic plasma dosage of modafinil, atomoxetine and guanfacine. Gene expression analyses revealed a high beta-2 adrenoceptor expression in hMSC, suggesting it as a possible pathway to stimulate action. In bone formation assays, all three cognitive enhancers caused a significant decrease in the mineralized matrix and an early slight reduction of cell viability without triggering apoptosis or necrosis. While there was no effect of the three substances on early differentiation, they showed differing effects on the expression of osterix (OSX), receptor activator of NF- κ B ligand (RANKL) and osteoprotegerin (OPG) in the later stages of osteoblast development, suggesting alternative modes of action. All three substances significantly inhibited hMSC migration. This effect could be rescued by a selective beta-blocker (Imperial Chemical Industries ICI-118,551) in modafinil and atomoxetine, suggesting mediation via beta-2 receptor stimulation. In conclusion, modafinil, atomoxetine and guanfacine negatively influence hMSC differentiation to bone-forming osteoblasts and cell migration through different intracellular pathways

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Int J Clin Pract. 2022;2022.

EFFECT OF VITAMIN D SUPPLEMENTATION ON INFLAMMATORY BIOMARKERS IN SCHOOL-AGED CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Samadi M, Gholami F, Seyedi M, et al.

Attention deficit hyperactivity disorder (ADHD) is one of the most prevalent psychiatric and developmental disorders in children. Low serum vitamin D concentration and elevated inflammation biomarkers might be involved in neuropsychiatric disorders, such as ADHD. The purpose of this study was to evaluate the effect of vitamin D supplementation on TNF- α and IL-6 levels in children with attention deficit hyperactivity disorder. Method. This randomized double-blind, placebo-controlled trial was conducted on 75 school-aged children with a diagnosis of ADHD based on DSM-V criteria. Children were randomly allocated to receive either vitamin D3 (2000 IU/day) or a placebo for 3 months. Serum IL-6, TNF- α , and 25(OH) D were assessed before and after the intervention to determine the effects of vitamin D on the highlighted parameters. Results. Serum levels of 25(OH) D increased significantly in the vitamin D group (P=0.01). However, no significant differences in serum IL-6 and TNF- α were found between both groups at the baseline and at the end of the intervention. Conclusion. The findings revealed that vitamin D supplementation for 3 months is not efficacious in reducing inflammatory cytokines in children with ADHD. Further studies are required to confirm these results

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Int J Environ Res Public Health. 2022;19.

CLASSIFYING YOUNG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BASED ON CHILD, PARENT, AND FAMILY CHARACTERISTICS: A CROSS-VALIDATION STUDY.

Law E, Sideridis G, Alkhadim G, et al.

We aimed to identify subgroups of young children with differential risks for ADHD, and cross-validate these subgroups with an independent sample of children. All children in Study 1 (N = 120) underwent psychological assessments and were diagnosed with ADHD before age 7. Latent class analysis (LCA) classified children into risk subgroups. Study 2 (N = 168) included an independent sample of children under age 7. A predictive model from Study 1 was applied to Study 2. The latent class analyses in Study 1 indicated preference of a 3-class solution (BIC = 3807.70, p < 0.001). Maternal education, income-to-needs ratio, and family history of psychopathology, defined class membership more strongly than child factors. An almost identical LCA structure from Study 1 was replicated in Study 2 (BIC = 5108.01, p < 0.001). Indices of sensitivity (0.913, 95% C.I. 0.814-0.964) and specificity (0.788, 95% C.I. 0.692-0.861) were high across studies. It is concluded that the classifications represent valid combinations of child, parent, and family characteristics that are predictive of ADHD in young children

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Int J Environ Res Public Health. 2022;19.

FETAL EXPOSURE TO AIR POLLUTION IN LATE PREGNANCY SIGNIFICANTLY INCREASES ADHD-RISK BEHAVIOR IN EARLY CHILDHOOD.

Liu B, Fang X, Strodl E, et al.

Background: Air pollution nowadays has seriously threatened the health of the Chinese population, especially in the vulnerable groups of fetuses, infants and toddlers. In particular, the effects of air pollution on children's neurobehavioral development have attracted widespread attention. Moreover, the early detection of a sensitive period is very important for the precise intervention of the disease. However, such studies focusing on hyperactive behaviors and susceptible window identification are currently lacking in China.

Objectives: The study aims to explore the correlation between air pollution exposure and hyperactive behaviors during the early life stage and attempt to identify whether a susceptible exposure window exists that is crucial for further precise intervention.

Methods: Based on the Longhua Child Cohort Study, we collected the basic information and hyperactivity index of 26,052 children using a questionnaire conducted from 2015 to 2017, and the Conners Parent Rating Scale-revised (CPRS-48) was used to assess hyperactive behaviors. Moreover, the data of air pollution concentration (PM10, PM2.5, NO2, CO, O3 and SO2) were collected from the monitoring station between 2011 to 2017, and a land-use random forest model was used to evaluate the exposure level of each subject. Furthermore, Distributed lag non-linear models (DLNMs) were applied for statistic analysis.

Results: The risk of child hyperactivity was found to be positively associated with early life exposure to PM10, PM2.5 and NO2. In particular, for an increase of per 10 $\mu\text{g}/\text{m}^3$ in PM10, PM2.5 and NO2 exposure concentration during early life, the risk of child hyperactivity increased significantly during the seventh month of pregnancy to the fourth month after birth, with the strongest association in the ninth month of pregnancy (PM10: OR = 1.043, 95% CI: 1.016-1.071; PM2.5: OR = 1.062, 95% CI: 1.024-1.102; NO2: OR = 1.043, 95% CI: 1.016-1.071). However, no significant associations among early life exposure to CO, O3 and SO2 and child hyperactive behaviors were observed.

Conclusions: Early life exposure to PM10, PM2.5 and NO2 is associated with an increased risk of child ADHD-like behaviors at the age around 3 years, and the late-prenatal and early postnatal periods might be the susceptible exposure windows

Ital J Pediatr. 2022 Sep;48:173.

INCREASED BEHAVIORAL PROBLEMS IN CHILDREN WITH SLEEP-DISORDERED BREATHING.

Csàbi E, et al.

Background: Healthy sleep is essential for the cognitive, behavioral and emotional development of children. Therefore, this study aimed to assess the behavioral consequences of sleep disturbances by examining children with sleep-disordered breathing compared with control participants.

Methods: Seventy-eight children with SDB (average age: 6.7 years (SD = 1.83); 61 had OSA and 17 had primary snoring) and 156 control subjects (average age: 6.57 years (SD = 1.46) participated in the study. We matched the groups in age ($t(232) = 0.578$, $p = 0.564$) and gender ($\chi^2(1) = 2.192$, $p = 0.139$). In the SDB group, the average Apnea-Hypopnea Index was 3.44 event/h (SD = 4.00), the average desaturation level was 87.37% (SD = 6.91). Parent-report rating scales were used to measure the children's daytime behavior including Attention Deficit Hyperactivity Disorder Rating Scale, Strengths and Difficulties Questionnaire, and Child Behavior Checklist.

Results: Our results showed that children with SDB exhibited a higher level of inattentiveness and hyperactive behavior. Furthermore, the SDB group demonstrated more internalizing (anxiety, depression, somatic complaints, social problems) ($p < 0.001$) and externalizing (aggressive and rule-breaking behavior) problems compared with children without SDB, irrespective of severity.

Conclusions: Based on our findings we supposed that snoring and mild OSA had a risk for developing behavioral and emotional dysfunctions as much as moderate-severe OSA. Therefore, clinical research and practice need to focus more on the accurate assessment and treatment of sleep disturbances in childhood, particularly primary snoring, and mild obstructive sleep apnea

J Affect Disord. 2022 Dec;318:314-30.

POSTPARTUM DEPRESSION AND ADHD IN THE OFFSPRING: SYSTEMATIC REVIEW AND META-ANALYSIS.

Christaki V, Ismirnioglou I, Katrali A, et al.

BACKGROUND: Postpartum depression (PPD) is a disorder that has a severe impact on a woman's mental state and mood after birth. Research has shown that postnatal levels of family adversity and maternal psychopathology are associated with Attention Deficit Hyperactivity Disorder (ADHD). This paper is intended to examine the association among maternal PPD and the risk of ADHD in the offspring.

METHODS: Keyword search was conducted for PsycINFO, PubMed, Google Scholar, and Embase up to Feb 28, 2021; studies in English were deemed eligible. Random-effects meta-analysis and meta-regression analysis took place. Subgroup analyses by study design, geographical region, level of adjustment and study setting were performed.

RESULTS: Nine cohort studies and two case-control studies published from 2003 to 2019 were included in the qualitative synthesis; among them, eight studies were synthesized in the meta-analysis. Overall, maternal PPD was associated with an increased risk of ADHD in the offspring (pooled relative risk, $RR\hat{A} = \hat{A} 1.69$, 95%CI: 1.27-2.26). Significant associations were noted in the subsets of cohort studies, studies implementing multivariate analyses and registry-based surveys.

LIMITATIONS: Overall, a larger number of studies of the field are needed. Data collection relied on self-report and attrition bias limited the validity of eligible studies. Studies from developing countries were underrepresented. There was significant publication bias ($p = 0.035$, Egger's test).

CONCLUSIONS: The relationship between PPD and ADHD in children was found to be significant in this systematic review and meta-analysis and reveals the need for further investigation in various geographical regions

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J Clin Endocrinol Metab. 2022 Sep;107:e4203-e4211.

ROLE OF EXCESSIVE WEIGHT GAIN DURING GESTATION IN THE RISK OF ADHD IN OFFSPRING OF WOMEN WITH GESTATIONAL DIABETES.

Perea V, et al.

CONTEXT: Although attention-deficit/hyperactivity disorder (ADHD) has been associated with gestational diabetes mellitus (GDM) and maternal obesity, excessive weight gain (EWG) during pregnancy has scarcely been evaluated.

OBJECTIVE: This study aimed to assess the joint effect of maternal weight and EWG on the risk of ADHD in offspring of GDM pregnancies.

METHODS: In this cohort study of singleton births ≥ 22 weeks of gestation of women with GDM between 1991 and 2008, gestational weight gain above the National Academy of Medicine (NAM) recommendations was classified into EWG. Cox-regression models estimated the effect of maternal pregestational weight and EWG on the risk of ADHD (identified from medical records), adjusted for pregnancy outcomes and GDM-related variables.

RESULTS: Of 1036 children who were included, with a median follow-up of 17.7 years, 135 (13%) were diagnosed with ADHD. ADHD rates according to pregestational maternal weight were 1/14 (7.1%) for underweight, 62/546 (11.4%) for normal weight, 40/281 (14.2%) for overweight, and 32/195 (16.4%) for obesity. Only maternal obesity was independently associated with ADHD (HRadjusted 1.66 [95% CI, 1.07-2.60]), but not maternal overweight or EWG. On evaluating the joint contribution of maternal weight and EWG, maternal obesity with EWG was associated with the highest risk of ADHD (vs normal weight without EWG; HRadjusted 2.13 [95% CI, 1.14-4.01]). Pregestational obesity without EWG was no longer associated (HRadjusted 1.36 [95% CI, 0.78-2.36]).

CONCLUSION: Among GDM pregnancies, pregestational obesity was associated with a higher risk of ADHD in offspring. Nonetheless, when gestational weight gain was taken into account, only the joint association of obesity and EWG remained significant

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JAMA Netw Open. 2022 Sep;5:e2234179.

TRENDS IN DIAGNOSED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG CHILDREN, ADOLESCENTS, AND ADULTS IN JAPAN FROM APRIL 2010 TO MARCH 2020.

Sasayama D, Kuge R, Toibana Y, et al.

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J Affective Disord. 2022;316:63-70.

FUNCTIONAL URINATION OR DEFECATION DISORDERS MAY BE WARNING SIGNS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG CHILDREN IN RURAL CHINA.

Liu X, Zhang G.

Background: This study was designed to investigate the prevalence of attention-deficit/hyperactivity disorder (ADHD) and its association with functional urination and defecation disorders among children in rural China.

Methods: A cross-sectional study was conducted with children aged 6-18 in rural schools in southwest China using a survey questionnaire. The Swanson, Nolan, and Pelham Questionnaire-IV (SNAP-IV) was used to measure ADHD symptoms, and standardized questions about urination and defecation were used to measure lower urinary tract symptoms (LUTS) and functional defecation disorders (FDDs). The association of ADHD with LUTS and FDDs was analyzed by matched logistic regression after propensity score matching was performed to minimize the influence of potential confounders, including demographic characteristics.

Results: A total of 17,279 participants were included in the analyses. The prevalence of ADHD was 2 % mainly among boys before age 12, after which it showed a decreasing trend with age, resulting in a concomitant reduction in gender differences. The risk of ADHD was positively associated with the presence of enuresis, holding maneuvers, intermittency, and encopresis, with encopresis having the strongest association ($P = 0.001$). The presence of holding maneuvers, intermittency, excessive volitional stool retention, and encopresis were associated with a higher risk of ADHD at 6-15 years-old, with intermittency exhibiting an increasingly positive association with ADHD risk across ages 6-15.

Conclusions: ADHD was associated with LUTS and FDDs, which highlights that functional urination and/or defecation disorders could serve as warning signs for ADHD that should trigger screening, especially in relatively backward regions with little ADHD awareness

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J Autism Dev Disord. 2022 Sep;52:3933-48.

TIME-TO-COLLISION ESTIMATIONS IN YOUNG DRIVERS WITH AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Svancara AM, Kana R, Bednarz H, et al.

Individuals with attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) may exhibit driving difficulties due to cognitive impairments such as time perception difficulties, a construct related to the perception of time-to-collision (TTC). This study examined the timing abilities of drivers with ASD and ADHD. Sixty participants ($n_{ADHD} = 20$, $n_{ASD} = 20$, $n_{TD} = 20$) completed a time reproduction task and a TTC estimation task in a driving simulator. Results indicated drivers with ASD were less precise in time reproduction across all time intervals and over-reproduced time at shorter intervals. Drivers with ASD produced larger TTC estimates when driving at a faster speed compared to typically developing drivers. Drivers with ASD, but not ADHD, appear to present difficulties in time estimation abilities

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Journal of Behavioral Addictions. 2022;11:143.

FREQUENCIES AND PREDICTORS OF PROBLEMATIC ONLINE BEHAVIOURS IN AN AUSTRALIAN SAMPLE.

Starcevic V, Berle D, Eslick G, et al.

Background: This study aimed to ascertain the frequencies and predictors of several problematic online behaviours (POBs) in an Australian community sample.

Method: The survey was administered to 1626 Australians aged 16 to 60. Participants were asked to complete the instruments assessing levels of anxiety, depression and attention deficit/hyperactivity disorder (ADHD), as well as 6 POBs: gaming, cyberchondria, cybersex, online shopping, use of social networking sites and gambling. Each POB was presumed to be present based on the scores on the corresponding self-

report instrument and at least one self-reported indicator of interference with functioning. Generalized Linear Models analyses were used to ascertain the predictors of each POB.

Results: The most common POB in the total sample was shopping (12.2%), followed by gambling (11.4%), use of social networking sites (6.0%), cybersex (5.3%), gaming (5.2%) and cyberchondria (4.1%). Except for cyberchondria, the rates of all POBs were the highest in the age group 27-36. The intensity of ADHD symptoms predicted all POBs, male gender predicted problematic online gaming and cybersex and younger age was a significant predictor of all POBs except for problematic cybersex and online gambling. Other demographic variables predicted only some POBs, whereas levels of anxiety and depression predicted no POB.

Conclusions: The frequencies of the specific POBs in the community appear to vary markedly between different age groups. Although the direction of causality, if any, cannot be inferred, a strong relationship between ADHD symptoms and all POBs may reflect a role of online environments in soothing ADHD-related distress

Journal of Behavioral Addictions. 2022;11:305-25.

PROBLEMATIC USE OF DIGITAL MEDIA IN CHILDREN AND ADOLESCENTS WITH A DIAGNOSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMPARED TO CONTROLS. A META-ANALYSIS.

Werling AM, Kuzhipallil S, Emery S, et al.

Objective: Problematic use of digital media and problematic use of the internet (PUI) in particular are growing problems in the general population. Moreover, studies have shown links between PUI and symptoms of attention-deficit/hyperactivity disorder (ADHD). This meta-analysis investigated whether children and adolescents with ADHD are more often affected by PUI compared to control groups.

Method: Multiple databases (EBSCOhost, Pubmed) were reviewed. Studies were eligible if individuals (aged 6-18 years) were diagnosed with ADHD, assessed on PUI-related measures, and compared to non-clinical or/and clinical controls without a diagnosis of ADHD. Out of 3,859 identified studies, 14 studies assessing 2,488 participants met all inclusion criteria. Four meta-analyses examining time-based and scale-based measures, different informants and non-clinical vs. clinical controls using random-effects models were performed. Funnel plots were used to investigate publication bias.

Results: The analyses revealed significantly more severe PUI in individuals with ADHD compared to controls, both when PUI was assessed via rating scale (scaled-based) and via units for time (time-based measures). Different informants (self- vs. parent-rating) had no impact on results. Differences in PUI between groups with ADHD and non-clinical controls were significant, whereas differences between ADHD and clinical controls were not. Due to the high heterogeneity observed and the small sample sizes, these latter findings should be interpreted cautiously.

Conclusion: Children and adolescents with ADHD show more severe PUI compared to non-clinical controls without ADHD. However, the small number of studies does not allow for a systematic comparison between ADHD and groups with other psychopathologies

Journal of Behavioral Addictions. 2022;11:141.

PROBLEMATIC GAMING IN YOUNG ADOLESCENCE: THE ROLE OF IN-GAME REWARDS AND INDIVIDUAL VULNERABILITIES.

Pirrone D, Van Den Eijnden R, Peeters M.

Background: Rewarding characteristics in games may amplify the transition from recreational to more problematic gaming behavior. This research explored the association between typical rewarding game elements and adolescents' problematic gaming behaviors and evaluated the interacting nature of individual vulnerabilities within this relationship.

Method: In a two-cohort-design the impact of rewarding elements (e.g., random rewards, contingencies rewards, social rewards, and meta-achievements) on adolescents' problematic gaming was investigated. Participants were 2708 (53.9% male, mean age 13.9 SD=1.20) and 2073 secondary school students in respectively in the first and second cohort (52.1% male, mean age 14.3 SD=1.49).

Results: Results revealed that random rewards, social rewards, and contingencies rewards, were predictors of adolescents' problematic gaming in both cohorts. Games including such type of rewards increased the risk for problematic game play. Regarding interactions with individual vulnerabilities, results indicated that for adolescents with attention deficit hyperactivity symptoms, the impact of contingencies rewards on problematic gaming behavior was amplified, while for adolescents with social problems the impact of social rewards on problematic gaming was amplified.

Conclusion: The findings illustrate that certain rewarding elements in games can increase problematic gaming behavior, particularly among adolescents with individual vulnerabilities. Prevention strategies can benefit from integrating this knowledge in education and intervention strategies may be tailored towards those with attention-deficit hyperactivity symptoms and social problems as these adolescents are at the greatest risk for being affected by the rewarding elements in games

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J Child Adolesc Psychopharmacol. 2021;31:697-98.

LETTER TO THE EDITOR: THE IMPACT OF THE COVID-19 PANDEMIC ON THE MENTAL HEALTH OF YOUTH WITH DEVELOPMENTAL DISABILITIES.

Valicenti-McDermott M, Rivelis E, Bernstein C, et al.

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J Child Adolesc Psychopharmacol. 2022 Aug;32:337-48.

IMPACT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMORBIDITY ON PHENOMENOLOGY AND TREATMENT OUTCOMES OF PEDIATRIC OBSESSIVE-COMPULSIVE DISORDER.

Efe A, Kaba D, Canli M, et al.

Objective: This study, with a case-control design, investigates the impact of attention-deficit/hyperactivity disorder (ADHD) comorbidity on the phenomenology and treatment outcomes in a clinical sample of pediatric obsessive-compulsive disorder (OCD).

Methods: The data were derived from an evaluation of the sociodemographic and clinical characteristics of 364 children with OCD who were regularly followed up over a 4-year period. Between-group analyses of psychiatric scales were used to compare patients with ADHD comorbidity (n = 144, 39.5%) with their ADHD-free opponents. The clinical course and treatment outcomes of each patient were evaluated based on 4-year clinical follow-up data.

Results: Substantial clinical variations in pediatric OCD caused by ADHD comorbidity were identified, including a male preponderance, higher rates of concurrent conduct problems, tic disorders, and learning disabilities, as well as prolonged symptom and treatment durations accompanied by poor response to first-line treatments and higher rates of treatment resistance. Contrary to previous findings, ADHD comorbidity had no impact on the age of OCD onset, and the severity of OCD symptoms was lower in ADHD. With ADHD comorbidity, the OCD symptom course tended to be chronically stable, which may have resulted in complaints persisting into adulthood. In ADHD-free patients, contamination, doubt, religious, somatic obsessions, and cleaning were all more common than in those with ADHD. There was a positive correlation between compulsion scores and the severity of ADHD symptoms, which may be related to increased compulsive coping in ADHD. Impulsivity or compulsivity dominance in the symptom presentation of OCD-ADHD comorbidity may determine phenomenological distinctions such as whether concurrent traits are more prone to tics, conduct problems, or internalizing problems. The primordial associations for clinical characteristics, which were independently associated with ADHD comorbidity, were adjusted using multivariate logistic regression analysis. Clinical variables such as being male, absence of cleaning compulsion, the existence of concurrent conduct problems, tic disorders, and dyslexia, as well as longer treatment duration and poorer treatment response, were all independent predictors of ADHD comorbidity. With an 80.8% accurate classification and relatively fine goodness-of-fit model, the regression model consisting of those predictors had good predictiveness for ADHD comorbidity ($R^2 = 0.543$).

Conclusions: The close association between pediatric OCD, ADHD, and tic disorders can be defined as a specific subtype of pediatric OCD, characterized by more conduct problems, a chronically stable course of OCD symptoms, and poorer treatment outcomes. Correlational analyses in a longitudinal design and the

inclusion of an impulsivity scale would be beneficial for further research to interpret the impulsivity-related correlates in the findings on tic and conduct problems

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J Clin Child Adolesc Psychol. 2022 Sep;51:688-700.

BODY MASS INDICES OF GIRLS WITH AND WITHOUT ADHD: DEVELOPMENTAL TRAJECTORIES FROM CHILDHOOD TO ADULTHOOD.

Porter PA, Henry LN, Halkett A, et al.

Objective: We examined the predictive relation between childhood-diagnosed ADHD and trajectories of body mass index (BMI) from childhood to adulthood in an all-female sample, accounting for socioeconomic status (SES), childhood comorbidities (e.g., depression/anxiety), and stimulant usage. Childhood executive functioning (i.e., planning, sustained attention, and response inhibition) was also evaluated as a possible predictor of BMI trajectories.

Method: We utilized longitudinal data from a full sample of 140 girls diagnosed with ADHD in childhood and 88 comparison girls matched on age and ethnicity. Girls were 6–12 years old at the first assessment and followed prospectively for 16 years. Data were collected on their BMI and stimulant medication usage across four evaluation waves. Using latent growth curve modeling, we evaluated the BMI trajectories of girls with ADHD and the comparison sample from childhood to adulthood.

Results: Although there was no significant difference in initial childhood BMI, girls with ADHD increased in BMI at a significantly faster rate than comparison girls across development, even when adjusting for covariates. Significant differences in BMI first emerged in adolescence; by adulthood, 40.2% of the ADHD sample met criteria for obesity versus 15.4% of the comparison sample. When covarying ADHD diagnosis, executive functioning measures were not significantly predictive of BMI increase. Adjusting for stimulant medication usage within the ADHD sample did not alter core findings.

Conclusions: We discuss health-related implications for girls with ADHD, potential underlying mechanisms, and how our findings may inform both ADHD and obesity interventions

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J Clin Child Adolesc Psychol. 2022 Sep;51:726-39.

BEHAVIORAL PARENT TRAINING FOR PRESCHOOL ADHD: FAMILY-CENTERED PROFILES PREDICT CHANGES IN PARENTING AND CHILD OUTCOMES.

Dale C, Parent J, Forehand R, et al.

Objective: Behavioral parent training (BPT) is the first line of treatment for preschool-aged children with attention-deficit hyperactivity disorder (ADHD); however, clinically significant improvements are not universal. In the current study, we employ a person-centered approach to create subgroups of families based on the intersection of multiple parent, child, and family pre-treatment factors. Further, we explore the utility of pre-treatment family profiles in predicting post-treatment differences in observed parenting behavior (i.e., behavioral control, parental warmth) and clinically significant change in child ADHD and oppositional symptoms.

Method: Longitudinal data were collected using observational and parent-, teacher- and clinician-reported assessments from 130 parent-child dyads (Mage = 3.57, range = 3.0– 4.11, 73.8% male, 69.2% White, 25.6% Hispanic) participating in BPT.

Results: Findings from the current study suggest three distinct family profiles, which consisted of one profile with high family stress (HFS) as evidenced by elevated symptomatology across parent, child, and family-level domains, a second profile with elevated parental anxiety (PA), and a final profile with elevated parental depression (PD). These family-centered profiles were differentially associated with changes in observed parenting practices. Specifically, the PD profile (39%) demonstrated minimal improvements in behavioral control and warmth following treatment. In contrast, the HFS profile (30%) only improved in behavioral control and the PA profile (31%) improved in both parenting domains following treatment. In addition, marginally significant differences in child oppositional and ADHD symptoms were observed across profiles.

Conclusions: Family-centered approaches may be useful for selecting and implementing interventions.

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J Clin Child Adolesc Psychol. 2022 Sep;51:750-63.

FOUR-YEAR FOLLOW-UP OF HIGH VERSUS LOW INTENSITY SUMMER TREATMENT FOR ADOLESCENTS WITH ADHD.

Sibley MH, Coxe SJ, Page TF, et al.

Objective: Despite an emergence of psychosocial treatments for adolescent ADHD, their long-term effects are unknown.

Method: We examine four-year outcomes of a randomized controlled trial (N = 218) comparing high-intensity (HI; 412 h, \$4,373 per participant) versus low-intensity (LI; 24 h, \$97 per participant) skills-based summer intervention delivered to adolescents with ADHD at two secondary school transitions (6th/9th grade). Quantitative and qualitative analyses evaluated group×time and group×gradexime effects on 4-year outcomes.

Results: Relative to LI, a single dose of HI had modest but lasting effects on teen organization skills ($d = .40$) and ADHD symptoms (9th grade only: $d = .27$ to $.31$) at 4-year follow-up. There was no long-term incremental effect of HI (vs. LI) for parent-teen conflict, GPA, or parent use of contingency management. Treatment appeared most effective when delivered to older adolescents (i.e., 9th versus 6th grade), suggesting the long-term impact of ADHD treatment may increase with age. Qualitative data corroborated that the primary long-term benefit of HI (vs. LI) treatment was to organization skills; many of the remaining perceived benefits were to parent and teen psychological variables (i.e., increased self-esteem, self-awareness, parental optimism). HI offered no incremental benefit to long-term educational or clinical service utilization or costs.

Conclusions: Modest therapeutic benefits of adolescent ADHD treatment are maintained long term. However, HI treatment did not impact outcomes that could defray the intervention's high costs (\$4,373) compared to LI treatment (\$97)

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J Clin Psychiatry. 2020;81.

ACUTE EFFECTS OF PARENT STIMULANT MEDICATION VERSUS BEHAVIORAL PARENT TRAINING ON MOTHERS' ADHD, PARENTING BEHAVIOR, AND AT-RISK CHILDREN.

Chronis-Tuscano A, French W, Strickland J, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is present in 25%-50% of parents of children with ADHD, compromising parenting and child behavioral treatment. Efforts to treat multiplex ADHD families have not compared behavioral parenting interventions to parent psychopharmacology without confounds of other treatments. This report describes a pilot early intervention study directly comparing parent lisdexamfetamine dimesylate (LDX) to behavioral parent training (BPT) in families in which the mother had currently untreated ADHD and the young child displayed ADHD symptoms.

Methods: Mothers with ADHD (N = 35) of 4- to 8-year-old stimulant-naive children (N = 35) were randomly assigned to an 8-week trial of LDX (starting at 20 mg/d and titrated to a maximum of 70 mg/d) or BPT. Outcomes included multi-method, multi-informant measures of (1) maternal ADHD symptoms (Conners' Adult ADHD Rating Scales) and impairment (Clinical Global Impressions-Severity of Illness scale [CGI-S] and CGI-Improvement scale [CGI-I]), (2) parenting (Alabama Parenting Questionnaire [APQ] and Dyadic Parent-Child Interaction Coding System, Fourth Edition), and (3) child ADHD symptoms (Conners Parent Rating Scale Revised-Short Form and Conners Early Childhood Scale) and impairment (CGI-S, CGI-I, and Child Impairment Rating Scale).

Results: At 8 weeks, both treatments improved mothers' self-reported emotion regulation and mothers' functioning on the CGI, but only LDX improved mothers' self-reported core ADHD symptoms. LDX was associated with improvement in parents' perception of their own ADHD symptoms (Conners Inattention [$P < .0001$] and ADHD Index scores [$P < .0001$]) and their child's ADHD symptoms ($P = .009$). Fifty-six percent of the mothers treated with LDX ($n = 10$) were much or very much improved with regard to their adult ADHD based on the CGI-I scores versus 6% of mothers receiving BPT ($n = 1$; $P = .003$). BPT improved parenting on self-reported positive parenting ($P = .007$), inconsistent discipline ($P > .0001$), and corporal punishment ($P = .001$), while LDX improved reported inconsistent discipline ($P = .001$) and corporal punishment ($P = .04$) on the APQ, consistent with prior research. In contrast to parental LDX, which did not improve observed parenting, BPT was associated with increased positive parenting during child-directed play ($P = .0002$) and clean-up ($P = .04$) and less negative parenting ($P = .04$) during child-directed play. Six percent of children ($n = 1$) whose mothers were randomized to LDX ($n = 18$) were much or very much improved on the CGI-I compared to 35% ($n = 16$) of those treated with BPT ($P = .04$).

Conclusions: LDX and BPT each had unique effects on maternal ADHD symptoms and parenting, but modest effects on at-risk children. In general, LDX was more effective at treating mothers' core ADHD symptoms, but both LDX and BPT improved mothers' emotion regulation, and BPT resulted in more consistent effects on parenting measures via both maternal report and direct observation. As most children remained significantly impaired after 8 weeks of unimodal treatment, combination treatment and/or longer treatment duration may be necessary to improve functioning of multiplex ADHD families

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Journal of Medical Internet Research. 2022;24.

DECIPHERING THE DIVERSITY OF MENTAL MODELS IN NEURODEVELOPMENTAL DISORDERS: KNOWLEDGE GRAPH REPRESENTATION OF PUBLIC DATA USING NATURAL LANGUAGE PROCESSING.

Kaur M, Costello J, Willis E, et al.

Background: Understanding how individuals think about a topic, known as the mental model, can significantly improve communication, especially in the medical domain where emotions and implications are high. Neurodevelopmental disorders (NDDs) represent a group of diagnoses, affecting up to 18% of the global population, involving differences in the development of cognitive or social functions. In this study, we focus on 2 NDDs, attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD), which involve multiple symptoms and interventions requiring interactions between 2 important stakeholders: parents and health professionals. There is a gap in our understanding of differences between mental models for each stakeholder, making communication between stakeholders more difficult than it could be.

Objective: We aim to build knowledge graphs (KGs) from web-based information relevant to each stakeholder as proxies of mental models. These KGs will accelerate the identification of shared and divergent concerns between stakeholders. The developed KGs can help improve knowledge mobilization, communication, and care for individuals with ADHD and ASD. **Methods:** We created 2 data sets by collecting the posts from web-based forums and PubMed abstracts related to ADHD and ASD. We utilized the Unified Medical Language System (UMLS) to detect biomedical concepts and applied Positive Pointwise Mutual Information followed by truncated Singular Value Decomposition to obtain corpus-based concept embeddings for each data set. Each data set is represented as a KG using a property graph model. Semantic relatedness between concepts is calculated to rank the relation strength of concepts and stored in the KG as relation weights. UMLS disorder-relevant semantic types are used to provide additional categorical information about each concept's domain.

Results: The developed KGs contain concepts from both data sets, with node sizes representing the co-occurrence frequency of concepts and edge sizes representing relevance between concepts. ADHD- and ASD-related concepts from different semantic types shows diverse areas of concerns and complex needs of the conditions. KG identifies converging and diverging concepts between health professionals literature (PubMed) and parental concerns (web-based forums), which may correspond to the differences between mental models for each stakeholder.

Conclusions: We show for the first time that generating KGs from web-based data can capture the complex needs of families dealing with ADHD or ASD. Moreover, we showed points of convergence between families and health professionals' KGs. Natural language processing-based KG provides access to a large sample size, which is often a limiting factor for traditional in-person mental model mapping. Our work offers a high throughput access to mental model maps, which could be used for further in-person validation, knowledge mobilization projects, and basis for communication about potential blind spots from stakeholders in interactions about NDDs. Future research will be needed to identify how concepts could interact together differently for each stakeholder

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J Pediatr. 2022.

GESTATIONAL AGE AT TERM AND TEACHER-REPORTED ATTENTION-DEFICIT HYPERACTIVITY DISORDER SYMPTOM PATTERNS.

Lingasubramanian G, Corman H, Noonan K, et al.

Objective: The objective of this study was to estimate associations between gestational age and teacher-reported attention-deficit hyperactivity disorder (ADHD) related symptom patterns at age 9 years among children born at term (37-41 weeks).

Study design: A secondary data analysis of approximately 1400 children in the Fragile Families and Child Wellbeing study, a US birth cohort study that oversampled nonmarital births, was conducted. At age 9 years, students were evaluated by their teachers using the Conners Teacher Rating Scale Revised Short Form that included subscales for symptoms of hyperactivity, ADHD, oppositional behavior, and cognitive problems/inattention. Unadjusted and adjusted negative binomial and logistic regression models of associations between gestational age and teacher-reported scores were estimated.

Results: Each week of gestational age at term was associated with hyperactivity scores that were 6% lower (adjusted incidence rate ratio [IRR]: 0.94; 95% CI: 0.89-0.99) and ADHD and cognitive problems/inattention scores that were 5% lower (adjusted IRR: 0.95; 95% CI: 0.91-0.98 in both cases). Early-term birth (37-38 weeks) was associated with 23% higher hyperactivity scores (adjusted IRR: 1.23; 95% CI: 1.07-1.41), 17% higher ADHD scores (adjusted IRR: 1.17; 95% CI: 1.05-1.30), and 50% higher odds of scoring 1.5+ SDs above the sample mean for hyperactivity (aOR: 1.51; 95% CI: 1.05-2.18) when compared with birth at 39-41 weeks. There were no significant associations between gestational age and oppositional behavior scores.

Conclusion: The findings add to growing evidence supporting current recommendations for delaying elective deliveries to at least 39 weeks and suggest that regular screenings for ADHD symptoms are important for children born at 37- to 38-weeks gestation

Journal of Personalized Medicine. 2022;12.

CYTOKINE LEVELS AND NEUROPSYCHOLOGICAL FUNCTION AMONG PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ATOPIC DISEASES.

Chang SJ, Kuo HC, Chou WJ, et al.

Since atopic disease and inflammatory cytokines are both involved in attention deficit hyperactivity disorder (ADHD), in this study, we examined the relationship among cytokine levels, neuropsychological function, and behavioral manifestations in patients with ADHD and atopic diseases. Participants were categorized into individuals with ADHD and atopic disease (n = 41), those with ADHD without allergy (n = 74), individuals without ADHD but with allergy (n = 23), and those without ADHD or allergy (n = 49). We used the Swanson, Nolan, and Pelham IV Scale (SNAP-IV), Conners Continuous Performance Test (Conners CPT), and Conners Continuous Auditory Test of Attention (CATA) to assess patients behavioral symptoms, visual attention, and auditory attention, respectively. Participants IFN- γ , IL-1B, IL-6, IL-10, IL-13, IL-17, MCP-1, and TNF- α plasma levels were assessed using multiplex assays. We found that the prevalence rates of atopic diseases (asthma, allergic rhinitis, or atopic dermatitis) were similar between individuals with ADHD and those without ADHD. ADHD behavioral symptoms (SNAP-IV), CPT omission scores, and CATA detectability scores demonstrated significant differences between individuals with ADHD and those without ADHD, regardless of atopic diseases. However, plasma levels of cytokines (TNF- α , IFN- γ , and IL-17) were negatively correlated with inattention symptoms. This study demonstrates a potential relationship between cytokine levels and neuropsychological function among patients with ADHD and atopic diseases

J Psychopathol Behav Assess. 2022.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND FORGETFULNESS: DOES TIME-RELATED DECAY REFLECT DEFICIENT REHEARSAL?

Rapport MD, Friedman LM, Pothoven C, et al.

The diminished ability to maintain verbal information in short-term memory (forgetfulness) mitigates the ability to follow instructions and acquisition of knowledge. Despite its acknowledged importance and involvement in multiple DSM-5 ADHD clinical symptoms, the construct remains under scrutinized in children with the disorder. The present study examined the extent to which children with ADHD (n = 15) were able to maintain multiple length word lists (2, 4, and 6 words) in phonological short-term memory (STM) for prolonged time intervals (12-s and 21-s) relative to typically developing (TD) children (n = 18). More crucially, it is the first to utilize a conventional suppression paradigm to determine whether deficient rehearsal contributes to

diminished word recall by children with ADHD over time. Children with ADHD exhibited clear evidence of forgetting when tasked with remembering a greater number of words and maintaining the words over longer time intervals relative to TD children. Follow-up analyses, however, revealed that the imposition of articulatory suppression (repeating an irrelevant syllable throughout recall intervals) diminished the recall performance of children in both groups to a similar degree relative to their performance under the recall only (non-suppression) conditions. Collectively, findings indicate that inadequate use of overt/covert rehearsal to refresh/maintain verbal memoranda in phonological STM is an unlikely explanation for the higher rates of forgetting in children with ADHD. Consideration of other sources that may contribute to higher rates of forgetfulness in ADHD, such as reduced attention control and/or higher susceptibility to internal interference, warrant attention in future investigations

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J Psychopathol Behav Assess. 2022 Sep;44:679-97.

IRRITABILITY AND EMOTIONAL IMPULSIVITY AS CORE FEATURE OF ADHD AND ODD IN CHILDREN.

Junghänel M, Thöne AK, Ginsberg C, et al.

[Correction Notice: An Erratum for this article was reported in Vol 44(3) of Journal of Psychopathology and Behavioral Assessment (see record [rid]2022-91690-001[rid]). The original publication of this article contained a mistake. The revised version of the article with tracked changes has been mistakenly added online as supplementary material 2. This should not be, as this is simply a word document of the revised manuscript with tracked changes. The original article has been corrected.] The categorical approach of diagnosing mental disorders entails the problem of frequently occurring comorbidities, suggesting a more parsimonious structure of psychopathology. In this study, we therefore aim to assess how affective dysregulation (AD) is associated with attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) in children. To assess AD in children aged 8–12 years (n = 391), we employed the parent version of a newly constructed parent rating scale. Following item reduction, we conducted exploratory and confirmatory factor analyses to establish a factorial structure of AD. One core dimension was identified, comprising irritability and emotional impulsivity, and two smaller dimensions, comprising positive emotionality and exuberance. Subsequently, we examined five different latent factor models – a unidimensional model, a first-order correlated factor model, a second-order correlated factor model, a traditional bifactor model, and a bifactor S-1 model, in which the first-order factor AD-Irritability/Emotional Impulsivity (II) was modeled as the general reference factor. A bifactor S-1 model with the a priori defined general reference domain AD-II provided the best fit to our data and was straightforward to interpret. This model showed excellent model fit and no anomalous factor loadings. This still held true, when comparing it to bifactor S-1 models with ADHD/ODD-related reference factors. Differential correlations with emotion regulation skills and the established Parent Proxy Anger Scale validate the interpretation of the different dimensions. Our results suggest that irritability/emotional impulsivity might be a common core feature of ADHD and ODD

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J Am Acad Child Adolesc Psychiatry. 2022;61:1273-84.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESTRICTED PHENOTYPES PREVALENCE, COMORBIDITY, AND POLYGENIC RISK SENSITIVITY IN THE ABCD BASELINE COHORT.

Cordova MM, Antovitch DM, Ryabinin P, et al.

Objective: To evaluate the prevalence and major comorbidities of ADHD using different operational definitions in a newly available national dataset and to test the utility of operational definitions against genetic and cognitive correlates.

Method: The US Adolescent Brain Cognitive Development (ABCD) Study enrolled 11,878 children aged 9-10 years at baseline. ADHD prevalence, comorbidity, and association with polygenic risk score and laboratory-assessed executive functions were calculated at 4 thresholds of ADHD phenotype restrictiveness. Bias from missingness, sampling, and nesting were addressed statistically.

Results: Prevalence of current ADHD for 9- to 10-year old children was 3.53% (95% CI 3.14%-3.92%) when Computerized Schedule for Affective Disorders and Schizophrenia for School-Age Children (K-SADS-COMP) score and parent and teacher ratings were required to converge. Of ADHD cases so defined, 70% had a comorbid psychiatric disorder. After control for overlapping comorbidity and ruling out for psychosis or

low IQ, 30.9% (95% CI 25.7%-36.7%) had a comorbid disruptive behavior disorder, 27.4% (95% CI 22.3%-33.1%) had an anxiety or fear disorder, and 2.1% (95% CI 1.2%-3.8%) had a mood disorder. Children in the top decile of polygenic load incurred a 63% increased chance of having ADHD vs the bottom half of polygenic load ($p < .01$) an effect detected only with a stringent phenotype definition. Dimensional latent variables for irritability, externalizing, and ADHD yielded convergent results for cognitive correlates.

Conclusion: This fresh estimate of national prevalence of ADHD in the United States suggests that the DSM-5 definition requiring multiple informants yields a prevalence of about 3.5%. Results may inform further ADHD studies in the ABCD sample

J Am Acad Child Adolesc Psychiatry. 2022.

ASSOCIATION OF PARENT-RATED SLEEP DISTURBANCES WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS: 9-YEAR FOLLOW-UP OF A POPULATION-BASED COHORT STUDY.

Gosling CJ, Cortese S, Konofal E, et al.

Objective: Symptoms of attention-deficit/hyperactivity disorder (ADHD) and sleep disturbances frequently co-occur, and can result in significant functional impairments that worsen quality of life. Despite a growing number of studies focusing on the association between sleep disturbances and ADHD symptoms over the last 20 years, the directionality of this association from childhood to early adulthood remains unclear.

Method: A sample of French parents ($n = 1,055$) were followed-up over a 9-year period. At children mean ages of 9, 13, and 18 years, parents were interviewed about their children's ADHD symptoms and sleep disturbances. Random-intercept cross-lagged panel models assessed the directionality of the association from childhood to early adulthood.

Results: Parent-reported sleep disturbances at a mean age of 13 years predicted increased ADHD symptoms 5 years later. Additional analyses suggested that this effect might be limited to inattentive symptoms, and that ADHD symptoms at a mean age of 9 predicted increased sleep disturbances 4 years later.

Conclusion: The present study provides evidence of a directional longitudinal association between parent-reported sleep disturbances and ADHD symptoms from adolescence to early adulthood. Our results highlight the importance of identifying sleep disturbances and ADHD symptoms for the design of preventive interventions. Future studies investigating this association in children with a clinical diagnosis of ADHD have the potential to provide important information for clinical practice

J Am Acad Child Adolesc Psychiatry. 2022.

ELECTROPHYSIOLOGICAL AND CLINICAL PREDICTORS OF METHYLPHENIDATE, GUANFACINE, AND COMBINED TREATMENT OUTCOMES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Michelini G, Lenartowicz A, Vera JD, et al.

Objective: The combination of d-methylphenidate and guanfacine (an α_1 -2A agonist) has emerged as a potential alternative to either monotherapy in children with attention-deficit/hyperactivity disorder (ADHD), but it is unclear what predicts response to these treatments. This study is the first to investigate pretreatment clinical and electroencephalography (EEG) profiles as predictors of treatment outcome in children randomized to these different medications.

Method: A total of 181 children with ADHD (aged 7-14 years; 123 boys) completed an 8-week randomized, double-blind, comparative study with d-methylphenidate, guanfacine, or combined treatments. Pretreatment assessments included ratings on ADHD, anxiety, and oppositional behavior. EEG activity from cortical sources localized within midfrontal and midoccipital regions was measured during a spatial working memory task with encoding, maintenance, and retrieval phases. Analyses tested whether pretreatment clinical and EEG measures predicted treatment-related change in ADHD severity.

Results: Higher pretreatment hyperactivity-impulsivity and oppositional symptoms and lower anxiety predicted greater ADHD improvements across all medication groups. Pretreatment event-related midfrontal beta power predicted treatment outcome with combined and monotherapy treatments, albeit in different directions. Weaker beta modulations predicted improvements with combined treatment, whereas stronger modulation during encoding and retrieval predicted improvements with d-methylphenidate and guanfacine,

respectively. A multivariate model including EEG and clinical measures explained twice as much variance in ADHD improvement with guanfacine and combined treatment ($R^2 = 0.34-0.41$) as clinical measures alone ($R^2 = 0.14-.21$).

Conclusion: We identified treatment-specific and shared predictors of response to different pharmacotherapies in children with ADHD. If replicated, these findings would suggest that aggregating information from clinical and brain measures may aid personalized treatment decisions in ADHD.

Clinical trial registration information: Single Versus Combination Medication Treatment for Children With Attention Deficit Hyperactivity Disorder; <https://clinicaltrials.gov>; NCT00429273 Diversity & Inclusion Statement: We worked to ensure sex and gender balance in the recruitment of human participants. We worked to ensure race, ethnic, and/or other types of diversity in the recruitment of human participants. One or more of the authors of this paper self-identifies as a member of one or more historically underrepresented racial and/or ethnic groups in science. We actively worked to promote sex and gender balance in our author group. We actively worked to promote inclusion of historically underrepresented racial and/or ethnic groups in science in our author group. While citing references scientifically relevant for this work, we also actively worked to promote sex and gender balance in our reference list

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J Am Acad Child Adolesc Psychiatry. 2022.

METHYLPHENIDATE, GUANFACINE, AND COMBINED TREATMENT EFFECTS ON ELECTROENCEPHALOGRAPHY CORRELATES OF SPATIAL WORKING MEMORY IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Michelin G, Lenartowicz A, Diaz-Fong JP, et al.

Objective: The combination of d-methylphenidate and guanfacine (an +1-2A adrenergic agonist) may be an effective alternative to either agent as monotherapy in children with attention-deficit/hyperactivity disorder (ADHD). This study investigated the neural mechanisms underlying medication effects using cortical source analysis of electroencephalography (EEG) data.

Method: A total of 172 children with ADHD (aged 7-14; 118 boys) completed an 8-week randomized, double-blind, comparative study with 3 treatment arms: d-methylphenidate, guanfacine, or their combination. EEG modulations of brain oscillations at baseline and end point were measured during a spatial working memory task from cortical sources localized within the anterior cingulate (midfrontal) and primary visual cortex (midoccipital), based on previously reported ADHD and control differences. Linear mixed models examined treatment effects on EEG and performance measures.

Results: Combined treatment decreased midoccipital EEG power across most frequency bands and task phases. Several midoccipital EEG measures also showed significantly greater changes with combined treatment than with monotherapies. D-methylphenidate significantly increased midoccipital theta during retrieval, while guanfacine produced only trend-level reductions in midoccipital alpha during maintenance and retrieval. Task accuracy improved with combined treatment, was unchanged with d-methylphenidate, and worsened with guanfacine. Treatment-related changes in midoccipital power correlated with improvement in ADHD severity.

Conclusion: These findings show that combined treatment ameliorates midoccipital neural activity associated with treatment-related behavioral improvements and previously implicated in visuo-attentional deficits in ADHD. Both monotherapies had limited effects on EEG measures, with guanfacine further showing detrimental effects on performance. The identified midoccipital EEG profile may aid future treatment monitoring for children with ADHD. Clinical trial registration information: Single Versus Combination Medication Treatment for Children With Attention Deficit Hyperactivity Disorder (Project1); <https://clinicaltrials.gov>; NCT00429273. Diversity & Inclusion Statement: We worked to ensure race, ethnic, and/or other types of diversity in the recruitment of human participants. We worked to ensure sex and gender balance in the recruitment of human participants. One or more of the authors of this paper self-identifies as a member of one or more historically underrepresented racial and/or ethnic groups in science. While citing references scientifically relevant for this work, we also actively worked to promote sex and gender balance in our reference list. We actively worked to promote inclusion of historically underrepresented racial and/or ethnic groups in science in our author group. We actively worked to promote sex and gender balance in our author group

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Malaysian Journal of Medical Sciences. 2022;29:152-59.

RELATIONSHIP BETWEEN PARENTING STYLE AND RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN ELEMENTARY SCHOOL CHILDREN.

Setyanisa AR, Setiawati Y, Irwanto I, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder in a child with three symptoms, which include inattention, hyperactivity and impulsiveness that may persist into adulthood for some conditions. Parenting style is thought to be one part that determines the risk of ADHD in children. This study aims to analyse the relationship between parenting styles and the risk of ADHD in children.

Methods: Employing a cross-sectional design, this study was conducted in Surabaya from November 2020 to January 2021. The respondents of the study were parents who had children at risk of ADHD with a total of 55 samples recruited using the purposive sampling technique. The questionnaires used are the demographic questionnaire, Abbreviated Conners Rating Scale (ACRS), and the Parenting Style Questionnaire for Children and Adolescents (KPAA), which were filled out online by the respondents. The data were processed and analysed using the bivariate analysis test, Pearson's chi-squared test, which has a significant value if the P-value < 0.05.

Results: The majority of the parents used the authoritative style (94.5%). There was a significant relationship between parenting style and the risk of ADHD in children with $P < 0.001$ for authoritarian and permissive styles and $P = 0.005$ for an authoritative style.

Conclusion: There is a significant relationship between parenting style and the risk of ADHD in children. This indicates the importance of early diagnosis of ADHD and treating the children with ADHD in the context of family environment, especially from parenting style

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Medicina (B Aires). 2022 Aug;82 Suppl 3:30-34.

SLEEP DISORDERS AND THEIR IMPACT ON NEURODEVELOPMENT.

Navarro VA, Gonzalez RG.

Sleep is the main activity of the developing brain and indispensable for the maturation of the central nervous system. Sleep habits are influenced by biological, social and cultural factors and play a role in learning and memory processes. It is estimated that 25-50% of children have sleep difficulties. There is consensus that insufficient sleep has a negative impact on neurodevelopment. Sleep disorders double their incidence in children with neurological disorders, with a bidirectional reciprocal causal link. They are classified into: insomnia, sleep-related breathing disorders, centrally caused hypersomnolence disorders, circadian cycle disorders, parasomnias, sleep-related movement disorders, and others. Despite the scientific evidence of the importance of sleep in early childhood, a high percentage of children do not comply with the recommended hours of sleep, which reflects the importance of training the pediatrician in this problem, which has increased during the pandemic

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Medicina (B Aires). 2022 Aug;82 Suppl 3:67-70.

Autism spectrum disorder and attention-deficit/hyperactivity disorder: challenge in diagnosis and treatment.

Velarde M, Cardenas A.

The coexistence of autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) definitely poses new challenges, such as making an early diagnosis, considering that the former is usually diagnosed 2 years later in children with ADHD comorbid with autism compared to those with ASD alone; this is a problem at a personal, family and social level, since they must receive timely intervention. This coexistence raises questions about the efficacy of treatment in ADHD in people with autism, genetic, anatomical and functional concordances, among others; these are the challenges that are currently posed. In this review, we present some responses to the challenges posed by such coexistence, and we highlight some pending issues to be solved, being these of great importance for their better understanding and management. In all patients with ADHD or ASD, a coexistence between them should be sought.

There are shared functional brain alterations in both disorders identified by functional brain magnetic resonance imaging; the treatment established for ADHD is also effective in this comorbidity

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Medicina (B Aires). 2022 Aug;82 Suppl 3:51-56.

THERAPEUTIC APPROACH TO ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Rojas MT, Mulas F, Gandá-a R, et al.

Attention deficit hyperactivity disorder (ADHD) is the most prevalent and frequent neurodevelopmental disorder in neuropediatrics, child psychiatry and child psychology consultations. The greater awareness of this condition, the information and, above all, the socio-cultural acceptance, has led to an earlier diagnosis, leading to more timely and effective treatment. Individualizing each case through systematic tools such as neuropsychological studies and their neuroanatomical and neurobiochemical correlation, related to ADHD, together with algorithms that analyze executive functions, is essential to indicate the optimal pharmacological treatment, together with the application of appropriate non-pharmacological therapies. Multimodal treatment, with cognitive behavioral intervention and pharmacological treatment, is the most effective therapeutic approach

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Medicine (Baltimore). 2022 Sep;101:e30545.

USING THE ALLUVIAL PLOT TO VISUALIZE THE NETWORK CHARACTERISTICS OF 100 TOP-CITED ARTICLES ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) SINCE 2011: BIBLIOMETRIC ANALYSIS.

Tsai YC, Chien TW, Wu JW, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is a common neuro developmental disorder that affects children and adolescents. It is estimated that the prevalence of ADHD is 7.2% throughout the world. There have been a number of articles published in the literature related to ADHD. However, it remains unclear which countries, journals, subject categories, and articles have the greatest influence. The purpose of this study was to display influential entities in 100 top-cited ADHD-related articles (T100ADHD) on an alluvial plot and apply alluvial to better understand the network characteristics of T100ADHD across entities.

Methods: Using the PubMed and Web of Science (WoS) databases, T100ADHD data since 2011 were downloaded. The dominant entities were compared using alluvial plots based on citation analysis. Based on medical subject headings (MeSH terms) and research areas extracted from PubMed and WoS, social network analysis (SNA) was performed to classify subject categories. To examine the difference in article citations among subject categories and the predictive power of MeSH terms on article citations in T100ADHD, one-way analysis of variance and regression analysis were used.

Results: The top 3 countries (the United States, the United Kingdom, and the Netherlands) accounted for 75% of T100ADHD. The most citations per article were earned by Brazil (=415.33). The overall impact factor (IF = citations per 100) of the T100ADHD series is 188.24. The most cited article was written by Polanczyk et al from Brazil, with 772 citations since 2014. The majority of the articles were published and cited in Biol Psychiatry (13%; IF = 174.15). The SNA was used to categorize 6 subject areas. On the alluvial plots, T100ADHD's network characteristics were successfully displayed. There was no difference in article citations among subject categories (F = 1.19, P = .320). The most frequently occurring MeSH terms were physiopathology, diagnosis, and epidemiology. A significant correlation was observed between MeSH terms and the number of article citations (F = 25.36; P < .001).

Conclusion: Drawing the alluvial plot to display network characteristics in T100ADHD was a breakthrough. Article subject categories can be classified using MeSH terms to predict T100ADHD citations. Bibliometric analyses of 100 top-cited articles can be conducted in the future

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Methods Mol Biol. 2022;2547:427-36.

THE PHARMACOGENETIC IMPACT ON THE PHARMACOKINETICS OF ADHD MEDICATIONS.

Brown JT.

ADHD is a common condition in both children and adults. The most prescribed medications for the treatment of ADHD include methylphenidate, mixed amphetamine salts, atomoxetine, guanfacine, and clonidine. While

each of these medications have their own distinct pharmacokinetic profile, the extent to which pharmacogenetics effects their pharmacokinetic parameters is best described in atomoxetine, followed by methylphenidate. Atomoxetine is predominantly metabolized by cytochrome p450 2D6 (CYP2D6), while methylphenidate is metabolized by carboxylesterase 1 (CES1). Both CYP2D6 and CES1 have multiple variants resulting in varying levels of enzyme activity; however, to date, the functional consequence of variants and alleles for CYP2D6 is better characterized as compared to CES1. Regarding CYP2D6, individuals who are poor metabolizers prescribed atomoxetine experience up to ten-fold higher exposure as compared to normal metabolizers at comparable dosing. Additionally, individuals prescribed methylphenidate with the rs71647871 variant may experience up to 2.5-fold higher exposure as compared to those without. Having this pharmacogenetic information available may aid clinicians and patients when choosing medications and doses to treat ADHD

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NeuroImage Clin. 2022;36.

BEHAVIORAL AND NEUROCOGNITIVE EFFECTS OF JUDO TRAINING ON WORKING MEMORY CAPACITY IN CHILDREN WITH ADHD: A RANDOMIZED CONTROLLED TRIAL.

Ludyga S, et al.

Background: Children with Attention Deficit Hyperactivity Disorder (ADHD) face deficits in working memory capacity that often persist into adulthood. In healthy peers, exercise targeting motor skill acquisition benefits visuospatial working memory, but its potential to reduce ADHD-related deficits remains unclear. We investigated the effect of a judo training program targeting motor skills on behavioral and neurocognitive indices of working memory capacity in children with ADHD.

Methods: Children with ADHD aged 8 to 12 years (N = 57) were randomly allocated to a judo training group and a wait-list control group. The training program encompassed 120 min of judo per week over three months. Before and after the intervention period, participants completed a bilateral Change Detection task with low and high memory load conditions and the Movement Assessment Battery for Children-2 (MABC-2). The contralateral delay activity (CDA) elicited by the cognitive task was recorded using electroencephalography.

Results: Compared to the control group, the judo training group showed a higher K-score on the Change Detection task and an increased negativity of the CDA on the high load condition following the intervention, when pretest scores (and confounders) were accounted for. In contrast, no group differences were found for MABC-2 score.

Conclusion: In children with ADHD, judo training may complement the pharmacological treatment by increasing the effectiveness of working memory maintenance processes. On a behavioral level, this improvement is accompanied with an increased capacity to store visuospatial information

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NeuroQuantology. 2022;20:2816-29.

EFFECTIVENESS OF ATOMOXETINE ON CHILDREN WITH AUTISM SPECTRUM DISORDER AND COMORBID ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Azouz HG, Ghareib B, Gad HA, et al.

Background: Early-onset neurodevelopmental abnormalities known as autism spectrum disorders (ASD) causes considerable impairment in social interaction and communication. It is well known that children with ASD are at risk for attention deficit/hyperactivity disorder (ADHD), with about one-third of these kids showing substantial inattention and/or hyperactivity issues. ADHD symptoms in ASD are frequently challenging to control and hinder the ability to perform at school, in the community, and at home. The objective of this study was to examine the short-term effects of atomoxetine on core symptoms of autism and hyperactivity in children and adolescents with ASD and ADHD.

Method: The Childhood Autism Rating Scale-2 (CARS-2), Conner's Parent Rating Scales-Revised (CPRS-R) and Autism Treatment Evaluation Checklist (ATEC), were used to evaluate the severity of autism and ADHD symptoms prior to the administration of atomoxetine (ATX) to 20 of the study's 40 ASD patients with ADHD. The other 20 children served as the control group, and after intervention.

Results: When the atomoxetine group was compared to the control group, a significant statistic was present. In the activity level relation to people subscales of the CARS-2, the health/physical/behavior and sociability

subscales of the ATEC, and the emotional liability in the Conner's test. Nevertheless, there was neither difference seen between CARS-2's and the ATEC's total scores.

Conclusion: In children with ASD and concomitant ADHD, atomoxetine demonstrated encouraging results for hyperactivity, sociability and emotional liability. These early findings need to be confirmed by larger research conducted in the future

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Pediatr Int. 2022 Jan;64:e15298.

A COMPARATIVE ANALYSIS OF CHILDREN BORN WITH LOW BIRTHWEIGHT AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Iai Y, Shimakawa S, Fukui M, et al.

BACKGROUND: We aimed to compare the profile of the Wechsler Intelligence Scale for Children Fourth Edition (WISC-IV) between Japanese schoolchildren born very preterm (VP) and with very low birthweight (VLBW) and those with attention deficit hyperactivity disorder (ADHD), and to identify the specific neurocognitive characteristics of VLBW/VP children.

METHODS: The VLBW/VP group in the present study included 50 (19 male, 31 female) first- to third-grade elementary school children born between January 2008 and February 2013 at Osaka Medical and Pharmaceutical University Hospital and Saiseikai Suita Hospital with birthweights <1,500g and <32 gestational weeks. The ADHD group included 18 (13 male, 5 female) first- to third-grade elementary school children who visited Osaka Medical and Pharmaceutical University Hospital between January 2019 and October 2021. Full-scale intelligence quotient scores, four indices, and 12 subtests of the WISC-IV were calculated for all participants and compared between the VLBW/VP and ADHD groups. We assessed whether the patients' clinical history was associated with a low score on the cancellation task in the VLBW/VP group.

RESULTS: The WISC-IV profiles showed similar between-group patterns, and the VLBW/VP group had lower cancellation task scores than the ADHD group.

CONCLUSIONS: This is the first study to compare WISC-IV profiles between VLBW/VP children and those with ADHD. Further investigation is needed on the association between academic performance and the score of the cancellation task, and the neural mechanism of low performance for cancellation tasks in VLBW/VP children

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Pediatrics. 2022 Oct;150.

PSYCHOTROPIC MEDICATION UTILIZATION AMONG CHILDREN DIAGNOSED WITH FETAL ALCOHOL SPECTRUM DISORDER.

Senturias Y, Ali MM, West K.

BACKGROUND AND OBJECTIVES: To date, there has been no large, population-based study estimating the prevalence of psychotropic medication use and cooccurring medical conditions among children with fetal alcohol syndrome disorder (FASD). In addition, it is not known how psychotropic medication use varies by mental health status of the children with FASD and their health insurance coverage. This study attempts to fill this gap by analyzing a large health insurance claims database covering Medicaid and private insurance.

METHODS: The study used the 2017 IBM Watson Health MarketScan Multistate Medicaid and Commercial Claims databases. The sample for the analysis includes children between the ages of 0 and 17 with either an FASD diagnosis or a mental health diagnosis (N = 848-721 Medicaid; N = 511-061 private insurance).

RESULTS: More than half of the children with an FASD diagnosis were prescribed psychotropic medications (63% Medicaid; 57% private). Utilization rates of psychotropic medication among children with cooccurring FASD and a mental health condition (79% Medicaid; 71% private) were higher compared to children with a mental health diagnosis but no FASD (57% Medicaid; 57% private). Stimulants were the most commonly prescribed. Encephalopathy, attention deficit hyperactivity disorder, and epilepsy were the 3 most common cooccurring diagnosis among children with FASD using psychotropic medication under Medicaid compared to encephalopathy, attention deficit hyperactivity disorder, and anxiety with private insurance.

CONCLUSIONS: These results exemplify the complexity of the neurobehavioral profile of children with FASD and the challenge of treatment. Future studies may determine how supportive services for these children will affect psychotropic medication use

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PLoS ONE. 2022;17.

THE ASSOCIATIONS BETWEEN ADHD, PAIN, INFLAMMATION, AND QUALITY OF LIFE IN CHILDREN AND ADOLESCENTS-A CLINICAL STUDY PROTOCOL.

Kerekes N, Lundqvist S, Hjalmarsson ES, et al.

New research shows that the prevalence of neurodevelopmental disorders, such as attention-deficit/hyperactivity disorder (ADHD), is increased in children and adolescents as well as in adults with chronic pain, compared to those without chronic pain. Children and adolescents with ADHD also have an increased incidence of various physical conditions associated with pain, and they more frequently suffer from inflammatory diseases. Moreover, parents of children with ADHD can often suffer from pain conditions. These epidemiological and clinical observations form the scientific basis of our study, which aims to map the relationships between ADHD, altered pain experiences/central sensitization, and inflammation in children and adolescents. We will investigate the presence of central sensitization in children and adolescents with newly diagnosed ADHD and compare it with those who have not been diagnosed with ADHD. Participants (and their biological parents) will complete surveys about their somatic health, pain experience, and quality of life. Biological samples (saliva and stool) will be collected, aiming to utilize proteome and metabolome data to discover disease mechanisms and to predict, prevent and treat them. The results from our investigation should enable an expanded understanding of the pathophysiology behind both ADHD and pain/central sensitization. Presently, there are no established protocols for addressing psychiatric symptoms when examining patients with pain conditions in a somatic care setting, nor is there any knowledge of offering patients with ADHD or other neurodevelopmental disorders adapted treatments for pain conditions. Our results, therefore, can contribute to the development of new treatment strategies for pathological pain conditions in children and adolescents with ADHD. They may also increase awareness about and provide opportunities for the treatment of attention and impulse control problems in children and adolescents with pain syndromes

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PLoS ONE. 2022;17:e0273805.

GEOGRAPHIC PROXIMITY TO PRIMARY CARE PROVIDERS AS A RISK-ASSESSMENT CRITERION FOR QUALITY PERFORMANCE MEASURES.

Bell N, et al.

IMPORTANCE: Previous studies have found a mixed association between Patient-Centered Medical Home (PCMH) designation and improvements in primary care quality indicators, including avoidable pediatric emergency department (ED) encounters. Whether these associations persist after accounting for the geographic locations of providers relative to where patients reside is unknown.

OBJECTIVE: To examine the association between geographic proximity to primary care providers versus hospitals and risk of avoidable and potentially avoidable ED visits among children with pre-existing diagnosis of attention-deficit/hyperactivity disorder or asthma.

METHODS: Retrospective cohort study of a panel of pediatric Medicaid claims data from the South Carolina from 2016-2018 for 2,959 beneficiaries having a pre-existing diagnosis of attention-deficit/hyperactivity disorder (ADD, ages 6-12) and 6,390 beneficiaries with asthma (MMA, ages 5-18), as defined using Healthcare Effectiveness Data and Information Set (HEDIS) performance measures. We calculated differences in avoidable and potentially avoidable ED visits by the beneficiary's PCMH attribution type and in relation to differences in proximity to their primary care providers versus hospitals. Outcomes were defined using the New York University Emergency Department Algorithm (NYU-EDA). Differences in ED visit risk were assessed using generalized estimation equations and compared using marginal effects models.

RESULTS: The 2.4 percentage point reduction in risk of avoidable ED visits among children in the ADD cohort who attended a PCMH versus those who did not increased to 3.9 to 7.2 percentage points as relative proximity to primary care providers versus hospitals improved ($p < 0.01$). Children in the ADD and MMA

cohorts that were enrolled in a medical home, but did not attend one for primary care services exhibited a 5.4 and 3.0 percentage point increase in avoidable ED visit compared to children who were unenrolled and did not attend medical homes ($p < 0.05$), but these differences were only observed when geographic proximity to hospitals was more convenient than primary care providers. Mixed findings were observed for potentially avoidable visits.

CONCLUSIONS: In several health care performance evaluations, patient-centered medical homes have not been found to reduce differences in hospital utilization for conditions that are treatable in primary care settings among children with chronic illnesses. Analytical approaches that also consider geographic proximity to health care services can identify performance benefits of medical homes. Expanding risk-adjustment models to also include geographic data would benefit ongoing quality improvement initiatives

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PLoS ONE. 2022;17:e0272593.

MATERNAL USE OF ACETAMINOPHEN DURING PREGNANCY AND NEUROBEHAVIORAL PROBLEMS IN OFFSPRING AT 3 YEARS: A PROSPECTIVE COHORT STUDY.

Sznajder KK, Teti DM, Kjerulff KH.

BACKGROUND: Acetaminophen is one of the most commonly used drugs during pregnancy globally. Recent studies have reported associations between prenatal exposure to acetaminophen and neurobehavioral problems in children, including attention-deficit hyperactivity disorders. Little research has investigated these associations in preschool-age children or the potential confounding effects of prenatal stress. The purpose of this study was to examine associations between prenatal acetaminophen exposure and offspring neurobehavioral problems at the age of 3 years, with a focus on the potentially confounding effects of prenatal stress.

METHODS: We used data from the First Baby Study, a prospective cohort study conducted in Pennsylvania, USA, with 2,423 mother-child pairs. Women reported medication use and completed a prenatal stress inventory during their third trimester. Child behavioral problems were measured at the age of 3 years, using the 7 syndrome scale scores from the Child Behavior Checklist (CBCL) for ages 1 ½ to 5.

RESULTS: There were 1,011 women (41.7%) who reported using acetaminophen during pregnancy. Children who were exposed to acetaminophen during pregnancy scored significantly higher on 3 of the 7 CBCL syndrome scales: withdrawn, sleep problems and attention problems. Scores on all 7 of the CBCL syndrome scales were significantly associated with prenatal stress. After adjustment for prenatal stress and other confounders, 2 syndrome scales remained significantly higher in children exposed to acetaminophen: sleep problems (aOR = 1.23, 95% CI = 1.01-1.51) and attention problems (aOR = 1.21, 95% CI = 1.01-1.45).

CONCLUSIONS: These findings corroborate previous studies reporting associations between prenatal exposure to acetaminophen and attention problems in offspring and also show an association with sleep problems at age 3 years. Because use of acetaminophen during pregnancy is common, these results are of public health concern and suggest caution in the use of medications containing acetaminophen during pregnancy

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PLoS ONE. 2022;17:e0273819.

IRON DEFICIENCY AND COMMON NEURODEVELOPMENTAL DISORDERS-A SCOPING REVIEW.

McWilliams S, Singh I, Leung W, et al.

BACKGROUND: A wealth of human and experimental studies document a causal and aggravating role of iron deficiency in neurodevelopmental disorders. While pre-, peri-, and early postnatal iron deficiency sets the stage for the risk of developing neurodevelopmental disorders, iron deficiency acquired at later ages aggravates pre-existing neurodevelopmental disorders. Yet, the association of iron deficiency and neurodevelopmental disorders in childhood and adolescence has not yet been explored comprehensively. In this scoping review, we investigate 1) the association of iron deficiency in children and adolescents with the most frequent neurodevelopmental disorders, ADHD, ASD, and FASD, and 2) whether iron supplementation improves outcomes in these disorders.

METHOD: Scoping review of studies published between 1994 and 2021 using "iron deficiency / iron deficiency anemia" AND "ADHD" OR "autism" OR "FASD" in four biomedical databases. The main inclusion

criterion was that articles needed to have quantitative determination of iron status at any postnatal age with primary iron markers such as serum ferritin being reported in association with ADHD, ASD, or FASD.

RESULTS: For ADHD, 22/30 studies and 4/4 systematic reviews showed an association of ADHD occurrence or severity with iron deficiency; 6/6 treatment studies including 2 randomized controlled trials demonstrated positive effects of iron supplementation. For ASD, 3/6 studies showed an association with iron deficiency, while 3/6 and 1/1 systematic literature review did not; 4 studies showed a variety of prevalence rates of iron deficiency in ASD populations; 1 randomized controlled trial found no positive effect of iron supplementation on behavioural symptoms of ASD. For FASD, 2/2 studies showed an association of iron deficiency with growth retardation in infants and children with prenatal alcohol exposure.

CONCLUSION: Evidence in favor of screening for iron deficiency and using iron supplementation for pediatric neurodevelopmental disorders comes primarily from ADHD studies and needs to be further investigated for ASD and FASD. Further analysis of study methodologies employed and populations investigated is needed to compare studies against each other and further substantiate the evidence created

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PLoS ONE. 2022;17:e0274375.

CO-PRODUCTION OF A NATURE-BASED INTERVENTION FOR CHILDREN WITH ADHD STUDY (CONIFAS): PROTOCOL FOR CO-PRODUCTION PHASES.

Armitt HA, Kingsley EN, Attwell L, et al.

Children with Attention Deficit Hyperactivity Disorder can face difficulties with inattention, hyperactivity, and impulsivity, which can impact many areas of their lives, including their educational attainment and social and emotional wellbeing. Involvement in nature-based activities can reduce these difficulties and improve wellbeing, but there are limited resources for supporting children with this diagnosis to access these approaches and no nature-based interventions designed with and for this group. This protocol describes a co-production study in which children diagnosed with Attention Deficit Hyperactivity Disorder aged 5-11 years old, their parents/guardians, and professionals will attend a series of workshops to share their knowledge to co-produce a new nature-based intervention for this population of children. We aim to understand how the children's' experiences of Attention Deficit Hyperactivity Disorder may affect their interactions with nature, identify how activity in and with nature may help with symptom reduction and general wellbeing, and co-produce an intervention for families which applies our learning. The result of this study will be the designed intervention and insights into how children and young people with Attention Deficit Hyperactivity Disorder interact with nature. The prototype intervention will then undergo feasibility testing in a future study.

Trail registration: NIHR203043; ISRCTN11763460

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Prev Chronic Dis. 2022 Sep;19:E60.

PSYCHOSOCIAL CORRELATES OF INSOMNIA AMONG COLLEGE STUDENTS.

Mbous YPV, Nili M, Mohamed R, et al.

INTRODUCTION: Among college students, insomnia remains a topic of research focus, especially as it pertains to its correlates and the extent of its association with mental conditions. This study aimed to shed light on the chief predictors of insomnia among college students.

METHODS: A cross-sectional survey on a convenience sample of college students (aged 18 years) at 2 large midwestern universities was conducted from March 18 through August 23, 2019. All participants were administered validated screening instruments used to screen for insomnia, depression, and attention deficit hyperactivity disorder (ADHD). Insomnia correlates were identified by using multivariate logistic regression.

RESULTS: Overall, 26.4% of students experienced insomnia; 41.2% and 15.8% had depression and had ADHD symptoms, respectively. Students with depression (adjusted odds ratio, 9.54; 95% CI, 4.50-20.26) and students with ADHD (adjusted odds ratio, 3.48; 95% CI, 1.48-8.19) had significantly higher odds of insomnia. The odds of insomnia were also significantly higher among employed students (odds ratio, 2.10; 95% CI, 1.05-4.18).

CONCLUSION: This study showed an association between insomnia and mental health conditions among college students. Policy efforts should be directed toward primary and secondary prevention programs that

enforce sleep education interventions, particularly among employed college students and those with mental illnesses

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Prim Care Companion CNS Disord. 2022 Sep;24.

SEX DIFFERENCES IN PSYCHIATRIC COMORBIDITIES IN ADOLESCENTS WITH AUTISM SPECTRUM DISORDER: A NATIONAL INPATIENT SAMPLE ANALYSIS.

Vadukapuram R, Elshokiry AB, Trivedi C, et al.

Objective: To investigate sex differences in psychiatric comorbidities in adolescents with autism spectrum disorder (ASD).

Methods: The US National Inpatient Sample dataset (January 2016 to December 2018) was used for this retrospective study. The patient population was selected by performing a query on all adolescent patients (aged 12-17 years) having ASD with the ICD-10-CM code starting with F84. All missing sex data were excluded. Additional data on mood disorders, anxiety disorders, personality disorders, adjustment disorders, psychotic disorders, attention-deficit/hyperactivity disorder (ADHD)/conduct disorders, sleep-wake disorders, and substance use disorders were collected. Data on psychiatric comorbidities were collected using the ICD-10-CM code provided in the Clinical Classifications Software of the dataset.

Results: Mood disorders (37.4% vs 44.1%, $P < .001$) and anxiety disorders (29.4% vs 37.0%, $P < .001$) were more prevalent in females compared to males. The prevalence of ADHD and other conduct disorders was significantly higher in males than females (47.7% vs 36.7%, $P < .001$). Substance use disorders were slightly higher among males compared to females (3.7% vs 3.0%, $P = .04$).

Conclusion: The study findings revealed statistically significant disparities in psychiatric comorbidities among adolescent male and female patients with ASD. These findings could serve as a pilot for larger-scale research with this patient population in the future

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Psychiatr Danub. 2022 Sep;34:214-19.

UNIQUE VARIABLE ANALYSIS OF REDUNDANCY IN ADHD ITEMS FROM THE CONNERS TEACHER RATING SCALE - REVISED: SHORT.

Till AC, Florquin R, Christensen AP, et al.

Attention deficit hyperactivity disorder (ADHD) is a neuropsychiatric disorder interfering with the normal development of the child. The disorder can be screened at school with the Conners Teacher Rating Scale Revised Short (CTRS-R:S). This scale goes beyond the disorder itself and covers a wider construct, that of abnormal child behavior. This can be understood as a complex system of mutually influencing entities. We analyzed a data set of 525 children in French-speaking primary schools from Belgium, and estimated a network structure, as well as to determine the local dependence of items through Unique Variable Analysis. A reduced network was computed including 15 non-locally dependent items. The structural consistency of the network was not affected by redundant items and was structurally sound. The reduction of the number of variables in network studies is important to improve the investigation of network structures as well as better interpret results from inference measures

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Psychiatry Clin Neurosci. 2022.

RISK OF INJURIES REQUIRING HOSPITALIZATION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND THE PREVENTIVE EFFECTS OF MEDICATION.

Pai MS, Yang SN, Chu CM, et al.

Aims: Patients with attention deficit hyperactivity disorder (ADHD) are prone to injury and frequently require treatment with hospital admission. This study aimed to evaluate the risk of injuries requiring hospitalization among children and adolescents with and without ADHD and assess the effects of medication on the risk reduction in patients with ADHD.

Methods: This is a retrospective population-based cohort study by using data from the Taiwan National Health Insurance Research Database. We compared 4658 6-18 year-old ADHD patients with 18 632 sex-, age-, and index day-matched non-ADHD controls between 2005 and 2012. Both groups were followed until

the end of 2013 to compare the risk of injuries requiring hospitalization. Cox regression analysis was performed to determine the hazard ratio (HR) with 95% confidence intervals (CI) after adjusting for confounders.

Results: Children and adolescents with ADHD had a significantly higher risk of injuries requiring hospitalization than the non-ADHD controls (HR=1.39, 95% CI=1.12-1.72), and a higher risk was especially observed in the male and adolescent subgroups. In ADHD patients, long-term users of ADHD medication were associated with a lower risk of injuries requiring hospitalization than nonusers (HR=0.51, 95% CI=0.30-0.85).

Conclusion: Healthcare providers should be aware of the potential risk of injury in patients with ADHD and highlight the importance of the duration and compliance with medication treatment

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Psychiatry Res Neuroimaging. 2022;326.

ALTERED FUNCTIONAL CONNECTIVITY IN CHILDREN WITH ADHD WHILE PERFORMING COGNITIVE CONTROL TASK.

Kumar U, Arya A, Agarwal V.

Response inhibition is one of the crucial cognitive domains that exhibit deficit in children with ADHD. To further elucidate it, this study examines the task-based functional-connectivity in children with attention deficit hyperactive disorder (ADHD). We acquired the fMRI data of 16 unmedicated children with ADHD and 16 typically developing (TD) children who performed the flanker task. MVPA and seed-based connectivity analysis was performed to identify the abnormal connectivity pattern across the whole brain. MVPA revealed that six important regions, namely the right IFG, right SMA, bilateral precentral gyrus, left DLPFC, and left cerebellum, had abnormal connectivity in children with ADHD while they performed the cognitive control task. Out of these six regions, four were further used for whole-brain seed-based functional connectivity analyses, which revealed patterns of significantly altered connectivity across multiple regions. Signal intensities changes were also extracted to perform BOLD- reaction time (RT) correlation analysis, that suggest positive correlation between left DLPFC and right IFG. Overall, the results suggest that children with ADHD are unable to endure high cognitive control demand. Our findings highlight the utility of analyzing brain connectivity data in identifying the abnormal connectivity in children with ADHD

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Psychol Assess. 2022 Sep.

TEMPERAMENT IN MIDDLE CHILDHOOD QUESTIONNAIRE: NEW DATA ON FACTOR STRUCTURE AND APPLICABILITY IN A CHILD CLINICAL SAMPLE.

Kozlowski MB, Antovich D, Karalunas SL, et al.

The Temperament in Middle Childhood Questionnaire (TMCQ) is one of a family of instruments representing one of the major conceptual models of child temperament. The present study reports new psychometric information on the TMCQ using a larger sample than in prior factor-analytic studies of this instrument. Data from parent ratings of 1,418 children were utilized. The sample of community volunteers included 697 typically developing youth and 721 defined by research diagnostic procedures as having attention-deficit/hyperactivity disorder. Results failed to support the original proposed structure of the TMCQ, but found support for a structure with 12 subscales that confirmed a substantial portion of the lower order factor structure. However, the intended three-factor higher order structure was not able to be fully recovered. Two-group invariance was supported in the final model, supporting use in studies of typical and atypical development. In conclusion, with some modifications the TMCQ remains a useful research measure at the lower order factor level. The validity of the higher order structure is less clear, likely due to measure-specific limitations, and suggests a need for some refinement to the measure.

This study provides evidence for the reliability and validity of a modified version of the Temperament in Middle Childhood Questionnaire, a commonly used instrument in developmental and psychopathology research

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Psychoneuroendocrinology. 2022;146.

LOW SERUM ALLOPREGNANOLONE LEVELS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Xahin, Say GN, et al.

Attention deficit hyperactivity disorder (ADHD) has increasing evidence for the role of neurohormones in its etiopathogenesis. It has been suggested that the effects of neurosteroids on the brain in the early developmental period may predispose to neurodevelopmental pathologies. In our study, we examined serum dehydroepiandrosterone (DHEA), dehydroepiandrosterone sulfate (DHEA-S), and allopregnanolone levels in children with ADHD and whether these neurosteroids differ in the presence of specific learning disorder (SLD) and oppositional defiant disorder (ODD) comorbidities (ADHD+SLD and ADHD+ODD). We also investigated the relationship between neurosteroid levels and the severity of ADHD symptoms. Thirty-five prepubertal children with ADHD and 33 prepubertal healthy children, all aged 6-10 years, were included in this study. The severity of ADHD symptoms was assessed with the parent-rated and teacher-rated Turgay DSM-IV Disruptive Behavior Disorders Rating Scale (T-DSM-IV-S). Serum allopregnanolone levels were significantly lower in the ADHD group compared to healthy controls. When analyzed according to comorbidity status, serum allopregnanolone levels were lower in ADHD+SLD and ADHD+ODD groups compared to healthy controls. However, when compared to healthy children, serum DHEA and DHEA-S levels in children with ADHD were not significantly different. Serum allopregnanolone levels were negatively associated with teacher-rated T-DSM-IV-S hyperactivity/impulsivity scores for all participants only. These findings suggest that allopregnanolone may play a role in the pathophysiology of ADHD, especially in the presence of ODD and SLD comorbidities

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Rev Neurol. 2022 Oct;75:189-97.

THE ROLE OF CANNABINOIDS IN NEURODEVELOPMENTAL DISORDERS OF CHILDREN AND ADOLESCENTS.

Dias-de FF, Pimenta S, Soares S, et al.

INTRODUCTION: Neurodevelopmental disorders have a multifactorial etiology that results from the interaction between biological and environmental factors. The biological basis of many of these disorders is only partially understood, which makes therapeutic interventions, especially pharmacological ones, particularly difficult. The impact of medical cannabis on neurological and psychiatric disorders has been studied for a long time. This study aimed to review the currently available clinical and pre-clinical studies regarding the use of cannabinoids in pediatric neurodevelopmental disorders and to draw attention to the potential therapeutic role of cannabidiol in this field.

DEVELOPMENT: Cannabidiol is an endocannabinoid system modulator and exerts its effects on both developing and mature brains through numerous mechanisms. Cannabidiol holds a relatively high toxicity limit and current literature suggests that it may have anxiolytic, antipsychotic, and neuroprotective properties. Clinical evidence suggests that early treatment with cannabidiol might be a promising therapy for neurodevelopmental disorders, including intellectual disability, autism spectrum disorders, tics, and attention/deficit hyperactivity disorder.

CONCLUSIONS: This review hopefully draws attention to an emerging body of evidence concerning cannabidiol's significant potential to safely improve many of the common symptoms affecting children and adolescents with neurodevelopmental disorders, especially autism spectrum disorder

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Sci Rep. 2022 Sep;12:15922.

ADGRL3 GENOMIC VARIATION IMPLICATED IN NEUROGENESIS AND ADHD LINKS FUNCTIONAL EFFECTS TO THE INCRETIN POLYPEPTIDE GIP.

Vidal OM, et al.

Attention deficit/hyperactivity disorder (ADHD) is the most common childhood neurodevelopmental disorder. Single nucleotide polymorphisms (SNPs) in the Adhesion G Protein-Coupled Receptor L3 (ADGRL3) gene are associated with increased susceptibility to developing ADHD worldwide. However, the effect of ADGRL3 non-synonymous SNPs (nsSNPs) on the ADGRL3 protein function is vastly unknown. Using several bioinformatics tools to evaluate the impact of mutations, we found that nsSNPs rs35106420, rs61747658, and rs734644, previously reported to be associated and in linkage with ADHD in disparate populations from

the world over, are predicted as pathogenic variants. Docking analysis of rs35106420, harbored in the ADGLR3-hormone receptor domain (HRM, a common extracellular domain of the secretin-like GPCRs family), showed that HRM interacts with the Glucose-dependent insulinotropic polypeptide (GIP), part of the incretin hormones family. GIP has been linked to the pathogenesis of diabetes mellitus, and our analyses suggest a potential link to ADHD. Overall, the comprehensive application of bioinformatics tools showed that functional mutations in the ADGLR3 gene disrupt the standard and wild ADGRL3 structure, most likely affecting its metabolic regulation. Further in vitro experiments are granted to evaluate these in silico predictions of the ADGRL3-GIP interaction and dissect the complexity underlying the development of ADHD

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Sci Rep. 2022 Sep;12:16235.

PRENATAL AND EARLY POSTNATAL EXPOSURE TO A NATURAL DISASTER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN INDIAN CHILDREN.

Hana T, Gomula A, Nowak-Szczepanska N, et al.

The aim of this study was to assess the relation between early exposure to stressful events and symptoms of the Attention-Deficit/Hyperactivity Disorder (ADHD) in children, based on the outcomes from a natural experiment. It was hypothesized that children pre- and postnatally exposed to cyclone Aila have increased ADHD symptoms compared to the control group, and the effect depends on the timing of the exposure. Indian children (8-11 years) prenatally (N=336) and early postnatally (N=216) exposed to cyclone Aila were compared to a non-exposed control peer group (N=285). ADHD symptoms were assessed using the Conner's Teacher Rating Scale Revised. The main effect of exposure to the cyclone on the total ADHD symptoms' score, ADHD index, Hyperactivity and Oppositional symptoms was significant and independent to covariates: age and sex of children, gestational age and birth weight, maternal stress during the year before the study and the socioeconomic status of a family. The timing of exposure and sex of the children were found to be a significant moderator of the relation between early exposure to the natural disaster and ADHD symptoms. The prenatal, but also early postnatal exposure to stressful experiences such as a natural disaster, may disturb the development of cognitive functions and behavioural control, thus increasing the risk of ADHD in children

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Transl Psychiatry. 2022 Sep;12:368.

DISTINCT BRAIN STRUCTURAL ABNORMALITIES IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND SUBSTANCE USE DISORDERS: A COMPARATIVE META-ANALYSIS.

Long Y, Pan N, Ji S, et al.

As two common mental disorders during the period of adolescence that extend to early adulthood, attention-deficit/hyperactivity disorder (ADHD) and substance use disorders (SUDs) have considerable diagnostic co-occurrence and shared neuropsychological impairments. Our study aimed to identify overlapping and distinct brain structural abnormalities associated with ADHD and SUDs among adolescents and young adults. A systematic literature search on voxel-based morphometry (VBM) studies of ADHD and SUDs was conducted in PubMed and Web of Science. Data were extracted and analyzed to identify brain abnormalities using Seed-based d-Mapping software. Data-driven functional decoding was conducted to identify the psychophysiological functioning associated with brain alterations. 13 and 14 VBM studies for ADHD (619 patients and 483 controls) and SUDs (516 patients and 413 controls), respectively, were included. Patterns of decreased gray matter volume (GMV) were found in the left precentral gyrus, bilateral superior frontal gyri, and left inferior frontal gyrus in the ADHD group compared to the control group. In contrast, individuals with SUDs, relative to controls, were characterized by increased GMV in the left putamen and insula. Comparative analysis indicated larger regional GMV in the right inferior parietal lobule and smaller volumes in the left putamen and left precentral gyrus in the ADHD group than in the SUDs group. Dissociable brain structural abnormalities in adolescents and young adults with ADHD and SUDs potentially implicate different pathogeneses and provide a reference for differential diagnosis and early detection for shared symptomology and comorbidity

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