

# NEWSLETTER



## INDICE:

Dalle banche dati bibliografiche

pag. 2

## **BIBLIOGRAFIA ADHD FEBBRAIO 2020**

Addictive Behaviors. 2020 Feb;101:8.

**PREDICTING LIKELIHOOD OF PSYCHOLOGICAL DISORDERS IN PLAYERUNKNOWN'S BATTLEGROUNDS (PUBG) PLAYERS FROM ASIAN COUNTRIES USING SUPERVISED MACHINE LEARNING.**

***Aggarwal S, Saluja S, Gambhir V, et al.***

Multiplayer Online Battle Arena (MOBA) has become one of the most popular genre of online video games played by gamers worldwide. Previous studies have exhibited that excessive engagement in games can lead to Internet Gaming Disorder (IGD). Internet Gaming Disorder has been associated with psychological disorders like impulsivity, anxiety and Attention Deficit Hyperactivity Disorder (ADHD). In this study, we propose an approach to use the game and player statistics along with self-esteem measure of a PlayerUnknown's Battlegrounds (PUBG, a MOBA game) player to predict whether he/she suffers from IGD and psychological disorders namely ADHD and Generalized Anxiety Disorder (GAD). We extract the game and player statistics of PUBG players from Asian countries and then run several state of the art supervised machine learning models to predict the occurrence of IGD, ADHD, and GAD. Initial experiments and results show that we are able to predict IGD, ADHD, and GAD with an accuracy of 93.18%, 81.81% and 84.9% respectively. Game statistics of PUBG players show strong positive correlation with IGD and ADHD indicating detrimental effects of MOBA games

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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.**

Adv Neurobiol. 2020;24:481-504.

**FOOD COLOR AND AUTISM: A META-ANALYSIS.**

***Bakthavachalu P, Kannan SM, Qoronfleh MW.***

Autism has been increasing dramatically since its description by Leo Kanner in 1943. The Centers for Disease Control and Prevention (CDC) in 2018 has identified 1 in 59 children (1 in 37 boys and 1 in 151 girls) has autism spectrum disorder (ASD). Autistic spectrum disorders and ADHD are complex conditions in which nutritional and environmental factors play major roles. It is important to understand how food can have an impact on their current and future health. Appealing food colors stimulate the consumption of different food products. Since 2011, it is evident that dyes are linked to harmful effects in children. Artificial dyes have neurotoxic chemicals that aggravate mental health problems. Many families with autistic children avoid food dyes in their diet in order to avoid behavioral issues. A study reported that there is a correlation between yellow dye and sleep disturbance. Food colors Blue 1 and 2, Green 3, Red 3, Yellow 5 and 6, Citrus Red 2, and Red 40 can trigger many behaviors in most kids. Artificial food color usually contains petroleum and is manufactured in a chemical process that includes formaldehyde, aniline, hydroxides, and sulfuric acids. Most impurities in the food color are in the form of salts or acids. Sometimes lead, arsenic, and mercury may be present as impurities. The U.S. FDA is yet to study the effects of synthetic dyes on behavior in children. A study conducted at Southampton University in England found a link between food dyes and hyperactive behavior in children. The research does not prove that food coloring actually causes autism spectrum disorder, but there seems to be a link. This chapter attempts to provide a broad review of the available literature on food color and the epidemiology, etiology, prevention, and treatment of autistic spectrum disorder

American Journal of Therapeutics. 2018;26:e742-e743.

**METHYLPHENIDATE-INDUCED YAWNING CHASM IN AN ADOLESCENT WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER THAT RESOLVED BY SWITCHING TO ATOMOXETINE.**

***Naguy A, Shoukry TM, Alamiri B.***

American Journal of Therapeutics. 2018;26:e730-e732.

**ADD-ON MILNACIPRAN BOOSTS METHYLPHENIDATE RESPONSE IN AN ADOLESCENT WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH COMORBID ANXIETY AND ENURESIS.**

***Naguy A, ElSORI DH, Alawadhi DS, et al.***

American Journal of Therapeutics. 2018;26:e718-e720.

**METHYLPHENIDATE FOR COMORBID EPILEPSY AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

***Naguy A, Alrashidi F, ElSORI D.***

Asian Biomedicine. 2019;13:19-25.

**PATHWAYS TO PARENTAL ANXIETY: EFFECT OF COPING STRATEGIES FOR DISRUPTIVE BEHAVIORS IN CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER.**

***Buathong N, Pityaratstian N, Unahalekhaka A.***

Disruptive behaviors are commonly found in children with attention deficit-hyperactivity disorder (ADHD) and affect the mental health of parents. However, a study of the direct and indirect effects between disruptive behaviors in children with ADHD and parental anxiety and coping strategies is apparently lacking. To examine the direct and indirect relationship between disruptive behaviors in children with ADHD and parental

anxiety and coping strategies as a mediator. A cross-sectional study was conducted at King Chulalongkorn Memorial Hospital, Thailand between March 2015 and January 2016. Participants comprised 200 parents whose children were diagnosed with ADHD by physicians. Participants completed questionnaires regarding sociodemographic characteristics including The Thai Hospital Anxiety and Depression Scale, The Swanson, Nolan and Pelham (SNAP-IV): Parent form (Thai version), and The Coping Scale Questionnaire (Thai version). The direct path between disruptive behaviors and anxiety was significant ( $b = 0.21$ ,  $P = 0.002$ ). Moreover, a significant indirect path was found between disruptive behaviors and coping behavior with escape-avoidance ( $\beta = 0.20$ ,  $P = 0.005$ ), and an indirect path was found between escape-avoidance and anxiety ( $b = 0.31$ ,  $P < 0.001$ ). Health care professionals should evaluate the use of coping strategies by parents of children with ADHD and encourage the parents to use a positive strategy for coping with the disruptive behaviors of their children

Autism. 2020.

**SLUGGISH COGNITIVE TEMPO: AN EXAMINATION OF CLINICAL CORRELATES FOR ADULTS WITH AUTISM.**

**Brewe AM, Simmons GL, Capriola-Hall NN, et al.**

Adults with autism spectrum disorder often experience co-occurring mental health problems such as attention-deficit/hyperactivity-disorder, as well as impairments in executive function. Sluggish cognitive tempo, a cluster of behaviors including slow processing, daydreaming, and mental foggy, has been shown to be associated with attention-deficit/hyperactivity-disorder. This study was designed to assess sluggish cognitive tempo in young adults with autism spectrum disorder. Specifically, we sought to establish a preliminary estimate of clinically significant sluggish cognitive tempo symptoms and to better understand its phenomenology and associations with executive function and psychiatric symptoms in the context of autism spectrum disorder. Young adults with autism spectrum disorder ( $n = 57$ ; age 16–25 years; 84.2% male) completed a laboratory-based executive function task, and parents and participants completed measures of the participants' sluggish cognitive tempo, attention-deficit/hyperactivity-disorder, depression, and anxiety symptoms. Nearly one-third of the sample exhibited clinically impairing levels of sluggish cognitive tempo. Although sluggish cognitive tempo and attention-deficit/hyperactivity-disorder symptoms were significantly correlated, findings suggest the constructs are distinct. Results also suggest that increased sluggish cognitive tempo is related to executive function impairment and depression, but not anxiety symptoms. Considerations for assessment and long-term impacts of sluggish cognitive tempo for adults with autism spectrum disorder are discussed. Lay abstract: Adults with autism spectrum disorder often experience a range of co-occurring mental health problems such as attention-deficit/hyperactivity-disorder, as well as difficulties with executive function. Sluggish cognitive tempo, a cluster of behaviors including slow processing, daydreaming, and mental foggy, has been shown to be associated with attention-deficit/hyperactivity-disorder, and limited research has suggested that individuals with autism spectrum disorder may experience sluggish cognitive tempo. We examined co-occurring mental health problems and executive function in 57 young adults with autism spectrum disorder, aged 16–25 years to better understand sluggish cognitive tempo in autism spectrum disorder. Parents of the young adults answered questions about their children's sluggish cognitive tempo, attention-deficit/hyperactivity-disorder, depression, and anxiety symptoms, and the young adults completed tests of their executive function. Results demonstrated that nearly one-third of the sample exhibited clinically impairing levels of sluggish cognitive tempo. Although sluggish cognitive tempo and attention-deficit/hyperactivity-disorder symptoms were related, our findings suggest they are not the same constructs. Increased sluggish cognitive tempo is related to more difficulties with executive function and increased depression, but not anxiety symptoms. Results demonstrate that sluggish cognitive tempo may pose heightened difficulties for adults with autism spectrum disorder, making it an important construct to continue studying. Considerations for assessment and long-term impacts of sluggish cognitive tempo for adults with autism spectrum disorder are discussed

Behav Genet. 2020.

**INTERGENERATIONAL TRANSMISSION OF EDUCATION AND ADHD: EFFECTS OF PARENTAL GENOTYPES.**

**De Zeeuw EL, Hottenga J-J, Ouwens KG, et al.**

It remains a challenge to determine whether children resemble their parents due to nature, nurture, or a mixture of both. Here we used a design that exploits the distinction between transmitted and non-transmitted alleles in genetic transmission from parent to offspring. Two separate polygenic scores (PGS) were calculated on the basis of the transmitted and non-transmitted alleles. The effect of the non-transmitted PGS is necessarily mediated by parental phenotypes, insofar as they contribute to the rearing environment of the offspring (genetic nurturing). We calculated transmitted and non-transmitted PGSs associated with adult educational attainment (EA) and PGSs associated with childhood ADHD in a general population sample of trios, i.e. child or adult offspring and their parents (N = 112072518). We tested if the EA and ADHD (non-)transmitted PGSs were associated with childhood academic achievement and ADHD in offspring. Based on the earlier findings for shared environment, we hypothesized to find genetic nurturing for academic achievement, but not for ADHD. In adults, both transmitted ( $R^2 = 7.6\%$ ) and non-transmitted ( $R^2 = 1.7\%$ ) EA PGSs were associated with offspring EA, evidencing genetic nurturing. In children around age 12, academic achievement was associated with the transmitted EA PGSs ( $R^2 = 5.7\%$ ), but we found no support for genetic nurturing ( $R^2 \sim 0.1\%$ ). The ADHD PGSs were not significantly associated with academic achievement ( $R^2 \sim 0.6\%$ ). ADHD symptoms in children were only associated with transmitted EA PGSs and ADHD PGSs ( $R^2 = 1\%$ ). Based on these results, we conclude that the associations between parent characteristics and offspring outcomes in childhood are mainly to be attributable to the effects of genes that are shared by parents and children

Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2020.

**COGNITIVE MODELING INFORMS INTERPRETATION OF GO/NO-GO TASK-RELATED NEURAL ACTIVATIONS AND THEIR LINKS TO EXTERNALIZING PSYCHOPATHOLOGY.**

**Weigard A, Soules M, Ferris B, et al.**

**Background:** Individuals with attention-deficit/hyperactivity disorder and other externalizing psychopathologies tend to display poor behavioral performance on the go/no-go task, which is thought to reflect deficits in inhibitory control. However, clinical neuroimaging studies using this task have yielded conflicting results, raising basic questions about what the task measures and which aspects of the task relate to clinical outcomes. We used computational modeling to provide a clearer understanding of how neural activations from this task relate to the cognitive mechanisms that underlie performance and to probe the implications of these relationships for clinical research.

**Methods:** A total of 143 young adults (8–21 years of age) performed the go/no-go task during functional magnetic resonance imaging scanning. We used the diffusion decision model (DDM), a cognitive modeling approach, to quantify distinct neurocognitive processes that underlie go/no-go performance. We then assessed correlations between DDM parameters and brain activation from standard go/no-go contrasts and assessed relationships of DDM parameters and associated neural measures with clinical ratings.

**Results:** Right-lateralized prefrontal activations on correct inhibition trials, which are generally assumed to isolate neural processes involved in inhibition, were unrelated to DDM parameters (and other performance indices). However, responses to failed inhibitions in brain regions associated with error monitoring were strongly related to more efficient task performance and correlated with externalizing behavior and attention-deficit/hyperactivity disorder symptoms.

**Conclusions:** Our findings cast doubt on conventional interpretations of go/no-go task-related activations as reflecting the neural basis of inhibitory functioning. We instead found evidence that error-related contrasts provide clinically relevant information about neural systems involved in monitoring and optimizing the efficiency of cognitive performance

Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2020.

**ATYPICAL CORTICAL ACTIVATION DURING RISKY DECISION MAKING IN DISRUPTIVE BEHAVIOR DISORDERED YOUTHS WITH HISTORIES OF SUICIDAL IDEATION.**

*Dir AL, Allebach CL, Hummer TA, et al.*

**Background:** Suicidality is a leading cause of death among adolescents. In addition to other psychiatric conditions, youths with attention-deficit/hyperactivity disorder (ADHD) and disruptive behavior disorders (DBDs) are at heightened risk for suicide. Decision-making deficits are a hallmark symptom of ADHD and DBDs and are also implicated in suicidal behavior. We examined behavioral and neural differences in decision making among youths with ADHD and DBDs with (SI+) and without (SI-) histories of suicidal ideation.

**Methods:** The Balloon Analog Risk Task, a risky decision-making task, was completed by 57 youths with ADHD and DBDs (38% SI+) during functional magnetic resonance imaging. Mean stop wager (mean wager at which youths bank money) was the primary measure of risk taking. We conducted whole-brain and region-of-interest analyses in the anterior cingulate cortex and orbitofrontal cortex (OFC) during choice (win vs. inflate) and outcome (inflate vs. explode) contrasts using parametric modulators accounting for probability of balloon explosion.

**Results:** There were no differences between SI+ and SI- youths in Balloon Analog Risk Task performance. SI+ youths showed decreasing activation in the right medial frontal gyrus when choosing inflate as explosion probability increased compared with SI- youths. During explosions, SI- youths showed increasing activation in the left OFC as explosions became more likely. SI+ showed increasing left medial OFC activity in response to inflations as explosion probability increased.

**Conclusions:** SI+ youths may show heightened sensitivity to immediate reward and decreased sensitivity to potential loss as evidenced by medial frontal gyrus activity. OFC findings suggest that SI+ youths may be drawn to reward even when there is high probability of loss

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Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2020.

**POLYGENIC RISK SCORE-DERIVED SUBCORTICAL CONNECTIVITY MEDIATES ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DIAGNOSIS.**

*Hermosillo RJM, Mooney MA, Fezcko E, et al.*

**Background:** Attention-deficit/hyperactivity disorder (ADHD) has substantial heritability, and a recent large-scale investigation has identified common genome-wide significant loci associated with increased risk for ADHD. Along the same lines, many studies using noninvasive neuroimaging have identified differences in brain functional connectivity in children with ADHD. We attempted to bridge these studies to identify differences in functional connectivity associated with common genetic risk for ADHD using polygenic risk score (PRS).

**Methods:** We computed ADHD PRSs for all participants in our sample (N = 315, children 7-13 years of age, 196 with ADHD and 119 unaffected comparison children) using ADHD data from the Psychiatric Genomics Consortium as a discovery set. Magnetic resonance imaging was used to evaluate resting-state functional connectivity of targeted subcortical structures.

**Results:** The functional connectivity between 2 region pairs demonstrated a significant correlation to PRS: right caudate parietal cortex and nucleus accumbens occipital cortex. Connectivity between these areas, in addition to being correlated with PRS, was correlated with ADHD status. The connection between the caudate and the parietal region acted as a statistical suppressor, such that when it was included in a path model, the association between PRS and ADHD status was enhanced.

**Conclusions:** Our results suggest that functional connectivity to certain subcortical brain regions is directly altered by genetic variants, and certain cortico subcortical connections may modulate ADHD-related genetic effects

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Biological Trace Element Research. 2020.

**POSSIBLE ASSOCIATIONS OF DISTURBED NEUROMETALS AND AMMONIA WITH GLYCAEMIC CONTROL IN TYPE 1 DIABETIC CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Sakhr HM, Hassan MH, Desoky T.**

The chronicity of type 1 diabetes mellitus (T1DM) is reported to be associated with various psychological disorders. The current study aimed to evaluate the levels of serum ammonia and various neurometals (zinc, copper, and magnesium) in patients with T1DM with and without ADHD and to correlate their levels with glycaemic status. A prospective case-control study was conducted with 60 diabetic children with T1DM (allocated into a group of 20 patients with a diagnosis of ADHD and a group of 40 patients without ADHD) who were comparable to 60 matched controls. Assays of glucose, glycated haemoglobin (HbA1c), ammonia, zinc, copper, and magnesium were performed. Overall, ammonia and copper levels were significantly higher in the diabetic patients especially those with ADHD than in the control group ( $p < 0.05$  for all). The calculated copper/zinc ratio was significantly higher in the diabetic patient group than in the control group and higher in diabetic children with ADHD than in diabetic children without ADHD ( $p < 0.05$  for all). Diabetic children had significantly lower magnesium levels than the controls ( $p < 0.05$ ), but no significant difference between the diabetic subgroups was detected. A positive correlation between glycaemic control (HbA1c %) and ammonia level was found in the diabetic group and subgroups, and a positive correlation was found between HbA1c % and the Cu/Zn ratio in diabetic children with ADHD ( $p < 0.05$  for all). The current study confirms an association of elevated ammonia and copper/zinc ratio with poor glycaemic control and ADHD development among children with T1DM

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BMC Med Genet. 2020 Jan;21:20.

**A NOVEL NONSENSE MUTATION IN THE STS GENE IN A PAKISTANI FAMILY WITH X-LINKED RECESSIVE ICHTHYOSIS: INCLUDING A VERY RARE CASE OF TWO HOMOZYGOUS FEMALE PATIENTS.**

**Afzal S, Ramzan K, Ullah S, et al.**

**BACKGROUND:** X-linked ichthyosis (XLI; OMIM# 308100) is a recessive keratinization disorder characterized by the presence of dark brown, polygonal, adherent scales on different parts of the body surface. It almost exclusively affects males and the estimated prevalence ranges from 1:2000-6000 in males worldwide. Extracutaneous manifestations are frequent including corneal opacities, cryptorchidism, neuropsychiatric symptoms or others. Up to 90% of XLI cases are caused by recurrent hemizygous microdeletion encompassing entire STS gene on chromosome Xp22.3, while only a minority of patients shows partial deletions or loss of function point mutations in STS. Larger deletions also involving contiguous genes are identified in syndromic patients.

**METHODS:** Here, we report clinical and genetic findings of a large Pakistani family having 16 affected individuals including 2 females with XLI. Molecular karyotyping and direct DNA sequencing of coding region of the STS gene was performed.

**RESULTS:** The clinical manifestations in affected individuals involved generalized dryness and scaling of the skin with polygonal, dark scales of the skin on scalp, trunk, limbs, and neck while sparing face, palms and soles. There were no associated extra-cutaneous features such as short stature, cryptorchidism, photophobia, corneal opacities, male baldness, and behavioral, cognitive, or neurological phenotypes including intellectual disability, autism or attention deficit hyperactivity disorder. Molecular karyotyping was normal and no copy number variation was found. Sanger sequencing identified a novel hemizygous nonsense mutation (c.287G > A; p.W96\*), in exon 4 of STS gene in all affected male individuals. In addition, two XLI affected females in the family were found to be homozygous for the identified variant.

**CONCLUSIONS:** This study is useful for understanding the genetic basis of XLI in the patients studied, for extending the known mutational spectrum of STS, diagnosis of female carriers and for further application of mutation screening in the genetic counseling of this family

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BMJ. 2020 Feb;368:m331.

**ASSOCIATIONS BETWEEN MACROLIDE ANTIBIOTICS PRESCRIBING DURING PREGNANCY AND ADVERSE CHILD OUTCOMES IN THE UK: POPULATION BASED COHORT STUDY.**

**Fan H, Gilbert R, O'Callaghan F, et al.**

**OBJECTIVE:** To assess the association between macrolide antibiotics prescribing during pregnancy and major malformations, cerebral palsy, epilepsy, attention deficit hyperactivity disorder, and autism spectrum disorder in children.

**DESIGN:** Population based cohort study.

**SETTING:** The UK Clinical Practice Research Datalink.

**PARTICIPANTS:** The study cohort included 104 605 children born from 1990 to 2016 whose mothers were prescribed one macrolide monotherapy (erythromycin, clarithromycin, or azithromycin) or one penicillin monotherapy from the fourth gestational week to delivery. Two negative control cohorts consisted of 82 314 children whose mothers were prescribed macrolides or penicillins before conception, and 53 735 children who were siblings of the children in the study cohort.

**MAIN OUTCOME MEASURES:** Risks of any major malformations and system specific major malformations (nervous, cardiovascular, gastrointestinal, genital, and urinary) after macrolide or penicillin prescribing during the first trimester (four to 13 gestational weeks), second to third trimester (14 gestational weeks to birth), or any trimester of pregnancy. Additionally, risks of cerebral palsy, epilepsy, attention deficit hyperactivity disorder, and autism spectrum disorder.

**RESULTS:** Major malformations were recorded in 186 of 8632 children (21.55 per 1000) whose mothers were prescribed macrolides and 1666 of 95 973 children (17.36 per 1000) whose mothers were prescribed penicillins during pregnancy. Macrolide prescribing during the first trimester was associated with an increased risk of any major malformation compared with penicillin (27.65 v 17.65 per 1000, adjusted risk ratio 1.55, 95% confidence interval 1.19 to 2.03) and specifically cardiovascular malformations (10.60 v 6.61 per 1000, 1.62, 1.05 to 2.51). Macrolide prescribing in any trimester was associated with an increased risk of genital malformations (4.75 v 3.07 per 1000, 1.58, 1.14 to 2.19, mainly hypospadias). Erythromycin in the first trimester was associated with an increased risk of any major malformation (27.39 v 17.65 per 1000, 1.50, 1.13 to 1.99). No statistically significant associations were found for other system specific malformations or for neurodevelopmental disorders. Findings were robust to sensitivity analyses.

**CONCLUSIONS:** Prescribing macrolide antibiotics during the first trimester of pregnancy was associated with an increased risk of any major malformation and specifically cardiovascular malformations compared with penicillin antibiotics. Macrolide prescribing in any trimester was associated with an increased risk of genital malformations. These findings show that macrolides should be used with caution during pregnancy and if feasible alternative antibiotics should be prescribed until further research is available.

**TRIAL REGISTRATION:** ClinicalTrials.gov NCT03948620

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Brain Dev. 2020;42:129-39.

**ATYPICAL GAMMA FUNCTIONAL CONNECTIVITY PATTERN DURING LIGHT SLEEP IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Ueda R, Takeichi H, Kaga Y, et al.**

**Introduction:** We examined functional connectivity analyses in electroencephalograms (EEGs) of patients with attention deficit hyperactivity disorder (ADHD) and in those of typically developing children (TDC) to uncover neurobiological abnormalities.

**Methodology:** We enrolled 31 children with ADHD (mean age 11.1 years; 23 boys) and 17 sex-, age-, and intelligence-matched TDC to undergo 19-channel EEGs during light sleep. We estimated functional connectivity using the phase lag index (PLI) and coherence measurements that capture the synchronization of EEG signals and graphed metrics with GREYNA. We also performed continuous performance tests (CPTs) on the children and obtained answered questionnaires on ADHD and autism spectrum disorder.

**Results:** The central-to-posterior gamma PLI was lower in children with ADHD than that in TDC. The other PLI frequency bands and all coherence frequency bands were not statistically different between both groups. Individuals with high hyperactivity scores on questionnaires and low reaction times (SDs) on CPT had low motor and occipital pairs of gamma PLIs. Graph metrics showed no differences between the groups.

**Conclusions:** The difference in averaged gamma PLI (especially with motor and occipital pairs) between groups was more suitable for diagnosis than the averaged coherence. Lower averaged gamma PLIs reflected more severe ADHD symptoms. A prospective study with more controlled conditions is warranted to determine if gamma-band PLI can be used as an auxiliary tool for ADHD diagnosis

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Brain Sciences. 2020;10.

**BEHAVIORAL AND ELECTROPHYSIOLOGICAL CORRELATES OF PERFORMANCE MONITORING AND DEVELOPMENT IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Liu Y, Hanna GL, Hanna BS, et al.**

The pathophysiology of attention-deficit/hyperactivity disorder (ADHD) involves deficits in performance monitoring and adaptive adjustments. Yet, the developmental trajectory and underlying neural correlates of performance monitoring deficits in youth with ADHD remain poorly understood. To address the gap, this study recruited 77 children and adolescents with ADHD and 77 age- and gender-matched healthy controls (HC), ages 8-18 years, who performed an arrow flanker task during electroencephalogram recording. Compared to HC, participants with ADHD responded more slowly and showed larger reaction time variability (RTV) and reduced post-error slowing; they also exhibited reduced error-related negativity (ERN) and error positivity effects, and reduced N2 and P3 congruency effects. Age effects were observed across groups: with increasing age, participants responded faster, with less variability, and with increased post-error slowing. They also exhibited increased ERN effects and increased N2 and P3 congruency effects. Increased RTV and reduced P3 amplitude in incongruent trials were associated with increased ADHD Problems Scale scores on the Child Behavior Checklist across groups. The altered behavioral and ERP responses in ADHD are consistent with the pattern associated with younger age across groups. Further research with a longitudinal design may determine specific aspects of developmental alteration and deficits in ADHD during performance monitoring

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Child Fam Behav Ther. 2020;42:20-36.

**EFFECTS OF WHITE NOISE ON OFF-TASK BEHAVIOR AND SLEEP FOR ELEMENTARY-AGE STUDENTS WITH ADHD.**

**Rosalez E, Johnson CM, Bradley-Johnson S, et al.**

Children with ADHD were administered 75 dB of continuous white noise during independent seat work in the classroom and during bedtime in their homes. Compared to baseline all three students exhibited decreases in off-task behavior. Off-task behavior returned to original baseline levels when white noise was removed and decreased again when reintroduced in classrooms. White noise also decreased bedtime sleep latency and spontaneous night wakings at home. Both sleep latencies and night wakings increased during return-to-baseline conditions. Surprisingly, when white noise was reintroduced only in the classrooms sleep improved a second time. White noise in classrooms with or without simultaneous treatment during sleep at night resulted in lower levels of off-task classroom behavior as well as less disruptive sleep. Results were independent of whether children were on ADHD medication. Children, teachers, and parents all rated white noise favorably

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Child Neuropsychol. 2000;6:185-94.

**THE ASSOCIATION OF NEUROFIBROMATOSIS TYPE 1 AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Koth CW, Cutting LE, Denckla MB.**

Some research and clinical observations have linked Neurofibromatosis Type 1 (NF-1) and Attention Deficit Hyperactivity Disorder (ADHD). In order to investigate whether ADHD is part of the phenotype of NF-1 or is a separate, unrelated disorder within families, we compared the ADHD status of children affected with NF-1 to that of their unaffected-NF-1 siblings and to that of their biological parents. Results of matched-pair analyses were calculated and revealed a significant within-pair discordance, when comparing children with

NF-1 and their siblings and when comparing children with NF-1 and their biological parents (in families with a sporadic, non-familial NF-1 child). These findings suggest that ADHD may occur as a component of the NF-1 phenotype

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Child Neuropsychol. 2000;6:209-17.

**A CLINICAL COMPARATIVE STUDY EVALUATING THE EFFECT OF EPILEPSY VERSUS ADHD ON TIMED COGNITIVE TASKS IN CHILDREN.**

**Aldenkamp AP, Van BK, Braken M, et al.**

Both children with epilepsy and children with ADHD may be characterized by slowing on reaction-time measurement. This is of particular interest, as neuropsychological assessment is often requested in the differential diagnosis between children with short non-convulsive epileptic seizures and children with ADHD. In this study we attempt to identify patterns of impairment on timed tasks that are specific for epilepsy, relative to ADHD. This study was an open, controlled parallel-group clinical investigation which included two groups of patients: 60 children with ADHD and 60 children with epilepsy. These children were compared with a control group (n = 30) on two types of timed cognitive tasks: tasks with low information load (simple reaction-time measurement) and tasks with high information load (multiple decision reaction-time measurement). The simple reaction-time measurements show significant differences between ADHD and controls (all except for visual RT non-dominant hand) and between epilepsy and controls (only one test). No significant differences were found between epilepsy and ADHD. The two tests with high information load show significant slowing compared with the controls for epilepsy on the Binary Choice Reaction-Time Test and for ADHD on the Visual Searching Test. On both tests also the differences between epilepsy and ADHD are significant. The two tests in combination have a relatively satisfactory potential to classify the children with ADHD (75% correct classification) and the children with epilepsy (55% correct classification). We may conclude that complex reaction-time tests (i.e., timed tasks with high information load) have potential for assessing the differential impact of ADHD and epilepsy on attentional function. These tasks specifically reveal general slowing for children with epilepsy and slowing as an effect of failures of inhibitory self control on unstructured tasks for ADHD

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Child Neuropsychol. 2000;6:241-50.

**TIME PERCEPTION IN BOYS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ACCORDING TO TIME DURATION, DISTRACTION AND MODE OF PRESENTATION.**

**West J, Douglas G, Houghton S, et al.**

In a recent theoretical model of attention-deficit/hyperactivity disorder (ADHD), Barkley (1997a) predicted that ADHD children experience impairments in their psychological sense of time. This was demonstrated in a series of experiments by Barkley, Koplowitz, Anderson, and McMurray (1997). The present study sought to investigate the effects of ADHD subtype, stimulus duration, mode of presentation (visual versus auditory) and distractors on the performance of a simple time reproduction task. Data were obtained from 44 ADHD children (14 predominantly inattentive and 30 combined type) and 44 age-matched Controls using the Time Perception Application version 1.0 (Barkley, University of Massachusetts Medical Center, 1998). Results revealed that the ADHD children made significantly larger errors on Visual time reproduction tasks than the Controls, regardless of ADHD subtype or the presence of distractors. Furthermore, ADHD children were more likely to overestimate the shorter time intervals (0.5 and 2 s) and underestimate the longer time intervals (3, 4 and 6 s) relative to Controls. No group differences were observed on the auditory time reproduction task, with both ADHD and Control groups consistently underestimating the durations to be reproduced. The results of this study provide further support for the prediction that children with ADHD have an impaired sense of time

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Child Neuropsychol. 2000;6:218-34.

**PROCESSING SPEED IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER, INATTENTIVE TYPE.**

**Weiler MD, Bernstein JH, Bellinger DC, et al.**

Attention Deficit/Hyperactivity Disorder (ADHD) is among the most common and most often reconceptualized neurobehavioral disorders of childhood. In the most recent DSM-IV, a primarily inattentive subtype of ADHD (AD) has again been identified. This study explores the neuropsychological profile of this group of children. Eighty-two children referred for school-related problems participated. Twenty-five met criteria for AD; 52 met criteria for reading disability (RD); 9 were comorbid for RD and AD. AD children performed poorly on measures of information processing speed. Children with comorbid AD/RD were distinguishable from those with RD on speed of processing measures only. Vulnerability to information processing load may be at the root of many of the behavioral manifestations of AD

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Child Neuropsychol. 2000;6:286-96.

**LACK OF INHIBITION: A MOTIVATIONAL DEFICIT IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND CHILDREN WITH TRAUMATIC BRAIN INJURY.**

**Konrad K, Gauggel S, Manz A, et al.**

Recent research has demonstrated that both brain-injured children and children with attention deficit/hyperactivity disorder (ADHD) suffer from response inhibition deficits. To investigate whether these deficits can be influenced by motivational factors, the stop-signal task was performed with and without reward contingencies for successful inhibition. Three groups of children between 8 and 12 years of age, participated in the study: 31 children with ADHD, 37 with traumatic brain injuries (TBI), and 26 normal controls. Results indicated that, although all groups showed comparable learning effects, reward contingencies had different effects on the groups. Whereas the performance of children with ADHD under reward contingencies were brought up to the performance level of normal controls, rewards were found less effective at improving response inhibition in children with TBI. The results further support a motivational/energetic explanation of the inhibitory deficit in children with ADHD, and of a primary response inhibition deficit due to structural brain damage in children with TBI

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Child Neuropsychol. 2020;26:219-41.

**ASPECTS OF ATTENTION AND INHIBITORY CONTROL ARE ASSOCIATED WITH ON-TASK CLASSROOM BEHAVIOUR AND BEHAVIOURAL ASSESSMENTS, BY BOTH TEACHERS AND PARENTS, IN CHILDREN WITH HIGH AND LOW SYMPTOMS OF ADHD.**

**Johnson KA, White M, Wong PS, et al.**

There is often weak association between performance on cognitive tasks and the behavioural symptoms of ADHD. One possible reason is the use of rating scales rather than direct observations of behaviours. This exploratory study used well established measures of attention and response inhibition with both direct observation and behavioural rating scales to examine these associations. Twenty-two children (mean age 9.6-áyears) identified by their teachers as displaying high levels of ADHD symptoms, and 22 matched controls (mean age 9.8-áyears), completed the Fixed and Random Sustained Attention to Response Tasks (SART). Their on-task classroom behaviour was assessed using the ASEBA Direct Observation Form (DOF). ADHD symptoms were also assessed using the Conners 3 Short Form and the SWAN. Children with high symptoms of ADHD performed the SARTs with more errors of commission and were more variable with their responding, and spent less time on-task in the classroom than controls. Performance on the Fixed SART was not associated with on-task classroom behaviour; in contrast three Random SART measures, commission and omission errors, moment-to-moment variability, were negatively associated with on-task classroom behaviour. There were strong associations between the commission error counts on both SARTs and the Teacher SWAN scores, and one of the Parent SWAN scores. The Teacher SWAN scores were associated with on-task classroom behaviour; the Parent SWAN scores were not. These findings provide

preliminary evidence of an association between cognitive measures of inhibitory control and some measures of inattention, and both observed behaviour and the ADHD behavioural symptoms

Child Neuropsychol. 2020;26:145-69.

**EFFECT OF READ1 ON LATENT PROFILES OF READING DISORDER AND COMORBID ATTENTION AND LANGUAGE IMPAIRMENT SUBTYPES.**

**Li M, Truong DT, DeMille M, et al.**

Recent studies of co-occurring reading disorder (RD) and attention deficit/hyperactivity disorder (ADHD), and co-occurring RD and language impairment (LI), support a core disability plus co-occurrence model focused on language and attention. Genetic factors have been associated with poor reading performance. However, little is known about whether different genetic variants independently contribute to RD co-occurrence subtypes. We aimed to identify subgroups of struggling readers using a latent profile analysis (LPA) in a sample of 1,432 Hispanic American and African American youth. RD classes were then tested for association with variants of READ1, a regulatory element within the candidate RD risk gene, DCDC2. Six groups were identified in the LPA using RD designation as a known-class variable. The three RD classes identified groups of subjects with neurocognitive profiles representing RD+ADHD, specific phonological deficit RD, and RD+LI. Genetic associations across RD subtypes were investigated against functional groupings of READ1. The RU1-1 group of READ1 alleles was associated with RD cases that were marked by deficits in both processing speed and attention (RD+ADHD). The DCDC2 microdeletion that encompasses READ1 was associated with RD cases showing a phonological deficit RD profile. These findings provide evidence for differential genetic contribution to RD subtypes, and that previously implicated genetic variants for RD may share an underlying genetic architecture across population groups for reading disorder

Child Care Health Dev. 2020 Jan;46:111-20.

**CLINICIAN PERSPECTIVES ON THE USE OF NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE GUIDELINES FOR THE PROCESS OF TRANSITION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Eke H, Janssens A, Newlove Delgado T, et al.**

**Background:** The UK National Institute for Health and Care Excellence (NICE) clinical guidelines recommends the following steps in the transition from child to adult services for young people with attention deficit hyperactivity disorder (ADHD): reassessment before and after transition, transition planning, formal meeting between services, and involvement from young person and carer, completed by age 18.

**Methods:** A UK surveillance study asked clinicians to report young people on their caseloads with ADHD in need of transition to adult services in 2016 to support their continued access to medication need. Clinicians reported young people as they aged to within 6 months of the transition boundary, a prospective questionnaire prior to transition asked about intended transition and the use of local transition protocols. A retrospective questionnaire sent 9 months later established which steps recommended by NICE were followed during transition. Clinicians (38) working in child or adult services were interviewed about their experiences of transition and the use of NICE guidelines during transition and were analysed using a framework approach.

**Results:** Information was shared between services in 85% of the 315 identified transition cases. A joint meeting was planned in 16% of cases; joint working before transfer occurred in 10% of cases. Clinicians were aware of NICE guidelines; they had mixed views on whether (local) guidelines or protocols were helpful. The main reason for not following guidelines was workload and resources: NICE recommends stuff that is miles above what we will ever be able to provide.

**Conclusions:** Clinicians involved in the transition process of young people with ADHD judged NICE guidelines to be unrealistic given the current limited resources and service organization. More open dialogue is needed for recommendations on service models to bridge the gap between guideline recommendations and what is viewed as feasible and how implementation of guidance is funded, monitored, and prioritized. This may lead to valuable changes in the consultation process, for example, consideration of a layered (gold,

standard, and minimal) system for some NICE guidelines. (PsycINFO Database Record (c) 2020 APA, all rights reserved) (Source: journal abstract)

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Clinical Epidemiology. 2020;12:163-71.

**ASSOCIATIONS BETWEEN PSYCHIATRIC DISORDERS AND ENURESIS IN TAIWANESE CHILDREN: A NATIONAL POPULATION-BASED STUDY.**

**Tsai H-L, Chang J-W, Chen M-H, et al.**

**Background:** Psychiatric disorders such as attention-deficit/hyperactivity disorder may negatively impact drug compliance and the prognosis of enuresis. However, existing studies regarding associations between lifetime psychiatric disorders and childhood enuresis are primarily from Western countries, and studies from Taiwan are lacking.

**Methods:** We conducted a population-based retrospective cohort analysis using the Taiwan Longitudinal Health Insurance Database 2010. A total of 1,146 children with enuresis (ICD-9-CM code: 307.6) and 4,584 randomly selected sex-and age-matched controls were identified between January 1, 1997 and December 31, 2011. Logistic regression was used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) for the development of psychiatric disorders in the children with enuresis.

**Results:** Enuresis was more common in the younger children, and the rate was significantly higher in boys (58.7%) than in girls (41.3%). A total of 171 patients (14.9%) in the enuresis group had at least one psychiatric diagnosis vs 259 (5.7%) in the control group ( $p < 0.001$ ). Multivariate analysis showed that the presence of enuresis increased the odds of developing major depressive/dysthymic disorder (OR=2.841, 95% CI: 1.619, 4.987), attention-deficit/hyperactivity disorder (OR=3.156, 95% CI: 2.446, 4.073), autism spectrum disorder (OR=2.468, 95% CI: 1.264, 4.822), anxiety disorders (OR=3.113, 95% CI: 2.063, 4.699), intelligence disability (OR=3.989, 95% CI: 2.476, 6.426), disruptive behavior disorders (OR=3.749, 95% CI: 1.756, 8.004), and tic disorder (OR=2.660, 95% CI: 1.642, 4.308).

**Conclusion:** Children with enuresis are likely to have psychiatric disorders, and physicians should consider this during their evaluation

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Clin Neuropharmacol. 2019;42:184-85.

**PRIAPISM WITH METHYLPHENIDATE USE IN A PRESCHOOL-AGED BOY RESOLVED WITH SWITCHING TO ATOMOXETINE.**

**Ekinci O, et al.**

**Background** Priapism is a persistent unwanted erection that is not linked with sexual stimulation. A number of previous case reports have shown priapism with methylphenidate (MPH) use, especially in adolescence and preadolescence period. In all of these cases, the unwanted erections ceased after the medication was discontinued and no further attention-deficit hyperactivity disorder medication was initiated. Hereby, we present the case of a boy who had priapism episodes with MPH, which resolved with switching to atomoxetine (ATX).

**Case Report** A 5-year, 10-month-old medically healthy boy was diagnosed with attention-deficit hyperactivity disorder and was prescribed methylphenidate immediate-release (10 mg/d). Two weeks later, his family communicated and reported penile erection episodes since the initiation of MPH. With the suspect of a medication-induced adverse reaction, MPH was discontinued and priapism resolved within a week. Thereafter, 10 mg/d of ATX was initiated. Four-week follow-up with ATX treatment revealed that the medication was tolerated well, and priapism or any other adverse effect was not reported.

**Conclusions** This case report suggests that ATX may be safely used in some children who experienced priapism with MPH. Future studies are needed to clarify the risk factors and etiologic mechanisms of this adverse reaction

Clin Neurophysiol. 2020.

**COMPARISON BETWEEN CONVENTIONAL AND HD-tDCS OF THE RIGHT INFERIOR FRONTAL GYRUS IN CHILDREN AND ADOLESCENTS WITH ADHD.**

**Breitling C, Zaehle T, Dannhauer M, et al.**

**Objective:** To investigate whether the effects of HD-tDCS and conventional tDCS of the right IFG are superior to the effects of sham stimulation for the improvement of working memory performance in ADHD.

**Methods:** 15 ADHD patients between 10 and 16 years underwent three tDCS sessions in which conventional, HD and sham tDCS of the right IFG were applied. In all sessions a 2-back working memory task was solved and EEG was recorded. Baseline data were assessed from 15 age matched healthy controls.

**Results:** In ADHD patients, increased positive values of P300 and N200 mean amplitudes were found after conventional and HD-tDCS. Thus, both components were more in resemblance to ERPs in healthy controls. Behavioral performance was not generally influenced by tDCS but effects of HD-tDCS depended on individual hyperactive/impulsive symptom load. The rate of responders for HD-tDCS was equivalent to the responder rate for conventional tDCS.

**Conclusions:** ERP data indicate that HD-tDCS is equally suitable as conventional tDCS for the recruitment of the right IFG in the context of working memory processing. Significance: HD-tDCS of the right IFG is a promising approach for neuromodulation in ADHD but further research is necessary to develop adaptations that produce reliable behavioral benefits

Clinical Nutrition ESPEN. 2020.

**EMPIRICALLY DERIVED DIETARY PATTERNS AND FOOD GROUPS INTAKE IN RELATION WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD): A SYSTEMATIC REVIEW AND META-ANALYSIS.**

**Shareghfarid E, Sangsefidi ZS, Salehi-Abargouei A, et al.**

**Background and aims:** Attention Deficit Hyperactivity Disorder (ADHD) is a prevalent chronic psychiatric condition in children world wide. This study was aimed to provide an overview of food groups and dietary patterns in ADHD children as a systematic review.

**Methods:** The relation between dietary patterns and this disorder was also investigated through meta-analysis. Databases including Google Scholar, SCOPUS, ISI Web of science, and PubMed were searched up to June 2017. Studies on posteriori derived dietary patterns and food intakes of ADHD children were included. The achieved Relative Risks (RR) and Odds Ratio (OR) were pooled together for ADHD to compare the most and the least adherence to major dietary patterns. The heterogeneity was assessed by Cochran's Q test and I-squared methods.

**Results:** This systematic review consisted of 6 dietary patterns and 6 foods or macronutrients studies. In this regard, 6 dietary patterns studies (n: 8816) were included in the meta-analysis. The pooled analysis established that healthy dietary pattern significantly decreased the risk of ADHD (OR: 0.463; 95% CI: 0.41, 0.496), whereas Western (OR: 1.92; 95% CI: 1.13, 3.26; p:0.016) and junk food (OR: 1.51; 95% CI: 1.06, 2.16; p: 0.024) dietary patterns increased it.

**Conclusions:** Healthy dietary pattern highly loaded with vegetables, fruits, legumes, and fish has decreased the odds of ADHD up to 37%. In addition, adherence to junk food pattern containing sweetened beverages and desserts as well as Western dietary pattern including red meat, refined grains, processed meats, and hydrogenated fat increased it

Clin Pediatr. 2020.

**CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ARE AT INCREASED RISK FOR SLOWED GROWTH AND SHORT STATURE IN EARLY CHILDHOOD.**

**Davallow GL, DeBoer MD.**

Our objective was to evaluate the risk of short stature in children with attention-deficit/hyperactivity disorder (ADHD) and the effect of ADHD and its treatment on height-for-age z score (HAZ) and body mass index-for-age z score (BMIZ) in early childhood. We evaluated 7603 children from the Early Childhood

Longitudinal Study of Kindergarten Cohort 2011 and found that children with ADHD had lower HAZ at second and fourth grades and lower BMIZ at K to fourth grade. Children with ADHD at fourth grade had almost 4 times higher odds of short stature. Children with ADHD at K grew at a slower rate from K to fourth grade (difference in  $\Delta$ HAZ = 0.23, 95% confidence interval = 0.04-0.42) and had less gain in BMI (difference in  $\Delta$ BMIZ = 0.16, 95% confidence interval = 0.03-0.29). Longer duration of ADHD medication use was associated with lower HAZ at fourth grade and slower growth from K to fourth grade. These data may assist pediatricians in considering risk of poor growth in children with ADHD

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CNS Spectr. 2020.

**INDIVIDUALIZATION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER TREATMENT: PHARMACOTHERAPY CONSIDERATIONS BY AGE AND CO-OCCURRING CONDITIONS.**

**Mattingly GW, Wilson J, Ugarte L, et al.**

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that manifests in childhood and can persist into adolescence and adulthood. Impairments associated with ADHD can impact quality of life, social interactions, and increase the risk of morbidity and mortality; however, for many patients, effective treatment can lessen these effects. Pharmacotherapy with stimulants or nonstimulants is recommended in conjunction with psychosocial therapy for most patients. Determining the optimal pharmacotherapy can be complex, and the clinician needs to consider many factors such as the patient's age, comorbidities, and lifestyle. Furthermore, the needs of the patient with ADHD will change over time, with specific challenges to consider at each stage of life. A variety of Food and Drug Administration (FDA)-approved stimulant and nonstimulant formulations are available with different modes of delivery and durations of effect. This armamentarium of ADHD medications can be used to individualize ADHD treatment for each patient's needs. This article combines current information from the literature and the first-hand experience of the authors to provide guidance on ADHD treatment options for patients of different ages and for some of the more common comorbidities

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Contemporary Clinical Trials Communications. 2020;17.

**PROTOCOL FOR A LONGITUDINAL STUDY OF MELATONIN THERAPY AND COST EFFECTIVENESS ANALYSIS IN STIMULANT-TREATED CHILDREN WITH ADHD AND INSOMNIA: AN N-OF-1 TRIAL.**

**Edelson J, Byrnes J, Mitchell G, et al.**

**Background:** Children with ADHD and sleep problems have more caregiver deficits and decreased school attendance than children with ADHD but without a sleep problem. We conducted an N-of-1 trial of melatonin for children with ADHD on stimulants. As a follow-up study, we aim to conduct a cost effectiveness analysis (CEA) of melatonin therapy by comparing costs of this condition (of using melatonin) to costs of the baseline condition (usual care with no N-of-1 trial).

**Methods:** The CEA will compare participants who remained on melatonin vs those who chose to cease melatonin. Costs will be determined by medication cost to the caregiver(s), school/work absences, other sleep remedy costs, and health service utilization costs, including incidentals like parking. These costs will be determined at baseline, end of 6-week trial, and 6 months post-trial. We will also calculate Quality-Adjusted Life-Years (QALY) based on responses to PedsQL or SF-12v2 for patients and caregiver(s) and assess differences between remaining on melatonin or not; and assess the intermediate-term effectiveness and adverse effects of melatonin at 6 months.

**Discussion:** We hypothesize that shorter sleep-onset-latency will be associated with improved QALYs for patients and caregivers. We also expect that targeting melatonin to positive responders will be cost effective both for individuals and society. Cost per QALY for positive responders to melatonin is useful for doctors when creating treatment plans since melatonin is not an over-the-counter pharmaceutical in Australia.

**Trial registration number:** ACTRN12614000542695

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Dev Psychol. 2020 Feb;56:251-60.

**ATTENTIONAL SYSTEM OF VERY PREMATURELY BORN PRESCHOOLERS.**

**Walczak-Kozłowska T, Małkowska A, Chrzan-Dątko M, et al.**

Recent studies indicate that premature children are at risk for difficulties with cognitive development and have increased incidence of ADHD as well as other behavioral disorders. Although the exact mechanism accounting for these children's neuropsychological abnormalities is unknown, there is evidence to suggest that the cognitive and behavioral disturbances seen in this population may result from a slower development of the attentional system. However, it remains unclear whether prematurity affects the development of the entire attention system or if prematurely born children have a selective insufficiency of components of this system (i.e., orienting, alerting, executive). We compared the efficiency of the attentional system of very prematurely born children and full-term controls at 5 years of age, using the Attention Network Task's Child Version. In comparison to full-term peers, very preterm children exhibited inefficient orienting of attention, whereas there was no group difference in the efficiency of alerting and executive aspects of attention. The reason for the selectively suboptimal orienting of attention in very prematurely born preschoolers remains unclear; it is possible that the neural substrates of this attentional subsystem are particularly underdeveloped in the preschool period in this cohort

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Dissertation Abstracts International Section A: Humanities and Social Sciences. 2020 Feb.

**USING THE SIMPLE VIEW OF READING TO EXAMINE READING COMPREHENSION PROFICIENCY IN YOUTH WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Mackenzie G.**

Reading comprehension may be an area of challenge for youth with ADHD but is currently understudied. The overarching goal of this study was to examine reading comprehension (RC) performance drawing on the Simple View of Reading (Gough & Tunmer, 1986). The first objective was to compare reading comprehension proficiency and related reading measures between youth with ADHD and typically developing youth. Findings showed that there were no statistically significant differences between the two groups on the measure of RC, word level decoding, and oral language comprehension. In contrast, youth with ADHD performed significantly lower than their peer group on the word level reading fluency measure and on a verbal working memory measure. Next, I explored predictors of performance on the RC measures. Multiple regression analyses revealed that only word level decoding and language comprehension proficiency were unique predictors of performance on each of the RC measures. A supplementary analysis revealed that the contribution of working memory to RC was mediated by the language comprehension composite. Finally, I tested the convergent validity of the two RC measures using latent profile analysis. As the latent profile analysis showed that profiles of performance converged across the three latent profile groups (lowest, middle, and highest performers), the findings supported the convergent validity of the two measures of RC. Further analyses of the three latent profile subgroups using a multinomial regression analysis revealed that language comprehension and word level decoding differentiated the low-performing group compared to the middle- and highest-performing groups. Overall, these findings suggest that youth with ADHD and their typically developing peers are more likely to demonstrate weaker RC if they have less proficiency in oral language comprehension skills and/or word level decoding ability, supporting the Simple View of Reading

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Dissertation Abstracts International Section A: Humanities and Social Sciences. 2020 Feb.

**A COMPARISON OF PRAGMATIC SKILLS IN CHILDREN WITH LANGUAGE AND/OR READING DISORDERS WITH AND WITHOUT ADHD.**

**Forbes AC.**

Although consensus supports the role of pragmatic competence issues in children with various psychopathology (e.g., Tucha et al., 2005; Boscolo, Ratner, & Rescorla, 2002; Cleave & Rice, 1997), little research has focused on what specific aspects of pragmatic problems are associated with participants with a diagnosis of language and/or reading disorders (LD/RD) with and without attention deficit hyperactivity

disorder (ADHD). This question holds particular relevance in identifying what pragmatic deficits look like in these populations. Narrative tasks and a questionnaire were used to examine pragmatic competency. In the first task, children were asked to tell the story of the wordless picture book *Frog, Where are you?* (Mayer, 1969). In the second task, children were asked to retell the wordless picture book *Frog, Where are you?* story. In the third task, children were asked to play "Tell The Best Story" game. The "Tell The Best Story" game asked the children to tell a story about a recent interesting experience. The children's fluency, complexity, and coherence skills were rated from these narrative tasks. Results, based on reliably coded narrative measures, indicated that: (a) there were significant main effects across the majority of measures for the three storytelling conditions; (b) no group by storytelling condition interactions were found; and (c) there were main effect group differences, with the comorbid group (LD/RD and ADHD) having more difficulties producing complex sentence structure and producing an organized clearly presented prose than the LD/RD group. Scores were also collected from the parental questionnaire in order to ascertain the participant's overall pragmatic competence, but findings were not significant. Results of the findings were discussed in terms of the impact they may have on these children's academic, social and communication functioning

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Dissertation Abstracts International Section A: Humanities and Social Sciences. 2020 Feb.

**A CLASSROOM SELF-REGULATION TOOLBOX: A COLLABORATIVE PROGRAM BETWEEN OCCUPATIONAL THERAPISTS AND TEACHERS FOR CHILDREN WITH ADHD.**

**Costa R.**

Children with attention deficit hyperactivity disorder have less successful school experiences, as well as lives as adults, related to their challenges with self-regulation (Brook, Zhang, Brook, & Leukefeld, 2015). Children spend most of their school career in classrooms; however, teachers may not provide teaching or classroom environments that are conducive for learning for children with ADHD (Straker, Harris, Joosten, & Howie, 2018). These factors contribute to barriers to their success in school occupations, as well as their self-efficacy and participation (Major, Martinussen, & Wiener, 2013). However, evidence suggests that providing self-regulation strategies in classrooms improves success in school occupations. This doctoral project proposes a face-to-face continuing education course educating kindergarten through third grade teachers on strategies with a Classroom Self-regulation Toolbox facilitated by an occupational therapist. Self-regulation strategies of mindfulness, cognitive-behavioral, sensory, seating arrangements and ergonomics are included in the Toolbox. This continuing education course fosters collaboration between elementary teachers as well as elementary teachers and occupational therapists. This project will contribute to school-based occupational therapy by providing more evidence-based classroom interventions (The American Occupational Therapy Association, 2014) and improving collaboration between elementary school professionals

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Dissertation Abstracts International Section A: Humanities and Social Sciences. 2020 Feb.

**DEVELOPMENT OF AN ECOLOGICAL MULTI-FAMILY THERAPY FOR CHINESE FAMILIES OF ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A MIXED-METHOD STUDY.**

**Lo WK.**

Previous studies have revealed that adolescents with Attention Deficit Hyperactivity Disorder (ADHD) were more likely to have lower self-efficacy than other adolescents and develop other psychiatric problems, suggesting these young people may encounter more challenges in self-development. A secure family relationship is crucial for an adolescent's self-searching to be effective. In Hong Kong, there is a lack of family-based intervention to support Chinese families of adolescents with ADHD. This practice research aimed to develop a Multi-Family Therapy (MFT) model to enhance the family relationships of Chinese families of adolescents with ADHD, and to facilitate the adolescent's self-efficacy and their acquisition of family collective efficacy. There are two research objectives: 1) to investigate the group design of the proposed MFT model through inquiring into the client-perceived helpful group characteristics, the characteristics of the participants and the characteristics of the worker team; and 2) to generate knowledge about the potential

facilitative power of the use of a rural environment for promoting inter-and-intra-familial interactions through MFT. Modified from the Ma et al.'s model, the current MFT model comprised two family days on a university campus and an overnight family camp in a rural area of Hong Kong. From June 2017 to September 2018, five MFTs were conducted, with a total of 20 Chinese families of adolescents with ADHD (aged 11 to 15) participating in this research project. In summary, 23 adolescents with ADHD, 19 fathers and 18 mothers joined the research. This study adopted a mixed-method research design. Multidimensional measures comprising photo-elicitation interviews with adolescents, parent post-treatment focus groups and family in-depth interviews, and Client Satisfaction and Group Process Questionnaires were employed to evaluate and explore the participatory experiences of the Chinese adolescents with ADHD and their parents. The results of the quantitative data analysis revealed that a high level of perceived satisfaction with the MFT model was found among the participating Chinese families of adolescents with ADHD. Further analysis revealed that younger parents, mothers and parents with lower monthly household income had a higher degree of satisfaction with the group and found it more helpful than did older parents and parents with higher incomes. The results of the thematic analysis of the multiple sources of qualitative data revealed six major client-perceived helpful group characteristics of the MFT model, namely the worker team, similar but- unfamiliar members, plenty of free time, a change of environment, family companionship and exchange. The former three group characteristics were found to conduce the development of a mutually supportive relational climate while the latter three group characteristics were found to be conducive to the development of changes in the MFT model. A discussion of the findings is given on the development of the current model, the development of MFT theories, and the development of social work practice for Chinese families of adolescents with ADHD in Hong Kong. Given that conducting intervention in outdoors has been reported by previous studies in the west to be helpful in working with adolescents with emotional and behavioural needs, the current MFT model would likely be applicable to adolescents with other mental health needs for non-Chinese populations. The implications of this study for theory and practice, research limitations, and recommendations are discussed

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Dissertation Abstracts International: Section B: The Sciences and Engineering. 2020 Feb.  
**CHILD-CENTERED PLAY THERAPY AND ADVERSE CHILDHOOD EXPERIENCES: EFFECTIVENESS ON IMPULSIVITY AND INATTENTION.**

***Kram K.***

Adverse childhood experiences (ACEs) are a certain set of abuse household dysfunction experiences that many children in the United States experience. Children who experience multiple ACEs are more likely to have negative mental and physical health issues as they grow older. These outcomes include ADHD, depression, cancer, heart disease, and early death. In this study, I examined the effectiveness of child centered play therapy (CCPT), a developmentally appropriate treatment modality, with children who have experienced two or more ACEs and who are also demonstrating inattention and impulsivity symptoms. Participants were 34 students from five Title 1 elementary schools in the southwest United States (28 males and 6 females; age range 5-8 years old with a mean age of 6.12). In the sample, participants were comprised of 29.4% African American (n = 10), 38.2% Caucasian (n = 13), 17.6% Hispanic/Latino (n = 6), and 14.7% identified as biracial (n = 5). Participants were randomly assigned to a treatment group that received 16 CCPT 30-minute sessions twice a week (n = 17) or a waitlist control group (n = 17) that received treatment at the conclusion of the study. Using a factorial ANOVA, results indicated statistically significant improvement of CCPT treatment group over waitlist control group on the ADDES-4 School Total and the DOF Attention Deficit/Hyperactivity Problems scale indicating that CCPT was an appropriate treatment model for children who have experienced ACEs and inattention and impulsivity symptoms

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Dissertation Abstracts International: Section B: The Sciences and Engineering. 2020 Feb.

**FRIENDSHIP QUALITY IN ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.**

**Rokeach A.**

The majority of research investigating the social functioning of youth with ADHD has examined peer rejection and social skills deficits while generally overlooking their friendships. The goal of this dissertation was to provide detailed information about friendship quality in adolescents with and without ADHD. The first manuscript compared ratings of social support and negative interactions in same- and other-sex friendship dyads in adolescents with and without ADHD, while examining the potentially moderating effects of age and gender. The second manuscript examined empirically supported correlates of friendship quality including friendship stability, co-morbid psychopathology, and interpersonal competence. A sample of 115 adolescents, ages 13-18, were recruited to participate in the present study of whom 61 were classified as having ADHD (21 female) and 54 without ADHD (29 female). The measures used included parent and self-report rating scales and questionnaires assessing ADHD symptoms, friendship quality, friendship stability, externalizing behaviour (conduct problems, oppositional behaviour), internalizing behaviour (anxiety, depression), and interpersonal competence (social skills, social perspective taking). Results from study one indicated that ratings of friendship social support diminished across age groups in youth with ADHD, but increased in typically developing youth. Adolescents with and without ADHD, however, did not differ on ratings of negative interactions experienced in their friendships. Compared to males, females rated their friendships to be more supportive, irrespective of ADHD status. Adolescents with and without ADHD rated their same-sex friendships to be simultaneously more supportive and more conflictual than their other-sex friendships. Results from study two indicated that friendship stability, social skills, social perspective-taking, oppositional behaviour, and anxiety explained unique variance in the prediction of friendship social support. However, results of exploratory mediation analyses indicated that the direct effects of oppositional behaviour and anxiety were no longer significantly predictive of friendship quality, after controlling for the mediators social skills and social perspective-taking, respectively. These findings, clinical implications, and future directions are discussed within the context of the existing peer relations literature

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Epidemiol Psychiatr Sci. 2020 Jan;29:e95.

**COMORBIDITY AND HEALTH SERVICES' USAGE IN CHILDREN WITH AUTISM SPECTRUM DISORDER: A NESTED CASE-CONTROL STUDY.**

**Dizitzer Y, Meiri G, Flusser H, et al.**

**AIMS:** Children with autism spectrum disorder (ASD) tend to suffer from various medical comorbidities. We studied the comorbidity burden and health services' utilisation of children with ASD to highlight potential aetiologies and to better understand the medical needs of these children.

**METHODS:** In this nested case-control study, ASD cases and controls - matched by age, sex and ethnicity in a 1:5 ratio - were sampled from all children born between 2009 and 2016 at a tertiary medical centre. Data were obtained from the hospital's electronic database. Comorbid diagnoses were classified according to pathophysiological aetiology and anatomical/systemic classification of disease. Standard univariate and multivariate statistics were used to demonstrate comorbidities and health services' utilisation patterns that are significantly associated with ASD.

**RESULTS:** ASD children had higher rates of comorbidities according to both pathophysiological and anatomical/systemic classifications ( $p < 0.001$ ). The most marked significant differences were observed for: hearing impairments (OR = 4.728; 95% CI 2.207-10.127) and other auricular conditions (OR = 5.040; 95% CI 1.759-14.438); neurological (OR = 8.198; 95% CI 5.690-11.813) and ophthalmological (OR = 3.381; 95% CI 1.617-7.068) conditions; and ADD/ADHD (OR = 3.246; 95% CI 1.811-5.818). A subgroup analysis revealed a more profound case-control difference in anaemia rates among girls than in boys (OR = 3.25; 95% CI 1.04-10.19 v. OR = 0.74; 95% CI 0.33-1.64 respectively) and an opposite trend (larger differences in males than in females in cardiovascular diseases (OR = 1.99; 95% CI 1.23-3.23 v. OR = 0.76; 95% CI 0.17-3.45, respectively)). In addition, larger case-control differences were seen among Bedouin children than in Jewish children in a number of medical comorbidities (Breslow-Day test for homogeneity of odds ratio  $p$ -value  $< 0.05$ ). Finally, we found that children with ASD tended to be referred to the emergency department and to be admitted to the hospital more frequently than children without ASD, even after adjusting for their

comorbidity burden (aOR = 1.28; 95% CI 1.08-1.50 and aOR = 1.28; 95% CI 1.11-1.47 for >1 referrals and admissions per year, respectively).

**CONCLUSIONS:** The findings of this study contribute to the overall understanding of comorbid conditions and health services' utilisation for children with ASD. The higher prevalences of comorbidities and healthcare services' utilisation for children with ASD highlight the additional medical burden associated with this condition

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Eur Child Adolesc Psychiatry. 2020.

**CAN AUDITORY WARNING SIGNALS NORMALIZE EYE MOVEMENTS IN CHILDREN WITH ADHD?**

**Kleberg JL, Frick MA, Brocki KC.**

Attenuated baseline arousal has been hypothesized to underlie symptoms of attention deficit/hyperactivity disorder (ADHD). A behavioral signature of reduced baseline arousal is an increased beneficiary effect of warning signals in reaction tasks. This paradoxical effect is believed to be caused by a temporary increase in arousal induced by warning signals. In a preregistered study, we tested the hypothesis that children with high levels of ADHD symptoms would be hyperresponsive to warning signals in a well-established visual attention task (the gap/overlap paradigm). Previous studies using this task have found slower and more variable saccadic reaction times in children with ADHD compared to typically developing children, suggesting that these eye movement metrics are candidate biomarkers. We examined 71 children, of which 1/3 had a diagnosis of ADHD, using both dimensional analyses and group comparisons. Previously reported findings of reduced saccadic latency and increased latency variability were replicated. Importantly, saccadic latency was normalized by auditory warning signals. Analyses of pupil dilation, a physiological index of arousal and locus coeruleus-noradrenergic activity, confirmed that warning signals led to enhanced arousal. Our findings are novel and contribute to our understanding of arousal and attention in ADHD and have implications for treatment and interventions

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Eur Child Adolesc Psychiatry. 2020.

**EMOTIONAL SCENE PROCESSING IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW.**

**Leroy A, Spotorno S, Faure S.**

Impairments in emotional information processing are frequently reported in attention deficit hyperactivity disorder (ADHD) at a voluntary, explicit level (e.g., emotion recognition) and at an involuntary, implicit level (e.g., emotional interference). Most of previous studies have used faces with emotional expressions, rarely examining other important sources of information usually co-occurring with faces in our every day experience. Here, we examined how the emotional content of an entire visual scene depicting real-world environments and situations is processed in ADHD. We systematically reviewed in PubMed, SCOPUS and ScienceDirect, using the PRISMA guidelines, empirical studies published in English until March 2019, about processing of visual scenes, with or without emotional content, in children and adolescents with ADHD. We included 17 studies among the 154 initially identified. Fifteen used scenes with emotional content (which was task-relevant in seven and irrelevant in eight studies) and two used scenes without emotional content. Even though the interpretation of the results differed according to the theoretical model of emotions of the study and the presence of comorbidity, differences in scene information processing between ADHD and typically developing children and adolescents were reported in all but one study. ADHD children and adolescents show difficulties in the processing of emotional information conveyed by visual scenes, which may stem from a stronger bottom-up impact of emotional stimuli in ADHD, increasing the emotional experience, and from core deficits of the disorder, decreasing the overall processing of the scene

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Eur J Neurosci. 2019.

**EEG SPECTRAL POWER, BUT NOT THETA/BETA RATIO, IS A NEUROMARKER FOR ADULT ADHD.**

**Kiiski H, Bennett M, Rueda-Delgado LM, et al.**

Adults with attention-deficit/hyperactivity disorder (ADHD) have been described as having altered resting-state electroencephalographic (EEG) spectral power and theta/beta ratio (TBR). However, a recent review (Pulini et al. 2018) identified methodological errors in neuroimaging, including EEG, ADHD classification studies. Therefore, the specific EEG neuromarkers of adult ADHD remain to be identified, as do the EEG characteristics that mediate between genes and behaviour (mediational endophenotypes). Resting-state eyes-open and eyes-closed EEG was measured from 38 adults with ADHD, 45 first-degree relatives of people with ADHD and 51 unrelated controls. A machine learning classification analysis using penalized logistic regression (Elastic Net) examined if EEG spectral power (11–45 Hz) and TBR could classify participants into ADHD, first-degree relatives and/or control groups. Random-label permutation was used to quantify any bias in the analysis. Eyes-open absolute and relative EEG power distinguished ADHD from control participants (area under receiver operating characteristic = 0.71). The best predictors of ADHD status were increased power in delta, theta and low-alpha over centro-parietal regions, and in frontal low-beta and parietal mid-beta. TBR did not successfully classify ADHD status. Elevated eyes-open power in delta, theta, low-alpha and low-beta distinguished first-degree relatives from controls (area under receiver operating characteristic = 0.68), suggesting that these features may be a mediational endophenotype for adult ADHD. Resting-state EEG spectral power may be a neuromarker and mediational endophenotype of adult ADHD. These results did not support TBR as a diagnostic neuromarker for ADHD. It is possible that TBR is a characteristic of childhood ADHD

Europ J Spec Needs Educ. 2020;35:115-27.

**WHAT'S IN A NAME: THE EFFECT OF CATEGORY LABELS ON TEACHERS' BELIEFS.**

**Gibbs S, Beckmann JF, Elliott J, et al.**

In this paper, we report an investigation of the possible influence on teachers' essentialist thinking and efficacy beliefs of category labels used to describe children's educational difficulties. A 2x2x2 counterbalanced design was employed in which primary school teachers in Finland and the UK were exposed to vignettes that portrayed a child exhibiting difficulties in one of two domains: either behaviour or reading. Vignettes were presented in two versions. In one, the child was labelled as having either ADHD or Dyslexia; in the alternate condition, no such label was ascribed, descriptions were identical in all other respects. Participating teachers were presented with two vignettes, one from each domain and in each condition. Responses to measures of Efficacy and Essentialist beliefs were solicited. Overall responses indicated that category labels evoked stronger essentialist beliefs but did not influence teachers' efficacy beliefs. Finnish teachers reported stronger essentialist and lower efficacy beliefs than their counterparts in the UK

Eur Neuropsychopharmacol. 2020.

**ANATOMICAL SUBSTRATES OF SYMPTOM REMISSION AND PERSISTENCE IN YOUNG ADULTS WITH CHILDHOOD ATTENTION DEFICIT/HYPERACTIVITY DISORDER.**

**Luo Y, Halperin JM, Li X.**

Attention deficit/hyperactivity disorder (ADHD) is a highly prevalent neurodevelopmental disorder that emerges in childhood and persists into adulthood in a sizeable portion of afflicted individuals. The persistence of ADHD symptoms elevates the risk of adverse outcomes that result in substantial individual and societal burden. The objective of this study was to delineate neuroanatomical substrates associated with the diversity of adult outcomes of childhood ADHD, which may have considerable value for development of novel interventions that target mechanisms associated with recovery. Structural MRI and diffusion tensor imaging data from 32 young adults who were diagnosed with ADHD combined-type during childhood and 35 group-matched controls were analyzed. Adults with childhood ADHD were divided into 16 remitters and 16

persists based on DSM-IV criteria. Compared to the controls, ADHD probands showed significantly reduced gray matter (GM) volume in right putamen and white matter (WM) volume in left parieto-insular fiber tracts. Within the ADHD probands, the remitters, as compared to persisters, showed significantly greater volume of right hippocampo-frontal and right parieto-insular WM fiber tracts, and those connecting caudate with the frontal, parietal, occipital, temporal, and insular cortices. Among ADHD probands, increased fractional anisotropy value of left caudate-parietal tract was significantly correlated with reduced hyperactive/impulsive symptoms. These findings suggest that optimal structural development in the WM tracts that connect caudate with cortical areas, especially in the caudate-parietal path, may play an important role in symptom remission in young adults with childhood ADHD

Frontiers in Genetics. 2020;11.

**GENOME-WIDE DNA METHYLATION PATTERNS IN PERSISTENT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND IN ASSOCIATION WITH IMPULSIVE AND CALLOUS TRAITS.**

**Meijer M, Klein M, Hannon E, et al.**

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder that often persists into adulthood. ADHD and related personality traits, such as impulsivity and callousness, are caused by genetic and environmental factors and their interplay. Epigenetic modifications of DNA, including methylation, are thought to mediate between such factors and behavior and may behave as biomarkers for disorders. Here, we set out to study DNA methylation in persistent ADHD and related traits. We performed epigenome-wide association studies (EWASs) on peripheral whole blood from participants in the NeuroIMAGE study (age range 12–23 years). We compared participants with persistent ADHD (n = 35) with healthy controls (n = 19) and with participants with remittent ADHD (n = 19). Additionally, we performed EWASs of impulsive and callous traits derived from the Conners Parent Rating Scale and the Callous-Unemotional Inventory, respectively, across all participants. For every EWAS, the linear regression model analyzed included covariates for age, sex, smoking scores, and surrogate variables reflecting blood cell type composition and genetic background. We observed no epigenome-wide significant differences in single CpG site methylation between participants with persistent ADHD and healthy controls or participants with remittent ADHD. However, epigenome-wide analysis of differentially methylated regions provided significant findings showing that hypermethylated regions in the APOB and LPAR5 genes were associated with ADHD persistence compared to ADHD remittance ( $p = 1.68 \times 10^{-24}$  and  $p = 9.06 \times 10^{-7}$ , respectively); both genes are involved in cholesterol signaling. Both findings appeared to be linked to genetic variation in cis. We found neither significant epigenome-wide single CpG sites nor regions associated with impulsive and callous traits; the top-hits from these analyses were annotated to genes involved in neurotransmitter release and the regulation of the biological clock. No link to genetic variation was observed for these findings, which thus might reflect environmental influences. In conclusion, in this pilot study with a small sample size, we observed several DNA-methylation disorder/trait associations of potential significance for ADHD and the related behavioral traits. Although we do not wish to draw conclusions before replication in larger, independent samples, cholesterol signaling and metabolism may be of relevance for the onset and/or persistence of ADHD

Front Human Neurosci. 2020;14.

**ATYPICAL DYNAMIC CONNECTIVITY RECRUITMENT IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER CHILDREN: AN INSIGHT INTO TASK-BASED DYNAMIC CONNECTIVITY THROUGH AN fNIRS STUDY.**

**Sutoko S, Monden Y, Tokuda T, et al.**

Connectivity between brain regions has been redefined beyond a stationary state. Even when a person is in a resting state, brain connectivity dynamically shifts. However, shifted brain connectivity under externally evoked stimulus is still little understood. The current study, therefore, focuses on task-based dynamic functional-connectivity (FC) analysis of brain signals measured by functional near-infrared spectroscopy (fNIRS). We hypothesize that a stimulus may influence not only brain connectivity but also the occurrence

probabilities of task-related and task-irrelevant connectivity states. fNIRS measurement (of the prefrontal-to-inferior parietal lobes) was conducted on 21 typically developing (TD) and 21 age-matched attention-deficit/hyperactivity disorder (ADHD) children performing an inhibitory control task, namely, the Go/No-Go (GNG) task. It has been reported that ADHD children lack inhibitory control; differences between TD and ADHD children in terms of task-based dynamic FC were also evaluated. Four connectivity states were found to occur during the temporal task course. Two dominant connectivity states (states 1 and 2) are characterized by strong connectivities within the frontoparietal network (occurrence probabilities of 40% and 26%), and presumptively interpreted as task-related states. A connectivity state (state 3) shows strong connectivities in the bilateral medial frontal-to-parietal cortices (occurrence probability of 7%). The strong connectivities were found at the overlapped regions related the default mode network (DMN). Another connectivity state (state 4) visualizes strong connectivities in all measured regions (occurrence probability of 10%). A global effect coming from cerebral vascular may highly influence this connectivity state. During the GNG stimulus interval, the ADHD children tended to show decreased occurrence probability of the dominant connectivity state and increased occurrence probability of other connectivity states (states 3 and 4). Bringing a new perspective to explain neuropathophysiology, these findings suggest atypical dynamic network recruitment to accommodate task demands in ADHD children

Gait Posture. 2019;73:489.

#### **NEUROCOGNITIVE EXERCISE PROGRAM IMPROVES THE BALANCE PERFORMANCE IN CHILDREN WITH ADHD: A FOLLOW-UP STUDY.**

**Buker N, Akay U, +ûzbek A, et al.**

**1. Introduction** Attention Deficit/Hyperactivity Disorder (ADHD) is a widespread neurodevelopmental disorder in childhood and causes inattention, impulsivity, and hyperactivity which are negatively affect daily living activities. Recent studies have shown that cerebellar dysfunction, which leads to impaired balance or postural deficit, is the most common symptom in children with ADHD. Also, these studies reported that children with ADHD had a worse static and dynamic balance when compared with typically developing children. It has shown that neurocognitive exercise programme (NEP) improve physical, cognitive or behavioral parameters in ADHD. NEP is which consists of balance and coordination exercises involves various cognitive tasks and using different sports equipment (ball, racket, rope, tulle etc.). However, there is no follow-up study investigating the long-term effect of NEP.

**2. Research Question** Is there a statistically significant difference in pre-, post-, and a year follow up effects of NEP on balance scores in children with ADHD?

**3. Methods** Twelve children who had just diagnosed with ADHD (12 males; age: 9.25 - 11.66 years) included the study. Children who were using drugs and having a comorbid disorder (developmental coordination disorder, anxiety, depression) were excluded. Each child completed one NEP session (each session 60 minutes) in a week among the 10-week of NEP. NEP is a multimodal exercise program that includes visual, verbal and tactile stimuli, with various balance-coordination exercises. The static balance was measured by the Balance Master system with and without cognitive dual task (mCTSIB and Unilateral Stance Test with eyes opened/closed). Dynamic balance was evaluated by the Y-Balance Test. All measurements were completed in the before and after the NEP and one-year follow up. Friedman Tests were conducted to test whether there is a significant difference in the balance variables. The Wilcoxon test was performed to test the significance of pairwise differences using Bonferroni correction to adjust for multiple comparisons.

**4. Results** There was no significant difference in after NEP and one-year follow-up of the children with ADHD during balance performance with and without dual task ( $p > 0.05$ ). There was a significant difference in dynamic balance levels of children after NEP (Dominant foot composite score) and this difference was found that continued to long term ( $p < 0.05$ ).

**5. Discussion** Most of the studies have reported that children with ADHD have impaired static, dynamic balance, and postural control. It has been reported that balance problems were more prominent in dynamic tasks in children with ADHD. Another study showed that the ADHD group had a poor ability to maintain or

improve the dynamic balance compared to children with typically developing. A significant improvement was observed in the dynamic balance after NEP in the current study. In addition, we found that the development of dynamic balance was maintained in one-year follow-up after NEP

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Hong Kong J Occup Ther. 2019;32:127-35.

**CONSTRUCT VALIDITY OF THE PERSIAN VERSION OF THE CHILD OCCUPATIONAL SELF-ASSESSMENT IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN IRAN.**

**Sattari M, Yazdani F, Rassafiani M, et al.**

**Objective:** This study aimed to assess the construct validity of the Child Occupational Self-Assessment, translated to Persian that could provide occupational therapists with a tool to evaluate occupational competence and values of children in Iran.

**Methods:** A total of 250 children (87 girls and 163 boys) with attention deficit hyperactivity disorder aged 7.5-11 years referred from two specialised children's hospitals were included. The researchers read the questions to the children and they identified their own answers. The data were analysed based on the Rasch Rating Scale Model.

**Results:** Four of the items showed misfit and as a result of deleting these items the Persian version of the questionnaire has 21 items with an appropriate validity.

**Conclusion:** The Persian version of Child Occupational Self-Assessment can be used with new items format. It could be also useful to replace the missing question to develop the tool further

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Hum Mov Sci. 2020;70.

**GAIT CONTROL IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Simmons RW, Taggart TC, Thomas JD, et al.**

The current profile of gait control in children with ADHD is incomplete and predominately based on children walking forward at a self-selected pace. There are no studies of potential gait deficits in this clinical population when walking in different directions in combination with varying rates of stepping that are freely selected and entrained to an external stimulus. The purpose of the current study was to address this lack of information by assessing gait of children aged 7-17 years with (n = 17) and without (n = 26) ADHD. Participants walked forward and backward along an electronically instrumented carpet at a self-selected stepping rate and in synchrony to a metronome that dictated an increased and decreased stepping rate. Using repeated measures analysis of covariance (ANCOVA) to assess spatiotemporal gait parameters, results showed that children with ADHD exhibited a significantly exaggerated, toes turned out, foot position for all walking conditions compared to typically developing children. When walking backward, children with ADHD produced an increased step width, higher stepping cadence, and increased velocity. Additionally, coefficient of variation ratios indicated that children with ADHD produced greater variability of velocity, cadence, and step time for all walking conditions, and greater variability for stride length when walking at an increased stepping rate. Results were interpreted in terms of clinical significance and practical ramifications that inform rehabilitation specialists in designing therapies that ameliorate the reported gait deficits

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J Abnorm Child Psychol. 2020 Feb;48:251-63.

**EXAMINING PSYCHOPATHIC TRAITS IN CHILDREN USING THE CHILD PSYCHOPATHY SCALE - REVISED.**

**Breaux R, Babinski DE, Willoughby MT, et al.**

Applying the affective dimension of psychopathy to youth has advanced understanding of conduct problems in youth, leading to suggestions that other aspects of psychopathy may do the same. This was addressed in the present study by examining the structure and validity of psychopathic traits in elementary-age children as rated by mothers and teachers on the Child Psychopathy Scale Revised (CPS-R). Participants were 222 children (80.2% male; Mage = 8.92), the majority (71.6%) of whom met criteria for both ADHD and conduct

problems. Confirmatory factor analysis supported a four-factor model consisting of prosocial-empathic (PE), grandiose-manipulative (GM), emotionally volatile (EV), and attentive-planful (AP) factors. The CPS-R demonstrated good criterion validity with well-established measures of child behavior problems and callousness. The EV and AP factors demonstrate incremental validity by moderating the relation between conduct problems and impairment. Latent profiles supported a three-profile solution for mothers and a four-profile solution for teachers, with profiles consisting of one group low, one group moderate, and one high on all measures for both informants, and a fourth group that was high on all measures except CD and limited PE. Profiles differed significantly from each other on callousness and impairment, with limited PE being the best differentiator of youth highest in antisocial behavior based on mother and teacher report. Findings suggest that mothers and teachers may be able to identify children at risk for a more negative trajectory of antisocial behavior, that it is worthwhile to examine multiple psychopathy dimensions (rather than just the affective dimension), and that the CPS-R may be useful to screen for youth who are most likely to display more severe antisocial behavior and impairment

J Abnorm Child Psychol. 2020 Feb;48:223-36.

**PATTERNS OF HOMOTYPIC AND HETEROTYPIC CONTINUITY BETWEEN ADHD SYMPTOMS, EXTERNALISING AND INTERNALISING PROBLEMS FROM AGE 7 TO 15.**

**Obsuth I, Murray AL, Di Folco S, et al.**

ADHD presents a serious community-health problem through its links to a wide range of negative outcomes. These outcomes are exacerbated when ADHD symptoms co-occur with other mental health problems. Research evidence suggests high rates of co-morbidity with a range of problems. However, there is a paucity of longitudinal research that examines the predictive links between ADHD symptoms and symptoms of other mental health problems. We examined a cross-lagged autoregressive model in order to assess homotypic and heterotypic continuity between ADHD symptoms, aggressive behavior, non-aggressive behavior problems and anxiety/depression in a community-based sample of 1571 youth (761 female, 810 male) assessed annually from age 7 to 13 and again at age 15. Consistently significant correlations between each pair of problem behaviors provided support for concurrent comorbidity. Furthermore, significant autoregressive pathways provided support for homotypic continuity. Support for heterotypic continuity was limited to ADHD symptoms predicting both aggressive behavior and non-aggressive behavior problems, but not vice versa. Our study highlights the importance of focusing on ADHD symptoms to identify children at risk not only for continued ADHD symptomatology but also a range of externalizing behavior problems including different types of aggression and non-aggressive behavior problems, such as rule-breaking. Identifying these patterns in a community-based sample provides support for the possibility of early identification of risk for a range of problem behaviors

J Abnorm Child Psychol. 2020 Feb;48:237-49.

**ACADEMIC MOTIVATION DEFICITS IN ADOLESCENTS WITH ADHD AND ASSOCIATIONS WITH ACADEMIC FUNCTIONING.**

**Smith ZR, Langberg JM, Cusick CN, et al.**

The present study evaluates differences in self-reported intrinsic and extrinsic academic motivation and amotivation between eighth-grade adolescents with (n = 162) and without (n = 140) ADHD. This study also examines associations between motivation and academic functioning with objective (i.e., grade point average, standardized reading and math scores) and cross-rater measurement (i.e., parent-reported homework performance). Multivariate analysis of variance controlling for sex, intelligence, and medication status found that adolescents with ADHD exhibited a significant motivational deficit compared to adolescents without ADHD across all areas of academic motivation, including intrinsic motivation (d = 0.49), extrinsic motivation (d = 0.43), and amotivation (d = 0.42). To examine whether motivation was differentially associated with academic impairment in the ADHD and comparison groups, a multi-group path analysis was conducted controlling for sex, intelligence, and medication status. Findings showed that motivation was differentially associated with academic impairment for adolescents with and without ADHD. For the

comparison group, higher amotivation was associated with poorer homework performance and lower intrinsic motivation was associated with lower reading accuracy. In the ADHD group, higher amotivation was associated with poorer homework performance and math fluency, higher extrinsic motivation was associated with better homework performance and higher GPA, and higher intrinsic motivation was associated with higher reading accuracy. This study builds upon previous research in demonstrating that adolescents with ADHD have academic motivational deficits when compared to their peers without ADHD. Research is needed to understand the longitudinal interplay of academic motivation and academic functioning, with an eye towards developing or modifying interventions to increase academic motivation and academic success

J Affective Disord. 2020;266:109-19.

**SUICIDAL IDEATION AND ATTEMPTS IN THE UNITED STATES OF AMERICA AMONG STIMULANT-TREATED, NON-STIMULANT-TREATED, AND UNTREATED PATIENTS WITH A DIAGNOSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Siffel C, DerSarkissian M, Kponee-Shovein K, et al.**

**Background:** Studies of the association between attention-deficit/hyperactivity disorder (ADHD) drug therapy and suicidal ideation and attempts (SIA) have conflicting results.

**Methods:** Cohorts of patients with ADHD aged 6 years or older with at least one pharmacy claim for a central nervous system (CNS) stimulant or a non-stimulant, or with no claims for ADHD pharmacotherapy, were identified in the US IBM-« MarketScan-« Research Database from January 2008 to March 2018. Incidence density rates (IDRs) of SIA (i.e., claims for suicide and self-inflicted poisoning, suicide and self-inflicted injuries, or suicidal ideation) were calculated. Cohorts were compared (CNS stimulants vs non-stimulants; CNS stimulants vs no pharmacotherapy) using hazard ratios (HRs) estimated from Cox proportional hazards models. Inverse-probability-of-treatment weighting (IPTW) was used to control for confounding.

**Results:** The study included 797,189 patients (CNS stimulants, 622,536; non-stimulants, 54,615; no pharmacotherapy, 120,038). IDRs of SIA (per 1000 patient-years) were: CNS stimulants, 5.8; non-stimulants, 10.5; and no pharmacotherapy, 10.0. The overall SIA risk was significantly lower with CNS stimulants than with non-stimulants (IPTW-adjusted HR = .0.70, 95% confidence interval = .0.61-0.81,  $p < 0.001$ ) and no pharmacotherapy (0.62, 0.57-0.67,  $p < 0.001$ ). Limitations: SIA assessment was based on diagnostic codes; suicidal ideation may not have been reported; completed suicides were generally not captured; and treatment was not verified.

**Conclusions:** In this population-based study of patients with ADHD, SIA risk was significantly lower in those receiving CNS stimulants relative to those receiving non-stimulants or no pharmacotherapy, suggesting that CNS stimulants may attenuate SIA risk

J Affective Disord. 2020;266:585-94.

**CLINICAL EXPRESSION AND TREATMENT RESPONSE AMONG CHILDREN WITH COMORBID OBSESSIVE COMPULSIVE DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Farrell LJ, Lavell C, Baras E, et al.**

**Background:** Paediatric obsessive-compulsive disorder (OCD) is highly comorbid with other psychological disorders, including attention deficit/hyperactivity disorder (ADHD). Preliminary evidence suggests that youth with comorbid OCD and ADHD may experience greater impairments than children with other comorbidities; however, there is limited research examining the clinical expression and treatment response of these youth.

**Methods:** Youth (7 to 17 years) with a primary diagnosis of OCD and comorbid ADHD ( $n = 40$ ) were compared a sample of age and gender matched youth with OCD and other comorbidity (without ADHD,  $n = 40$ ). The study investigated symptoms, severity, functioning, comorbidity, family accommodation, in addition to parental psychopathology and rearing styles. Treatment response was investigated at post-treatment and six-month follow-up.

**Results:** Youth with comorbid OCD and ADHD had fewer sexual obsessions, higher rates of comorbidity, poorer executive functioning and higher family impairment. Families of comorbid youth engaged in

significantly more accommodation and reported more negative rearing. Finally, comorbid youth were significantly less likely to be responders or remitters at post-treatment.

**Limitations and Conclusions:** Limitations include the cross-sectional design, relatively small clinical sample, and lack of an experimental control group of youth with ADHD without OCD. Current approaches to treatment may be improved for youth with comorbid OCD and ADHD by addressing cooccurring anxiety, behavioural difficulties, and maladaptive family accommodation and rearing. Moreover, given pronounced deficits in executive function, these youth may require a stronger initial dose of CBT to achieve an adequate response

J Appl Dev Psychol. 2020 Jan;66:12.

**EXPLORING RELATIONSHIPS BETWEEN TEACHERS AND STUDENTS WITH DIAGNOSED DISABILITIES: A MULTI-INFORMANT APPROACH.**

**Zee M, de Bree E, Hakvoort B, et al.**

This study explored unique associations of student disabilities (ADHD, ASD, dyslexia) with teacher-, student- and peer-perceptions of student-teacher relationship quality. Sixty-three teachers, 510 students, and classmates from 24 Dutch mainstream elementary schools completed questionnaires about the student-teacher relationship quality. Teachers indicated whether students were diagnosed with disabilities. Multilevel models indicated that both teachers and classmates, but not students with ADHD themselves, reported higher levels of conflict in relationships. Additionally, teachers experienced less closeness and more conflict in relationships with children with ASD. The lower levels of closeness were also reported by classmates, but not by students with ASD themselves. Last, students with dyslexia experienced less closeness and conflict with their teacher, whereas their classmates and teachers reported more closeness and less conflict in relationships

J Autism Dev Disord. 2020 Jan;50:42-50.

**ADAPTIVE BEHAVIOR IN YOUTH WITH AUTISM SPECTRUM DISORDER: THE ROLE OF FLEXIBILITY.**

**Bertollo JR, Strang JF, Anthony LG, et al.**

Cognitive and behavioral flexibility are important predictors of adaptive behavior in school-age autistic youth. While prior research has utilized broad measures of flexibility, the current study uses the multi-dimensional Flexibility Scale-Revised to examine which specific flexibility skills relate to adaptive functioning. Through parent-report measures on 216 autistic youth, flexibility explained 22.2% of variance in adaptive socialization skills ( $p < 0.001$ ). Specifically, Social Flexibility accounted for significant variance in adaptive socialization skills, while Transitions/Change approached significance. In exploratory analyses, flexibility explained 11.5% of variance in Communication skills ( $p < 0.001$ ). This pattern remained after controlling for co-occurring ADHD symptoms. The current study helps to refine the relationship between flexibility and adaptive behavior, which may ultimately help to inform more targeted interventions

J Clin Child Adolesc Psychol. 2020 Jan;49:134-45.

**FUTURE DIRECTIONS FOR PSYCHOSOCIAL INTERVENTIONS FOR CHILDREN AND ADOLESCENTS WITH ADHD.**

**DuPaul GJ, Evans SW, Mautone JA, et al.**

Multiple psychosocial interventions are efficacious for children and adolescents with attention-deficit/hyperactivity disorder (ADHD) including behavioral parent training, behavioral classroom management, behavioral peer interventions, and organization training programs. Unfortunately, there is a significant gap between research and practice such that evidence-based treatments often are not implemented in community and school settings. Using a life course model for ADHD treatment implementation, we discuss future research directions that support movement from the current, fragmented system of care to a more comprehensive, integrated, and multisystemic approach. Specifically, we offer six

recommendations for future research. Within the realm of treatment development and evaluation, we recommend (1) identifying and leveraging mechanisms of change, (2) examining impact of youth development on treatment mechanisms and outcomes, and (3) designing intervention research in the context of a life course model. Within the realm of implementation and dissemination, we recommend investigating strategies to (4) enhance access to evidence-based treatment, (5) optimize implementation fidelity, and (6) examine and optimize costs and cost-effectiveness of psychosocial interventions. Our field needs to go beyond short-term, efficacy trials to reduce symptomatic behaviors conducted under ideal controlled conditions and successfully address the research-to-practice gap by advancing development, evaluation, implementation, and dissemination of evidence-based treatment strategies to ameliorate ADHD-related impairment that can be used with fidelity by parents, teachers, and community health providers

Journal of Experimental Psychology: General. 2020 Feb.

**PARTICIPANT-EXPERIMENTER RAPPORT IN EXPERIMENTAL SETTINGS: A TEST CASE OF EXECUTIVE FUNCTIONS AMONG CHILDREN WITH ADHD.**

***Gidron M, Sabag M, Yarmolovsky J, et al.***

There is a growing interest in the effects of social engagement on cognition, yet, research on the effects of social engagement with the experimenter in empirical contexts has been sparse. During an experiment, the experimenter and participant form a dyad, establishing a certain level of rapport—a sense of a positive and congruent relationship. This rapport is thought to promote performance by providing a comfortable testing environment, thereby reducing resource demand, and enhancing participant engagement and willingness to exert effort to perform. The current study sought to better understand the role of rapport by examining the effects of perceived rapport on effortful control, that is, inhibition and shifting, in an experimental setting among children with and without attention-deficit/hyperactivity disorder (ADHD). Forty-nine children (9 to 12 years old) were divided into two groups based on ADHD classification (i.e., typically developing children,  $n = 27$ ; children with ADHD,  $n = 22$ ). Participants completed the day/night Stroop task and the Wisconsin Card Sorting Task following a short rapport-building conversation with the experimenter. Later, both participant and experimenter filled the CHARM questionnaire reporting the rapport constructed during the experiment. Results show moderating effects of ADHD on the relationship between perceived rapport quality and congruency, and participant's executive functions performance. Specifically, children with ADHD showed higher susceptibility to rapport quality and were impervious to the effects of rapport congruency. Results highlight the importance of rapport with the experimenter in experimental research and suggest incorporating considerations concerning rapport, both in designing the experimental paradigm as well as an independent factor affecting task performance and outcome

J Invest Med. 2020;68:A164.

**PRIMARY CARE MANAGEMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AGED 2 -5 YEARS.**

***Bannett Y, Feldman HM, Gardner RM, et al.***

Purpose of study Attention-deficit/hyperactivity disorder (ADHD) affects approximately 2% of US preschool-age children. Little is known regarding preschool ADHD diagnosis and management by primary care providers (PCPs). This study assessed (1) rates of PCP diagnosis of ADHD in preschool-age children, (2) PCP adherence to select aspects of ADHD clinical practice guidelines, and (3) patient factors influencing variation in PCP diagnosis and management. Methods used Retrospective cohort study of electronic health record (EHR) data from all office visits of children aged 2-5 years, seen >2 times between 2015 and 2019, in 10 practices of a community-based California primary healthcare network. Study outcomes included ADHD diagnosis (symptom- or disorder-level), and adherence to guidelines in (1) documentation of comorbidities at or after an ADHD diagnosis, (2) choice of ADHD medication, and (3) follow-up of medicated patients. Summary of results Of 29,408 eligible children aged 2 to 5 years, 195 (0.7%) carried an ADHD diagnosis (0.04%-0.85% from 2-5 years, respectively). Of those, 109 (56%) had only symptom-level ADHD diagnoses (e.g., hyperactivity); 105 (54%) had documented comorbidities (e.g., language delay/disorder). ADHD

medications were prescribed only to children aged 4-5 years (40/195 (21%)); 34 of those 40 received stimulants as the first-line medication, and 19 of 40 had a follow-up visit within 2 months. In logistic regression models, children with public or military insurance were more likely to have an ADHD diagnosis (OR=1.64; CI: (1.17, 2.26); OR=2.22; CI: (1.32, 3.56)); ADHD patients initially diagnosed at a younger age and those with military insurance were more likely to have documented comorbidities (OR=1.06 (1.03, 1.10); OR=2.94; CI: (1.064, 3.529)). Conclusions The rates of PCP diagnosis of ADHD in preschoolers in this network were below estimated population prevalence. PCPs mostly followed guidelines in identification of comorbid conditions and in choice of stimulant medications, but had low rates of timely follow-up. Preschool-age children with ADHD may have remained undetected, with evidence of sociodemographic disparities in diagnosis of young children with ADHD

J Magn Reson Imaging. 2020;51:719-26.

#### **ABERRANT GRAY MATTER VOLUMES AND FUNCTIONAL CONNECTIVITY IN ADOLESCENT PATIENTS WITH ADHD.**

**Zhao Y, Cui D, Lu W, et al.**

**Background:** Altered gray matter (GM) volumes and functional connectivity (FC) happens in attention-deficit/hyperactivity disorder (ADHD) patients and the intelligence quotient (IQ) of ADHD patients is generally lower than healthy subjects, while few studies have focused on the association among the three.

**Purpose:** To investigate the abnormal changes of GM volumes and FC in ADHD patients compared with typically-developing control (TD-C), as well as the association between the changes and IQ.

**Study Type:** Case control. Population: 36 ADHD patients and 36 TD-C, aged 8-17. Field Strength/Sequence: 3.0T/single shot echo planar imaging (EPI).

**Assessment:** Preprocessing of fMRI data and seed-based FC calculation using DPABI4.0, and VBM was performed by CAT12.

**Statistical Tests:** Comparison between groups of smoothed GM volumes was performed using two-sample t-test within SPM 12, age and total intracranial volume (TIV) were returned as covariates. Comparison between groups of FCs was performed using a two-sample t-test within RESTplus; age was returned as a covariate. False discovery rate (FDR)-corrected and  $P < 0.05$  was considered statistically significant.

**Results:** Compared with TD-C, reduced GM volumes occurred in the left superior frontal gyrus ( $t = 3.61$ ,  $P < 0.001$ ), right middle frontal gyrus ( $t = 3.97$ ,  $P < 0.001$ ), left middle cingulum ( $t = 3.93$ ,  $P < 0.001$ ), and left cuneus ( $t = 4.42$ ,  $P < 0.001$ ). Decreased FC was found between the left precuneus and left middle cingulum ( $t = 5.86$ ,  $P < 0.001$ ), left middle temporal gyrus, and left superior frontal gyrus ( $t = 5.67$ ,  $P < 0.001$ ), as well as left medial superior frontal gyrus and left superior frontal gyrus ( $t = 6.73$ ,  $P < 0.001$ ).

**Data Conclusion:** The results confirmed that FCs between the regions with declined GM volumes and others were altered in ADHD patients. We speculated that abnormal changes of GM volume and FC maybe used as an imaging metric of ADHD.

**Level of Evidence:** 2.

**Technical Efficacy:** Stage 4.

Journal of Mental Health. 2020.

#### **UTILIZING THE COMMON-SENSE MODEL OF ILLNESS REPRESENTATIONS TO EXPLORE CHILDREN'S PERCEPTIONS OF, AND COPING WITH ADHD.**

**Ringer N.**

**Background:** Attention Deficit Hyperactivity Disorder (ADHD) among children is associated with difficulties in everyday functioning. According to the Common-Sense Model of Illness Representations (CSM), individuals beliefs about their illness condition guide their attempts to cope with it. The model suggests five dimensions of illness representations: beliefs regarding the identity of the symptoms, its duration, causes, consequences, and one's ability to achieve control over it.

**Aims:** The study aimed to explore the validity of the CSM-dimensions of illness representations for children with ADHD, while also exploring the possible relationships between types of beliefs and coping strategies.

**Method:** A deductive qualitative content analysis was used for analyzing data constructed from semi-structured individual interviews with 14 children diagnosed with ADHD. Results: The results have shown that there is a variation in children's beliefs regarding their ADHD. Those beliefs are, for the most part, captured by the five CSM-dimensions. An additional dimension of Uniqueness is suggested, which reflects children's beliefs on the way ADHD distinguishes them from other children. Patterns regarding types of beliefs and types of coping strategies were identified.

**Conclusions:** The CSM is a useful theoretical model to understand children's beliefs of, and coping with their ADHD

J Mol Neurosci. 2020.

**ASSOCIATION ANALYSIS BETWEEN THE RS1899663 POLYMORPHISM OF HOTAIR AND RISK OF PSYCHIATRIC CONDITIONS IN AN IRANIAN POPULATION.**

**Sayad A, Badrlou E, Ghafouri-Fard S, et al.**

Recent studies have shown contribution of long non-coding RNAs (lncRNAs) in the pathogenesis of a number of psychiatric disorders. In the current study, we investigated the association between a single nucleotide polymorphism in the lncRNA HOX transcript antisense intergenic RNA (HOTAIR) and risk of diverse neuropsychiatric conditions in Iranian population. The selected polymorphism (rs1899663) is an intronic variant of this lncRNA which has been associated with several cancers in different populations. This SNP was genotyped in 323 individuals with methamphetamine addiction, 55 children with attention-deficit hyperactive disorder (ADHD), 138 patients with bipolar disorder 1 (BPD1), 86 patients with BPD2, 53 patients with major depressive disorder (MDD), and 194 patients with schizophrenia (SCZ). There was no significant association between rs1899663 genotypes and risk of methamphetamine addiction or SCZ in any assessed inheritance model. There was a significant association between rs1899663 SNP and risk of BPD1 in allelic, co-dominant, and dominant models (P values of 0.003, 0.009, and 0.003, respectively). The T allele of this SNP conferred risk of BPD1 (OR (95% CI) = 1.70 (1.20-2.41)). This SNP was associated with risk of BPD2 in allelic and dominant models (P values of 0.02 and 0.04). The T allele of this SNP was revealed to be the risk allele for BPD2 as well (OR (95% CI) = 1.61 (1.09-2.40)). Besides, the mentioned SNP was associated with susceptibility to MDD in allelic and dominant models (P values of 0.01 and 0.03). Finally, the rs1899663 was associated with risk of ADHD in allelic, co-dominant, and dominant models (P values of 3.6E-4, 0.002, and 1.2E-4, respectively). The current investigation highlights the role of rs1899663 in conferring risk of BPD1, BPD2, MDD, and ADHD and suggests a similar underlying genetic background for these conditions

J Neurodevelopmental Disord. 2020;12.

**COGNITIVE CORRELATES OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS WITH HIGH INTELLECTUAL ABILITY.**

**Cadenas M, Hartman C, Faraone S, et al.**

**Background:** There is an ongoing debate as to whether attention-deficit hyperactivity disorder (ADHD) in highly intelligent individuals has a similar presentation as in average intelligent individuals. The aim of this study was to examine the cognitive correlates of ADHD in highly intelligent children and adolescents with ADHD.

**Method:** Two independent samples (N = 204 and N = 84) of (1) high intelligence quotient (IQ) (IQ  $\geq$  120) children and adolescents with ADHD were used, carefully matched on age, gender, ADHD severity, and IQ with (2) control participants with high intelligence, (3) participants with ADHD with an average intelligence (IQ 90-110), and (4) control participants with an average intelligence. These samples were selected from the Dutch node of the International Multicenter ADHD Genetics (NeuroIMAGE) and Tracking Adolescents' Individual Lives Survey (TRAILS) cohorts, respectively, in which a large battery of cognitive tasks was administered. Linear mixed models were used to examine the main effects of ADHD and IQ and their interaction on cognitive performance.

**Results:** ADHD-control group differences were not moderated by IQ; mostly equally large ADHD-control differences in cognitive performance were found for high versus average intelligent groups. The small moderating effects found mostly indicated somewhat milder cognitive problems in highly intelligent individuals with ADHD. Overall, highly intelligent children and adolescents with ADHD performed at the level of the average intelligent control children.

**Conclusions:** Our findings indicate the cognitive profile of ADHD is similar in highly versus average intelligent individuals with ADHD, although ADHD-related cognitive deficits may be easily overlooked in the high intelligence population when compared to the typical (i.e., average intelligent) control group

J Pediatr Neurol. 2020;18:1-6.

**OMEGA-3 SUPPLEMENTATION FOR CHILDREN WITH LEARNING DIFFICULTIES AND ATTENTION DEFICIT DISORDER: IS IT BENEFICIAL?**

**Gadoth N.**

The use of natural medicines, food supplements, and in particular long-chain polyunsaturated fatty acids (omega-3/6) for a large variety of ailments including attention deficit hyperactivity disorder (ADHD) and other developmental behavioral disorders has dramatically increased in the past few years. In recent publications, doubts have been raised in regard to the benefits and risks of this form of treatment for ADHD. In this article, a short history of the way this treatment has evolved, its theoretical basis, and evidence-based data on the value of this popular supplementation will be reviewed

J Pediatr. 2020.

**HOMICIDAL IDEATION AMONG CHILDREN AND ADOLESCENTS: EVIDENCE FROM THE 2012-2016 NATIONWIDE EMERGENCY DEPARTMENT SAMPLE.**

**Vaughn MG, Carbone J, DeLisi M, et al.**

**Objective:** To assess the prevalence and behavioral, sociodemographic, and psychiatric/psychological correlates of homicidal ideation among a sample of children and adolescents.

**Study design:** We employed descriptive and multivariate logit models of homicidal ideation using data from the 2012-2016 Nationwide Emergency Department Sample from the Healthcare Cost and Utilization Project. This study was conducted with data from emergency departments in the US, and we used a sample of (N = 17 041 346) children and adolescents between the ages of 5 and 17 years.

**Results:** Pediatric homicidal ideation is rare with a prevalence estimate of 0.09%; however, its prevalence increases substantially from age 5 years to age 15 years when it peaks, and then declines through the end of adolescence. Conduct disorders conferred 1483% increased odds, attention deficit hyperactivity disorder conferred 616% increased odds, and other behavioral and emotional disorders increased a 2-fold to nearly 4-fold increased liability for homicidal ideation net the effects of sex, age, urban residence, insurance status, and zip code median household income.

**Conclusion:** In the wake of homicide tragedies, it is often the case that numerous behavioral and clinical red flags were present in the developmental history of the perpetrator, but these were overlooked. Identifying children and adolescents who present with homicidal ideation is a crucial pediatric and public health matter that can inform prevention and behavioral interventions that forestall lethal violence

J Pediatr. 2020.

**PARENTAL WEIGHT STATUS AND OFFSPRING BEHAVIORAL PROBLEMS AND PSYCHIATRIC SYMPTOMS.**

**Robinson SL, Ghassabian A, Sundaram R, et al.**

**Objectives:** To assess relations of prepregnancy maternal and paternal obesity with offspring behavioral problems and psychiatric symptoms at 7-8 years in the Upstate KIDS study, a prospective cohort study.

**Study design:** Maternal body mass index (BMI) was calculated from prepregnancy height and weight provided in vital records or self-report at 4 months postpartum. Mothers reported paternal height and weight. At 7-8 years, mothers indicated if their children had been diagnosed with ADHD or anxiety (n = 1915). Additionally, children's behavior was measured with the Strengths and Difficulties Questionnaire at 7 years of age (n = 1386) and the Vanderbilt ADHD Diagnostic Parent Rating Scale at 8 years of age (n = 1484). Based on Strengths and Difficulties Questionnaire scores, we identified children with borderline behavioral problems. Adjusted risk ratios (aRR) and 95% CIs were estimated with robust multivariable Poisson regression.

**Results:** Compared with children of mothers with a BMI of <25, children whose mothers had BMI 25-30, 30-35, and  $\geq 35$  kg/m<sup>2</sup> had higher risks of reported ADHD (aRR, 1.14, 95% CI, 0.78-1.69; aRR, 1.96, 95% CI, 1.29-2.98; and aRR, 1.82, 95% CI, 1.21-2.74, respectively). Risks of hyperactivity problems identified by the Strengths and Difficulties Questionnaire and a positive screen for inattentive or hyperactive/impulsive behavior with the Vanderbilt ADHD Diagnostic Parent Rating Scale were also higher with increasing maternal prepregnancy BMI. Paternal BMI was not associated with child outcomes.

**Conclusions:** Our findings suggest that maternal, rather than paternal, obesity is associated with maternal report of child ADHD diagnosis and inattentive or hyperactivity problems. Further research is needed to understand how maternal obesity might influence these behavioral changes during or after pregnancy

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J Psychopathol Behav Assess. 2020.

**LONELINESS ACCOUNTS FOR THE ASSOCIATION BETWEEN DIAGNOSED ATTENTION DEFICIT-HYPERACTIVITY DISORDER AND SYMPTOMS OF DEPRESSION AMONG ADOLESCENTS.**

**Houghton S, Lawrence D, Hunter SC, et al.**

The heightened levels of peer relationship difficulties associated with Attention Deficit/Hyperactivity Disorder (ADHD) potentially predispose adolescents to feelings of loneliness and depressive symptoms. The current study explores whether feelings of loneliness mediate the effects of ADHD on depressive symptoms. Eighty-four adolescents (Mage = 13.01-áyears, 75% Male) in Western Australian schools completed mental health and wellbeing surveys. Multivariate analysis of variance assessed whether adolescents with ADHD had greater loneliness and depressive symptoms, and mediation analysis explored whether loneliness mediated the relationship between ADHD and depressive symptoms. Adolescents with ADHD reported significantly greater depressive symptomatology and feelings of isolation and lower quality of friendships. Together, friendship and isolation related loneliness fully mediated the relationship between ADHD and depressive symptoms. Loneliness is associated with depression in adolescents with ADHD and may be an important consideration when addressing symptoms of depression among young people diagnosed with ADHD

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J Psychopharmacol. 2020.

**POST HOC ANALYSES OF RESPONSE RATES TO PHARMACOLOGICAL TREATMENTS IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Coghill DR, Newcorn JH, Chen J, et al.**

**Introduction and objectives:** Lack of consensus regarding how best to define treatment response hinders translation from trials to the clinic. These post hoc analyses examine three commonly used response criteria in six trials of lisdexamfetamine dimesylate (LDX) in children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

**Methods:** Data from four short-term randomised controlled trials (RCTs) and two long-term open-label studies were analysed. Children and adolescents with ADHD received either dose-optimised (30-70 mg/day) or fixed-dose (70 mg/day) LDX. The RCTs included osmotic-release oral system methylphenidate (OROS-MPH) or atomoxetine (ATX) as a head-to-head comparator or as a reference treatment. Three definitions of response were used in these analyses: reductions of 30% or 50% in ADHD Rating Scale IV (ADHD-RS-IV) total score plus a Clinical Global Impressions Improvement (CGI-I) score of 1 or 2, or an ADHD-RS-IV total score of 18.

**Results:** At the end point, LDX response rates for the least stringent criterion of 30% reduction in ADHD-RS-IV total score plus a CGI-I score of 1 or 2 ranged from 69.6% to 82.6%. The proportion achieving the more stringent criterion of a reduction in ADHD-RS-IV total score of 50% plus a CGI-I score of 1 or 2 at the end point ranged from 59.8% to 74.8%. An ADHD-RS-IV total score of 18 at the end point was achieved by 56.7-79.9% of participants. Response rates remained stable throughout the long-term open-label studies.

**Conclusions:** Response rates were similar for the two more stringent response criteria. The less stringent criterion resulted in higher response rates and may include partial responders

Kindheit und Entwicklung: Zeitschrift für Klinische Kinderpsychologie. 2020 Jan;29:40-51.

**BELASTUNGSERLEBEN VON MÄTTERN MIT KINDERN MIT ADHS: EINFLUSS DER ADHS-ERSCHEINUNGSFORMEN UND DER ELTERLICHEN SYMPTOMATIK.**

**SchwÄrer MCI, Nitkowski D, Petermann F, et al.**

Parents of children with attention deficit hyperactivity disorder (ADHD) report a high level of psychological stress associated with the child's symptoms, but this can also be attributed to the frequently comorbid oppositional defiant disorder (ODD). In addition, parents often have their own psychopathological symptoms, which contributes to the stress experience. The study involved 207 children (M = 9.00 years; SD = 1.52; 65.2% male). The aim of the study was first to analyze whether the maternal stress differs depending on ADHD presentation and whether there is a comorbid symptomatology of ODD. The children with ADHD symptoms (n = 138) were divided into groups depending on ADHD presentation and signs of ODD (DSM-5; ADHS-KJ; Petermann & Petermann, 2019) and were examined in terms of maternal stress experience (EBI, Eltern-Belastungs-Inventar; Traster, 2011). Group differences were analyzed using a multivariate variance analysis. Furthermore, it was investigated, which symptoms and control variables best explain maternal stress in children (ADHD and ODD) and parents (depression; EBI and ADHD; Schmidt & Petermann, 2013), which was calculated with a stepwise multiple regression (n = 157). The results show a significant main effect between the different ADHD presentations on the scales of Mood and Adaptability. In addition, a significant interaction effect of ADHD presentation, sex, and ADHD-specific drug use was demonstrated on the EBI scale of Acceptability. Sidak post-hoc tests showed the highest maternal stress for children with ADHD+ODD (independent of ADHD presentation); medium-to-large effect sizes were found (d = .69 to 1.50). Furthermore, maternal depression proved to be the most important predictor of maternal stress ( $\hat{\rho}^2 = 0.45$ ). Combined presentation with ODD ( $\hat{\rho}^2 = 0.37$ ), inattentive presentation with ODD ( $\hat{\rho}^2 = 0.16$ ), the impulse control/disinhibition of mothers ( $\hat{\rho}^2 = 0.15$ ), the number of children living in the household ( $\hat{\rho}^2 = 0.11$ ), and the attention control of mothers ( $\hat{\rho}^2 = 0.11$ ) were able to clarify further variance, resulting in an overall model of  $R^2 = 0.60$ . In the clinical context, mothers of children with ADHD should be specifically examined for depressive symptoms, and questionnaire procedures for parental symptoms should be collected. In the case of indications of the presence of their own symptoms, clinical diagnostic or therapy recommendations should be made, as otherwise the therapy goals would be at risk (e. g., owing to lack of support in practicing the therapy contents). The parental ADHD should be clarified because of the high heredity, since this can intensify the symptoms of the child. Additionally, behavioral therapeutic measures should be carried out that are adapted to the ADHD presentation of the child in order to guarantee a targeted stress reduction in mothers

Konuralp Derg. 2019;11:397-403.

**EVALUATION OF SOCIODEMOGRAPHIC AND CLINICAL PROFILES OF ADOLESCENTS UNDER-18 YEARS OF AGE REFERRED BY THE JUDICIAL AUTHORITIES FOR MARRIAGE LICENSE.**

**Yektas C, Buken B.**

**Objective:** The aim of this study was to investigate the sociodemographic and clinical characteristics of adolescents referred to a university hospital by the judicial authority for determining whether any mental and physical impediments to marriage exist.

**Methods:** 70 adolescents who were consulted to child and adolescent psychiatry inquired by the judicial authorities if there was any impediment to marriage were included to study. Psychiatric examination of the

adolescents was performed according to DSM 5. Data obtained from the study were examined retrospectively with the method of file scanning system.

**Results:** Mostly (94.3%) female children with a mean age of 16.05 -1 0.2 years were included in the study. None of the children attended to school during the assessment. Most (89.5%) of the children were living in a family environment with a low socioeconomic level. The most frequently psychiatric diagnoses were; attention-deficit hyperactivity disorder (%4.3, n=3), depressive disorder (%4.3, n=3), mental retardation (%2.8, n=2) and post-traumatic stress disorder (%1.4, n=1). 85.7% of the children decided to marry individuals they got acquainted from their immediate circle or from social media, while marriage of only 14.3% (n=10) of them were previously arranged by their families.

**Conclusions:** Socio-economic level, family characteristics and attending to school are important predisposing factors for early marriages. It was also considered that marriage at this age means an attempt for gaining an early autonomy. Encouraging to continue formal education for the development of healthy autonomy will be an important factor to prevent early marriages

Konuralp Derg. 2019;11:269-73.

**AN EXAMINATION OF EMOTION REGULATION AND ASSOCIATED FACTORS IN ATTENTION DEFICIT-HYPERACTIVITY DISORDER.**

**Baykal S, Nalbantoglu A.**

**Objective:** Emotion regulation difficulties (ERD) such as anger, irritability and frustration intolerance leading to severe functional losses may be observed in attention deficit-hyperactivity disorder (ADHD). The purpose of this study was to compare children and adults diagnosed with ADHD and a healthy control group in terms of emotion regulation characteristics and to examine factors potentially associated with ERD.

**Methods:** The study was performed with 72 children/adults aged 6-18 diagnosed with ADHD based on DSM-V diagnostic criteria at the Nam-ik Kemal University Medical School of Child and Adolescent Psychiatry Polyclinic, Turkey, and 30 healthy controls. The Schedule for Affective Disorders and Schizophrenia for School-Age Children - Present and Lifetime Version (K-SADS-PL), a semi-structured interview form, was used to determine comorbidities. ERD scores (ERD=attention+anxiety/depression+aggression subscales) were determined using the Childhood Behavior Checklist (CBCL).

**Results:** Mean ERD scores were 189.45-119.33 in the ADHD group and 164.13-119.94 in the healthy control group. A significant difference was determined in ERD scores between the two groups ( $p < 0.001^{**}$ ). When the ADHD group was evaluated in terms of clinical characteristics, comorbid psychiatric disorders were not associated with ERD, but combined type ADHD characteristics emerged as significant predictors for ERD ( $p = 0.011^{*}$ ).

**Conclusions:** The results of this research revealed significantly greater ERD in individuals diagnosed with ADHD compared to healthy controls, and that combined type ADHD is a predictor for ERD. Since ERD accompanying ADHD lead to greater function loss in the individual and are associated with persistence of the disorder in adulthood, these are important clinical characteristics also requiring evaluation during the diagnosis and treatment of ADHD

Lancet Psychiatry. 2020 Feb;7:148-61.

**THE BURDEN OF MENTAL DISORDERS ACROSS THE STATES OF INDIA: THE GLOBAL BURDEN OF DISEASE STUDY 1990-2017.**

*Anon.*

**BACKGROUND:** Mental disorders are among the leading causes of non-fatal disease burden in India, but a systematic understanding of their prevalence, disease burden, and risk factors is not readily available for each state of India. In this report, we describe the prevalence and disease burden of each mental disorder for the states of India, from 1990 to 2017.

**METHODS:** We used all accessible data from multiple sources to estimate the prevalence of mental disorders, years lived with disability (YLDs), and disability-adjusted life-years (DALYs) caused by these

disorders for all the states of India from 1990 to 2017, as part of the Global Burden of Diseases, Injuries, and Risk Factors Study. We assessed the heterogeneity and time trends of mental disorders across the states of India. We grouped states on the basis of their Socio-demographic Index (SDI), which is a composite measure of per-capita income, mean education, and fertility rate in women younger than 25 years. We also assessed the association of major mental disorders with suicide deaths. We calculated 95% uncertainty intervals (UIs) for the point estimates.

**FINDINGS:** In 2017, 197.3 million (95% UI 178.4-216.4) people had mental disorders in India, including 45.7 million (42.4-49.8) with depressive disorders and 44.9 million (41.2-48.9) with anxiety disorders. We found a significant, but modest, correlation between the prevalence of depressive disorders and suicide death rate at the state level for females ( $r(2)=0.33$ ,  $p=0.0009$ ) and males ( $r(2)=0.19$ ,  $p=0.015$ ). The contribution of mental disorders to the total DALYs in India increased from 2.5% (2.0-3.1) in 1990 to 4.7% (3.7-5.6) in 2017. In 2017, depressive disorders contributed the most to the total mental disorders DALYs (33.8%, 29.5-38.5), followed by anxiety disorders (19.0%, 15.9-22.4), idiopathic developmental intellectual disability (IDID; 10.8%, 6.3-15.9), schizophrenia (9.8%, 7.7-12.4), bipolar disorder (6.9%, 4.9-9.6), conduct disorder (5.9%, 4.0-8.1), autism spectrum disorders (3.2%, 2.7-3.8), eating disorders (2.2%, 1.7-2.8), and attention-deficit hyperactivity disorder (ADHD; 0.3%, 0.2-0.5); other mental disorders comprised 8.0% (6.1-10.1) of DALYs. Almost all (>99.9%) of these DALYs were made up of YLDs. The DALY rate point estimates of mental disorders with onset predominantly in childhood and adolescence (IDID, conduct disorder, autism spectrum disorders, and ADHD) were higher in low SDI states than in middle SDI and high SDI states in 2017, whereas the trend was reversed for mental disorders that manifest predominantly during adulthood. Although the prevalence of mental disorders with onset in childhood and adolescence decreased in India from 1990 to 2017, with a stronger decrease in high SDI and middle SDI states than in low SDI states, the prevalence of mental disorders that manifest predominantly during adulthood increased during this period.

**INTERPRETATION:** One in seven Indians were affected by mental disorders of varying severity in 2017. The proportional contribution of mental disorders to the total disease burden in India has almost doubled since 1990. Substantial variations exist between states in the burden from different mental disorders and in their trends over time. These state-specific trends of each mental disorder reported here could guide appropriate policies and health system response to more effectively address the burden of mental disorders in India. **FUNDING:** Bill & Melinda Gates Foundation; and Indian Council of Medical Research, Department of Health Research, Ministry of Health and Family Welfare, Government of India

Med Lett Drugs Ther. 2020 Jan;62:9-15.

#### **DRUGS FOR ADHD.**

Anon.

Med Care. 2020;58:273-79.

#### **THE PREVALENCE AND INCIDENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN THE VETERANS HEALTH ADMINISTRATION FROM 2009 TO 2016.**

**Hale AC, Bohnert KM, Spencer RJ, et al.**

**Background:** The prevalence and incidence of attention-deficit/hyperactivity disorder (ADHD) have increased substantially among children and adolescents over the past decade; however, little is known regarding trends in adult populations.

**Objective:** The objective of this study was to explore trends in the prevalence, incidence, and correlates of adult ADHD in a national sample of veterans receiving care at Veteran Affairs (VA) hospitals and clinics.

**Research Design:** A retrospective design was used to examine ADHD diagnosed in all VA primary care (PC) and mental health clinics (MHCs) from fiscal years (FYs) 2009 to 2016. Age-adjusted prevalence and incidence were calculated using direct standardization, and Poisson regressions modeled differences in trends between demographic groups.

**Subjects:** All veterans with VA PC or MHC visits during the observation period.

**Measures:** ADHD incidence and prevalence, psychiatric comorbidity, neuropsychological evaluation.

**Results:** An annual average of 5.09 million (range: 4.63-5.42 million) VA patients attended a PC or MHC appointment between FY09 and FY16. During this period, age-adjusted annual prevalence increased 258% from 0.23% to 0.84% and incidence increased 240% from 0.14% to 0.48%. Black veterans and older veterans had the lowest prevalence and incidence across all years. Increases in prevalence and incidence occurred across all demographic subgroups. The proportion of patients who had a neuropsychological evaluation within 6 months before or after a new ADHD diagnosis decreased from 12.6% to 10.8% [ $\chi^2(1)=16.59$ ,  $P<0.001$ ].

**Conclusion:** Overall increases and demographic differences in adult veterans diagnosed with ADHD suggest a growing need to establish the reliability of diagnostic practices to ensure appropriate and equitable care

Mol Psychiatry. 2020.

**META-ANALYSIS AND SYSTEMATIC REVIEW OF ADGRL3 (LPHN3) POLYMORPHISMS IN ADHD SUSCEPTIBILITY.**

**Bruxel EM, Moreira-Maia CR, Akutagava-Martins GC, et al.**

The gene encoding adhesion G protein-coupled receptor L3 (ADGRL3, also referred to as latrophilin 3 or LPHN3) has been associated with ADHD susceptibility in independent ADHD samples. We conducted a systematic review and a comprehensive meta-analysis to summarize the associations between the most studied ADGRL3 polymorphisms (rs6551665, rs1947274, rs1947275, and rs2345039) and both childhood and adulthood ADHD. Eight association studies (seven published and one unpublished) fulfilled criteria for inclusion in our meta-analysis. We also incorporated GWAS data for ADGRL3. In order to avoid overlapping samples, we started with summary statistics from GWAS samples and then added data from gene association studies. The results of our meta-analysis suggest an effect of ADGRL3 variants on ADHD susceptibility in children ( $n = 8724/14,644$  cases/controls and 1893 families): rs6551665 A allele (Z score =  $1.701$ ;  $p = 0.0069$ ); rs1947274 A allele (Z score =  $2.033$ ;  $p = 0.0421$ ); rs1947275 T allele (Z score =  $2.339$ ;  $p = 0.0978$ ); and rs2345039 C allele (Z score =  $3.806$ ;  $p = 0.0026$ ). Heterogeneity was found in analyses for three SNPs (rs6551665, rs1947274, and rs2345039). In adults, results were not significant ( $n = 6532$  cases/ $15,874$  controls): rs6551665 A allele (Z score =  $2.005$ ;  $p = 0.0450$ ); rs1947274 A allele (Z score =  $2.179$ ;  $p = 0.0293$ ); rs1947275 T allele (Z score =  $0.822$ ;  $p = 0.4109$ ); and rs2345039 C allele (Z score =  $1.544$ ;  $p = 0.1226$ ). Heterogeneity was found just for rs6551665. In addition, funnel plots did not suggest publication biases. Consistent with ADGRL3's role in early neurodevelopment, our findings suggest that the gene is predominantly associated with childhood ADHD

Neurol Sci. 2020.

**ARE ATTENTIONAL INSTRUCTION AND FEEDBACK TYPE AFFECT ON LEARNING OF POSTURAL AND SUPRA-POSTURAL TASKS?**

**Shams A, Dehkordi PS, Tahmasbi F, et al .**

Optimum postural control and balance is dependent on the individual, the environment, and the task limitations. Thus, the present study investigated the effect of attentional instruction and feedback type on postural and supra-postural tasks. The 96 participants aged 11-19 years with attention deficit hyperactivity disorder (ADHD) were randomly assigned to one of the eight groups such as attentional instruction (internal and external), feedback (external and internal), and task (postural and supra-postural). Following a pre-test, the participants underwent four training sessions. Each session included 20 trials of 30-seconds with 20-seconds of rest between trials. Twenty-four hours after the training session, they performed two trials of warm-up and then took part in a retention test. Twenty-four hours after the retention test, they again performed two trials of warm-up and then participated in the transfer test. The result showed that the external attentional feedback and external attentional instruction groups performed better on supra-postural and postural tasks than the other experimental groups ( $P > 0.05$ ). The external attentional instruction group performed better on postural and supra-postural tasks in the delayed retention and transfer tests ( $P > 0.05$ ).

Also, the external feedback group scored highest on postural and supra-postural tasks in the delayed retention and transfer tests. The results suggest that external attentional feedback and instruction is more effective than internal attention when learning supra-postural tasks to maintain balance

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Neuropsychiatr Dis Treat. 2020;16:465-77.

**INDEXING EXECUTIVE FUNCTIONS WITH TEST SCORES, PARENT RATINGS AND ERPS: HOW DO THE MEASURES RELATE IN CHILDREN VERSUS ADOLESCENTS WITH ADHD?**

**Häger LA, Øgrim G, Danielsen M, et al.**

**Objective:** Rating scales and neuropsychological tests including continuous performance tests (CPTs) are widely used to assess executive functions (EFs). Event-related potentials (ERPs) are also used to index certain EFs such as action preparation and inhibition. In this descriptive study, we examined the associations between results on an EF rating scale, a CPT and ERP components in ADHD as a function of age.

**Methods:** Fifty-nine patients with ADHD (and more often than not with comorbid dis-orders) in two age groups (9-12 years and 13-17 years) were assessed using EF ratings, a visual CPT and ERPs (CueP3, P3go and P3no-go).

**Results:** There were age related changes in the ERPs with the CueP3 amplitude being stronger in children, and the P3no-go amplitude stronger in adolescents. The associations between the EF measures were different in the two age groups. In particular, the P3no-go seemed to reflect different EF-related processes in children versus adolescents.

**Conclusion:** Age group effects were seen on a selection of ERP amplitudes in this sample of patients with ADHD. Ratings, test scores and EF-related ERPs seem to capture different aspects of EF in ADHD, and the associations differed depending on age group. The results show that different measures of EF are not interchangeable and highlight the importance of age when interpreting ERPs

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Paediatr Perinat Epidemiol. 2020.

**NEONATAL THYROID-STIMULATING HORMONE AND ASSOCIATION WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Villanger GD, Ystrom E, Engel SM, et al.**

**Background:** Normal brain development is dependent on maternal, fetal and neonatal thyroid function. Measuring neonatal thyroid-stimulating hormone (TSH) 48-72 hours after birth screens for congenital hypothyroidism, allowing early treatment to avoid serious impairment. However, even within sub-clinical ranges, disrupted thyroid homeostasis during brain development has been linked to adverse neurodevelopmental outcomes, including attention-deficit/hyperactivity disorder (ADHD). Objectives: To estimate the association between neonatal TSH below threshold for potential congenital hypothyroidism and subsequent ADHD diagnosis using a population-based birth cohort.

**Methods:** Children with a diagnosis of ADHD in the Norwegian Mother, Father and Child Cohort Study (MoBa) were identified through linkage with the Norwegian Patient Registry using ICD-10 codes for hyperkinetic disorders. The study included 405 ADHD cases and 1,092 controls (born 2003-2008) with available neonatal TSH concentrations below 10 mU/L (cut-off for potential congenital hypothyroidism) measured in dried blood spots sampled 48-72 hours after birth.

**Results:** In multivariable, quintile models the relationship appeared to follow a U-shaped pattern with elevated odds ratios (ORs) at lower and higher TSH levels. Among children with TSH in the lowest quintile, odds of ADHD was approximately 1.5-fold higher than children in the middle quintile (OR = 1.60, 95% CI 1.09, 2.34), which was driven by substantially elevated risk among girls, with no association among boys (Pinteraction = 0.02; girls OR = 3.10, 95% CI 1.53, 6.30; boys OR = 1.16, 95% CI 0.73, 1.84).

**Conclusions:** ADHD risk appeared to be elevated among newborns with low TSH levels (i.e. with hyperthyroid status), and this association was mainly found among girls. Because our findings are suggestive of increased risk at very low TSH concentrations, where analytical accuracy is low, future studies should employ highly sensitive assays capable of accurate quantitation at very low concentrations. Also, larger

studies are needed to investigate these associations at higher neonatal TSH concentrations where data are more widely distributed

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Pediatrics. 2018;142.

**A TECHNOLOGY DRIVEN APPROACH FOR SHARING PATIENT-REPORTED OUTCOMES IN ADHD BETWEEN PARENTS, PEDIATRICIANS AND TEACHERS.**

**Michel JJ, Fiks A, Mayne S, et al.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is the most common chronic childhood neurobehavioral disorder. Although portals have been developed for pediatricians to collect information from parents and teachers, we lack systems that share relevant information between families, pediatricians and teachers in order to overcome fragmented care that worsens outcomes. Our institution developed a Clinical Decision Support (CDS) system (Figures 1 & 2) to collect information from families and teachers by sending survey links by email following parental consent and presents this information to the pediatrician within the electronic health record (EHR). Information collected from parents included treatment preferences and goals and the Vanderbilt rating scales for ADHD symptoms, co-morbidities and performance (validated measures).

**Aims:** To update this CDS to better address priorities of families and teachers including enabling information sharing of results between families, pediatricians, and teachers.

**Methods:** We conducted a prospective technology development and implementation evaluation, engaging 8 parents, 11 pediatricians and 8 educators in the iterative process. From 9/2015 to 9/2016, we held 2 family advisor, 3 educator, 3 pediatrician and 2 joint parent-educator meetings that set priorities. We added features to support parent-directed sharing of results directly to teachers. T-tests and chi-square tests assessed the association of child symptoms, performance and co-morbidities with parents' willingness to share.

**Results:** The stakeholder-engaged design process prioritized the following features: (1) parents' ability to control which survey components (goals, symptoms, performance, medication side-effects) were shared with teachers and (2) parents' and teachers' ability to receive information entered by each other and retain their own submitted information. These features were added in January, 2017. Supplemental questions on the ADHD parent surveys provided control of sharing and we utilized already in place software for secure emailing to control access to completed surveys. A total of 209 parents submitted survey responses within 28 days of the upgrade. Of these, 138 (66%) agreed to share information (114 (83%) sharing all information). Parents of children with greater hyperactivity ( $p=.03$ ) as well as impaired performance (76% versus 46%,  $p < .001$ ) were more likely to share than others. We observed a trend toward information sharing among parents of children with ADHD co-morbidities (oppositonality, anxiety, depression) (92% versus 71%,  $p=.2$ ).

**Conclusion:** A stakeholder-engaged process developed feasible and acceptable upgrades to an EHR-linked system that support parents' information sharing with pediatricians and teachers for a common chronic condition. Results indicate that parents of children with greater symptomatology and impairments - those likely to benefit most - were most likely to share. This system provides a model for how patient-reported outcomes may be shared between families and interdisciplinary care teams

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Pediatrics. 2018;142.

**EFFICACY AND SAFETY OF HLD200, A NOVEL DELAYED-RELEASE AND EXTENDED-RELEASE METHYLPHENIDATE FORMULATION, IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESULTS FROM A PIVOTAL PHASE 3 TRIAL.**

**Pliszka S, Wilens T, Bostrom S, et al.**

**Purpose:** Evening-dosed HLD200 is a novel delayed-release and extended-release formulation of methylphenidate (DR/ER-MPH) designed to address the unmet need for a once-daily medication for children with attention-deficit/hyperactivity disorder (ADHD) that provides efficacy upon awakening, but not at the expense of efficacy later in the day. The objective was to determine whether DR/ER-MPH improves control of ADHD symptoms, and at-home early morning, late afternoon, and evening functional impairments versus placebo in children with ADHD. Safety and tolerability were also assessed.

**Methods:** This was a pivotal, randomized, double-blind, placebo-controlled, parallel-group, phase 3 trial of DR/ER-MPH (40-80 mg/d) in children (6-12 years) with ADHD (NCT02520388). Participants had current or prior response on methylphenidate. Following a screening period of <2 weeks with a 3- to 7-day washout, participants were randomized (1:1) to DR/ER-MPH or placebo administered in the evening for 3 weeks. After 1 week, the initial 40 mg dose was titrated in 20-mg weekly increments to 60 mg and 80 mg, as tolerated, with one down-titration step permitted. The primary endpoint was the ADHD Rating Scale-IV (ADHD-RS-IV) Total Score following 3 weeks of treatment. The key secondary endpoints were the Before School Functioning Questionnaire (BSFQ) and Parent Rating of Evening and Morning Behavior-Revised, Morning (PREMB-R AM) and Evening (PREMB-R PM) subscales. Safety measures included treatment-emergent adverse events (TEAEs), with direct questioning for sleep- and appetite-related TEAEs; vital signs; laboratory tests; electrocardiograms; and physical exams.

**Results:** A total of 161 participants were included in the intent-to-treat population (DR/ER-MPH, n = 81; placebo, n = 80). The mean DR/ER-MPH dose after 3 weeks of treatment was 68.1 mg. After 3 weeks, children on DR/ER-MPH achieved significant improvements versus those on placebo in ADHD symptoms (least squares [LS] mean ADHD-RS-IV: 24.1 vs 31.2; P=0.002), and at-home early morning functioning (LS mean BSFQ: 18.7 vs 28.4; P < 0.001; LS mean PREMB-R AM: 2.1 vs 3.6; P < 0.001) and late afternoon/evening functioning (LS mean PREMB-R PM: 9.4 vs 12.2; P=0.002). Significant improvements in ADHD symptoms and early morning functional impairments were also evident after 1 week (ADHD-RS-IV: P < 0.001; BSFQ: P=0.001) and 2 weeks of treatment (ADHD-RS-IV: P=0.002; BSFQ: P=0.004) with DR/ER-MPH. All TEAEs and vital signs were consistent with those expected for methylphenidate. No serious TEAEs were reported, and only 1 participant on DR/ER-MPH (1.2%) and 4 on placebo (5.0%) had TEAEs leading to early withdrawal. Most common TEAEs (>10%) reported by children on DR/ER-MPH were decreased appetite and insomnia. Sleep-related TEAEs were mild or moderate in severity and 96.6% resolved during the study.

**Conclusions:** Following daily evening administration, DR/ER-MPH was well tolerated and demonstrated significant improvements versus placebo in ADHD symptoms and at-home functional impairments in the early morning, late afternoon, and evening in children with ADHD

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Pediatrics. 2018;142.

**NORMATIVE DATA FOR THE BEFORE SCHOOL FUNCTIONING QUESTIONNAIRE (BSFQ) IN YOUTH WITH AND WITHOUT A HISTORY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Faraone S, Nullmeier R, DeSousa N, et al.**

**Purpose:** The validated Before School Functioning Questionnaire (BSFQ) assesses commonly reported areas of dysfunction in early morning, before school activities (eg, breakfast, hygiene, time awareness, getting to school) associated with attention-deficit/hyperactivity disorder (ADHD) in children and adolescents. The objectives of this study were to: (1) obtain normative data for the BSFQ; (2) determine whether parent ratings differentiate youth with and without a history of ADHD; and (3) determine whether ratings are affected by age, gender, or comorbidities.

**Methods:** A normative survey was conducted with 1200 respondents derived from a representative U.S. sample of primary caregivers of children and adolescents (6-17 years; 50 males and 50 females per age category) using an online questionnaire. Caregivers were enrolled if their child: (1) never had ADHD, (2) had a past history of ADHD; or (3) currently had untreated ADHD (no treatment during the past 3 months). Using the 20-item BSFQ, caregivers rated their child's at-home early morning functional (EMF) impairments between the time of awakening and before the school day or other morning activities (ie, 6:00 AM and 9:00 AM). Each item was rated on a severity scale of 0 to 3 (0 = no impairment; 3 = severe impairment). Total BSFQ scores can range from 0 to 60, with a higher total score indicating greater EMF impairment. Differences in total BSFQ scores were determined by an ANOVA with post hoc comparisons, and differences in individual item scores were determined by a Chi-squared test.

**Results:** Of the 1200 youth (children [6-12 years]: n = 700; adolescents [13-17 years]: n = 500) rated by a caregiver (mothers/step-mothers: 68.9%), 1079 (90%) had no history of ADHD, 41 (3%) had a history of ADHD, and 80 (7%) had current untreated ADHD. There were no differences in the total BSFQ score distributions between males and females (P=0.554); however, scores were 23.7% higher for children versus

adolescents, and 54.4% higher for youth with one or more comorbidities versus no comorbidities (both  $P < 0.001$ ). There were significant differences in the total BSFQ score distributions between youth without ADHD, those with a history of ADHD, and those with current untreated ADHD (mean -| SD: 12.70 -| 11.00 vs. 21.17 -| 14.58 vs. 29.60 -| 13.15, respectively;  $P < 0.001$ ), and also across all 20 items ( $P < 0.001$ ). The effect of ADHD on the total BSFQ score and all 20 items remained significant after adjusting for psychiatric comorbidity (all  $P < 0.001$ ).

**Conclusions:** Normative data suggest that the BSFQ discriminates between youth with and without a history of ADHD. Age and comorbidities, but not gender, had significant effects on the total BSFQ score

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Pediatrics. 2018;142.

**NORMATIVE DATA FOR THE PARENT RATING OF EVENING AND MORNING BEHAVIOR SCALE, REVISED (PREMB-R) IN YOUTH WITH AND WITHOUT A HISTORY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Faraone S, Nullmeier R, DeSousa N, et al.**

**Purpose:** The validated 11-item Parent Rating of Evening and Morning Behavior Scale, Revised assesses at-home functioning (ie, behaviors that impact activities of daily living, such as getting up and out of bed, doing or completing homework, and falling asleep) during the early morning (PREMB-R AM subscale) and late afternoon/evening (PREMB-R PM subscale) in children with attention-deficit/hyperactivity disorder (ADHD). The objectives of this study were to: (1) obtain normative data for PREMB-R AM and PREMB-R PM; (2) determine whether parent ratings differentiate youth with and without a history of ADHD; and (3) determine whether ratings are affected by age, gender, or comorbidities.

**Methods:** A normative survey was conducted with 1200 respondents derived from a representative U.S. sample of primary caregivers of youth (6-17 years; 50 males and 50 females per age category) using an online questionnaire. Caregivers were enrolled if their child never had ADHD, had a past history of ADHD, or currently had untreated ADHD (during the past 3 months). Caregivers rated their child's at-home early morning functional impairments on the 3-item PREMB-R AM, and their child's at-home late afternoon/evening functional impairments on the 8-item PREMB-R PM. Each item was rated from 0 (no difficulty) to 3 (a lot of difficulty), with PREMB-R AM having a maximum total score of 9 and PREMB-R PM having a maximum total score of 24, and a higher score indicating greater temporal functional impairment. Differences in total and individual item scores were determined by an ANOVA with post hoc comparisons and Chi-squared test, respectively.

**Results:** Of the 700 children (6-12 years) and 500 adolescents (13-17 years) rated by caregivers (mothers/step-mothers: 68.9%), 1079 had no history of ADHD, 41 had a history of ADHD, and 80 had current untreated ADHD. PREMB-R AM/PREMB-R PM scores were significantly higher for children versus adolescents ( $P=0.042/P < 0.001$ ), and those with  $>1$  comorbidities versus no comorbidities (both  $P < 0.001$ ); however, there were no gender differences. There were significant differences in the total score distributions between youth without ADHD, with a history of ADHD, and with current untreated ADHD in PREMB-R AM (mean -| SD: 2.27 -| 2.13, 4.07 -| 2.69, and 4.19 -| 2.39;  $P < 0.001$ ) and PREMB-R PM (mean -| SD: 5.05 -| 4.80, 10.27 -| 6.70, and 12.53 -| 5.77;  $P < 0.001$ ), and across all individual items ( $P < 0.001$ ). The effect of ADHD on total scores and individual items of the PREMB-R AM and PREMB-R PM remained significant after adjusting for psychiatric comorbidity (all  $P < 0.001$ , except  $P=0.01$  for item 1 on PREMB-R AM).

**Conclusions:** Normative data suggest that both PREMB-R AM and PREMB-R PM discriminate between youth with and without a history of ADHD. Age and comorbidities, but not gender, had significant effects on the total scores of PREMB-R AM and PREMB-R PM

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Pediatrics. 2018;142.

**EFFECT OF HLD200 ON CAREGIVER-REPORTED ADHD SYMPTOM IMPROVEMENT IN CHILDREN WITH ADHD AND CAREGIVER STRAIN: RESULTS FROM A PHASE 3 TRIAL.**

**Pliszka S, Wilens T, Bostrom S, et al.**

**Purpose:** Evening-dosed HLD200 is a novel delayed-release and extended-release formulation of methylphenidate (DR/ER-MPH) designed to address the unmet need for a once-daily medication for children with attention-deficit/hyperactivity disorder (ADHD) that provides efficacy upon awakening, but not at the expense of efficacy later in the day. The objective was to evaluate whether 3 weeks of treatment with HLD200 in children with ADHD: (1) demonstrates an improvement in caregiver-rated ADHD symptoms, as measured by the Conners' Global Index - Parent (CGI-P), and (2) reduces caregiver strain, as measured by the Caregiver Strain Questionnaire (CGSQ), versus placebo.

**Methods:** Caregiver-rated ADHD symptoms (CGI-P) and caregiver strain (CGSQ) were assessed as secondary endpoints following 3 weeks of treatment in a randomized, double-blind, multicenter, placebo-controlled, parallel-group, phase 3 trial of DR/ER-MPH in children (6-12 years) with ADHD (NCT02520388). Using the 10-item CGI-P, parents rated their child's ADHD symptoms on a 4-point scale (0 = never/seldom; 3 = very often/frequently), with total scores ranging from 0 to 30. Caregivers also rated the impact of caring for a child with emotional and behavioral challenges on the 21-item CGSQ (5-point scale: 0 = not at all; 4 = very much), with total scores ranging from 0 to 84. A reduction on individual item and total scores for both measures indicated an improvement.

**Results:** Of 163 children enrolled across 22 sites, 161 were included in the intent-to-treat population (DR/ER-MPH, n = 81; placebo, n = 80). The mean DR/ER-MPH dose after 3 weeks of treatment was 68.1 mg. Mean CGI-P scores at baseline and CGSQ scores at screening (ie, before washout of prior ADHD therapy) were comparable for both DR/ER-MPH (CGI-P: 22.8, CGSQ: 54.5) and placebo (CGI-P: 21.8; CGSQ: 54.9) groups. After 3 weeks of treatment, caregivers of children on DR/ER-MPH reported significant reductions in CGI-P scores versus those on placebo (least-squares [LS] mean: 12.3 vs 17.4;  $P < 0.001$ ). Additionally, there was a significant reduction in CGSQ scores after 3 weeks of treatment with DR/ER-MPH versus placebo (LS mean: 41.2 vs 49.1;  $P < 0.001$ ). Post hoc analyses on the effect of DR/ER-MPH versus placebo on individual items of CGI-P and CGSQ, and the two subscales of CGI-P will be presented. No serious TEAEs were reported and all TEAEs were consistent with previously reported studies of methylphenidate.

**Conclusions:** Caregivers reported significant improvements in their child's ADHD symptoms and these improvements coincided with reductions in caregiver strain after 3 weeks of treatment on evening-dosed DR/ER-MPH versus placebo

Pediatr Int. 2019.

**CLINICAL CHARACTERISTICS OF BOYS WITH COMORBID AUTISM SPECTRUM DISORDER AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER.**

**Yamawaki K, Ishitsuka K, Suyama S, et al.**

**Background:** Autism spectrum disorder (ASD) and attention deficit / hyperactivity disorder (ADHD) are frequently comorbid and, as both are defined as neurodevelopmental disorders in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, simultaneous diagnosis is possible. However, despite the frequency of this comorbid state, its endophenotypic features remain unclear. This study thus aimed to describe the behavioral and emotional problems in boys with comorbid ASD and ADHD using the Strengths and Difficulties Questionnaire (SDQ).

**Methods:** In total, 102 boys (age, 6-12 years) diagnosed with one or both disorders were divided into three groups according to their clinical diagnosis: ASD-á+-áADHD (N-á=-á39), ASD (N-á=-á37), and ADHD (N-á=-á25). Symptoms and related behaviors were compared among the groups using parents ratings of the autism spectrum quotient, ADHD rating scale-IV, and SDQ.

**Results:** In the ASD-á+-áADHD group, the proportion of clinical-range cases was as high as 76.9% for the SDQ total difficulties score (TDS). The ASD-á+-áADHD and ADHD groups had significantly higher TDS as well as behavioral problems and hyperactivity subscale scores than did the ASD group; however, the ASD-á+-áADHD group did not have significantly different scores on any subscale compared with the other two

groups. The ASD+ADHD and ASD groups also had significantly lower prosocial behavior scores than the ADHD group.

**Conclusions:** When using the SDQ as a screening tool for neurodevelopmental disorders, a high TDS, conduct problems, hyperactivity, and low prosocial behavior can be considered characteristic of ASD and ADHD comorbidity in 6- to 12-year-old boys

Pharmacoepidemiol Drug Saf. 2020.

**USE OF METHYLPHENIDATE AND RISK FOR VALVULAR HEART DISEASE: A CASE-CONTROL STUDY NESTED IN THE BIFAP COHORT.**

**Saiz LC, Gil M, Alonso A, et al.**

**Purpose:** To examine the association between use of methylphenidate and the risk for valvular heart disease (VHD) in the Spanish primary care database BIFAP.

**Methods:** Case-control study nested in a cohort of patients aged 5 to 25 years between 2002 and 2014, based in a general practice research database. Cases were people with a validated diagnosis of VHD. Ten controls per case were matched on age, sex, and calendar year. Multivariable conditional logistic regression was used to estimate odds ratios (ORs) of VHD comparing patients ever treated with methylphenidate vs never users, as well as by time since last use, treatment duration, and variations in case inclusion criteria.

**Results:** From a cohort of 1 596 284 patients, we identified 262 valid cases of VHD. No difference in the incidence of VHD was observed when comparing ever users of methylphenidate with never users (adjusted OR 0.52, 95%CI 0.16-1.69). A similar result was found comparing current, recent, or past users of methylphenidate. Differences were not significant when both valid and probable cases were included as events of interest (adjusted OR 0.59, 95%CI 0.22-1.63).

**Conclusions:** In this first-ever population-based study on this issue, association between methylphenidate and the incidence of VHD among persons in the 5 to 25 years age range was neither confirmed nor excluded. Additional studies may be required to clarify the presence or absence of this relationship

Physician and Sportsmedicine. 2020.

**THE EFFECTS OF METHYLPHENIDATE ON STRESS FRACTURES IN PATIENTS' AGES 10-29: A NATIONAL DATABASE STUDY.**

**DeFroda SF, Quinn M, Yang DS, et al.**

**Objectives:** Current literature is divided on the effect of methylphenidate (MP) on stress fracture development and if this medication increases fracture, or is actually protective for it. This study further investigates this effect utilizing a large national database. We hypothesized that individuals on MP would have a reduced risk of SF compared against controls.

**Methods:** This study utilized the Humana insurance data set within the PearlDiver Patient Records Database (PearlDiver Inc, Fort Wayne, Indiana). All patients ages 10-29 were included and patients were identified without ADHD, with ADHD not on MP, and with ADHD on MP. ADHD and stress fracture diagnoses were identified by International Classification of Disease, Tenth Revision codes. Bivariate analysis of stress fracture occurrence was conducted using chi-square analysis. Multivariate logistic regression was used to calculate odds ratios, controlling for age, sex, race, and Charlson Comorbidity Index (CCI). Statistical analysis was performed using the PearlDiver software, which runs R, Version 1.1.442. An alpha value of .05 was set as the level of significance.

**Results:** The study included 29,590 patients on MP and 831,439 patients not on MP from ages 10-29. The highest proportions of patients who filled MP prescriptions were in the age range 10 to 14 years old (51.2%), followed by 15 to 19 (41.0%). Patients rarely continue MP from years 20 to 24 (16.5%) or 25 to 29 (9.6%). ADHD patients on MP had the lowest calculated risk of stress fractures (0.45%) compared to patients without ADHD (0.54%) and ADHD patients not on methylphenidate (0.58%). In all three patient groups, most stress fractures occurred in 15 to 19-year olds. Patients with ADHD on MP conferred lower odds of stress fracture than ADHD patients not on MP and patients without ADHD (aOR = 0.64, p = 0.0002). The older age

groups 20-24 and 25-29 involved less risk of stress fracture compared to the youngest age group 10-14 ( $p < 0.0001$ ;  $p < 0.0001$ ), as well as did male gender ( $p < 0.0001$ ).

**Conclusions:** This database-based study of the effect of MP on SF adds to the growing body of literature providing evidence that MP may offer protective benefit for stress fracture

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PLoS ONE. 2020;15.

**UNMET CARE NEEDS OF CHILDREN WITH ADHD.**

*Vijverberg R, Ferdinand R, Beekman A, et al.*

**Background** Non-compliance to, or drop-out from treatment for childhood ADHD, result in suboptimal outcome. Non-compliance and drop-out may be due to mismatches between patients' care needs and treatments provided. This study investigated unmet care needs in ADHD patients. Unmet needs were assessed in two different treatment settings (general outpatient setting versus youth-ACT). Youth-ACT treatment is an intensive outreach-oriented treatment for patients with severe psychiatric and psychosocial problems. Comparison of a general outpatient sample with a youth-ACT sample enabled us to assess the influence of severity of psychiatric and psychosocial problems on perceived care needs.

**Methods** Self-reported unmet care needs were assessed among 105 ADHD patients between 6 and 17 years of age in a general outpatient ( $n = 52$ ) and a youth-ACT setting ( $n = 53$ ).

**Results** ADHD patients most frequently reported unmet needs regarding mental health problems, information on diagnosis/treatment, and future prospects. Outpatients differed from youth- ACT patients with respect to 30% of the unmet care needs that were investigated. Outpatients perceived more unmet needs regarding information on diagnosis/treatment ( $p = 0.014$ ). Youth-ACT patients perceived more unmet needs concerning medication side effects ( $p = 0.038$ ), quality and/or quantity of food ( $p = 0.016$ ), self-care abilities ( $p = 0.016$ ), regular/suitable school or other daytime activities ( $p = 0.013$ ), making and/or keeping friends ( $p = 0.049$ ), and future prospects ( $p = 0.045$ ).

**Conclusions** Focusing treatment of ADHD patients on unmet needs may reduce non-compliance and drop-out. In clinical practice, systematic assessment of unmet care needs in all ADHD patients may be warranted, e.g. using the CANSAS questionnaire during the screening/ intake phase

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Psychiatry Res. 2020;285.

**EMOTIONAL LABILITY AND IRRITABILITY HAVE SPECIFIC ASSOCIATIONS WITH SYMPTOMATOLOGY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

*Maire J, Galera C, Bioulac S, et al.*

Irritability and emotional lability have been shown to be severity and impairment factors in community and clinical sample studies and are frequent comorbid features of Attention Deficit Hyperactivity Disorder (ADHD). However, while irritability and emotional lability seem to be closely linked, the differential effect of these two features has received little attention. This study assessed the distinct associations of irritability and emotional lability on symptomatology in children with ADHD. One hundred and eight children diagnosed with ADHD participated in the study. Children were rated by parents on ADHD and comorbid symptomatology with the Conners Rating Scale 7<sup>th</sup> Revised. Irritability was the most significant predictive factor of the severity of anxiety and oppositional symptoms. Regarding emotional lability, it was significantly predictive of the severity of hyperactivity symptoms. While emotional lability shares common theoretical characteristics with irritability, each seems to be associated with specific areas. Irritability is a symptom of Oppositional Defiant Disorder, a frequent ADHD comorbidity, and also seems to be related to internalizing disorder (e.g. anxiety). Emotional lability seems to be related to ADHD severity symptoms per se. Both could be clinically informative in the diagnosis of ADHD and its comorbidities

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Psychiatry Res. 2020;284.

**TRENDS IN INCIDENCE RATES OF DIAGNOSED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) OVER 12 YEARS IN TAIWAN: A NATIONWIDE POPULATION-BASED STUDY.**

**Huang CLC, Wang J-J, Ho C-H.**

We investigated time trends in the incidence rate (IR) of attention-deficit/hyperactivity disorder (ADHD) across the lifespan and potential factors affecting them using a Taiwanese population-based database. IR per 10,000 person-years (PY) of newly diagnosed ADHD based on ICD-9-CM was calculated annually for the total population, gender, 5 age groups, and 3 ADHD subtypes from 2000 to 2011. Among the 265,932 patients, IR increased from 7.92 to 13.92; the male-to-female ratio decreased from 3.61 to 2.90. The largest increase in IR was noted in young adults (19–30 years), followed by preschoolers (0–6 years), while the smallest increase was in adults (>31 years). The IR trends showed a more prominent increase in males than females among children, adolescents, and young adults, yet a reserved relationship existed among adults, with a more prominent increase in women. The combined type of ADHD exhibited a prominently increasing trend in the child/adolescent group (age ≤18) and the inattentive type ADHD in the adult group (age >18). In conclusion, the ADHD IR is increasing with distinct differences among age, sex, and subtypes. The diminishing gap between those who need treatment and those actually treated might partly contribute to this trend, especially among young adults, preschoolers, and females

Psychiatry Res. 2020;285.

**ALTERED BRAIN WHITE MATTER MICROSTRUCTURAL ASYMMETRY IN CHILDREN WITH ADHD.**

**Wu Z-M, Wang P, Yang L, et al.**

**Objectives:** We aimed to examine brain white matter integrity in children with ADHD.

**Methods:** In a cohort of children with ADHD (n = 83) and healthy controls (n = 122), we used tract-based spatial statistics on Diffusion Tensor Imaging (DTI) data to obtain the mean fractional anisotropy (FA) in 40 bilateral regions of interest (ROIs). Lateralization Index (LI) was calculated. The difference in LI between groups and correlations between the LI of each ROI and ADHD symptom scores as well as cognitive function were examined.

**Results:** Children with ADHD had significantly greater LI at the posterior thalamic radiation (PTR) compared with healthy controls (mean LI in ADHD = 0.0096; in Control = 0.0044, p = 0.0143), and LI of the external capsule (EC) was significantly correlated with inattention symptoms in both groups (+1 = -0.00059, p = 0.0181). LI of the PTR was significantly correlated with inhibitory function in healthy controls (+1 = -0.0008510, p = 0.0248), but not in children with ADHD.

**Conclusion:** We found increased brain white matter asymmetry (leftward) in children with ADHD compared with healthy controls at the posterior thalamic radiation. Leftward lateralization of FA values at the external capsule was negatively correlated with ADHD symptoms in both children with ADHD and healthy controls

Psychiatry Res. 2020;285.

**MIND-WANDERING, DEPRESSION, ANXIETY AND ADHD: DISENTANGLING THE RELATIONSHIP.**

**Figueiredo T, Lima G, Erthal P, et al.**

**Background:** Mind Wandering (MW) has been associated with ADHD in a very small number of studies with adults and children. However, anxiety and depression have also been associated with MW and both are often comorbid with ADHD. The aim of this study was to investigate the role of anxiety and depression in MW in patients with ADHD.

**Methods:** The Mind Excessively Wandering Scale (MEWS) compared the levels of MW controlling for the presence of anxiety and depression symptoms in 78 adolescents (53 males and 25 females) comprising ADHD, clinical controls and typically developing individuals. Correlational analysis between MEWS score, demographic variables, ADHD, anxiety and depressive symptoms was performed using simple and multiple linear regression analysis demonstrating that only anxiety predicted MW scores. On a second analysis, we compared Anxiety and Non-Anxiety as well as ADHD and non-ADHD groups.

**Results:** Levels of MW were significantly correlated with anxiety symptoms, but not with depression. In addition, there were no differences in ADHD and non-ADHD groups regarding MW levels.

**Conclusions:** Our results suggest MW is associated with anxiety levels, independently of an ADHD diagnosis

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Psychol Addict Behav. 2019 Dec.

**EARLY SUBSTANCE USE IN THE PATHWAY FROM CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) TO YOUNG ADULT SUBSTANCE USE: EVIDENCE OF STATISTICAL MEDIATION AND SUBSTANCE SPECIFICITY.**

**Howard AL, Kennedy TM, Mitchell JT, et al.**

This study tested whether early and developmentally atypical substance use mediates risk for adult substance use among children with attention-deficit/hyperactivity disorder (ADHD), and whether that risk is substance-specific. Participants were children with ADHD previously enrolled in a randomized controlled trial (RCT), and a demographically similar non-ADHD group, assessed at 2 through 16 years after the original RCT baseline. Self-reports of heavy drinking, marijuana use, daily smoking, and other illicit drug use were collected at follow-ups to establish atypically early and frequent use. Models estimated statistically mediated effects of childhood ADHD on adult substance use via early substance involvement, with planned comparisons to evaluate substance specificity. Results supported the mediation hypothesis, showing that childhood ADHD was associated with more frequent adult substance use via early substance involvement for marijuana, cigarettes, illicit drugs, and to a lesser extent, alcohol. Mediation was not escalated by comorbid childhood conduct disorder or oppositional defiant disorder except for early use of nonmarijuana illicit drugs. Substance-specificity in the mediational pathway was largely absent except for cigarette use, where ADHD-related early smoking most strongly predicted adult daily smoking. Findings from this study provide new evidence that atypically early substance use associated with childhood ADHD signals important cross-drug vulnerability by early adulthood, but cigarette use at a young age is especially associated with increased risk for habitual (daily) smoking specifically. Efforts to prevent, delay, or reduce substance experimentation should occur early and focus on factors relevant to multiple drugs of abuse in this at-risk population

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Rev Neurol. 2020;70:84-92.

**USE OF SINGLE-ELECTRODE EEG IN THE EVALUATION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Moreno-Garcia I, Servera M, Meneres-Sancho S, et al.**

**Introduction.** Attention deficit/hyperactivity disorder (ADHD) maintains a diagnosis based on behavioral data despite its involvement in neuropsychophysiological models. The monopolar electroencephalography (EEG) record focused on differentiating children with ADHD versus controls based on a higher theta/beta ratio has been proposed as an alternative to objectify the diagnosis and guide neurofeedback-based intervention, but its results have been controversial.

**Aim.** To analyze the viability of a single electrode to detect differences in the main cerebral rhythms and especially in theta/ beta ratio, in children diagnosed with ADHD, analyzing the differences by subtype, age, sex and type of experimental task.

**Patients and methods.** 92 children (range: 7-13 years) diagnosed with ADHD were evaluated in a monopolar EEG record on four experimental tasks (rest, reading, active listening and copying a figure). Seven measures on slow and fast EEG rhythms were obtained, plus theta/beta ratio.

**Results.** There were no differences by ADHD subtypes. The task of greatest cognitive demand obtained the highest wave amplitudes. Smaller participants and boys presented higher amplitudes in slow waves and in theta/beta ratio in all the experimental tasks, showing a greater tendency to attentional regulation problems.

**Conclusion.** Monopolar record and theta/beta ratio are a viable alternative in the clinical setting to complement the evaluation of ADHD

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Revista Ecuatoriana de Neurologia. 2019;28:41-46.

**INHIBITORY CONTROL AND SYMPTOMATOLOGY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Ramos-Galarza C, Acosta-Rodas P, Páez-Salas C, et al.**

**Background.** Inhibitory control has been described as a factor causing difficulties in the regulation present in the ADHD.

**Objective.** The aim was to analyze the relationship between inhibitory control and symptoms of ADHD in a sample of 81 subjects diagnosed with ADHD (Mage=10.05, SD=2.53).

**Methods.** A quantitative, cross-sectional and correlational scope research was carried out. The instruments used were the ADHD RS IV and SIMON experiment. Correlation inferential statistical regression and regression processes were applied.

**Results.** Three regression models were tested, where inhibitory control presents a significant prediction with the (a) attention deficit  $F(1,79)=20.69$ ,  $p<.001$ ,  $R^2=.21$ , (b) hyperactivity and impulsivity  $F(1,79)=5.90$ ,  $p=.01$ ,  $R^2=.07$  and (c) the combination of both (a+b)  $F(1,79)=13.25$ ,  $p<.01$ ,  $R^2=.14$ .

**Conclusions.** The findings suggest that inhibitory control is one of the main executive functions that determines the degree of affectation of the symptomatology of the child population with ADHD

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Schizophr Res. 2020;215:190-96.

**PSYCHOTIC-LIKE EXPERIENCES DURING EARLY ADOLESCENCE PREDICT SYMPTOMS OF DEPRESSION, ANXIETY, AND CONDUCT PROBLEMS THREE YEARS LATER: A COMMUNITY-BASED STUDY.**

**Isaksson J, Vadlin S, Olofsdotter S, et al.**

Psychotic-like experiences (PLEs), such as delusions and hallucinations, are risk markers for psychiatric symptoms and functional impairment. However, the unique contribution of PLEs to psychiatric symptoms remains unclear. Thus, the aim of this study was to investigate the effect of PLEs on psychiatric symptoms, adjusting for the baseline of such symptoms. We assessed a community-based cohort of young adolescents (N = 1445; mean age = 14.38 years, SD = 1.04) to establish a baseline and reassessed them three years later (mean age = 17.31 years, SD = 1.04). Participants reported PLEs they had experienced in the last year and any internalizing (depression and anxiety) or externalizing (attention-deficit/hyperactivity disorder and conduct problems) psychiatric symptoms. The experience of more PLEs predicted more internalizing symptoms three years later, and to a lesser extent, more conduct problems as well, even when adjusting for the baseline occurrence of these symptoms. The association was not sex-specific, although girls reported more PLEs than did boys. The strongest predictor of internalizing/externalizing symptoms was the occurrence of those same symptoms at baseline. These findings highlight the importance of PLEs as markers for a wide range of psychiatric symptoms, emphasizing the importance of assessing PLEs in early adolescence

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Statistical Methods in Medical Research. 2020.

**THE CURE MODEL IN PERINATAL EPIDEMIOLOGY.**

**Stoltenberg EA, Nordeng HME, Ystrom E, et al.**

In the statistical literature, the class of survival analysis models known as cure models has received much attention in recent years. Cure models seem not, however, to be part of the statistical toolbox of perinatal epidemiologists. In this paper, we demonstrate that in perinatal epidemiological studies where one investigates the relation between a gestational exposure and a condition that can only be ascertained after several years, cure models may provide the correct statistical framework. The reason for this is that the hypotheses being tested often concern an unobservable outcome that, in view of the hypothesis, should be thought of as occurring at birth, even though it is only detectable much later in life. The outcome of interest can therefore be viewed as a censored binary variable. We illustrate our argument with a simple cure model analysis of the possible relation between gestational exposure to paracetamol and attention-deficit hyperactivity disorder, using data from the Norwegian Mother, Father and Child Cohort Study conducted by

the Norwegian Institute of Public Health, and information about the attention-deficit hyperactivity disorder diagnoses obtained from the Norwegian Patient Registry

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Tunis Med. 2019;97:874-81.

**REHABILITATION OF ADHD CHILDREN BY SPORT INTERVENTION: A TUNISIAN EXPERIENCE.**

**Hattabi S, Bouallegue M, Yahya HB, et al.**

**Introduction:** Childhood attention-deficit/hyperactivity disorder is associated with impairment across multiple domains, including social, familial, emotional and academic functioning. Available therapies, and in particular medical treatment, fail to produce improvement in this impairment. In this context, interest has grown in physical activity and exercise as potential interventions for the treatment of children with ADHD. Aim: The present study investigates the effect of a recreational swimming program on cognitives functions on Tunisian children with attention deficit hyperactivity disorder (ADHD).

**Methods:** The study recruited school children aged 9 to 12 years (n total = 40) with diagnosis of ADHD. They were randomly assigned into exercise or control groups. Neuropsychological tasks; the complex figure of Rey (ROCF), the stroop test and the Hayling test were assessed before and after the exercise program.

**Results:** The results indicates that there were significant improvements in memory accuracy (p=0,000), selective attention (p=0,000), and inhibition process (p=0,000), in experimental group compared with the control group after the intervention. In the post-program, children experienced an overall shortening of task execution times with fewer errors of omissions. They also made fewer errors in interference situations, signaling better cognitive functioning.

**Conclusion** These findings suggest that a recreational swimming program may have positive implications for cognitive function and may provide preliminary support for alternative therapeutic interventions that can be used by researchers, parents, educators, and clinicians and they support that reinforcement approved by recreational program can normalize cognitive deficiencies in children with ADHD

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Zhongguo Dang Dai Er Ke Za Zhi. 2020 Feb;22:152-57.

**ASSOCIATION OF MICRORNA EXPRESSION BEFORE AND AFTER DRUG THERAPY WITH CLINICAL SYMPTOMS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Zhang F, Zhu P, Wu LH.**

**OBJECTIVE:** To study the association of microRNA expression before and after drug therapy with clinical symptoms in children with attention deficit hyperactivity disorder (ADHD).

**METHODS:** A total of 80 previously untreated children with ADHD who were diagnosed from May 2017 to October 2018 were enrolled. The children who were willing to receive drug therapy were randomly divided into concerta-treated group with 31 children and strattera-treated group with 33 children. The children who were unwilling to receive treatment were enrolled as the untreated group with 16 children. A total of 60 children who underwent physical examination during the same period of time were enrolled as the healthy control group. SNAP-V score was determined at initial diagnosis and 3 and 6 months of follow-up. Serum samples were collected from the children with ADHD and the healthy control group. Quantitative real-time PCR was used to measure the relative expression of miR-4566-3p and miR-7641.

**RESULTS:** The repeated measures analysis of variance showed that the SNAP-V score of attention deficit symptoms were different among the two treatment groups and the untreated group at the first visit and 3 months and 6 months after treatment (P<0.05). There were significant differences in the relative expression of the two miRNAs among the two treatment groups and the healthy control group at the first visit and 3 months and 6 months after treatment (P<0.05). The SNAP-V score of attention deficit symptoms and the relative expression of the two miRNAs were different in different time points in the subjects (P<0.05). There were interactions between grouping and time factors in the SNAP-V score of attention deficit symptoms and the relative expression of the two miRNAs (P<0.05). The SNAP-V score of hyperactive impulsive symptoms was different in different time points in the two treatment groups and the untreated group (P<0.05), but the significant difference in the score was not observed between two treatment groups and the untreated group

( $P > 0.05$ ), and there was no interaction between the time factor and the grouping factor ( $P > 0.05$ ). The SNAP-V score of attention deficit symptoms was negatively correlated with the relative expression of miRNA-4655-3p and miRNA-7641 ( $r = -0.314, -0.495$  respectively;  $P < 0.05$ ) in ADHD children after drug treatment.

**CONCLUSIONS:** Drug therapy can significantly improve the clinical symptoms of children with ADHD. The expression of miR-4655-3p and miR-7641 in serum can be used as biomarkers for the diagnosis and outcome evaluation of ADHD

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