NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI · IRCCS

BIBLIOGRAFIA ADHD NOVEMBRE 2020

Acta Neuropsychiatr. 2020 Oct;32:237-46.

DIFFERENTIATING DEPRESSION AND ADHD WITHOUT DEPRESSION IN ADULTS WITH PROCESSING-SPEED MEASURES.

Martiny K, Nielsen NP, Wiig EH.

Objective: We evaluated processing-speed and shift-cost measures in adults with depression or attention-deficit hyperactivity disorder (ADHD) and monitored the effects of treatment. We hypothesised that cognitive-speed and shift-cost measures might differentiate diagnostic groups.

Methods: Colour, form, and colour–form stimuli were used to measure naming times. The shift costs were calculated as colour–form-naming time minus the sum of colour- and form-naming times. Measurements were done at baseline and end point for 42 adults with depression and 42 with ADHD without depression. Patients with depression were treated with transcranial pulsed electromagnetic fields and patients with ADHD with methylphenidate immediate release.

Results: During depression treatment, reductions in naming times were recorded weekly. One-way analysis of variance indicated statistical between-group differences, with effect sizes in the medium range for form and colour–form. In both groups, naming times were longer before than after treatment. For the ADHD group, shift costs exceeded the average–normal range at baseline but were in the average–normal range after stabilisation with stimulant medication. For the depression group, shift costs were in the average–normal range at baseline and after treatment. Baseline colour–form-naming times predicted reductions in naming times for both groups, with the largest effect size and index of forecasting efficiency for the ADHD group.

Conclusions: The cognitive-processing-speed (colour–form) and shift-cost measures before treatment proved most sensitive in differentiating patients with depression and ADHD. Reductions in naming times for the depression group were suggested to reflect improved psychomotor skills rather than improved cognitive control

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

Am J Orthod Dentofacial Orthop. 2020 Nov;158:694-99.

DENTAL MALOCCLUSION AMONG CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Roy A, Ferraz Dos SB, et al.

INTRODUCTION: Children with attention deficit hyperactivity disorder (ADHD) have more sleep breathing problems and parafunctional oral habits than individuals without ADHD. However, there is scarce information on the correlation between their dental malocclusion and these functional disorders. The objective of this study was to assess the severity of malocclusion in patients with and without ADHD and to evaluate the correlation between their functional disorders and dental malocclusion.

METHODS: Eighty-eight patients aged 6-17Â years were divided into 2 groups: ADHD (nÂ =Â 44) and control (nÂ =Â 44). A medical questionnaire to assess functional disorders and an orthodontic examination to evaluate malocclusion were completed for each patient. Distribution of the data was evaluated using Shapiro-Wilk test, whereas the 2 groups were compared with a t test, Mann-Whitney U test, Fisher exact test, and Spearman correlation. The association between parafunctional oral habits, ADHD drug intake, and malocclusion severity were assessed with a t test and Mann-Whitney U test.

RESULTS: Patients with ADHD had significantly higher severity of malocclusion (PÂ =Â 0.042), more dental rotation (PÂ =Â 0.021) and more parafunctional oral habits (PÂ =Â 0.001), specifically bruxism (PÂ =Â 0.005), and a history of pacifier use (PÂ =Â 0.009), than the control group.

CONCLUSIONS: It is important to be aware of the increased risk of parafunctional oral habits and dental malocclusion among ADHD patients to develop preventive programs, as well as therapeutic strategies for them

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American Journal of Geriatric Psychiatry. 2020.

A CALL FOR RESEARCH ON THE VALIDITY OF THE AGE-OF-ONSET CRITERION APPLICATION IN OLDER ADULTS BEING EVALUATED FOR ADHD: A REVIEW OF THE LITERATURE IN CLINICAL AND COGNITIVE PSYCHOLOGY.

Sharma MJ, Lavoie S, Callahan BL.

Roughly 3% of adults aged 50 years or older experience significant symptoms of attention-deficit/hyperactivity disorder (ADHD). They are often diagnosed for the first time in later adulthood, because ADHD is a relatively new diagnosis with only recent awareness of later-life cases, and because many symptomatic adults have high early-life functioning due to supportive environmental and social structures. Current Diagnostic and Statistical Manual of Mental Disorders-5 criteria require evidence of symptom onset prior to age 12, which rests on self-report in older adults for whom ancillary sources are unavailable or unreliable. In this review, we summarize evidence from several bodies of literature which suggest this criterion may be invalid in older adults. The authors hypothesize that demonstrating childhood symptom onset in older adults is not feasible (i.e., no awareness of ADHD prior to 1970; no good current ancillary sources of childhood behaviors), unreliable (i.e., severely flawed retrospective self-report) and unethical (i.e., unreasonable denial of support to people who need it, with demonstrated poor outcomes associated with untreated ADHD in adults). The authors outline additional research that is needed to establish the validity of self-reported childhood symptom onset in this under-studied demographic, including the identification of contextual factors (perhaps unique to late life) that are associated with the emergence of ADHD symptoms in older adulthood; determining the impact of memory biases on recall of childhood symptoms in older adults with ADHD; quantifying self-perception deficits; and investigating the usefulness of executive functioning rating scales to complement diagnostic assessment in older adults

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Am J Psychiatry. 2020;177:834-43.

SUBCORTICAL BRAIN VOLUME, REGIONAL CORTICAL THICKNESS, AND CORTICAL SURFACE AREA ACROSS DISORDERS: FINDINGS FROM THE ENIGMA ADHD, ASD, AND OCD WORKING GROUPS.

Boedhoe PSW, van Rooij D, Hoogman M, et al.

Objective: Attention deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and obsessive-compulsive disorder (OCD) are common neurodevelopmental disorders that frequently co-occur. The authors sought to directly compare these disorders using structural brain imaging data from ENIGMA consortium data.

Methods: Structural T1-weighted whole-brain MRI data from healthy control subjects (N=5,827) and from patients with ADHD (N=2,271), ASD (N=1,777), and OCD (N=2,323) from 151 cohorts worldwide were analyzed using standardized processing protocols. The authors examined subcortical volume, cortical thickness, and cortical surface area differences within a mega-analytical framework, pooling measures extracted from each cohort. Analyses were performed separately for children, adolescents, and adults, using linear mixed-effects models adjusting for age, sex, and site (and intracranial volume for subcortical and surface area measures).

Results: No shared differences were found among all three disorders, and shared differences between any two disorders did not survive correction for multiple comparisons. Children with ADHD compared with those with OCD had smaller hippocampal volumes, possibly influenced by IQ. Children and adolescents with ADHD also had smaller intracranial volume than control subjects and those with OCD or ASD. Adults with ASD showed thicker frontal cortices compared with adult control subjects and other clinical groups. No OCD-specific differences were observed across different age groups and surface area differences among all disorders in childhood and adulthood.

Conclusions: The study findings suggest robust but subtle differences across different age groups among ADHD, ASD, and OCD. ADHD-specific intracranial volume and hippocampal differences in children and adolescents, and ASD-specific cortical thickness differences in the frontal cortex in adults, support previous work emphasizing structural brain differences in these disorders

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Anadolu Psikiyatr Derg. 2020;21:633-40.

DECREASED SERUM LEVELS OF TOTAL AND HIGH MOLECULAR WEIGHT ADIPONECTIN IN TREATMENT-NAÏVE CHILDREN WITH ADHD.

Yurteri N, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is considered to be one of the most common childhood psychiatric disorders. The aim of this study was to examine serum levels of total and High Molecular Weight (HMW) adiponectin, and also HMW/total adiponectin ratio with respect to ADHD symptomatology in children.

Methods: Serum levels of total adiponectin and HMW adiponectin were measured by commercial enzyme-linked immune-sorbent assay kits in 44 treatment-naïve children with ADHD and age, gender matched 44 healthy controls. ADHD symptoms were scored by Conners Parent Rating Scale-Revised Short (CPRS-RS) and ADHD Rating Scale (ADHD-RS). Body Mass Index-Standart Deviation Scores (BMI-SDS) of all children were evaluated.

Results: There were no significant difference in terms of gender, age and BMI-SDS between ADHD and healthy control groups (respectively, p=1, p=0.475, p=0.097). We found that serum total, HMW adiponectin levels and HMW adiponectin/ total adiponectin ratio were significantly lower in ADHD group compared to controls (p<0.001). In logistic regression analysis, adjusting for age, gender and BMI-SDS, we observed that serum total and HMW adiponectin levels as well as HMW/total adiponectin ratio were associated with ADHD (p<0.001). Additionally, in partial correlations adjusting for age and BMI-SDS in ADHD group, we detected significantly negative correlations between total adiponectin, HMW adiponectin, HMW/total adiponectin ratio and CPRS-RS hyperactivity (p=0.031, p=0.016, p=0.007, respectively), ADHD-RS hyperactive-impulsive (p<0.001), ADHD-RS total symptom scores (p=0.015, p=0.010, p=0.005, respectively).

Discussion: To our knowledge, the present study is the first to examine serum HMW adipo-nectin levels in ADHD children and also to investigate the relationship between ADHD symptoms and serum levels of total

and HMW adiponectin. The results of our study indicate that total and HMW adiponectin may be associated with ADHD

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Ann Trop Med Public Health. 2020;23.

ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AND SPORTS ΓÇô WHAT CAUSES ADHD AND HOW DOES SPORT HELP DEAL WITH IT?

Verma A, Bagchi A.

Background: Attention Deficit Hyperactivity Disorder (ADHD) is a complex multidimensional syndrome where it results in restlessness, hyperactivity, and inattention. The purpose of this analysis was intended towards determining the scientific causes that result in ADHD and examine its various ways of inheritance and factors. Certain diet and hereditary factors have also been identified that trigger ADHD where the intake of protein in the diet of an athlete increases the neurotransmitters in the brain which reduces the symptoms of ADHD. Along with this, the cerebellum region of the brain is responsible for generating hereditary abnormalities which cause ADHD.

Methods: To witness how practising sports, assist in subsiding the symptoms of ADHD, the methodology of systematic literature reviews were conducted which involved numerous facts that supported the hypothesis. It also involved a detailed study of the infamous American competitive swimmer Michael Fred Phelps and his past experiences related to ADHD provided an insight intothe importance of sports to a person with this syndrome.

Conclusion: The results suggested that participating in sports builds a kind of neurotransmitter called norepinephrine which is derived from dopamine, the lack of which results in ADHD. There are also a few behavioural therapies that can be practised that minimize the symptoms in the children

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Arch Pediatr. 2020.

PSYCHIATRIC COMORBIDITIES OF CHILDREN WITH ELIMINATION DISORDERS.

Gizli Coban O., +ûnder A, S++rer Adan-¦r A.

Enuresis and encopresis can be stressful for children and parents. We investigated the comorbid psychiatric disorders and the emotional and behavioral symptoms associated with elimination disorders. A total of 97 children and adolescents (aged 4ΓÇô17 years) with an elimination disorder participated in this study. The elimination disorder group consisted of three subgroups: 50 subjects with enuresis nocturna, 26 with encopresis, and 21 subjects with enuresis + encopresis. The control group with no elimination disorder comprised 50 healthy subjects. All children were interviewed by a child and adolescent psychiatrist. Comorbid psychiatric disorders were assessed using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL). Parents completed the Strengths and Difficulties Questionnaire. The most common diagnosis was attention-deficit/hyperactivity disorder, followed by oppositional defiant disorder. The highest rate of psychiatric comorbidity was observed in the enuresis + encopresis subgroup, followed by the enuresis nocturna and encopresis subgroups. All the subgroups had higher total difficulties scores than the control group. Screening for psychiatric disorders should be performed for all children with incontinence

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Archives of Physical Medicine and Rehabilitation. 2020;101:e105.

TEXTING AND WALKING IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): EFFECT OF TASK AND ENVIRONMENT.

Korytny T, Kizony R, Hamady H, et al.

Research Objectives: Attention Deficit Hyperactivity Disorder (ADHD) impacts quality of life of children and adolescents. During the past decade walking and performing concurrent activities (Dual-task) such as talking or texting on a mobile phone has increased dramatically (1), potentially posing higher risk for injury for children and adolescents with ADHD (2). This study aimed to evaluate texting and walking performance in children with ADHD and age-matched, typically developing (TD) children, across two environments.

Design: An observational, cross-sectional study. Setting: A University setting, including a quiet corridor and a busy outdoor sidewalk.

Participants: Nineteen children and adolescents (mean age 13.12-¦2.2y, 54.8%F) with ADHD and 31 TD children (12.3-¦1.9y, 63.2%F) were recruited using convenience sampling.

Interventions: Parents completed the Conners-3 screening. Participants walked for 1minute periods along a 30m path with/without a concurrent texting task (copying sentences) on a mobile phone with a custom-written software. In addition, the texting task was performed while standing. Walking trials were performed in both quiet and busy environments and order of trials and environments was block randomized between participants.

Main Outcome Measures: Walking kinematics (gait speed, stride length and time) and gait variability (coefficient of variation of stride length and time) were captured using Mobility Lab sensors (APDM). Texting speed and accuracy were calculated from output of the mobile app, using MATLAB.

Results: Dual-task conditions similarly decreased walking and texting speed, and increased gait variability in both groups and across both environments. Among children with ADHD, hyperactivity and aggression were associated with increased dual-task costs for walking ($r>0.55$, $p < 0.05$) only when outdoors.

Conclusions: In light of mixed reports on dual-task performance in ADHD (3,4), we show that children with ADHD are able to perform a texting and walking task similarly to TD children. Specific impairments in dual-task walking in children with ADHD are identified when walking outdoors. Author(s)

Disclosures: None.

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Assessment. 2020 Oct;27:1463-75.

CORRELATED TRAIT–CORRELATED METHOD MINUS ONE ANALYSIS OF THE CONVERGENT AND DISCRIMINANT VALIDITY OF THE CONNERS 3 SHORT FORMS.

Gomez R, Vance A, Stavropoulos V.

This study used the correlated trait–correlated method minus one model to examine the convergent and discriminant validity of the scales of the Conners 3 Short [C 3 (S)]. The C 3 (S) scales in the analysis were inattention (IN), hyperactivity/impulsivity (HY), learning problems (LP; learning problems/executive functioning from the teacher version), aggression (AG), and peer relations (PR, only for parent and teacher versions). A total of 529 adolescents and children (75% males, mean age = 11.75 years, SD = 2.97 years) provided self-ratings, and were also rated by their mothers and teachers. The findings indicated no support for the convergence of IN and HY across the three respondents. In contrast, there was convergence for LP, AG, and PR. There was support for the discriminant validity of the traits, except between IN and HY. The findings are discussed in relation to the convergent and discriminant validity of the C 3 (S) measures, and the clinical use of the C 3 (S)

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Behav Genet. 2020.

NO EVIDENCE FOR PASSIVE GENE-ENVIRONMENT CORRELATION OR THE INFLUENCE OF GENETIC RISK FOR PSYCHIATRIC DISORDERS ON ADULT BODY COMPOSITION VIA THE ADOPTION DESIGN.

Hunjan AK, Cheesman R, Coleman JRI, et al.

The relationship between genetic and environmental risk is complex and for many traits, estimates of genetic effects may be inflated by passive gene-environment correlation. This arises because biological offspring inherit both their genotypes and rearing environment from their parents. We tested for passive gene-environment correlation in adult body composition traits using the natural experiment of childhood adoption, which removes passive gene-environment correlation within families. Specifically, we compared 6165 adoptees with propensity score matched non-adoptees in the UK Biobank. We also tested whether passive gene-environment correlation inflates the association between psychiatric genetic risk and body composition. We found no evidence for inflation of heritability or polygenic scores in non-adoptees compared to adoptees for a range of body composition traits. Furthermore, polygenic risk scores for anorexia nervosa, attention-deficit/hyperactivity disorder and schizophrenia did not differ in their influence on body composition traits in adoptees and non-adoptees. These findings suggest that passive gene-environment correlation does not inflate genetic effects for body composition, or the influence of psychiatric disorder genetic risk on body composition. Our design does not look at passive gene-environment correlation in childhood, and does not test for pure environmental effects or the effects of active and evocative gene-environment correlations, where child genetics directly influences home environment. However, these findings suggest that genetic influences identified for body composition in this adult sample are direct, and not confounded by the family environment provided by biological relatives

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Behav Modif. 2020 Sep;44:698-726.

ENHANCING SOCIAL SKILLS OF YOUNG CHILDREN WITH ADHD: EFFECTS OF A SIBLING-MEDIATED INTERVENTION.

Daffner MS, DuPaul GJ, Kern L, et al.

Children with attention deficit/hyperactivity disorder (ADHD) are at risk for experiencing problems with social functioning that are associated with adverse outcomes in adolescence and adulthood. To date, the most common ADHD treatments for children, psychostimulants and adult-mediated interventions, have had limited success reducing social impairments associated with ADHD. Using a non-concurrent multiple baseline across participants design, we examined the efficacy of a sibling-mediated social intervention for reducing negative and increasing positive social behaviors of three children with ADHD. We also assessed implementation integrity by the siblings, and acceptability from the perspective of the participant with ADHD, the siblings, and the parents. Results indicated that siblings learned and used specific social skills strategies with their siblings with ADHD that lead to increases in sharing, helping, and compromising behaviors for children with ADHD compared with baseline (Tau-U = 0.9531, $p < .001$). Summary of findings, study limitations, implications for research, and practice are discussed

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BJPsych Open. 2020;6.

REGIONAL ANALYSIS OF UK PRIMARY CARE PRESCRIBING AND ADULT SERVICE REFERRALS FOR YOUNG PEOPLE WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Price A, Ford T, Janssens A, et al.

Background Approximately 20% of children with attention-deficit hyperactivity disorder (ADHD) experience clinical levels of impairment into adulthood. In the UK, there is a sharp reduction in ADHD drug prescribing over the period of transition from child to adult services, which is higher than expected given estimates of ADHD persistence, and may be linked to difficulties in accessing adult services. Little is currently known about geographical variations in prescribing and how this may relate to service access.

Aims To analyse geographic variations in primary care prescribing of ADHD medications over the transition period (age 16 19 years) and adult mental health service (AMHS) referrals, and illustrate their relationship with UK adult ADHD service locations.
Method Using a Clinical Practice Research Datalink cohort of people with an ADHD diagnosis aged 10 20 in 2005 (study period 2005 2013; n = 9390, 99% diagnosed <18 years), regional data on ADHD prescribing over the transition period and AMHS referrals, were mapped against adult ADHD services identified in a linked mapping study.
Results Differences were found by region in the mean age at cessation of ADHD prescribing, range 15.8 17.4 years (P<0.001), as well as in referral rates to AMHSs, range 4 21% (P<0.001). There was no obvious relationship between service provision and prescribing variation.
Conclusions Clear regional differences were found in primary care prescribing over the transition period and in referrals to AMHSs. Taken together with service mapping, this suggests inequitable provision and is important information for those who commission and deliver services for adults with ADHD

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BJPsych Open. 2020;6.

INVESTIGATING GENDER-SPECIFIC EFFECTS OF FAMILIAL RISK FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND OTHER NEURODEVELOPMENTAL DISORDERS IN THE SWEDISH POPULATION.

Martin J, Ghirardi L, Chen Q, et al.

Background Many psychiatric disorders show gender differences in prevalence. Recent studies suggest that female patients diagnosed with anxiety and depression carry more genetic risks related to attention-deficit hyperactivity disorder (ADHD) compared with affected males.
Aims In this register-based study, we aimed to test whether female patients who received clinical diagnoses of anxiety, depressive, bipolar and eating disorders are at higher familial risk for ADHD and other neurodevelopmental disorders, compared with diagnosed male patients.
Method We analysed data from a record-linkage of several Swedish national registers, including 151 025 sibling pairs from 103 941 unique index individuals diagnosed with anxiety, depressive, bipolar or eating disorders, as well as data from 646 948 cousin pairs. We compared the likelihood of having a relative diagnosed with ADHD/neurodevelopmental disorders in index males and females.
Results Female patients with anxiety disorders were more likely than affected males to have a brother with ADHD (odd ratio (OR) = 1.13, 95% CI 1.05-1.22). Results for broader neurodevelopmental disorders were similar and were driven by ADHD diagnoses. Follow-up analyses revealed similar point estimates for several categories of anxiety disorders, with the strongest effect observed for agoraphobia (OR = 1.64, 95% CI 1.12-2.39). No significant associations were found in individuals with depressive, bipolar or eating disorders, or in cousins.
Conclusions These results provide modest support for the possibility that familial/genetic risks for ADHD may show gender-specific phenotypic expression. Alternatively, there could be gender-specific biases in diagnoses of anxiety and ADHD. These factors could play a small role in the observed gender differences in prevalence of ADHD and anxiety

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BMC Med Genomics. 2020;13.

BIOMARKER DISCOVERY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: RNA SEQUENCING OF WHOLE BLOOD IN DISCORDANT TWIN AND CASE-CONTROLLED COHORTS.

McCaffrey TA, St.Laurent G, Shtokalo D, et al.

Background: A variety of DNA-based methods have been applied to identify genetic markers of attention deficit hyperactivity disorder (ADHD), but the connection to RNA-based gene expression has not been fully exploited.
Methods: Using well defined cohorts of discordant, monozygotic twins from the Michigan State University Twin Registry, and case-controlled ADHD cases in adolescents, the present studies utilized advanced single

molecule RNA sequencing to identify expressed changes in whole blood RNA in ADHD. Multiple analytical strategies were employed to narrow differentially expressed RNA targets to a small set of potential biomarkers of ADHD.
Results: RNA markers common to both the discordant twin study and case-controlled subjects further narrowed the putative targets, some of which had been previously associated with ADHD at the DNA level. The potential role of several differentially expressed genes, including ABCB5, RGS2, GAK, GIT1 and 3 members of the galactose metabolism pathway (GALE, GALT, GALK1) are substantiated by prior associations to ADHD and by established mechanistic connections to molecular pathways relevant to ADHD and behavioral control.
Conclusions: The convergence of DNA, RNA, and metabolic data suggests these may be promising targets for diagnostics and therapeutics in ADHD

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BMC Pediatr. 2020;20.

UTILITY OF MEDICAL RECORD DIAGNOSTIC CODES TO ASCERTAIN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND LEARNING DISABILITIES IN POPULATIONS OF CHILDREN.

Shi Y, Schulte PJ, Hanson AC, et al.

Background: To develop and evaluate machine learning algorithms to ascertain attention-deficit/hyperactivity (ADHD) and learning disability (LD) using diagnostic codes in the medical record.
Method: Diagnoses of ADHD and LD were confirmed in cohorts of children in Olmsted County of Minnesota based on validated research criteria. Models to predict ADHD and LD were developed using ICD-9 codes in a derivation cohort of 1057 children before evaluated in a validation cohort of 536 children.
Results: The ENET-MIN model using selected ICD-9 codes at prior probability of 0.25 has a sensitivity of 0.76, PPV of 0.85, specificity of 0.98, and NPV of 0.97 in the validation cohort. However, it does not offer significant advantage over a model using a single ICD-9 code of 314.X, which shows sensitivity of 0.81, PPV of 0.83, specificity of 0.98, and NPV of 0.97. None of the models developed for LD performed well in the validation cohort.
Conclusions: It is feasible to utilize diagnostic codes to ascertain cases of ADHD in a population of children. Machine learning approaches do not have advantage compared with simply using a single family of diagnostic codes for ADHD. The use of medical record diagnostic codes is not feasible to ascertain LD

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BMC Psychiatry. 2020;20.

USING THE DRUG REPOSITIONING APPROACH TO DEVELOP A NOVEL THERAPY, TIPEPIDINE HIBENZATE SUSTAINED-RELEASE TABLET (TS-141), FOR CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Saito T, Yamashita Y, Tomoda A, et al.

Background: Asverin (tipepidine hibenzate) has been used as an antitussive for > 50 years in Japan. Studies revealed that tipepidine modulates monoamine levels, by inhibiting G-protein-activated inwardly rectifying potassium (GIRK) channels, expecting the potential therapeutic effects of tipepidine for attention-deficit/hyperactivity disorder (ADHD) in recent years. In this study, TS-141, a sustained-release tablet of tipepidine, was developed for the treatment of ADHD through a drug repositioning approach.
Methods: The sustained-release profile of TS-141 in healthy adults was investigated, and tipepidine exposure in the plasma after the TS-141 administration was compared to that of Asverin in the phase I study. Phase II study was conducted to examine the effects of TS-141 30 (once a day), 60 (once a day), 120 mg (60 mg twice a day), or placebo, that is within the exposure in the maximum dosage of Asverin, in children and adolescents with ADHD, and was designed as an 8-week treatment, randomized, parallel group, double-blind, placebo-controlled trial recruiting 6-17-year-old children and adolescents diagnosed with ADHD. A total of 216 patients were randomized according to the CYP2D6 phenotype. The primary end-point was ADHD

Rating Scale IV-J changes. Furthermore, effects of CYP2D6 phenotype on the efficacy in the subgroup analysis were investigated.
Results: TS-141 had the sustained-release profile, and the CYP2D6 phenotype had effects on the plasma exposure of tipepidine. ADHD RS-IV-J scores in all TS-141 dosages decreased from their baseline scores; however, no significant difference was observed in ADHD RS-IV-J score changes between the placebo and TS-141-administered groups. In patients with intermediate metabolizer CYP2D6, ADHD RS-IV-J score changes in the 120 mg group tended to be larger than that in the placebo group.
Conclusions: ADHD RS-IV-J changes on TS-141 may depend on the interaction between the TS-141 dose and CYP2D6 phenotype, suggesting that further clinical trials should be conducted with careful consideration of polymorphism. Drug repositioning approach of TS-141 was attempted at the same dose as that of antitussive; however, dose setting according to the indication was necessary.
Trial registration: Phase I study: JapicCTI-205235 (Registered 25 March 2020), Phase II study: JapicCTI-163244 (Registered 9 May 2016), https://www.clinicaltrials.jp/cti-user/trial/Show.jsp

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BMC Psychiatry. 2020;20.

LATE-ONSET ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AS A DIFFERENTIAL DIAGNOSIS OF DEMENTIA: A CASE REPORT.

Sasaki H, Jono T, Fukuhara R, et al.

Background: Although adult attention-deficit/hyperactivity disorder has recently gained increased attention, few reports on attention-deficit/hyperactivity disorder in the pre-elderly or elderly have been published. Here, we present the case of a patient with attention-deficit/hyperactivity disorder who gradually developed dementia-like symptoms as she aged, which initially made her condition difficult to distinguish from early onset Alzheimer's disease. This report illustrates that some types of attention-deficit/hyperactivity disorder may be misdiagnosed as dementia.
Case presentation: The patient was a 58-year-old woman. Although she presented with a tendency for inattentiveness and forgetfulness since childhood, she did not have a history of psychiatric disorders prior to consultation. Around the age of 52 years, her inattentiveness and forgetfulness gradually progressed, and at 57 years of age, she became inattentive and forgetful that it interfered with her work and daily life. For example, she forgot meetings with important clients and transferred money to the wrong bank account; these failures resulted in poor management of her company. At home, she experienced increasing difficulties with remembering prior commitments with her family and misplacing items, which her family members noticed. With the encouragement of her family and employees, who worried that she was suffering from dementia, she visited our memory clinic, whereby she was suspected of having early onset Alzheimer's disease. However, neuropsychological tests and brain imaging evaluations did not reveal any significant abnormalities. After dismissing various possible diagnoses, including dementia, other organic diseases, mood disorders, and delirium, we diagnosed her with attention-deficit/hyperactivity disorder. Treatment with 18 mg of methylphenidate was initiated, and significant improvements in her symptoms were observed within a few days; for example, she stopped losing her things, was able to concentrate for long durations, and could complete more tasks than she could before treatment. Since initiating treatment, she has returned to work and has been able to perform her daily activities without difficulty.
Conclusions: This case supports that some patients with late-onset attention-deficit/hyperactivity disorder may gradually develop dementia-like symptoms during the pre-elderly and elderly stages of life. Therefore, clinicians should consider late-onset attention-deficit/hyperactivity disorder as a differential diagnosis of some types of dementias

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BMJ Open. 2020;10.

INFLUENCE OF THE MONTH OF BIRTH ON PERSISTENCE OF ADHD IN PROSPECTIVE STUDIES: PROTOCOL FOR AN INDIVIDUAL PATIENT DATA META-ANALYSIS.

Gosling CJ, Pinabiaux C, Caparos S, et al.

Introduction Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder with symptoms, especially the hyperactive ones, that tend to decrease in severity with age. Interestingly, children born just before the school-entry cut-off date (ie, the youngest pupils of a classroom) are at higher risk of being diagnosed with ADHD compared with children born just after the cut-off date. Noteworthy, this month-of-birth effect tends to disappear with increasing absolute age. Therefore, it is possible that young children erroneously diagnosed with ADHD due to their month of birth present a lower chance to have their diagnosis confirmed at a later age, artificially reinforcing the low persistence of ADHD across the lifespan. This protocol outlines an individual patient data (IPD) meta-analysis of prospective observational studies to explore the role of the month of birth in the low persistence of ADHD across the lifespan.

Methods and analysis Five databases will be systematically searched in order to find prospective observational studies where the presence of ADHD is assessed both at baseline and at a follow-up of at least 4 years. We will use a two-stage IPD meta-analytic approach to estimate the role of the month of birth in the persistence of ADHD. Various sensitivity analyses will be performed to assess the robustness of the results.

Ethics and dissemination No additional data will be collected and no de-identified raw data will be used. Ethics approval is thus not required for the present study. Results of this IPD meta-analysis will be submitted for publication in a peer-reviewed journal. PROSPERO registration number CRD42020212650

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Brain Sciences. 2020;10:1-13.

CHILDHOOD ADHD AND EARLY-ONSET BIPOLAR DISORDER COMORBIDITY: A CASE REPORT.

Tatsiopoulou P, Porfyri GN, Bonti E, et al.

Introduction: Recent research has highlighted an increased rate of co-morbidity between the neurodevelopmental-behavioral disorder of attention deficit hyperactivity disorder (ADHD) and a variety of psychiatric disorders, such as mood disorders or bipolar disorder (BD). The etiology and clinical course of BD are considered to be determined by both genetic and environmental factors, either aggravating or improving.

Aim: This follow-up study of an adolescent aimed to clarify the co-morbidity between ADHD and BD. We also discuss the controversies surrounding the two diagnoses in younger populations and describe several aspects of concern regarding diagnosis, differential diagnosis, therapeutic planning/intervention, and prognosis.

Methods: Reporting of a two-year follow-up study of a bipolar 15-year-old female patient with a previous diagnosis of ADHD during childhood.

Results: Despite the occurrence of major risk factors, such as early onset and positive family history, the patient's condition rapidly remitted with medication, without relapse and/or rehospitalization during the following two years, due to the stability of her cooperation, and support of a stable and caring familial environment. Early diagnosis of BD and differential diagnoses of ADHD are considered crucial protective factors leading to an appropriate planning of treatment. In addition, parental involvement and empathic attitude towards the patient supported the latter to cooperate and comply with the treatment, enhancing positive outcomes and stability.

Conclusions: Research is required into the reliability and validity of diagnostic protocols and criteria for BD in children and adolescents, and also into the development of individualized therapeutic planning

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Brain Sciences. 2020;10:1-13.

IMPROVEMENT OF PURSUIT EYE MOVEMENT ALTERATIONS AFTER SHORT VISUO-ATTENTIONAL TRAINING IN ADHD.

Caldani S, Delorme R, Moscoso A, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder without validated and objective diagnostic procedures. Several neurological dysfunctions in the frontal circuit, in the thalamus, and in the cerebellum have been observed in subjects with ADHD. These cortical and subcortical areas are responsible for eye movement control. Therefore, studying eye movements could be a useful tool to better understand neuronal alterations in subjects with ADHD. The aim of the present study was firstly to compare the quality of pursuit eye movements in a group of 40 children with ADHD (age 8.2 -¦ 1.2) and in a group of 40 sex-, IQ-, age-matched typically developing (TD) children; secondly, we aimed to examine if a short visuo-attentional training could affect pursuit performances in children with ADHD. Findings showed that children with ADHD presented a greater number of catch-up saccade and lower pursuit gain compared to TD children. Differently to TD children, in children with ADHD, the number of catch-up saccades and the pursuit gain were not significantly correlated with childrenΓÇÖs age. Furthermore, a short visuo-attentional training period can only slightly improve pursuit performance in children with ADHD, leading to a decrease of the occurrence of catch-up saccades only, albeit the effect size was small. The absence of any improvement in pursuit performance with age could be explained by the fact that the prefrontal and fronto-cerebellar circuits responsible for pursuit triggering are still immature. Pursuit eye movements can be used as a useful tool for ADHD diagnosis. However, attentional mechanisms controlled by these cortical structures could be improved by a short visuo-attentional training period. Further studies will be necessary to explore the effects of a longer visuo-attentional training period on oculomotor tasks in order to clarify how adaptive mechanisms are able to increase the attentional capabilities in children with ADHD

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Brain Behav Immun. 2020 Oct;89:9-19.

EFFECTS OF A SYNBIOTIC ON SYMPTOMS, AND DAILY FUNCTIONING IN ATTENTION DEFICIT HYPERACTIVITY DISORDER—A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL.

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

Some prebiotics and probiotics have been proposed to improve psychiatric symptoms in children with autism. However, few studies were placebo-controlled, and there is no study on persons with an attention deficit hyperactivity disorder (ADHD) diagnosis. Our aim was to study effects of Synbiotic 2000 on psychiatric symptoms and functioning in children and adults with ADHD without an autism diagnosis. Children and adults (n = 182) with an ADHD diagnosis completed the nine weeks randomized double-blind parallel placebo-controlled trial examining effects of Synbiotic 2000 on the primary endpoints ADHD symptoms, autism symptoms and daily functioning, and the secondary endpoint emotion regulation, measured using the questionnaires SNAP-IV, ASRS, WFIRS, SCQ, AQ and DERS-16. Levels at baseline of plasma C-reactive protein and soluble vascular cell adhesion molecule-1 (sVCAM-1), central to leukocyte-endothelial cell adhesion facilitating inflammatory responses in tissues, were measured using Meso Scale Discovery. Synbiotic 2000 and placebo improved ADHD symptoms equally well, and neither active treatment nor placebo had any statistically significant effect on functioning or sub-diagnostic autism symptoms. However, Synbiotic 2000, specifically, reduced sub-diagnostic autism symptoms in the domain restricted, repetitive and stereotyped behaviors in children, and improved emotion regulation in the domain of goal-directed behavior in adults. In children with elevated sVCAM-1 levels at baseline as well as in children without ADHD medication, Synbiotic 2000 reduced both the total score of autism symptoms, and the restricted, repetitive and stereotyped behaviors. In adults with elevated sVCAM-1 at baseline, Synbiotic 2000 significantly improved emotion regulation, both the total score and four of the five subdomains. To conclude, while no definite Synbiotic 2000-specific effect was detected, the analysis of those with elevated plasma sVCAM-1 levels proposed a reduction of autism symptoms in children and an improvement of emotion regulation in adults with ADHD

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Br J Dev Psychol. 2020 Sep;38:442-57.

DO MOTOR COORDINATION AND SLEEP DIFFICULTIES PREDICT PEER FUNCTIONING IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT AND HYPERACTIVITY DISORDER AFTER ACCOUNTING FOR EXISTING ADHD SYMPTOMOLOGY?

Mancini VO, Althorpe KE, Chen W.

Children with attention-deficit and hyperactivity disorder (ADHD) are more likely to experience peer problems compared to their non-ADHD peers, though ADHD-specific symptoms only partially explain this association. This study examined whether sleep difficulties and motor coordination problems are additional predictors of peer problems in an ADHD population. An ADHD sample of 72 participants aged 6–14 years (M = 9.86 years, SD = 1.79 years) was evaluated for an association of peer problems with measures of motor coordination, sleep difficulties as well as ADHD and comorbidity symptoms. Hierarchical multiple regression analysis (HMRA) was used to test the current study aims. Motor coordination, but not sleep difficulties, predicted additional variance in peer problems after controlling for inattention, hyperactivity/impulsivity, internalizing problems, oppositionality, and conduct problems. Poor motor coordination predicts peer problems beyond ADHD symptoms. Clinicians seeking to improve peer functioning in children with ADHD should also consider motor coordination difficulties in addition to existing treatment strategies

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Br J Psychiatry. 2020;217:616-22.

TRANSITION BETWEEN CHILD AND ADULT SERVICES FOR YOUNG PEOPLE WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): FINDINGS FROM A BRITISH NATIONAL SURVEILLANCE STUDY.

Eke H, Ford T, Newlove-Delgado T, et al.

Background Optimal transition from child to adult services involves continuity, joint care, planning meetings and information transfer; commissioners and service providers therefore need data on how many people require that service. Although attention-deficit hyperactivity disorder (ADHD) frequently persists into adulthood, evidence is limited on these transitions.

Aims To estimate the national incidence of young people taking medication for ADHD that require and complete transition, and to describe the proportion that experienced optimal transition. Method Surveillance over 12 months using the British Paediatric Surveillance Unit and Child and Adolescent Psychiatry Surveillance System, including baseline notification and follow-up questionnaires.

Results Questionnaire response was 79% at baseline and 82% at follow-up. For those aged 17-19, incident rate (range adjusted for non-response) of transition need was 202-511 per 100 000 people aged 17-19 per year, with successful transition of 38-96 per 100 000 people aged 17-19 per year. Eligible young people with ADHD were mostly male (77%) with a comorbid condition (62%). Half were referred to specialist adult ADHD and 25% to general adult mental health services; 64% had referral accepted but only 22% attended a first appointment. Only 6% met optimal transition criteria.

Conclusions As inclusion criteria required participants to be on medication, these estimates represent the lower limit of the transition need. Two critical points were apparent: referral acceptance and first appointment attendance. The low rate of successful transition and limited guideline adherence indicates significant need for commissioners and service providers to improve service transition experiences

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Can Fam Phys. 2020;66:732-36.

APPROACH TO DIAGNOSIS AND MANAGEMENT OF CHILDHOOD ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Jerome D, Jerome L.

Objective To provide primary care clinicians with an approach to the diagnosis and management of attention deficit hyperactivity disorder (ADHD) by reviewing and summarizing the relevant practice guidelines and recent evidence from the literature. Sources of information Published guidelines on the management of ADHD were reviewed. A PubMed search was conducted with the MeSH terms attention deficit disorder and family practice.

Results were limited to articles published in English within the past 15 years. Main message Attention deficit hyperactivity disorder is a common neurodevelopmental disorder. Guidelines agree that diagnosis and management of ADHD is appropriate within primary care. Attention deficit hyperactivity disorder is diagnosed by applying the criteria defined within the Diagnostic and Statistical Manual of Mental Disorders, 5th edition, and is supplemented by validated rating scales. Behavioural management is firstline management in all patients, and stimulant medications are first-line management in patients 6 years of age and older. The Canadian ADHD Resource Alliance provides free resources to help clinicians care for patients with ADHD.
Conclusion Most patients with ADHD can be managed by family physicians. It is a chronic condition that requires ongoing follow-up. Attention deficit hyperactivity disorder that is complicated by comorbidities might require referral to a specialist

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Child Adolesc Psychiatr Clin North Am. 2021;30:143-57.
RESTLESS LEGS SYNDROME IN CHILDREN AND ADOLESCENTS.
DelRosso LM, Mogavero MP, Baroni A, et al.
Children with psychiatric comorbidities frequently are referred for evaluation of sleep complaints. Common sleep symptoms can include difficulty falling asleep, frequent nocturnal awakening, restless sleep, and symptoms of restless legs syndrome (RLS). The understanding of the sleep condition in relation to the psychiatric comorbidity often is a challenge to the physician and often sleep disorders remain undiagnosed, untreated, or undertreated. Restless legs syndrome has been associated with psychiatric comorbidities and with certain medications, such as antidepressants, antihistamines, and antipsychotics. This article reviews the presentation of RLS and restless sleep, the association with psychiatric comorbidities, and treatment options

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Chinese Journal of Biomedical Engineering. 2020;39:265-70.
INVESTIGATING BRAIN NETWORKS FOR ADHD CHILDREN BASED ON PHASE SYNCHRONIZATION OF RESTING STATE FMRI.
Jie X, Xunheng W, Lihua L.
In this study, we explored the application of complex network methods based on phase synchronization of brain network mechanisms for attention deficit hyperactivity disorder (ADHD). A total of 135 patients with ADHD and 102 normal controls were selected as subjects. The time series of functional magnetic resonance images of these 237 subjects were used as research data to study the brain network of children with ADHD. The phase synchronization method was used to obtain the connection relationship of each pair of brain regions. The brain network was constructed by using this connection relationship. Then, the resting state brain function was evaluated by using the local efficiency index of the complex network, and statistical methods such as multiple linear regression and variance analysis are used to analyze whether there was a significant difference in the local efficiencies of patients with ADHD and normal controls in the resting brain region. There were no significant differences in age, gender, scale scores (inattention and impulsivity), and three IQ values (verbal IQ, performance IQ and full IQ) between patients with ADHD and normal controls. The significance of the study was statistically significant (P<0. 05) in the diagnosis labels and head movement parameters. In terms of diagnosis, 11 brain regions with statistical difference (P<0. 05) between the control group with normal local efficiency and the ADHD group were found, among which the main brain regions were: left cauda nucleus (0. 118-¦0. 317 vs 278-¦0.433), thalamus (0. 345-¦0.425 vs 0. 541-¦0. 435), heschl gyrus (0. 467-¦0. 476 vs 0. 654-¦0. 444) and right dorsolateral superior frontal gyrus (0. 536-¦0. 401 vs 0. 681-¦0. 333), middle frontal gyrus (0.505-¦0.377 vs 0. 641 -¦0. 331), caudate nucleus (0. 144-¦0.329 vs 0. 298 -¦0. 423). There is a significant difference in the local efficiency of the left anterior gyrus, caudate nucleus,

thalamus between patients with ADHD and normal controls. These differences might be related to functional abnormalities in specific brain regions such as the caudate nucleusandthalamus, or neural network damage associated with patient attention and execution

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Clin Ther. 2020.

A Post Hoc Comparison of Prior ADHD Medication Dose and Optimized Delayed-release and Extended-release Methylphenidate Dose in a Pivotal Phase III Trial.

Childress AC, Uchida CL, Po MD, et al.

Purpose: HLD200 is the first evening-dosed, delayed-release and extended-release methylphenidate (DR/ER-MPH) designed to delay initial release of MPH and provide treatment effects throughout the day and into the evening for individuals with attention-deficit/hyperactivity disorder (ADHD). Because DR/ER-MPH is uniquely absorbed in the colon, it cannot be substituted for other ADHD medications on a milligram-per-milligram basis. To provide clinicians with a target dose range for DR/ER-MPH when transitioning patients from a prior ADHD medication, dose conversion ratios (DCRs) between prior medication doses and optimized doses of DR/ER-MPH were determined post hoc from a pivotal Phase III study of children (aged 6ΓÇô12 years) with ADHD.

Methods: DR/ER-MPH doses were optimized over a 6-week open-label period. DCRs were calculated between optimized doses of DR/ER-MPH at week 6 and prior stable doses of ADHD medication.

Findings: Mean DCRs ranged from 1.8 to 4.3 for optimized DR/ER-MPH dose versus previous stable dose for individuals taking an extended-release stimulant monotherapy. DCRs for those taking an immediate-release stimulant monotherapy ranged from 4.7 to 6.0.

Implications: In a Phase III trial of children with ADHD, optimized doses of DR/ER-MPH were higher than doses of prior ADHD medications, but the adverse event profile was consistent with that of other MPHs. Higher DCRs compared with those predicted by bioavailability differences are consistent with a predicted dose-dependent duration of effect for DR/ER-MPH: with increasing doses, absorption is extended but with an attenuated increase in Cmax compared with MPH formulations absorbed in the upper bowel. These data may help guide clinicians to optimize DR/ER-MPH doses.

ClinicalTrials.gov identifier: NCT02493777

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CNS Spectr. 2020.

Successful Agomelatine Monotherapy for an Adolescent with ADHD and comorbid Migraine.

Naguy A, Alamiri B.

Migraine has been demonstrated to be overrepresented in children with ADHD. Here, authors report on an interesting case of difficult-to-treat ADHD in an adolescent who failed sequential trials of atomoxetine and methylphenidate and ultimately favourably responded to agomelatine monotherapy. Strikingly, a parallel improvement in migraine headaches control was noticed. Purported pharmacodynamic mechanisms are briefly discussed. This is followed by a focussed literature review

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Codas. 2020;32:e20190086.

Phonological remediation in schoolchildren with ADHD and dyslexia.

Martins RA, Ribeiro MG, Pastura GMC, et al.

PURPOSE: To compare the performance in phonological processing skills, reading speed and reading comprehension before and after phonological remediation in a restricted group of schoolchildren with Attention Deficit Hyperactivity Disorder (ADHD) and with dyslexia.

METHODS: Thirty-two schoolchildren from the 2nd to 8th year of Elementary School of both genders, with diagnosis of ADHD and Dyslexia according to the DSM-5, participated in this study. All patients underwent Phonological Remediation Program consisted of 18 weekly sessions.
RESULTS: The results, expressed in z scores, showed a statistically significant difference between before and after remediation assessments in phonological processing skills, such as syllabic and phonemic awareness, working memory and lexical access. Rhyming task was analyzed separately because it represents another level of segmentation and, for this result, there was no significance. Besides these results, there was a statistically significant difference in reading speed and reading comprehension.
CONCLUSION: The phonological remediation program contributes to the development of phonological processing, reading speed and reading comprehension in this population

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Curr Med Res Opin. 2020;36:1717-35.
REVIEW OF LISDEXAMFETAMINE DIMESYLATE IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.
Najib J, Didenko E, Meleshkina D, et al.
Objective: Lisdexamfetamine dimesylate is a stimulant prodrug with low abuse and diversion potential that is used in treatment of attention deficit hyperactivity disorder (ADHD) in children, adolescents and adults. This current literature review article aims to examine safety and efficacy of LDX in children and adolescents for the treatment of ADHD based on currently available data.
Methods: Relevant English language articles were identified through computerized searches of the MEDLINE database (PubMed and EMBASE) and clinical trials registry up to January 2020 using the following search terms: lisdexamfetamine dimesylate, pro-drug stimulant, attention-deficit and hyperactivity disorders, ADHD, safety, efficacy, children, adolescents, Vyvanse. Forty-two articles were reviewed, 34 of which were included into this review, selected by the limit clinical trials. This article represents the pharmacological profile, efficacy and safety data of LDX for the treatment of ADHD in children and adolescents.
Results: The collection of studies reviewed identified that LDX was both safe and efficacious in the treatment of ADHD. The most commonly exhibited side effects were appetite suppression, weight loss, headache and insomnia. In comparison to placebo, LDX significantly improved ADHD symptoms and overall quality of life in children and adolescents. In comparison to atomoxetine, LDX showed statistically significant improvements in inattention, impulsivity, and activities of daily living. In comparison to OROS-MPH and placebo, LDX and OROS-MPH showed improvements with the CGI-I score, and ADHD-RS-IV, however, LDX was superior.
Conclusion: Patients have seen statistically significant improvements in their ADHD symptomatology in the classroom environment, health related quality of life, and their overall behavior in comparison to placebo, atomoxetine, and OROS-MPH. However, clinical judgment should be utilized when prescribing LDX due to patient specific needs and the side effect profile

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Current Obesity Reports. 2020;9:451-61.
THE CO-OCCURRENCE OF PEDIATRIC OBESITY AND ADHD: AN UNDERSTANDING OF SHARED PATHOPHYSIOLOGY AND IMPLICATIONS FOR COLLABORATIVE MANAGEMENT.
O'Hara VM, Curran JL, Browne NT.
Purpose of Review: To describe what is known about the association between obesity and attention-deficit hyperactivity disorder (ADHD) in children along with the co-occurring conditions of sleep dysfunction, loss of control/binge eating disorder (LOC-ED/BED), and anxiety.
Recent Findings: Obesity and ADHD share common brain pathways (hypothalamic, executive, and reward centers) with pathophysiology in these areas manifesting in partial or complete expression of these diseases. Sleep dysfunction, LOC-ED/BED, and anxiety share similar pathways and are associated with this disease dyad.

Summary: The association of obesity and ADHD with sleep dysfunction, LOC-ED/BED, and anxiety is discussed. An algorithm outlining decision pathways for patients with obesity and with and without ADHD is presented. Future research exploring the complex pathophysiology of both obesity and ADHD as well as co-occurring conditions is needed to develop clinical guidelines and ultimately assist in providing the best evidence-based care

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Current Psychiatry. 2019;18:42+44-42+48.
SEEING SNAKES THAT AREN'T THERE.
Shoemaker E, Nader F.

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Curr Psychiatry Rep. 2020;22.
ADHD AND EXPOSURE TO MALTREATMENT IN CHILDREN AND YOUTH: A SYSTEMATIC REVIEW OF THE PAST 10 YEARS.
Craig SG, Bondi BC, OΓÇÖDonnell KA, et al.
Purpose of the Review: The purpose of the current paper was to review and summarize the literature on ADHD and maltreatment over the past 10-áyears.
Recent Findings: The majority of research on ADHD and exposure to maltreatment focuses on the high rates of comorbidity, including international studies from Asia, South America, North America, and Europe. Longitudinal studies showed that early exposure to maltreatment is a risk factor for ADHD symptoms later in development; however, this finding was not consistent. There were some preliminary studies on the neurological and genetic mechanisms underlying the link between ADHD and exposure to maltreatment. Finally, ADHD and exposure to maltreatment were found to have an additive effect on clinically salient outcomes (e.g., aggression, suicide attempts).
Summary: Results from the review have direct clinical and future implications, including the need to understand the effect of comorbid ADHD and exposure to maltreatment in treatment studies

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Eas As A Psyc. 2020;30:88-90.
PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG PRIMARY SCHOOL CHILDREN IN OFORIKROM, GHANA BASED ON THE DISRUPTIVE BEHAVIOR DISORDERS RATING SCALE.
Anokye R, Acheampong E, Edusei A, et al.
Objective: To determine the prevalence of attention-deficit/hyperactivity disorder (ADHD) among primary school children in Oforikrom, Kumasi, Ghana.
Methods: 10 of 35 primary schools in Oforikrom were readily available. Of 2000 children aged 5 to 13 years selected, 1540 (77%) of their parents/guardians consented to participate. Their parents/guardians and six teachers from each school were asked to complete the Disruptive Behavior Disorders Rating Scale to screen children for the presence of ADHD, oppositional defiant disorder, or conduct disorder. Children who displayed symptoms (pretty much or very much) in most related items as determined by parents and/or teachers were considered positive cases.
Results: The mean age of 1540 pupils was 9 -¦ 2.16 years. Most (31%) were primary 4 pupils. 5% of pupils displayed ADHD symptoms (attention deficit disorder subtype in 36%, hyperactivity disorder subtype in 27%, and combined subtype in 37%). Of them, 51% were male. Most (19%) of those who displayed the symptoms were in primary 5.

Conclusion: The prevalence of ADHD among primary school children in Oforikrom was 5%. 51% of those with ADHD symptoms were male. Most (19%) of those with ADHD symptoms were in primary 5

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Eas As A Psyc. 2020;30:79-83.

EMOTIONAL/BEHAVIOURAL PROBLEMS AND FUNCTIONAL IMPAIRMENT IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Tengsujaritkul M, Louthrenoo O, Boonchooduang N.

Objective: This study aimed to compare the emotional/behavioural problems and functional impairment between early school-age children with attention-deficit/hyperactivity disorder (ADHD) and non-ADHD controls. Factors associated with behavioural problem scores were also evaluated.

Methods: Children aged 6 to 10 years who were diagnosed with ADHD based on the Swanson, Nolan and Pelham version IV Scale (SNAP-IV) and the DSM-5 criteria for ADHD were compared with age- A nd sex-matched controls with negative SNAP-IV results in terms of emotional/behavioural problems (as assessed by the Child Behavioural Checklist) and functional impairment (as assessed by the Strength and Difficulties Questionnaire).

Results: 40 children with ADHD and 40 non-ADHD controls with a mean age of 8.40 -¦ 1.44 years were included. The ADHD group scored significantly higher than controls in terms of all eight subscales of emotional/behavioural problems ($p<0.001$ to $p<0.01$). Regarding functional impairment, the ADHD group reported significantly higher scores than controls in terms of total difficulties, conduct problems, and hyperactivity (all $p<0.01$); and significantly lower prosocial scores ($p<0.03$). In the multiple linear regression analysis, among the ADHD group, comorbid medical disorders were associated with higher total problem score, internalising behaviour problems score, and externalising behaviour problems score; whereas combined subtype ADHD was associated with higher total difficulties score.

Conclusions: Early school-age children with ADHD have more emotional/behavioural problems and functional impairment than non-ADHD controls, and they need further evaluation and intervention for psychosocial functioning, particularly those with comorbid medical disorder or combined subtype ADHD

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Environ Sci Pollut Res Int. 2020 Dec;27:44757-70.

PHTHALATES EXPOSURE AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN: A SYSTEMATIC REVIEW OF EPIDEMIOLOGICAL LITERATURE.

Praveena SM, Munisvaradass R, Masiran R, et al.

Epidemiological studies have proven that children mental health can be affected by environmental pollutants which are believed to be visible in the form of psychological disorder later in their childhood. Moreover, the effects of children mental health are evidently clear in the case of phthalates which have been observed to increase psychological disorder, specifically attention-deficit hyperactivity disorder (ADHD). Hence, the present study aims to conduct a systematic review and provide an overview of the existing literature on the association between urinary phthalate metabolite concentrations and ADHD symptoms among children by emphasizing the confounding factors and limitations. Additionally, this review addressed the possible phthalate mechanism insights in human body including its impact on ADHD symptoms. In this case, 16 epidemiological studies (five cross-sectional, nine cohort and two case control studies) that met all the inclusion criteria were selected out of the total of 427 papers screened to show varying quantitative associations between phthalate exposure and ADHD symptoms among children with confounding factors and limitations in the existing studies in regard to the exposure and outcomes. This review also attempted to present possible explanation on phthalate mechanism in children body and its connection on neurodevelopment and ADHD symptom development which remains unclear in most of the studies. Finally, it is highly recommended for further research to carefully design cohort studies from prenatal to later

childhood development with a complete sample size in order to understand phthalate impacts on children health

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Erciyes Medical Journal. 2020;42:480-82.

DYSKINESIA IN A PREPUBERTAL BOY AFTER THE FIRST DOSE OF METHYLPHENIDATE AND THE ASSOCIATION OF FOCAL EPILEPTIFORM ACTIVITY: A CASE REPORT.

Cevikaslan A., Duman +, Kutluk MG.

Background: Methylphenidate is a piperidine derivative stimulant drug. It inhibits the reuptake of dopamine and norepi-nephrine and improves the primary symptoms of Attention-Deficit/Hyperactivity Disorder. Methylphenidate may cause dysk-inesias in children with Attention-Deficit/Hyperactivity Disorder, and concomitant irregularity in Electroencephalography may increase the likelihood of the neuropsychiatric side effects.

Case Report: A case of a 6.5-years-old boy who was admitted to the emergency room with unintended and uncontrolled behaviours after the first dose of this drug was presented. He was diagnosed with acute dyskinesia in the orofacial region and extremities, and then he was cured with biperiden lactate infusion in eighteen hours. Focal biphasic waves at right tem-poroparietal areas were recorded on his sleep-Electroencephalography.

Conclusion: In our case with both attention-deficit/hyperactivity disorder and epileptiform activity, dyskinesia occurrence after one single dose of 20 mg methylphenidate was discussed with the results of previous studies

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Eur Child Adolesc Psychiatry. 2020 Nov;29:1537-45.

MACROSOMIA AND PSYCHIATRIC RISK IN ADOLESCENCE.

Van Lieshout RJ, Savoy CD, Ferro MA, et al.

The prenatal environment can exert important effects on mental health. While much research has linked low birth weight to psychopathology, the intrauterine environment associated with high birth weight (macrosomia;>4000 g) is also sub-optimal and may increase risk. Given the increasing prevalence of macrosomic births, understanding the mental health outcomes of infants born macrosomic can help refine theories of etiology, predict disorder, and target preventive interventions. Using data from the 2014 Ontario Child Health Study (OCHS), we examined the risk for psychiatric disorders in adolescents born macrosomic. Youth (N=2151) aged 12-17 years completed the Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID). Rates of common mental disorders assessed by the MINI-KID were compared between those born at normal birth weight (NBW; 2500-4000 g, n=1817) and adolescents born macrosomic (>4000 g, n=334). These associations were then adjusted for participant age, sex, socioeconomic status (SES) of the family, parental mental health, and gestational diabetes mellitus. After adjustment for covariates, adolescents born macrosomic had higher odds of conduct disorder (CD; OR=3.19, 95% CI: 1.37-7.43), oppositional defiant disorder (ODD; OR=1.79, 95% CI: 1.11-2.91), and ADHD (OR=1.77, 95% CI: 1.21-2.80). Moderation analyses revealed that males born macrosomic were more likely to have psychiatric problems than their female peers. Socioeconomic disadvantage also amplified the risk posed by macrosomia for ODD, ADHD, major depressive disorder, and generalized anxiety disorder. In this study, macrosomia was associated with an increased risk of clinically significant externalizing problems in adolescence, most notably among boys and those facing socioeconomic disadvantage

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Eur Child Adolesc Psychiatry. 2020 Dec;29:1717-27.

PRESCRIBING ANTIPSYCHOTICS IN CHILD AND ADOLESCENT PSYCHIATRY: GUIDELINE ADHERENCE.

Dinnissen M, Dietrich A, van der Molen JH, et al.

Antipsychotics are often prescribed to children and adolescents, mostly off-label. We aimed to assess adherence to recommendations of guidelines for antipsychotic prescription. We reviewed 436 medical records from 155 clinicians from 26 clinics within three Dutch child and adolescent psychiatry organizations (n=398 outpatient, n=38 inpatient care). We assessed target symptoms, diagnostic process, prior and concomitant treatment, and consideration of contra-indications. Multiple logistic regression assessed the role of age, sex, and psychiatric diagnosis on adherence to three main recommendations: to (1) prescribe antipsychotics only after other treatments proved insufficient, (2) always combine antipsychotics with psychosocial interventions, and (3) not prescribe multiple antipsychotics simultaneously. Most patients received off-label antipsychotics. Main target symptoms were inattention/hyperactivity (25%), aggression (24%), and other disruptive behaviors (41%). Most patients underwent diagnostic evaluation before the first prescription; however, screening of contra-indications was low (0.2-19%). About 84% had previously received psychosocial treatment and 48% other psychoactive medication, but 9% had not received any treatment. Notably, only 37% continuously received concomitant psychosocial treatment. Simultaneous use of multiple antipsychotics occurred in 3.2%. Younger children were at higher risk of non-adherence to guideline recommendations regarding prior and concomitant treatment, children with autism spectrum disorder or attention-deficit/hyperactivity disorder more likely not to receive concomitant psychosocial treatment. Sex did not significantly affect adherence. Our findings implicate insufficient adherence to important recommendations regarding antipsychotic use in children and adolescents. Especially younger children are at higher risk of receiving suboptimal care. There is an urgency to consistently offer psychosocial interventions during antipsychotic treatment

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Eur Child Adolesc Psychiatry. 2020.

SUBGROUPING CHILDREN AND ADOLESCENTS WITH DISRUPTIVE BEHAVIORS: SYMPTOM PROFILES AND THE ROLE OF CALLOUS-UNEMOTIONAL TRAITS.

Rosa-Justicia M, Saam MC, Flamarique I, et al.

Disruptive behavior during childhood and adolescence is heterogeneous and associated with several psychiatric disorders. The identification of more homogeneous subgroups might help identify different underlying pathways and tailor treatment strategies. Children and adolescents (aged 8ΓÇô18) with disruptive behaviors (N = 121) and healthy controls (N = 100) were included in a European multi-center cognition and brain imaging study. They were assessed via a battery of standardized semi-structured interviews and questionnaires. K-means cluster-model analysis was carried out to identify subgroups within the group with disruptive behaviors, based on clinical symptom profiles, callousΓÇôunemotional (CU) traits, and proactive and reactive aggression. The resulting subgroups were then compared to healthy controls with regard to these clinical variables. Three distinct subgroups were found within the group with disruptive behaviors. The High CU Traits subgroup presented elevated scores for CU traits, proactive aggression and conduct disorder (CD) symptoms, as well as a higher proportion of comorbidities (CD + oppositional defiant disorder + attention deficit hyperactivity disorder (ADHD). The ADHD and Affective Dysregulation subgroup showed elevated scores for internalizing and ADHD symptoms, as well as a higher proportion of females. The Low Severity subgroup had relatively low levels of psychopathology and aggressive behavior compared to the other two subgroups. The High CU Traits subgroup displayed more antisocial behaviors than the Low Severity subgroup, but did not differ when compared to the ADHD and Affective Dysregulation subgroup. All three subgroups differed significantly from the healthy controls in all the variables analyzed. The present study extends previous findings on subgrouping children and adolescents with disruptive behaviors using a multidimensional approach and describes levels of anxiety, affective problems, ADHD, proactive aggression and CU traits as key factors that differentiate conclusively between subgroups

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Eur Child Adolesc Psychiatry. 2020.

A MULTI-TRAJECTORY ANALYSIS OF COMMONLY CO-OCCURRING MENTAL HEALTH ISSUES ACROSS CHILDHOOD AND ADOLESCENCE.

Murray AL, Eisner M, Nagin D, et al.

Developmental trajectories of mental health issues can often be usefully summarised in a small number of clinically meaningful subtypes. Given the high levels of heterotypic and homotypic comorbidity in child and adolescent mental health symptoms, we explored-áwhether it was possible to identify clinically meaningful developmental subtypes of multiple commonly co-occurring mental health issues. We evaluated the combined developmental trajectories of the most common and commonly co-occurring child and adolescent mental health issues: attention-deficit/hyperactivity disorder (ADHD), internalising, and externalising symptoms in a normative sample of youth with data (n = 1620) at ages 7, 8, 9, 10, 11, 12, 13 and 15 using group-based multi-trajectory modelling. Multinomial logistic regression was used to evaluate predictors of group membership. Our optimal model included six trajectory groups, labelled unaffected, normative maturing, internalising, multimorbid late onset, multimorbid remitting, and multimorbid with remitting externalising. Examining covariates of group membership suggested that males and bully victims tend to have complex mental health profiles; academic achievement and smoking during pregnancy have general associations with mental health irrespective of symptom developmental trajectories or combination; and maternal post-natal depression is primarily related to symptoms that are already in evidence by the beginning of the school years. Results suggest that developmental trajectories of commonly co-occurring mental health issues can be usefully summarised in terms of a small number of developmental subtypes. These subtypes more often than not involve multiple co-occurring mental health issues. Their association with mental health covariates depends on the combination and developmental timing of symptoms in ways that suggest they can be clinically informative

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Eur Child Adolesc Psychiatry. 2020.

SLEEP PROBLEMS AMONG ADOLESCENTS WITHIN CHILD AND ADOLESCENT MENTAL HEALTH SERVICES. AN EPIDEMIOLOGICAL STUDY WITH REGISTRY LINKAGE.

Hysing M, Heradstveit O, Harvey AG, et al.

Sleep problems are prevalent among adolescents, especially among those diagnosed with mental health disorders. There is insufficient knowledge about sleep among adolescents within child and adolescent mental health services (CAMHS) in comparison to the general population. The data are drawn from the youth@hordaland study, a large population-based study conducted in 2012, linked to the Norwegian Patient Registry (NPR) (n = 9077). Psychiatric disorders were based on clinical diagnoses from the NPR, while insomnia, delayed sleep ΓÇôwake-phase disorder (DSWPD), and other sleep problems/patterns were assessed by self-report questionnaires from youth@hordaland. The prevalence of diagnosed sleep disorders among adolescents seeking mental health services was 0.6%, yielding an estimated prevalence of 0.07% of the population. However, questionnaire-based measurement of insomnia from the youth@hordaland study indicated that insomnia was highly prevalent across disorders in comparison to a reference group of adolescents who were not within mental health care. Insomnia ranged from 29% among adolescents diagnosed with ADHD (PR = 1.79; 95% CI 1.41ΓÇô2.29) to 48% among adolescents diagnosed with depression (PR = 2.53, 95% CI 2.19ΓÇô2.92). All diagnostic groups had a mean sleep efficiency below (85%), indicating poor sleep quality. Insomnia, delayed sleep-phase wake disorder, and poor sleep efficiency were confirmed as transdiagnostic sleep problems across psychiatric disorders. In addition, some disorder-specific patterns emerged, such as a higher prevalence of insomnia among adolescents with depression, and DSWPS among adolescents with conduct disorder. This underscores the need for treating sleep problems in CAMHS, and transdiagnostic treatment approaches are warranted

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Eur Neuropsychopharmacol. 2020.

PROINFLAMMATORY MEDIATORS AND THEIR ASSOCIATIONS WITH MEDICATION AND COMORBID TRAITS IN CHILDREN AND ADULTS WITH ADHD.

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

Peripheral immune activation can influence neurodevelopment and is increased in autism, but is less explored in attention deficit hyperactivity disorder (ADHD). Patients with ADHD often display comorbid autism traits and gastrointestinal (GI) symptoms. Plasma protein levels of two acute phase reactants, C-reactive protein (CRP) and serum amyloid A (SAA), and two endothelial adhesion molecules, soluble intercellular adhesion molecule 1 (sICAM-1) and soluble vascular cell adhesion molecule 1 (sVCAM-1), which share important roles in inflammation, were analyzed in 154 patients with ADHD and 61 healthy controls. Their associations with ADHD diagnosis, severity, medication and comorbid autistic symptoms, emotion dysregulation and GI symptoms were explored. The ADHD patients had increased levels of sICAM-1 and sVCAM-1 compared to healthy controls (p = 8.6eΓÇô05, p = 6.9eΓÇô07, respectively). In children with ADHD, the sICAM-1 and sVCAM-1 levels were higher among those with ADHD medication than among children (p = 0.0037, p = 0.0053, respectively) and adults (p = 3.5eΓÇô09, p = 1.9eΓÇô09, respectively) without ADHD medication. Among the adult ADHD patients, higher sICAM-1 levels were associated with increased comorbid autistic symptoms in the domains attention to detail and imagination (p = 0.0081, p = 0.00028, respectively), and higher CRP levels were associated with more GI symptoms (p = 0.014). sICAM-1 and sVCAM-1 levels were highly correlated with each other, and so were CRP and SAA levels. To conclude, vascular inflammatory activity may be overrepresented in ADHD, with elevated sICAM-1 and sVCAM-1 levels and this may in children be a consequence of current ADHD medication, and in adults relate to increased comorbid autistic symptoms. Replication is warranted

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Front Behav Neurosci. 2020;14.

CHRONIC PHYSICAL ACTIVITY FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER AND/OR AUTISM SPECTRUM DISORDER IN CHILDREN: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS.

Zhang M, Liu Z, Ma H, et al.

Purpose: To explore the effects of physical activity (PA) intervention on executive function (EF) and motor skills (MS) among children with attention deficit hyperactivity disorder and/or autism spectrum disorder (ASD).

Methods: Relevant studies were sourced from PubMed, Web of Science, EMBASE, Cochrane Library, CNKI and Wanfang Data. Only randomized controlled trials (RCT) were included based upon the following criteria: (1) participants were children and clinically diagnosed with ADHD/ASD, (2) intervention strategies were identified as chronic physical activity, and (3) EF (e.g., cognitive flexibility) and/or MS (e.g., gross motor skills) were measured at baseline and post-intervention and compared with an eligible control group.

Results: Eleven studies involving 346 participants were finally identified. PA elicited significant improvements in EF and MS in children with ADHD/ASD. Regarding changes in the EF of participants, PA showed a great improvement in overall EF [standardized mean difference (SMD): 0.90, 95% confidence interval (CI) 0.49ΓÇô1.30, p < 0.00001], inhibitory control (SMD: 1.30, 95% CI 0.58-2.02, p = 0.0004) and cognitive flexibility (SMD: 0.85, 95% CI 0.42-1.29, p = 0.0001), but no significant improvement in working memory (SMD: 0.28, 95% CI 0.15-0.71, p = 0.20). Significant improvements were also found with respect to gross motor skills (SMD: 0.80, 95% CI 0.30 1.30, p = 0.002), but no significant changes were found in fine motor skills (SMD: 0.30, 95% CI 0.91-1.52, p = 0.62).

Conclusion: Chronic PA interventions may promote EF and MS in children with ADHD/ASD, especially in inhibitory control, cognitive flexibility, and gross motor skills. However, PA interventions seemed to have insignificant effects on working memory and fine motor skills to children with ADHD/ASD. PROSPERO registration number: CRD42019118622

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Frontiers in Neurology. 2020;11.

IMPAIRED MOTOR TIMING IN TOURETTE SYNDROME: RESULTS FROM A CASE-CONTROL STUDY IN CHILDREN.

Graziola F, Pellorca C, Di Criscio L, et al.

Tourette syndrome (TS) is a neurodevelopmental disorder characterized by motor and vocal tics. Co-occurrence of attention-deficit/hyperactivity disorder (ADHD) or obsessive compulsive disorder (OCD) is very frequent in the pediatric population as well as the presence of an impairment of the executive functions. The aim of our study was to investigate motor timing, that is, the temporal organization of motor behavior, in a pediatric population of Tourette patients. Thirty-seven Tourette patients (divided in 22 pure Tourette patients and 15 with ADHD) were compared with 22 healthy age- and gender-matched subjects. All subjects underwent a neuropsychiatric screening and were tested for their planning and decision-making abilities by using a standardized test, such as Tower of London (ToL). Two experimental paradigms were adopted: finger-tapping test (FTT), a free motor tapping task, and synchronization continuation task. An accuracy index was calculated as measure of ability of synchronization. We found that pure TS as well as TS+ADHD showed lower scores in the FTT for the dominant and non-dominant hands than controls. Moreover, in the synchronization and continuation test, we observed an overall lack of accuracy in both TS groups in the continuation phase for 2,000 ms (supra-second interval), interestingly, with opposite direction of accuracy index. Thus, pure TS patients were classified as behind the beat, whereas, TS+ADHD as ahead of the beat. The performance in the finger tapping was inversely correlated to ToL total scores and execution time, whereas we did not find any correlation with the accuracy index of the synchronization and continuation test. In conclusion, here, we explored motor timing ability in a childhood cohort of Tourette patients, confirming that patients exhibit an impaired temporal control of motor behavior and these findings may be explained by the common underlying neurobiology of TS and motor timing

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Front Psychiatry. 2020;11.

ANTIDEPRESSANTS IN CHILDREN AND ADOLESCENTS: META-REVIEW OF EFFICACY, TOLERABILITY AND SUICIDALITY IN ACUTE TREATMENT.

Boaden K, Tomlinson A, Cortese S, et al.

Antidepressants are prescribed for the treatment of a number of psychiatric disorders in children and adolescents, however there is still controversy about whether they should be used in this population. This meta-review aimed to assess the effects of antidepressants for the acute treatment of attention-deficit/hyperactivity disorder (ADHD), anxiety disorders (ADs), autistic spectrum disorder (ASD), enuresis, major depressive disorder (MDD), obsessive-compulsive disorder (OCD), and posttraumatic stress disorder (PTSD) in children and adolescents. Efficacy was measured as response to treatment (either as mean overall change in symptoms or as a dichotomous outcome) and tolerability was measured as the proportion of patients discontinuing treatment due to adverse events. Suicidality was measured as suicidal ideation, behavior (including suicide attempts) and completed suicide. PubMed, EMBASE, and Web of Science were systematically searched (until 31 October 2019) for existing systematic reviews and/or meta-analyses of double-blind randomized controlled trials. The quality of the included reviews was appraised using AMSTAR-2. Our meta-review included nine systematic reviews/meta-analyses (2 on ADHD; 1 on AD; 2 on ASD; 1 on enuresis; 1 on MDD, 1 on OCD and 1 on PTSD). In terms of efficacy this review found that, compared to placebo: fluoxetine was more efficacious in the treatment of MDD, fluvoxamine and paroxetine were better in the treatment of AD; fluoxetine and sertraline were more efficacious in the treatment of OCD; bupropion and desipramine improved clinician and teacher-rated ADHD symptoms; clomipramine and tianeptine were superior on some of the core symptoms of ASD; and no antidepressant was more efficacious for PTSD and enuresis. With regard to tolerability: imipramine, venlafaxine, and duloxetine were less well tolerated in MDD; no differences were found for any of the antidepressants in the treatment of anxiety disorders (ADs), ADHD, and PTSD; tianeptine and citalopram, but not clomipramine, were less well tolerated in children and adolescents with ASD. For suicidal behavior/ideation, venlafaxine (in MDD) and paroxetine (in AD) were associated with a significantly increased risk; by contrast, sertraline (in AD) was associated with a reduced risk. The majority of included systematic reviews/meta-analyses were rated as being of high or moderate in quality by the AMSTAR-2 critical appraisal tool (one and five, respectively). One included study was of low

quality and two were of critically low quality. Compared to placebo, selected antidepressants can be efficacious in the acute treatment of some common psychiatric disorders, although statistically significant differences do not always translate into clinically significant results. Little information was available about tolerability of antidepressants in RCTs of OCD and in the treatment of ADHD, ASD, MDD, and PTSD. There is a paucity of data on suicidal ideation/behavior, but paroxetine may increase the risk of suicidality in the treatment of AD and venlafaxine for MDD. Findings from this review must be considered in light of potential limitations, such as the lack of comparative information about many antidepressants, the short-term outcomes and the quality of the available evidence

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Front Psychiatry. 2020;11.

RELIABILITY AND VALIDITY OF THE SIMPLIFIED CHINESE VERSION OF THE ABERRANT BEHAVIOR CHECKLIST IN CHINESE AUTISM POPULATION.

Kat S, Xu L, Guo Y, et al.

Background: The Aberrant Behavior Checklist (ABC) is a widely used scale in autism clinical intervention research for the assessment of core symptoms and comorbid emotional and behavioral problems among people with autism. The aim of this study was to examine the psychometric properties of the Simplified Chinese version of the Aberrant Behavior Checklist (SC-ABC) using a sample of people with autism in a Chinese population.

Methods: In total, we enrolled 799 patients aged 1.5-33 years old. We collected data using the SC-ABC (n = 799), Autism Behavior Checklist (n = 743), Attention Deficit Hyperactivity Disorder Rating Scale-IV (ADHD-RS-IV) (n = 433) and Achenbach Child Behavior Checklist (CBCL) (n = 319). Eighty-four patients were separately assessed with the SC-ABC by two caregivers simultaneously. Forty-four patients were assessed with the SC-ABC again by same caregiver 2 weeks after the first assessment. SC-ABC data from the whole sample were used for confirmatory factor analysis. We evaluated criterion validity using Spearman's correlation coefficient between scores of the SC-ABC and scores of the Autism Behavior Checklist, ADHD-RS-IV and CBCL separately in the whole sample and different age groups. We calculated the intragroup correlation coefficients and Spearman's correlation coefficient for interrater reliability in 84 samples and test-retest reliability in 44 samples. We conducted Cronbach's +¦ for internal consistency.

Results: For the SC-ABC, the intragroup correlation coefficients of five subscales and the total score in interrater and test-retest reliability ranged from 0.87 to 0.92 and from 0.93 to 0.97 (all P < 0.01). The Spearman's correlation coefficient of five subscales and the total score in interrater and test-retest reliability ranged from 0.78 to 0.85 and 0.86 to 0.94, respectively (all P < 0.01). Cronbach's +¦ of five subscales and the total score ranged from 0.75 to 0.96 (all P < 0.01). The Spearman's correlation coefficient for criterion validity for the whole sample and different age groups ranged from 0.39 to 0.76 (all P < 0.01). The model fit for the original five factor model was acceptable, with fit indices of SMR = 0.062 and RMSEA = 0.052.

Conclusions: The SC-ABC has satisfactory psychometric properties and can be used in the assessment of core symptoms and comorbid emotional and behavioral problems in patients with autism

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Galen Medical Journal. 2020;9.

WHEY PROTEIN (MA-ALJOBON) AS A COMPLEMENTARY THERAPY FOR TREATMENT OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER (ADHD): A RANDOMIZED OPEN-LABEL CONTROLLED CLINICAL TRIAL.

Mostajeran Z, Mosavat SH, Najafi M, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is a common, chronic, neurodevelopmental disorder that manifests in childhood with symptoms of hyperactivity, inattention, and impulsivity. MaΓÇÖaljobon (a kind of whey protein) that is derived from milk during cheese producing process is a popular dietary traditional product supposed to provide immune modulation and prevent neuropsychiatric disorder. We aimed to evaluate the efficacy of ma aljobon in management of Attention-deficit/hyperactivity disorder (ADHD).

Materials and Methods: In this open-label randomized, double arm, and controlled clinical trial, sixty four patients with ADHD who referred to out-patient child and adolescent clinic of Khorshid Hospital of Isfahan, Iran, were randomly assigned in the intervention group (ma aljobon 25 g once daily plus standard conventional treatment (SCT)) or control group (SCT only) for a period of 8 weeks. Scores of the Strengths and Difficulties Questionnaire (SDQ) and Conners Continuous Performance Test (CPT) were set as the outcome measures.
Results: Parent reported hyperactivity scale of SDQ showed a significant decrease in the intervention group compared to the control group (P=0.04). However, no significant between groups differences were observed in other scales of parent-reported SDQ. Also, according to the results of CPT, there was a significant improvement in the intervention group regarding attention and focus score (P=0.01).
Conclusion: Ma aljobon might be considered as a complementary remedy for improving hyperactivity, attention and focus of children with ADHD. However, further researches with larger sample size and longer duration should be done for achieving more reliable results

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International Journal of Pharmaceutical Research. 2020;12:3652-56.

SIGNIFICANT RELATIONSHIP ASSOCIATED BY THE SYMPTOMS OF ADHD ADULTS ON PROFESSIONAL AND NON-PROFESSIONAL COURSES.

Gopinath TT, Pandiyan KR, Kumari R, et al.

The present study aims to explore association among socio-demographic characteristics and adult ADHD of students. The sample of the present study comprised of 300 college going students in Manipur within the age group of 17 to 29 years. Out of the 300 college going students, 150 were undergoing professional courses and 150 were undergoing non-professional courses. College drop-outs and those with history of head injury and with other psychiatric / psychological disorders other than ADHD were excluded. Adult ADHD Self-Report Scale (ASRS-v1.1) Symptoms Checklist was used to assess symptoms of adult ADHD. Parameters such as Age-range was found to be insignificant which signifies that adult ADHD persists throughout adult life. Also, parameters such as residence, family annual income, religion, number of siblings and birth order was also found to be statistically insignificant. Result shows significant relationship between symptoms of adult ADHD with the students undergoing professional course and non-professional course. Those undergoing non-professional courses have more symptom of adult ADHD as compared to those undergoing professionalcourses

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Int J Psychophysiol. 2020;158:215-24.

CROSS-SECTIONAL AND PROSPECTIVE ASSOCIATIONS OF P300, REWP, AND ADHD SYMPTOMS IN FEMALE ADOLESCENTS.

Kallen AM, Perkins ER, Klawohn J, et al.

Attention-deficit/hyperactivity disorder (ADHD), a neurodevelopmental syndrome characterized by impulsivity and distractibility, has been linked to blunted neural indicators of executive function and motivational processing. In the current study, we examined cross-sectional and prospective associations between P300 to feedback stimuli, the reward positivity (RewP), and interview-based and parent-reported ADHD symptoms in a sample of 300 female adolescents aged 8 to 14 who were re-assessed two years later. Cross-sectional analyses indicated that a smaller P300, but not RewP, was associated with greater interview-based and parent-reported ADHD symptoms. Moreover, both the P300 and RewP predicted interview-based symptom exacerbation among participants with some ADHD symptoms at baseline. These effects were found to be independent, supporting the notion of equifinal neurodevelopmental pathways to ADHD: one related to executive function (P300) and the other to motivational processing (RewP). Our results suggest that

incorporating psychophysiological measures into early assessment could be valuable for identifying youths likely to have a persistent course of ADHD

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JAMA Network Open. 2020;3.

MAGNETIC RESONANCE SPECTROSCOPY OF Y-AMINOBUTYRIC ACID AND GLUTAMATE CONCENTRATIONS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Hai T, Swansburg R, Kahl CK, et al.

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J Abnorm Child Psychol. 2020 Sep;48:1197-210.

NEUROCOGNITIVE CORRELATES OF RUMINATION RISK IN CHILDREN: COMPARING COMPETING MODEL PREDICTIONS IN A CLINICALLY HETEROGENEOUS SAMPLE.

Harmon SL, Kistner JA, Kofler MJ.

The current study examined associations between rumination and executive function difficulties in preadolescent youth, using predictions outlined in the attentional scope and multiple systems models of rumination. This study aimed to (a) extend current conceptual models of rumination to youth, (b) clarify disparate model predictions regarding working memory updating ('updating'), inhibition, and shifting abilities, and (c) examine differential neurocognitive predictions between two forms of rumination, sadness and anger. One hundred and fifty-nine youths oversampled for ADHD and other forms of child psychopathology associated with executive dysfunction (aged 8–13; 53.5% male; 59.1% Caucasian) completed a battery of assessments, including self-report measures of rumination and computerized neurocognitive tasks. Multiple regression analyses were conducted assessing relations between rumination and each executive function, controlling for both sadness and anger rumination to assess their unique associations. Sadness rumination was associated with poorer updating (ß = -0.18, p = 0.046) and shifting abilities (ß = 0.20, p = 0.03) but not inhibition (ß = -0.04, p = 0.62), offering partial support to the attentional scope and multiple systems models. In contrast, anger rumination was associated with better updating abilities (ß = 0.20, p = 0.03) but not shifting (ß = -0.15, p = 0.11) or inhibition (ß = 0.08, p = 0.35). Together, these results suggest (a) developmental differences in the neurocognitive correlates associated with rumination risk in youth compared to findings from the adult literature, and (b) that the executive function correlates of children's responses to negative emotions are affect-specific, such that sadness rumination is associated with difficulties replacing negative thoughts and shifting between mental sets, while anger rumination is associated with a better ability to maintain negative thoughts

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J Abnorm Child Psychol. 2020 Sep;48:1143-53.

EXECUTIVE FUNCTIONING AND ACTIVITY IN CHILDREN: A MULTIMETHOD EXAMINATION OF WORKING MEMORY, INHIBITION, AND HYPERACTIVITY.

Smith JN, Raiker JS, Fosco WD, et al.

Two primary methods of quantifying executive functioning include self- or other-reports (i.e., questionnaire-based EF) and cognitive test performance (i.e., task-based EF). Despite their lack of concordance with one another and relatively inconsistent associations with attention-deficit/hyperactivity disorder (ADHD) symptoms, both approaches have been utilized in attempts to advance our understanding of the role of EF in symptoms of ADHD. The current study is the first to incorporate a direct assessment of behavior (i.e., actigraphy) to further clarify the relation between EF and hyperactivity using a multi-method approach in a sample of children with a range of ADHD symptoms. Fifty-two children between the ages of 8 and 12 completed a testing session during which performance on working memory and inhibition computerized tasks, as well as actigraphy data, were collected. Additionally, parent reports of hyperactivity/impulsivity,

working memory, and inhibition were obtained. As expected, questionnaire-based measures of working memory and inhibition were strongly associated with parent-reported hyperactivity/impulsivity, whereas only the latter was associated significantly with mechanically assessed movement. In contrast, task-based working memory performance was more strongly associated with parent-reported hyperactivity/impulsivity relative to task-based inhibition. Further, both task-based working memory and task-based inhibition were similarly associated with mechanically-assessed movement. Finally, compared to questionnaire-based EF, both measures of task-based EF accounted for more variance in objectively-assessed movement. Collectively, these results highlight the measurement issues in the present literature, the importance of careful task and questionnaire design, and the value that alternative approaches (e.g., actigraphy) may provide with respect to advancing our understanding of EF

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J Abnorm Child Psychol. 2020 Sep;48:1115-28.

MODERATING THE RISK FOR ATTENTION DEFICITS IN CHILDREN WITH PRE-ADOPTIVE ADVERSITY: THE PROTECTIVE ROLE OF SHORTER DURATION OF OUT OF HOME PLACEMENT AND CHILDREN'S ENHANCED ERROR MONITORING.

Frenkel TI, Donzella B, Frenn KA, et al.

Early institutional-deprivation has been found to increase risk for inattention/hyperactivity (ADHD). Notably, studies suggest that children with a history of adversity evidencing an enhanced ERP (the error-related-negativity; ERN) may be protected against attention problems. However, such protective effects of the ERN have been studied in children whom typically experienced residential instability. It is unknown whether error-monitoring is similarly protective for children with stable post-deprivation placements. The present study examined the protective effect of the ERN in a sample of children who experienced at least 3-years of stable, relatively enriched caregiving after being internationally-adopted as infants/toddlers from institutional-care. We included two groups of children adopted internationally before age three, one group adopted from institutional-care (PI:n = 80) and one comparison group adopted from foster-care (FC;n = 44). A second comparison group consisted of non-adopted children (NA;n = 48) from demographically comparable families. At five-years of age, we assessed child ADHD symptoms (parent-report) and behavioral performance and neural correlates of error-monitoring (Go/No-Go task). PI children displayed lower Go/No-Go accuracy relative to FC children, and higher levels of ADHD symptoms relative to NA controls. In both FC and PI groups, longer duration of pre-adoptive out-of-home placement was associated with inattention, especially for children with deficits in error-monitoring. Enhancing cognitive control in the form of error monitoring might be a useful intervention target to protect children from some of the negative outcomes associated with adverse early care. Furthermore, results underscore that regardless of type of pre-adoptive care, we should aim to place children in stable/permanent homes as early as possible

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J Autism Dev Disord. 2020.

THE ROLE OF DECISION-MAKING IN PSYCHOLOGICAL WELLBEING AND RISKY BEHAVIOURS IN AUTISTIC ADOLESCENTS WITHOUT ADHD: LONGITUDINAL EVIDENCE FROM THE UK MILLENNIUM COHORT STUDY.

Hosozawa M, Mandy W, Cable N, et al.

This study examined the development of decision-making and its association with psychological wellbeing and risky behaviours in adolescents with and without autism. Participants included 270 autistic and 9,713 typically developing adolescents. In both samples, those with a diagnosis of attention-deficit/hyperactivity disorder (ADHD) were excluded. Data came from the Millennium Cohort Study, a nationally representative population-based birth cohort. Decision-making was assessed using the Cambridge Gambling Task at ages 11 and 14. Psychological wellbeing (happiness, self-esteem, depressive symptoms and self-harm) and risky/antisocial behaviours were self-reported at age 14. After adjusting for sex, cognitive ability, spatial working memory, socioeconomic status and pubertal status, autistic adolescents showed comparable quality

of decision-making to that of their peers at both ages but also a more deliberative decision-making style as they aged. Only in autistic adolescents was this decision-making style associated with positive outcomes

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J Autism Dev Disord. 2020.

FACTOR STRUCTURE OF REPETITIVE BEHAVIORS ACROSS AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Brierley NJ, McDonnell CG, Parks KMA, et al.

Restricted interests and repetitive behaviors (RRBs) are core symptoms of autism spectrum disorder (ASD), and commonly occur in attention-deficit/hyperactivity disorder (ADHD). Little is known about how RRBs manifest in ADHD. We quantified and compared factor structures of RRBs in children with ASD (n = 634) or ADHD (n = 448), and related factors to sex and IQ. A four-factor solution emerged, including Stereotypy, Self-Injury, Compulsions, and Ritualistic/Sameness. Factor structures were equivalent across diagnoses, though symptoms were more severe in ASD. IQ negatively correlated with Stereotypy, Self-Injury, and Compulsions in ASD, and negatively correlated with Compulsions and Ritualistic/Sameness behaviors in ADHD. In ASD only, females exhibited higher Self-Injury.-áThus, patterns of RRBs are preserved across ASD and ADHD, but severity and relationship with IQ differed

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J Child Adolesc Psychopharmacol. 2020;30:549-57.

A PHASE 3, RANDOMIZED DOUBLE-BLIND STUDY OF THE EFFICACY AND SAFETY OF LOW-DOSE SHP465 MIXED AMPHETAMINE SALTS EXTENDED-RELEASE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Mattingly G, Arnold V, Yan B, et al.

Objectives: In a previous pivotal study of children and adolescents (aged 6-17 years) with attention-deficit/hyperactivity disorder (ADHD), dose-optimized SHP465 mixed amphetamine salts (MAS) extended-release (12.5-25 mg once daily) was superior to placebo in reducing ADHD symptoms. This study evaluated the efficacy, tolerability, and safety of 6.25 mg SHP465 MAS once daily (one-half the lowest approved dose for adolescents and adults) versus placebo in children aged 6-12 years with ADHD.

Methods: Children (aged 6-12 years) with Diagnostic and Statistical Manual of Mental Disorders, Fifth edition-defined ADHD; baseline ADHD-Rating Scale, Fifth Edition, Child, Home Version total scores (ADHD-RS-5-HV-TS) 28; and baseline Clinical Global Impressions-Severity scores 4 were eligible. Participants received 6.25 mg SHP465 MAS once daily or placebo for 4 weeks. The primary (ADHD-RS-5-HV-TS change from baseline at week 4) and key secondary (Clinical Global Impressions-Improvement [CGI-I] score at week 4) efficacy end points were assessed using linear mixed-effects models for repeated measures. Safety and tolerability assessments included treatment-emergent adverse events (TEAEs) and vital sign changes.

Results: Of 89 randomized participants, 83 completed the study (placebo, n = 41; SHP465 MAS, n = 42). At week 4, the least squares mean (95% confidence interval) treatment differences (SHP465 MAS-placebo) were not statistically significant for ADHD-RS-5-HV-TS change (-1.9 [-6.8 to 3.1], p = 0.451; effect size [ES] = 0.17) or CGI-I score (-0.1 [-0.5 to 0.3], nominal p = 0.597; ES = 0.12). The percentage of participants reporting TEAEs was 16.3% with placebo and 24.4% with SHP465 MAS. The most frequently reported TEAEs (placebo; SHP465 MAS) were headache (7.0%; 4.4%) and decreased appetite (4.7%; 2.2%). Minimal increases in blood pressure were observed with SHP465 MAS at the final on-Treatment assessment.

Conclusions: SHP465 MAS 6.25 mg once daily (one-half the lowest dose approved for adolescents and adults) was well tolerated in children aged 6-12 years but was not superior to placebo in reducing ADHD symptoms, suggesting that this dose of SHP465 MAS was subtherapeutic in this age group. The Clinical Trial Registration number: NCT03325881

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J Child Neurol. 2020.

How Are They Doing? Neurodevelopmental Outcomes at School Age of Children Born Following Assisted Reproductive Treatments.

Farhi A, Glasser S, Gabis LV, et al.

Objective: The purpose of this study was to assess major neurodevelopmental aspects of children conceived by assisted reproductive treatments compared to spontaneously conceived children during the early school years.

Material & Methods: In this follow-up study, mothers of 358 children born following assisted reproductive treatments and 401 spontaneously-conceived children were interviewed by telephone regarding their childrenΓÇÖs health and development, when the children were 7-8 years old. The main outcomes were maternal responses to 4 questionnaires: Developmental Coordination Disorder Questionnaire, Short Sensory Profile, Autism Spectrum Screening Questionnaire, and the Attention-deficit hyperactive disorder (ADHD) Child Symptom Inventory-4 subscale. Mothers reported diagnoses of ADHD and autism spectrum disorder.

Results: No significant differences were found between the groups in Developmental Coordination Disorder Questionnaire or Short Sensory Profile scores upon univariate or multivariable analyses. There was a slightly higher but nonsignificant rate of diagnosed ADHD among children in the assisted reproductive treatment group (9.6% vs 5.5%; P =.18); on multivariable analysis, a nonsignificant increase in ADHD was also found for assisted reproductive treatment children (hazard ratio 1.45, 95% confidence interval 0.81-2.61). Regarding the Child Symptom Inventory-4 criteria for ADHD among the children who had never been diagnosed, there was also a slightly higher but nonsignificant rate among the assisted reproductive treatments compared to spontaneously-conceived children on univariate (2.4% vs 1.8%; P =.50) and multivariable analysis (odds ratio 0.88, 95% confidence interval 0.27-2.86). Autism spectrum disorder diagnosis or Autism Spectrum Screening Questionnaire scores were not significantly different; however, 5 of the 6 children with autism spectrum disorder diagnoses were in the assisted reproductive treatment group.

Conclusions: Neurodevelopmental measures were similar in both groups, although nonconclusive regarding ADHD and autism spectrum disorder risk. These findings contribute to the knowledge regarding long-term assisted reproductive treatment outcomes

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J Child Neurol. 2020.

Implementation of the Mini-Child Tourette Syndrome Impairment Scale: Relationships to Symptom Severity and Treatment Decisions.

Garris JF, Huddleston DA, Jackson HS, et al.

Functional impairment is an important factor in Tic Disorder treatment decisions. We evaluated the mini Child Tourette Syndrome Impairment Scale (mini-CTIM) for correlation with symptom severity and association with interventions. A total of 61 randomly selected tic encounters were retrospectively analyzed for mini-CTIM correlation with symptom severity scores and compared between patients who received treatment and those who did not. Regression models identified factors associated with treatment decisions. Mini-CTIM-tic scores correlated with tic severity and mini-CTIM-non-tic scores correlated with attention-deficit hyperactivity disorder (ADHD) severity. Tic treatment was associated with higher child, but not parent, mini-CTIM-tic scores. Regression models identified that comorbidity treatment was predicted by ADHD severity, obsessive compulsive disorder severity, and parent but not child mini-CTIM-non-tic scores. These findings suggest children have valuable insight into their tic-related impairment, but parent assessment is important for evaluating comorbidity-related impairment. The mini-CTIM may be a useful clinical tool for assessing tic-related impairment

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Journal of Child Science. 2020;10:E163-E168.

EFFECT OF DEMOGRAPHIC FACTORS ON QUALITY OF LIFE IN CHILDREN WITH ADHD UNDER ATOMOXETINE TREATMENT: 1-YEAR FOLLOW-UP.

Ragab MM, Eid EM, Badr NH.

Attention-deficit hyperactivity disorder (ADHD) is the most common psychiatric disorder in children and adolescents. Symptoms of ADHD and its treatment can impact an individual's quality of life (QoL). The present study aimed to evaluate the effect of atomoxetine treatment, demographic characteristics, and seasonal variation on QoL in children with a recent diagnosis of ADHD and their parents. The present study included a cohort of 200 children diagnosed with ADHD. In addition to the recruited children, one of their parents was included in the study. ADHD symptoms were assessed using Conners' Parent Rating Scale. QoL of the participants was assessed with the PedsQL, while parents' QoL was evaluated using the World Health Organization Quality of Life questionnaire (WHOQOL-Bref). There was significant improvement in pediatric and parental QoL after treatment with atomoxetine. Significant factors related to better QoL in the participants included spring season, above average Conner's score, male sex, and rural residence. However, after using multivariate regression analysis, only patients' sex and Conner's score were significant predictors of pediatric QoL at the end of treatment with atomoxetine. Medical treatment significantly improved QoL in children with ADHD and their parents. Level of improvement was affected by patients' sex and ADHD severity

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J Clin Psychopharmacol. 2020;40:314-15.

SUCCESSFUL MANAGEMENT OF METHYLPHENIDATE OR ATOMOXETINE-RELATED PRIAPISM DURING ATTENTION-DEFICIT HYPERACTIVITY DISORDER TREATMENT.

Karayagmurlu A, Coskun M.

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J Educ Psychol. 2020 Nov.

COGNITIVE DIMENSIONS OF LEARNING IN CHILDREN WITH PROBLEMS IN ATTENTION, LEARNING, AND MEMORY.

Holmes J, Guy J, Kievit RA, et al.

A data-driven, transdiagnostic approach was used to identify the cognitive dimensions linked with learning in a mixed group of 805 children aged 5 to 18 years recognized as having problems in attention, learning, and memory by a health or education practitioner. Assessments included phonological processing; information processing speed; short-term and working memory; executive functions; and attainments in word reading, spelling, and math. Data reduction methods identified 3 dimensions of phonological processing, processing speed, and executive function for the whole sample. This model was comparable for children with and without attention-deficit/hyperactivity disorder (ADHD). The severity of learning difficulties in literacy was linked with phonological processing skills, and in math with executive control. Associations between cognition and learning were similar across younger and older children and individuals with and without ADHD, although stronger links between learning-related problems and both executive skills and processing speed were observed in children with ADHD. These results establish clear domain-specific cognitive pathways to learning that distinguish individuals in the heterogeneous population of children struggling to learn. (PsycInfo Database Record (c) 2020 APA, all rights reserved)

Educational Impact and Implications Statement—Understanding how cognitive skills relate to learning can inform educational practice. Links between cognition and learning were explored in a group of children who represent a substantial majority of poor learners, including those with relatively mild problems through to those with complex and co-occurring needs. The ability to process the sound structure of words (phonological processing) was linked to the severity of word reading problems, whereas the high-level cognitive control of processes such as problem solving was related to mathematical difficulties. Understanding these specific associations may be useful in guiding support for children who are struggling at school

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J Med Genet. 2020;57:717-24.

PATHOGENIC VARIANTS IN TNRC6B CAUSE A GENETIC DISORDER CHARACTERISED BY DEVELOPMENTAL DELAY/INTELLECTUAL DISABILITY AND A SPECTRUM OF NEUROBEHAVIOURAL PHENOTYPES INCLUDING AUTISM AND ADHD.

Granadillo JL, Stegmann APA, Guo H, et al.

Background Rare variants in hundreds of genes have been implicated in developmental delay (DD), intellectual disability (ID) and neurobehavioural phenotypes. TNRC6B encodes a protein important for RNA silencing. Heterozygous truncating variants have been reported in three patients from large cohorts with autism, but no full phenotypic characterisation was described.

Methods Clinical and molecular characterisation was performed on 17 patients with TNRC6B variants. Clinical data were obtained by retrospective chart review, parent interviews, direct patient interaction with providers and formal neuropsychological evaluation.

Results Clinical findings included DD/ID (17/17) (speech delay in 94% (16/17), fine motor delay in 82% (14/17) and gross motor delay in 71% (12/17) of subjects), autism or autistic traits (13/17), attention deficit and hyperactivity disorder (ADHD) (11/17), other behavioural problems (7/17) and musculoskeletal findings (12/17). Other congenital malformations or clinical findings were occasionally documented. The majority of patients exhibited some dysmorphic features but no recognisable gestalt was identified. 17 heterozygous TNRC6B variants were identified in 12 male and five female unrelated subjects by exome sequencing (14), a targeted panel (2) and a chromosomal microarray (1). The variants were nonsense (7), frameshift (5), splice site (2), intragenic deletions (2) and missense (1).

Conclusions Variants in TNRC6B cause a novel genetic disorder characterised by recurrent neurocognitive and behavioural phenotypes featuring DD/ID, autism, ADHD and other behavioural abnormalities. Our data highly suggest that haploinsufficiency is the most likely pathogenic mechanism. TNRC6B should be added to the growing list of genes of the RNA-induced silencing complex associated with ID/DD, autism and ADHD

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J Neurosci Rural Pract. 2020.

IMPACT OF COVID-19 AND LOCKDOWN ON CHILDREN WITH ADHD AND THEIR FAMILIES-AN ONLINE SURVEY AND A CONTINUITY CARE MODEL.

Shah R, Raju VV, Sharma A, et al.

Background Little is known about the impact of the coronavirus disease 2019 pandemic on children with attention-deficit hyperkinetic disorder (ADHD). This study aimed to assess the impact of lockdown on children with the ADHD, and their families. Additionally, feasibility of carrying out text message-based intervention was evaluated.

Methods An online survey was performed to evaluate the impact of lockdown on children with ADHD and their family members. Additionally, a text message-based intervention was performed over 2 weeks. Along with the text-based intervention, we also provided reading materials and an option of telephonic consultation.

Results Of the 80 parents who initially consented to participate, 48 filled the baseline survey, and 41 agreed to receive intervention. Out of 41, 29 filled satisfaction survey. During the lockdown period, there was worsening of symptoms of ADHD in the form of increase (slight or marked) in the activity level (50.1%), irritability (45.8%), and disturbing or disruptive behavior (47.7%) in children. In terms of behavior of family members, there was marked/slight increase in irritability (37.5%), and shouting at the child (43.8%), verbal abuse (25%), and punishing the child (27.1%). Additionally, there was an increase in the praising (67.6%) and spending time with the child (72.9%). Text-based messages on a scale of 0 to 10 were rated as 5.79 for the content, 5.76 for the usefulness, and 6 for satisfaction.

Conclusion Lockdown resulted in worsening of symptoms among children of ADHD and it had impact on the interaction pattern of the children and parents. A text message-based intervention is a feasible and possibly acceptable option to deal with the behavioral problem of the children and adolescents with ADHD

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J Pediatr. 2020.

ASSOCIATION OF ANEMIA WITH NEURODEVELOPMENTAL DISORDERS IN A NATIONALLY REPRESENTATIVE SAMPLE OF US CHILDREN.

Yang W, Liu B, Gao R, et al.

Objective: To examine the associations of anemia with autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and learning disability in US children.

Study design: We included children and adolescents aged 3-17 years from the National Health Interview Survey (NHIS), 1997-2018. Information about physician-diagnosed history of anemia, ASD, ADHD, and learning disability was reported by a parent or guardian. Multiple logistic regression with sample weights was used to estimate the ORs and 95% CIs of neurodevelopmental disorders according to the presence of anemia.

Results: Of the total population of 213 893 children aged 3-17 years (mean age [SE], 10.01 [0.01] years), 2379 were reported to have a diagnosis of anemia, for a weighted prevalence of 1.06% (95% CI, 1.01-1.12). The prevalence of ASD was 1.94% (95% CI, 1.20-2.68) among children with anemia and 1.07% (95% CI, 1.01-1.14) among those without anemia. The corresponding prevalences were 12.24% (95% CI, 10.47-14.00) and 7.73% (95% CI, 7.58-7.88) for ADHD and 15.03% (95% CI, 13.08-16.99) and 7.75% (95% CI, 7.39-7.70) for learning disability, respectively. Compared with those without anemia, children with anemia were more likely to have neurodevelopmental disorders, with an aOR of 2.07 (95% CI, 1.39-3.08) for ASD, 1.84 (95% CI, 1.55-2.19) for ADHD, and 2.22 (95% CI, 1.90-2.60) for learning disability.

Conclusions: In a nationally representative sample of US children, we found significant associations between anemia and neurodevelopmental disorders including ASD, ADHD, and learning disability. Further investigation is warranted to assess the causality and elucidate the underlying mechanisms

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J Psychiatr Res. 2021;132:65-71.

ASSOCIATION BETWEEN THE GROUP III METABOTROPIC GLUTAMATE RECEPTOR GENE POLYMORPHISMS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND FUNCTIONAL EXPLORATION OF RISK LOCI.

Zhang Q, Chen X, Li S, et al.

Existing evidence suggests that the group III metabotropic glutamate receptor (mGluR) gene variations are involved in attention-deficit/hyperactivity disorder (ADHD), but few studies have fully explored this association. We conducted a case-control study with 617 cases and 636 controls to investigate the association between functional single-nucleotide polymorphisms (SNPs) from the group III mGluR gene polymorphisms (GRM4, GRM7, GRM8) and ADHD in the Chinese Han population and initially explored the function of positive SNPs. The GRM4 rs1906953 T genotype showed a significant association with a decreased risk of ADHD (TT:CC, OR = 0.55, 95% CI = 0.40ΓÇô0.77; recessive model, OR = 0.58, 95% CI = 0.43ΓÇô0.78). GRM7 rs9826579 C showed a significant association with an increased risk of ADHD (TC:TT, OR = 1.81, 95% CI = 1.39ΓÇô2.36; dominant model, OR = 1.74, 95% CI = 1.35ΓÇô2.24; additive model, OR = 1.56, 95% CI = 1.24ΓÇô1.97). In addition, compared with subjects with the rs1906953 TT genotype, subjects with of the CC genotype showed more obvious attention deficit behaviours and hyperactivity/impulsive behaviours. Dual-luciferase reporter gene assays showed that a promoter reporter with the rs1906953 TT genotype significantly decreased luciferase activity compared with the CC genotype. According to electrophoretic mobility shift assays, the binding capacity of rs1906953 T probe with nucleoprotein was lower than that of the rs1906953 C probe. Our results revealed the association of GRM4 rs1906953 and GRM7 rs9826579 with ADHD. Moreover, we found that rs1906953 disturbs the transcriptional activity of GRM4

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J Am Acad Child Adolesc Psychiatry. 2020.

EDITORIAL: TWO CENTIMETERS MORE OR LESS. HOW MUCH DOES IT MATTER TO AN ADOLESCENT OR A YOUNG ADULT WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?

Carucci S.

Stimulants are the first-line medication for attention-deficit/hyperactivity disorder (ADHD), and methylphenidate (MPH) is the first choice in Europe, with good efficacy and acceptable tolerability in a short-term course during childhood and adolescence.1 ADHD is, however a chronic condition, and patients can receive pharmacological treatment for a long period of time with understandable concerns related to long-term risks. Beside the well-known mild and transient adverse effects (ie, sleep disturbance, nervousness, anorexia, headache, and abdominal pain), in the last decade, emphasis has been placed on several less common, but potentially more serious, effects occurring with prolonged use, and in particular on a possible drug-related impact of medications on growth and pubertal maturation

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Journal of the Endocrine Society. 2020;4:1-12.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG US CHILDREN AND ADOLESCENTS WITH CONGENITAL ADRENAL HYPERPLASIA.

Harasymiw LA, Grosse SD, Sarafoglou K.

Background: Little is known regarding risk for co-occurring mental health conditions among pediatric patients with congenital adrenal hyperplasia (CAH). The objective of the current study was to investigate the prevalence of medically managed attention-deficit/ hyperactivity disorder (ADHD) in 2 large administrative samples of insured children and adolescents with and without CAH in the United States.

Methods: We assessed the prevalence of CAH and of medically managed ADHD using algorithms defined from diagnosis codes and filled prescriptions data using the IBM Market Scan Commercial and Multi-State Medicaid claims databases. We evaluated subjects who were continuously enrolled for 12 months with a first claim during October 2015 through December 2017 when they were 5 to 18 years old.

Results: The administrative prevalence of CAH in the Commercial (N = 3 685 127) and Medicaid (N = 3 434 472) samples was 10.1 per 100 000 (n = 372) and 7.2 per 100 000 (n = 247), respectively. The prevalence of medically managed ADHD in the non-CAH population was 8.4% in the Commercial sample and 15.1% in the Medicaid sample. Among children with CAH, there was no increased prevalence of ADHD in the Commercial (9.2%, prevalence ratio [PR] = 1.1; 95% confidence interval [CI], 0.82-1.54; P = 0.48) or Medicaid (13.8%; PR = 0.91; 95% CI, 0.67-1.24; P = 0.55) samples compared with the general population.

Conclusions: Using 2 large samples of insured children and adolescents in the United States, we found similar prevalence of medically managed ADHD among those with CAH and the general population. Future research to assess the validity of our claims algorithm for identifying pediatric CAH cases is warranted

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J Formos Med Assoc. 2020.

MONTELUKAST DOES NOT INCREASE THE RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN PEDIATRIC ASTHMA PATIENTS: A NATIONWIDE POPULATION-BASED MATCHED COHORT STUDY.

Huang PY, Yang YH, Huang YH, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) has been linked to pediatric asthma patients treated with montelukast. This study is the first to use a nationwide health insurance research database (NHIRD) to study whether asthmatic children using montelukast are at an increased risk of ADHD.

Methods: We used data from the Taiwan NHIRD, which is a longitudinal database of one million randomly selected subjects. The enrolled patients were followed up until 2013. Patients younger than and equal to 12 years old with new-onset asthma (ICD-9 CM code 493.X) diagnosed between 1997 and 2013 were enrolled. A multivariate Cox regression analysis was conducted to evaluate the association between montelukast treatment and the risk of ADHD (ICD-9-CM code 314.X).

Results: We enrolled a total of 54,487 asthmatic children younger than and equal to 12 years old who had at least one claim of inpatient admission or at least three claims of an ambulatory visit. Montelukast users and match controls were identified by matching age, gender, residence, the comorbidities including allergic rhinitis and atopic dermatitis, admission or emergency department visits due to asthma attack, and index date of starting montelukast in a 1:1 ratio, with 12,806 in the montelukast group and 12,806 in the non-montelukast group. The montelukast group had a similar risk of ADHD (n = 632, 4.94%) as the non-montelukast group (n = 610, 4.76%) [adjusted hazard ratio 1.04; 95% confidence interval, 0.93 to 1.17]. In children treated with montelukast, high cumulative days of montelukast use did not increase the risk of ADHD. **Conclusion**: This nationwide population-based cohort study reveals that asthma children treated with montelukast were not at an increased risk of developing ADHD. Nevertheless, validation of our retrospective survey requires further prospective study

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Mol Psychiatry. 2020.

PREDICTING THE COURSE OF ADHD SYMPTOMS THROUGH THE INTEGRATION OF CHILDHOOD GENOMIC, NEURAL, AND COGNITIVE FEATURES.

Sudre G, Sharp W, Kundzicz P, et al.

Childhood attention deficit hyperactivity disorder (ADHD) shows a highly variable course with age: some individuals show improving, others stable or worsening symptoms. The ability to predict symptom course could help individualize treatment and guide interventions. By studying a cohort of 362 youth, we ask if polygenic risk for ADHD, combined with baseline neural and cognitive features could aid in the prediction of the course of symptoms over an average period of 4.8 years. Compared to a never-affected comparison group, we find that participants with worsening symptoms carried the highest polygenic risk for ADHD, followed by those with stable symptoms, then those whose symptoms improved. Participants with worsening symptoms also showed atypical baseline cognition. Atypical microstructure of the cingulum bundle and anterior thalamic radiation was associated with improving symptoms while reduction of thalamic volume was found in those with stable symptoms. Machine-learning algorithms, trained and tested on independent groups, performed well in classifying those never affected against groups with worsening, stable, and improving symptoms (area under the curve >0.79). We conclude that some measures of polygenic risk, cognition, and neuroimaging show significant associations with the future course of ADHD symptoms and may have modest predictive power. These features warrant further exploration as prognostic tools

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NeuroImage. 2021;225.

CHARACTERIZING INSCAPES AND RESTING-STATE IN MEG: EFFECTS IN TYPICAL AND ATYPICAL DEVELOPMENT.

Vandewouw MM, Dunkley BT, Lerch JP, et al.

Examining the brain at rest is a powerful approach used to understand the intrinsic properties of typical and disordered human brain function, yet task-free paradigms are associated with greater head motion, particularly in young and/or clinical populations such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). Inscapes, a non-social and non-verbal movie paradigm, has been introduced to increase attention, thus mitigating head motion, while reducing the task-induced activations found during typical movie watching. Inscapes has not yet been validated for use in magnetoencephalography (MEG), and it has yet to be shown whether its effects are stable in clinical populations. Across typically developing (N = 32) children and adolescents and those with ASD (N = 46) and ADHD (N = 42), we demonstrate that head motion is reduced during Inscapes. Due to the task state evoked by movie paradigms, we also expectedly observed concomitant modulations in local neural activity (oscillatory power) and functional connectivity (phase and envelope coupling) in intrinsic resting-state networks and across the frequency spectra compared to a fixation cross resting-state. Increases in local activity were accompanied by decreases in low-frequency connectivity within and between resting-state networks, primarily the visual network, suggesting that task-state evoked by Inscapes moderates ongoing

and spontaneous cortical inhibition that forms the idling intrinsic networks found during a fixation cross resting-state. Importantly, these effects were similar in ASD and ADHD, making Inscapes a well-suited advancement for investigations of resting brain function in young and clinical populations

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NeuroImage Clin. 2020;28.

BEYOND DIAGNOSIS: CROSS-DIAGNOSTIC FEATURES IN CANONICAL RESTING-STATE NETWORKS IN CHILDREN WITH NEURODEVELOPMENTAL DISORDERS.

Choi EJ, Vandewouw MM, Taylor MJ, et al.

Children with neurodevelopmental disorders (NDDs) share common behavioural manifestations despite distinct categorical diagnostic criteria. Here, we examined canonical resting-state network connectivity in three diagnostic groups (autism spectrum disorder, attention-deficit/hyperactivity disorder and paediatric obsessive compulsive disorder) and typically developing controls (TD) in a large single-site sample (N = 407), applying diagnosis-based and dimensional approaches to understand underlying neurobiology across NDDs. Each participant's functional network graphs were computed using five graph metrics. In diagnosis-based comparisons, an analysis of covariance was performed to compare all NDDs to TD, followed by pairwise comparisons between NDDs. In the dimensional approach, participantsΓÇÖ functional network graphs were correlated with continuous behavioural measures, and a data-driven k-means clustering analysis was applied to determine if subgroups of participants were seen, without diagnostic information having been included. In the diagnosis-based comparisons, children with NDDs did not differ significantly from the TD group and the NDD categorical groups also did not differ significantly from each other, across all graph metrics. In the dimensional, diagnostic-independent approach, however, subcortical functional connectivity was significantly correlated with participants general adaptive functioning across all participants. The clustering analysis identified an optimal solution of two clusters, and participants assigned in the same data-driven cluster were highly heterogeneous in diagnosis. Neither cluster exclusively contained a specific diagnostic group, nor did NDDs separate cleanly from TDs. Each participant's distance ratio between the two clusters was significantly correlated with general adaptive functioning, social deficits and attentional problems. Our results suggest the neurobiological similarity and dissimilarity between NDDs need to be investigated beyond DSM/ICD-based, behaviourally-defined diagnostic categories

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Neuropsychiatr Dis Treat. 2020;16:2397-406.

APPLICATION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DIAGNOSTIC TOOLS: STRENGTHS AND WEAKNESSES OF THE KOREAN ADHD RATING SCALE AND CONTINUOUS PERFORMANCE TEST.

Won GH, Choi TY, Kim JW.

Purpose: We aimed to compare the Korean version of the ADHD Rating Scale (K-ARS) and Integrated Visual and Auditory Plus (IVA+Plus), a continuous performance test, by analyzing their abilities to distinguish different groups (attention-deficit/hyperactivity disorder [ADHD], ADHD-not otherwise specified [NOS], and normal control [NC]).

Patients and Methods: Individuals of 7ΓÇô12 years of age who visited our child and adolescent psychiatric clinic were recruited. Seventy-four participants (58 males, 16 females) were classified into three groups according to results from the Korean Version of Diagnostic Interview Schedule for Children Version IV. The K-ARS and IVA+Plus were administered. An analysis of covariance (ANCOVA) was conducted. The tools accuracy in discriminating patients with ADHD or NOS from NCs was evaluated using a receiver operating characteristic (ROC) curve analysis.

Results: ANCOVA revealed significant differences in the K-ARS results of the three groups (ADHD [n=29], NOS [n=33], NC [n=12]), whereas a difference in IVA+Plus results was observed only between the ADHD and NC groups. In the ROC curve analysis of the K-ARS, the areas under the curve (AUCs) for each group were 0.960 (ADHD vs NC), 0.885 (NOS vs NC), 0.920 (ADHD+NOS vs NC), and 0.779 (ADHD vs NOS+NC). In the ROC curve analysis for the IVA+Plus hyperactivity-impulsiveness scale, the AUCs for each group were

0.740 (ADHD vs NC), 0.643 (NOS vs NC), 0.688 (ADHD+NOS vs NC), and 0.626 (ADHD vs NOS+NC); those for the inattention scale were 0.731 (ADHD vs NC), 0.658 (NOS vs NC), 0.692 (ADHD+NOS vs NC), and 0.625 (ADHD+NOS vs NC).
Conclusion: The K-ARS was useful to distinguish the ADHD and NOS groups from the NC group, while the IVA+Plus was useful to distinguish the ADHD group from the NC group. Clinicians should ensure they understand the properties of each tool and apply them appropriately in the diagnosis of ADHD

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Neuropsychology. 2020 Nov;34:894-905.

THE ROLE OF TOP-DOWN ATTENTIONAL CONTROL AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN PREDICTING FUTURE MOTOR VEHICLE CRASH RISK.

Aduen PA, Kofler MJ, Bradshaw CP, et al.

Objective: Attention-deficit/hyperactivity disorder (ADHD) confers elevated risk for automobile crashes, both as a clinical syndrome and continuously when examining risk as a function of symptom severity. However, the neurocognitive mechanisms and processes underlying this risk remain poorly understood. The current longitudinal study examined whether attention network components reflect neurocognitive pathways linking ADHD symptoms with adverse driving outcomes.
Method: Drivers from six U.S. sites participating in the Strategic Highway Research Program Naturalistic Driving Study (N=3,226) were prospectively monitored for objectively identified crashes, near-crashes, and crash/near-crash fault. At study entry, drivers were assessed for ADHD symptoms; completed the Conners' Continuous Performance Test, Second Edition; and were then followed continuously for 1–2 years of routine, on-road driving using technology-enhanced in-car monitoring. Bias-corrected, bootstrapped mediation models examined the extent to which attention network components mediated the association between ADHD symptoms and future driving risk, controlling for known risk factors.
Results: As expected, self-reported ADHD symptoms predicted all markers of future driving risk. Higher ADHD symptoms were associated with reduced inhibitory control, lower levels of top-down attentional control (endogenous orienting), and greater arousal decrements (phasic alertness). Controlling for ADHD symptoms, top-down attentional control uniquely predicted future crashes, near-crashes, and culpability for future crashes/near-crashes; only arousal decrements portended future near-crashes. Only top-down attentional control significantly mediated the association between baseline ADHD symptoms and future driving risk.
Conclusions: The driving risks associated with ADHD appear to be conveyed in part by impairments in the top-down, voluntary control of attention, rather than by difficulties sustaining attention over time or inhibiting impulses, as is often assumed.
Key Points—Question: Why do drivers with attention-deficit/hyperactivity disorder (ADHD) experience more motor vehicle crashes and near-crashes than their peers?
Findings: The driving risks associated with ADHD appear to be conveyed in part by impairments in the top-down, voluntary control of attention, rather than by difficulties sustaining attention over time or inhibiting impulses, as is often assumed.
Importance: These findings provide the first longitudinal evidence linking neurocognitive impairments in specific components of the attention network with adverse motor vehicle driving outcomes during routine, on-road driving.
Next Steps: Investigating additional neuropsychological functions (e.g., working memory) and linking these abilities with the in-car behaviors that immediately proceed crashes/near-crashes will be important for developing harm reduction strategies that improve driving safety for individuals with neurocognitive vulnerabilities

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Neuropsychopharmacology. 2020.

INTEGRATION OF BRAIN AND BEHAVIOR MEASURES FOR IDENTIFICATION OF DATA-DRIVEN GROUPS CUTTING ACROSS CHILDREN WITH ASD, ADHD, OR OCD.

Jacobs GR, Voineskos AN, Hawco C, et al.

Autism spectrum disorder (ASD), obsessive-compulsive disorder (OCD) and attention-deficit/hyperactivity disorder (ADHD) are clinically and biologically heterogeneous neurodevelopmental disorders (NDDs). The objective of the present study was to integrate brain imaging and behavioral measures to identify new brain-behavior subgroups cutting across these disorders. A subset of the data from the Province of Ontario Neurodevelopmental Disorder (POND) Network was used including participants with different NDDs (aged 6Γ Çô16 years) that underwent cross-sectional T1-weighted and diffusion-weighted magnetic resonance imaging (MRI) scanning on the same 3T scanner, and behavioral/cognitive assessments. Similarity Network Fusion was applied to integrate cortical thickness, subcortical volume, white matter fractional anisotropy (FA), and behavioral measures in 176 children with ASD, ADHD or OCD with complete data that passed quality control. Normalized mutual information was used to determine top contributing model features. Bootstrapping, out-of-model outcome measures and supervised machine learning were each used to examine stability and evaluate the new groups. Cortical thickness in socio-emotional and attention/executive networks and inattention symptoms comprised the top ten features driving participant similarity and differences between four transdiagnostic groups. Subcortical volumes (pallidum, nucleus accumbens, thalamus) were also different among groups, although white matter FA showed limited differences. Features driving participant similarity remained stable across resampling, and the new groups showed significantly different scores on everyday adaptive functioning. Our findings open the possibility of studying new data-driven groups that represent children with NDDs more similar to each other than others within their own diagnostic group. Future work is needed to build on this early attempt through replication of the current findings in independent samples and testing longitudinally for prognostic value

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Neuropsychopharmacology. 2020.

EFFECTS OF SUBSTANCE MISUSE ON REWARD-PROCESSING IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Paraskevopoulou M, van Rooij D, Batalla A, et al.

Attention-Deficit/Hyperactivity Disorder (ADHD) and Substance Use Disorder (SUD) often co-occur and are associated with treatment resistance. Both disorders are characterized by similar reward-processing deficits with decreased striatal responses to reward anticipation, though literature is inconsistent. It is unclear whether substance misuse exaggerates reward-processing deficits observed in ADHD. The aim of this study was to examine substance misuse effects on reward-processing in ADHD. Functional MRI data in a Monetary Incentive Delay (MID) task from a multi-site study were compared across ADHD groups with and without substance misuse (ADHD + SM and ADHD-only, respectively) and healthy controls (n = 40/group, 74 males and 46 females, aged 13.7ΓÇô25.9 years). Substance misuse was defined as misuse of alcohol, nicotine, or drugs. Groups were matched with presence/absence of parental SUD to avoid interference with SUD trait effects. Compared to ADHD-only and controls, ADHD + SM showed hyperactivation in putamen during reward anticipation. Compared to controls, the ADHD groups showed hypoactivation in motor/sensory cortices and hyperactivation in frontal pole and OFC during reward outcome. ADHD + SM also showed hyperactivation in frontal pole during neutral outcome. Moreover, ADHD + SM patients showed higher callous-unemotional (CU) traits that were positively correlated with putamen responses to reward anticipation. Our results show distinct condition-independent neural activation profile for ADHD + SM compared to ADHD-only and controls. Effects of comorbid substance misuse and variability of its prevalence across ADHD studies might have contributed to inconsistencies in ADHD literature. Contrasted with findings for reward-processing in SUD literature, results potentially suggest distinct underlying mechanisms for SUD subgroups with different characteristics, like antisocial/psychopathic traits

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Neurosci Lett. 2020;738.

ASSOCIATIONS OF ATTENTION DISTRACTIBILITY WITH ATTENTION DEFICIT AND WITH VARIATION IN THE KTN1 GENE.

Tuvi I, Harro J, Kiive E, et al.

Attention distractibility in a low load visual search experiment with a rare irrelevant distractor could be an objective continuous measure in adulthood that correlates well with the symptoms of attention deficit throughout lifespan. This was studied using a birth cohort representative sample in a longitudinal study. The expected correlations were not found between the distractor cost measured in the experiment in adulthood and the inattention questionnaire scores from ages 15Γêǽ33. However, the coefficient of variability for RT (CVRT) correlated negatively with self-reported motor restlessness (age 15) and attention deficit (age 25). We suggest that hyperactivity in childhood improved motor control at age 33. Associations with the gene KTN1 rs945270 (found to affect putamen size) were explored. CVRT, motor restlessness at age 15 and attention deficit scores at age 25 were especially low for male C-allele carriers. A possible association with the volume of putamen of individual participants is considered

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Nord J Psychiatry. 2020 Nov;74:558-68.

THE USE OF DIET INTERVENTIONS TO TREAT SYMPTOMS OF ADHD IN CHILDREN AND ADOLESCENTS - A SYSTEMATIC REVIEW OF RANDOMIZED CONTROLLED TRIALS.

Uldall Torp NM, Thomsen PH.

Background: For over forty years diet interventions have been investigated as a treatment of ADHD in children and adolescents and, with the new discoveries of the microbiota-gut-brain axis, this research becomes more relevant than ever. The aim of this systematic review was therefore to investigate the current knowledge of diet interventions as a treatment of ADHD in children and adolescents

Methods: A systematic literature search in PubMed was conducted, identifying randomized controlled trials investigating diet interventions to treat ADHD in children and adolescents.

Results: The study populations were generally small and the studies varied in duration and nature of the exposure. Overall 10 out of 12 studies spoke in favour of an elimination diet, 2 out of 6 of eliminating artificial food colourings from the diet and none in favour of eliminating sucrose or aspartame from the diet to treat ADHD.

Conclusion: The current evidence is not enough to recommend treating ADHD with diet interventions, but a subgroup of children and adolescents might warrant from elimination of certain food-items. Further investigations of the mechanism and effect of diet interventions to treat ADHD is needed

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Nutrients. 2020;12:1-15.

OMEGA-3 LONG-CHAIN POLYUNSATURATED FATTY ACIDS INTAKE IN CHILDREN: THE ROLE OF FAMILY-RELATED SOCIAL DETERMINANTS.

Martinez-Martinez MI, et al.

Omega-3 long-chain polyunsaturated fatty acids play a central role in neuronal growth and in the development of the human brain, since they are essential elements which depend on intake through diet to ensure an adequate amount. Fish and seafood are the main dietary sources of these fatty acids in Spain and in other countries. In order to assess the effect of the intake of common foods containing high amounts of omega-3 polyunsaturated fatty acids, a food frequency questionnaire was administered to parents of children and adolescents attending a primary school in Valencia (Spain), and the intake of dietary omega-3 such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) was estimated based on their fish/seafood consumption. Low frequencies of intake were significantly ($p < 0.05$) lower for many types of fish/seafood in children compared to adolescents. 27.5% of children/adolescents did not eat lean fish or other types (19.8% of the sample did not eat fatty fish, and 71.8% did not eat smoked fish) and 20-60% of the sample consumed seafood only once three times a month, leading to a reduced estimated intake of EPA+DHA below that recommended for both groups by public health agencies. Social aspects, such as the type of work done by

mothers and their educational levels are significant factors ($p < 0.05$ in both cases) affecting children's/adolescents' intake of DHA+EPA. Dietary interventions to increase the consumption of fish and seafood are strongly advised, and health promotion strategies should be aimed at the family level and fight against gender disparities

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Nutrients. 2020;12:1-34.

NEGATIVE AFFECTIVITY AND EMOTION DYSREGULATION AS MEDIATORS BETWEEN ADHD AND DISORDERED EATING: A SYSTEMATIC REVIEW.

El Archi S, Cortese S, Ballon N, et al.

Attention-Deficit/Hyperactivity Disorder (ADHD) is associated with disordered eating, especially addictive-like eating behavior (i.e., binge eating, food addiction, loss of control overeating). The exact mechanisms underlying this association are unclear. ADHD and addictivelike eating behavior are both associated with negative affectivity and emotion dysregulation, which we hypothesized are mediators of this relationship. The purpose of this systematic review was to review the evidence related to this hypothesis from studies assessing the relationship between childhood or adulthood ADHD symptomatology, negative affectivity, emotion dysregulation and addictive-like eating behavior. The systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) recommendations. The literature search was conducted in PubMed and PsycINFO (publication date: January 2015 to August 2020; date of search: 2nd September 2020). Out of 403 potentially relevant articles, 41 were retained; 38 publications reported that ADHD and disordered eating or addictive-like eating behavior were significantly associated, including 8 articles that suggested a mediator role of negative affectivity or emotion dysregulation. Sixteen publications reported that the association between ADHD symptomatology and disordered eating or addictive-like eating behavior differed according to gender, eating behavior and ADHD symptoms (hyperactivity, impulsivity and inattention). We discuss the practical implications of these findings and directions future research

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Pediatrics. 2020;146.

ADHD AT AGE 7 AND FUNCTIONAL IMPAIRMENTS AT AGE 10.

Efron D, Nicholson JM, Anderson V, et al.

BACKGROUND AND OBJECTIVES: Attention-deficit/hyperactivity disorder (ADHD) cohort studies have typically involved clinical samples and have usually recruited children across wide age ranges, limiting generalizability across complexity and developmental stage. We compared academic, emotional-behavioral and social functioning at age 10, and predictors of outcomes, in a nonreferred cohort of children recruited at age 7, between those with full-syndrome (FS) ADHD and controls with no ADHD.

METHODS: This was a prospective cohort study with a 3-year follow-up period. Children were recruited from 43 socioeconomically diverse schools in Melbourne, Australia. Multi-informant outcomes at age 10 were academic functioning (Wide Range Achievement Test 4; Social Skills Improvement System), emotional-behavioral functioning (Strengths and Difficulties Questionnaire total), and social functioning (Strengths and Difficulties Questionnaire peer problems). Outcomes were compared across the groups by using adjusted random-effects linear regression analyses.

RESULTS: In total, 477 children (62% male) were recruited at a mean (SD) age of 7.3 years (0.4). There were 179 participants with FS ADHD, 86 with ST ADHD, and 212 controls. Sample retention was 78.2% at 3-year follow-up. Both the FS and ST groups were functioning worse than controls on almost all outcome measures. The best predictors of outcome for children with ADHD were working memory (academic outcome, P, .001), ADHD symptom severity (emotional-behavioral outcome, parent: P, .001; teacher: P, .01), and autism spectrum disorder symptoms (emotional-behavioral outcome, parent P = .003; social outcome, parent P = .001).

CONCLUSIONS: Children with FS and ST ADHD at age 7 experience persisting functional impairments across domains at age 10. The predictors identified at age 7 present potential targets for intervention to ameliorate impairments

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Pilot and Feasibility Studies. 2020;6.

PEDIATRIC TUINA FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) SYMPTOMS IN PRESCHOOL CHILDREN: STUDY PROTOCOL FOR A PILOT RANDOMIZED CONTROLLED TRIAL.

Chen SC, Yu J, Suen LKP, et al .

Background: Medication and behavior therapy are the conventional treatments for attention deficit hyperactivity disorder (ADHD), but they have limitations for preschool children. Evidence suggests that pediatric tuina, which is a modality of traditional Chinese medicine, might have beneficial effects on this condition.

Objective: To assess the feasibility of conducting an RCT in terms of recruitment, use, and acceptability of the parent-administered pediatric tuina for ADHD symptoms in preschoolers.

Methods: It is a single-center, two-arm, parallel, open-label, pilot randomized controlled trial (RCT). Sixty children with pre-specified ADHD symptoms (hyperactivity, anxiety, and sleep disturbance) together with one of their parents will be recruited and randomized into two groups at a 1:1 ratio. Parents in the parent-administered tuina group (intervention group, n = 30) will attend an online training program to learn pediatric tuina skills for ADHD symptoms and conduct this treatment on their children at home. Parents in the parent-child interaction group (comparison group, n = 30) will attend an online training about progressive muscle relaxation exercise and do this exercise with their children at home. Additional teaching materials will be provided to the participants in both groups. Both interventions should be carried out every other day during a 2-month treatment period, with each time around 20 min. Assessment will be performed at baseline, week 4, and week 8. The primary outcome measure is the Swanson, Nolan, and Pelham parent scale; the secondary outcomes include preschool anxiety scale, children's sleep habits questionnaire, and parental stress scale. A process evaluation embedded within the outcome evaluation will be performed. Differences in the scale scores and test parameters between groups will be examined using a linear mixed-effects model. Qualitative data will be analyzed using thematic content analysis, facilitated by QSR NVivo.

Discussion: This study will provide evidence on the acceptability and feasibility of pediatric tuina for ADHD in preschool children. The process evaluation will help to better understand the facilitators and barriers of the intervention functioning.

Trial registration: The study was registered at ClinicalTrials.gov (Identifier: NCT04237259) on 14 February 2020.

Protocol version: 2; date, 23 June 2020

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PLoS ONE. 2020;15.

DISORDER-SPECIFIC BRAIN VOLUMETRIC ABNORMALITIES IN ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER RELATIVE TO AUTISM SPECTRUM DISORDER.

Saenz A.A., Van Schuerbeek P, Baijot S, et al.

The overlap/distinctiveness between Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) has been increasingly investigated in recent years, particularly since the DSM-5 allows the dual diagnosis of ASD and ADHD, but the underlying brain mechanisms remain unclear. Although both disorders are associated with brain volumetric abnormalities, it is necessary to unfold the shared and specific volume abnormalities that could contribute to explain the similarities and differences in the clinical and neurocognitive profiles between ADHD and ASD. In this voxel-based morphometry (VBM) study, regional grey matter volumes (GMV) were compared between 22 children with ADHD, 18 children with ASD and 17 typically developing (TD) children aged 8 to 12 years old, controlling for age and total intracranial volume. When compared to TD children or children with ASD, children with ADHD had a larger left precuneus, and a

smaller right thalamus, suggesting that these brain abnormalities are specific to ADHD relative to ASD. Overall, this study contributes to the delineation of disorder-specific structural abnormalities in ADHD and ASD

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PLoS ONE. 2020;15.

ATTENTION DEFICIT HYPERACTIVITY DISORDER AND EDUCATIONAL LEVEL IN ADOLESCENT AND ADULT INDIVIDUALS AFTER ANESTHESIA AND ABDOMINAL SURGERY DURING INFANCY.

Håkanson CA, Fredriksson F, Engstrand Lilja H.

Aim Several studies in animal models have found that exposure to anesthetics in early life can cause cognitive dysfunction. Human studies show conflicting results and studies of cognitive function after anesthesia and neonatal surgery are scarce. The aim of this study was to investigate whether exposure to anesthesia and abdominal surgery during infancy was associated with cognitive dysfunction from the perspective of educational level, disposable income and attention deficit hyperactivity disorders (ADHD) in adolescent and adult individuals.

Methods A cohort study with patients born 1976 to 2002 that underwent abdominal surgery during infancy at a pediatric surgical center were matched by age, sex, and gestational age to ten randomly selected individuals from the Swedish Medical Birth Register. Individuals with chromosomal aberrations were excluded. Data on highest level of education and annual disposable income were attained from Statistics Sweden and the diagnosis of ADHD were retrieved from the Swedish National Patient Register.

Results 485 individuals and 4835 controls were included. Median gestational age was 38 weeks (24-44) and median age at surgery was seven days (0-365). Three hundred sixty-six individuals (70.0%) underwent surgery during the neonatal period (< 44 gestational weeks). Median operating time was 80 minutes (10-430). The mean age at follow-up was 28 years. Fisher's exact test for highest level of education for the exposed and unexposed groups were respectively: University 35% and 33%, upper secondary 44% and 47%, compulsory 21% and 20% (p = 0.6718). The median disposable income was 177.7 versus 180.9 TSEK respectively (p = 0.7532). Exposed individuals had a prevalence of ADHD of 5.2% and unexposed 4.4% (p = 0.4191).

Conclusions This study shows that exposure to anesthesia and abdominal surgery during infancy is not associated with cognitive dysfunction from the perspective of educational level, disposable income and ADHD in adolescent and adult individuals. Further studies in larger cohorts at earlier gestational ages are needed to verify these findings

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Psychiatr Q. 2020.

HELPING CLINICIANS TO DETECT ODD IN CHILDREN WITH ADHD IN CLINICAL SETTINGS.

Tahillio-Ƒlu A, Dogan N, Ercan ES, et al.

The objectives of this study were to provide a basic tool for pediatricians or other physicians to suspect and detect ODD in children with ADHD and to distinguish the symptomatic profile of ODD from ADHD. 101 subjects with ADHD, 83 with both ADHD and ODD and 342 controls aged 8 to 15 years were included in the study. A semi-structured interview was performed for evaluation of psychiatric diagnoses. Both parents and teachers completed DSM-IV Disruptive Behavior Disorders Rating Scale. We found differences among all three diagnostic subsamples in two-by-two analyses for all dimensions (Inattention, Hyperactivity/Impulsivity and ODD) both according to parent and teacher reports (p < 0.03 for all analyses). Based on parental ODD scores, ROC Curve analyses between only ADHD and ADHD+ODD groups showed that AUC was equal 0.80 (95%CI = 0.73-0.86) and the best cutoff point for ODD diagnosis in the ADHD subjects was 0.68. This study demonstrates the presence of a basic tool for detection and suspicion of ODD in children with ADHD for primary care clinicians or pediatricians in clinical settings. Findings also indicate that patients with ODD

and ADHD have more severe inattention, hyperactivity/impulsivity and oppositional symptoms than those with only ADHD have

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Psychiatry Res. 2020;294.

THIOLS AND CERULOPLASMIN LEVELS IN SERUM OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CROSS-SECTIONAL STUDY.

Ogutlu H, et al.

Attention deficit hyperactivity disorder (ADHD) is a childhood onset disorder with well-known findings that include impulsivity, hyperactivity, and inattention. This study aims to explore the relationship between the levels of ceruloplasmin, native thiol, total thiol, and disulfide and ADHD by comparing case and control groups. The study case group comprised 50 children aged 6-16 years who had been diagnosed with ADHD. The control group included 47 healthy children. Clinical interviews were conducted and the Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version Turkish Adaptation and the Conners Parent Rating Scale were administered. Additionally, blood samples were taken and native thiol, total thiol, disulfide, and ceruloplasmin levels measured. In the ADHD group, the mean native thiol, total thiol, and disulfide levels were significantly lower than the control group. There was no significant difference between the ADHD and control groups in ceruloplasmin levels. Total thiol and native thiol levels were inversely correlated with scores on the Conners Inattention and Hyperactivity subscales; total thiol was negatively correlated with the ADHD index. Thiol disulfide homeostasis was impaired in ADHD children and was related to symptom severity. Oxidative stress balance may play a role in ADHD

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Res Dev Disabil. 2021;108.

RELATIONSHIP BETWEEN INTRAINDIVIDUAL AUDITORY AND VISUAL ATTENTION IN CHILDREN WITH ADHD.

Lin HY, Chang WD, Hsieh HC, et al.

Background and aim: Most previous attention-deficit/hyperactivity disorder (ADHD) studies have used only a single sensory modality (usually vision) to investigate attentional problems, although patients with ADHD might display deficits of auditory attention similar to their visual attention. This study explored intraindividual auditory and visual attention in children with and without ADHD to examine the relationship between these two dimensions of attention.

Methods: Attentional performances of 140 children (70 children with ADHD and 70 typically developing peers) were measured through the Test of Variables of Attention (TOVA) in the present study.

Results: For both groups, most attentional indices showed significant differences between the two modalities (d ranging from 0.32 to 0.72). The correlation coefficients of most of the attentional variables in children with ADHD were lower than their typically developing peers. All attentional indices of children with ADHD (ranging from 12.8%ΓÇô55.7%) were much higher than those of their typically developing peers (ranging from 1.4% 8.6%).

Conclusion: These results not only indicate that typically developing children display more consistent attentional performance, but also support the view that children with ADHD may show attention deficiency in one modality but not necessarily in the other

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SAJCH South African Journal of Child Health. 2020;14:115-19.

UNDERSTANDING DAILY PARENTING STRESSES IN CARING FOR CHILDREN WITH AUTISM SPECTRUM DISORDERS.

Simelane AP.

Background. There is a growing body of knowledge related to stress levels in parents of children diagnosed with developmental challenges. However, limited research has focused on the stress levels among parents raising children with ASD in the South African context.

Objectives. To determine the stress levels experienced by parents raising children with ASD and whether experiences differ between mothers and fathers.

Methods. An independent-sample t-test was conducted to understand the differences between mothers and fathers stress levels.

Results. The study found that parents raising children with ASD experience significant stress and that mothers experienced higher parental stress levels than fathers.

Conclusion. The results of this study are pertinent to understanding challenges experienced by parents of children with ASD. Gender-based differences in parenting roles are still experienced. Mothers of children with ASD experienced more stress as measured according to the Parenting Daily Hassle Scale. The results suggest that a qualitative follow-up study is required to understand the nature of and background associated with struggles experienced by mothers

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Seizure. 2020.

COGNITIVE DISORDERS IN EPILEPSY I: CLINICAL EXPERIENCE, REAL-WORLD EVIDENCE AND RECOMMENDATIONS.

Kanner AM, Helmstaedter C, Sadat-Hossieny Z, et al.

This is the first of two narrative reviews on cognitive disorders in epilepsy (companion publication: Cognitive disorders in epilepsy II: Clinical Targets, Indications and Selection of Test Instruments). Its focus is on clinical experience, real-world evidence, and clinical recommendations. Cognitive disorders are a common comorbidity in children and adults with epilepsy. These cognitive disturbances may preceed the onset of seizures and are multifactorial including contributions by pre-existing brain damage, seizures, interictal epileptic discharges, and treatments including medications and surgery. Comorbid cognitive impairments can have a negative impact on the quality of life in people with epilepsy. They are under-identified and frequently not treated. Comorbid psychiatric disorders, such as ADHD can also contribute to a worse cognitive performance and can benefit from pharmacotherapy with CNS stimulants. Likewise, mood disorders cause a subjective perception of poor memory and attention, which can be reversed with antidepressants of the SSRI family. This narrative review discusses these issues from a real-world clinical perspective in children and adults with newly diagnosed and chronic epilepsy. The need for further research to understand and treat these disorders is noted

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Sleep. 2020;43:A342-A343.

OBSTRUCTIVE SLEEP APNEA SEVERITY, SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AND OTHER COMORBID PSYCHIATRIC DISORDERS IN CHILDREN AND ADOLESCENTS: A RETROSPECTIVE DATA ANALYSIS.

Skoulos M, Sedky K, Bennett D.

Introduction: Children and adolescents with obstructive sleep apnea (OSA) are often diagnosed with attention deficit hyperactivity disorder (ADHD). However, the connection between the severity of Apnea/Hypopnea Index (AHI) and ADHD is controversial with research evidence pointing in opposing directions.

Methods: A retrospective study was conducted in a pediatric sleep center at a university hospital setting to investigate the effect between AHI severity, ADHD and/or other comorbid psychiatric disorders. One hundred and thirty-eight participants between the age of 6 and 18 were examined in terms of AHI severity level and their correlation with scores from the Child Behavior Checklist (CBCL) using SPSS program.

Results: A negative correlation between AHI scores and Attention Problems for the entire group of participants was found. Additionally, female adolescents had positive correlations between AHI scores and several affective disorder variables from the CBCL, while male adolescents had negative correlations between AHI levels and several CBCL scores that are typically associated with ADHD and Anxiety disorders.
Conclusion: This study suggests a relationship between OSA severity and psychiatric conditions. However, this relationship can vary depending on age, gender and AHI severity. More research is required to understand this relationship

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Sleep. 2020;43:A334-A335.

ASSOCIATION OF OBSTRUCTIVE SLEEP APNEA WITH INTERNALIZING SYMPTOMS VS. EXTERNALIZING BEHAVIORS IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Puzino K, Calhoun SL, He F, et al.

Introduction: Attention deficit hyperactivity disorder (ADHD) in children has been associated with insomnia, obstructive sleep apnea (OSA), and abnormal periodic limb movements (PLMS). However, there is lack of data examining the contribution of OSA to ADHD-related internalizing symptoms and externalizing behaviors in adolescents.
Methods: We studied the Penn State Child Cohort, a random general population sample of 700 children (8.7-¦1.7y), of whom 421 were followed-up 8.3 years later during adolescence (17.0-¦2.3y, 53.9% male). All adolescents underwent a 9-hour PSG, clinical history and physical examination. ADHD was ascertained by a parent- or self-report of having been diagnosed with ADHD. OSA was defined as an apnea hypopnea index (AHI) of 2 events per hour of sleep, while a periodic limb movement index (PLMI) 5 events per hour of sleep was indicative of PLMS. Controls, OSAalone, ADHD-alone and ADHD+OSA were identified. The Child or Adult Behavior Checklist were used to ascertain internalizing and externalizing behaviors. Multivariable-adjusted models controlled for sex, race, age, and body mass index (BMI) percentile.
Results: As compared to controls, adolescents with ADHD-alone or ADHD+OSA had significantly greater externalizing behaviors ($p<0.001$), inattention ($p<0.001$) and thought problems ($p<0.001$). While adolescents with ADHD-alone had higher internalizing symptoms ($p=0.021$), specifically withdrawn-depression ($p<0.01$), adolescents with ADHD+OSA had more somatic problems than controls ($p=0.048$). There were no statistically significant differences in behavioral outcomes between controls and adolescents with OSA-alone or between adolescents with ADHD-alone and ADHD+OSA.
Conclusion: Adolescents with comorbid ADHD and OSA do not present with worse behavioral outcomes than those with ADHD alone. Future studies should examine whether the progression of these adolescents into young adulthood differs in terms of their behavioral outcomes and development of mental health disorders

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Sleep. 2020;43:A363-A364.

THE ASSOCIATION BETWEEN SLEEP AND SUSTAINED ATTENTION DIFFERS IN CHILDREN VS. ADOLESCENTS WITH ADHD.

Gagnon K, Theoret R, Rudd E, et al.

Introduction: Sleep disturbance in children with attention-deficit/ hyperactivity disorder (ADHD) is frequent, and lead to shorter sleep duration which has been associated with lower performance on sustained attention tasks. However, no study has investigated this association in adolescents with ADHD. We sought to explore whether the association between sleep and sustained attention performance of children with ADHD is similar in adolescents with ADHD given that sleep patterns are different.
Methods: Parents of 32 children (mean age = 8.0; SD = 1.3) and 10 adolescents (mean = 15.2; SD = 1.3) with ADHD completed a developmental questionnaire including sleep questions. Children and adolescents were medication free and underwent a comprehensive neuropsychological evaluation. Three sleep variables were extracted from the questionnaire, namely the duration of the sleep period during week nights and weekends as well as the difference between the two (weekend shift). The Continuous Performance Test was

used to measure sustained attention (omission, commission, hit reaction time). Pearson correlations between sleep variables and sustained attention measures were calculated.
Results: Children showed a positive correlation between hit reaction time and the duration of the sleep period during week nights (r = 0.37; p =0.04), weekends (r = 0.51; p = 0.004) and the weekend shift (r = 0.37; p =0.04). No significant correlations were found in the adolescent group.
Conclusion: The fact that no significant associations were found in the adolescent group suggest an improvement of the arousal system through brain development in ADHD, or that other mechanisms could be involved in the etiology of ADHD in adolescents

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Sleep. 2020;43:A367.

CLINICAL CHARACTERISTICS OF CHILDREN WITH SLEEP PROBLEMS AND COMORBID PSYCHIATRIC DISORDERS.

McIntyre E, Oles SK, Walsh K, et al.

Introduction: Anxiety and Attention Deficit Hyperactive Disorder (ADHD) are common psychiatric comorbidities in children with sleep disorders. It is known that comorbid psychiatric disorders increase the risk of sleep problems. However, no study has compared the clinical characteristics of children presenting with sleep problems and various common psychiatric disorders.
Methods: Retrospective chart review of all children presenting to the sleep clinic for sleep problems between March 2016 to June 2017 was performed. Demographics, sleep intake patient questionnaires, polysomnograms and ICD-9/10 codes for comorbidities and sleep diagnoses were collected. In children with diagnoses of anxiety (ICD-9 300/ICD-10 F41) and ADHD (ICD-9 314/ICD- 10 F90), demographics, presenting symptoms, Epworth sleepiness scores and prevalence of sleep comorbidities were compared. T-test (continuous) and Chi Square (categorical) were used. Unadjusted odds ratio was calculated for presenting symptoms and sleep comorbidities. P value of <0.05 was considered significant.
Results: 250 (F=145, 58%) children were evaluated. 71.2% children were diagnosed with anxiety and 28.8% diagnosed with ADHD. Mean age at presentation was 8.53 -¦ 4.2 years. Age, gender and race of children presenting with sleep problems and comorbid anxiety/ ADHD were statistically similar. Children with anxiety spent less time in stage N3 sleep (25.2% -¦ 9.1 versus 28.6% -¦ 9.2) and had lower arousal indices (7.19 -¦ 3.8 versus 8.86 -¦ 5.5) compared to children with ADHD. Children with anxiety were more likely to present with chief complaint of feeling tired or sleepy during the day (OR:2.38, 1.32-4.37) and were more likely to have a diagnosis of hypersomnia (OR: 11.67, 3.19-42.75) versus children with ADHD.
Conclusion: Children with psychiatric comorbidities have distinct polysomnographic characteristics. Children with anxiety are more likely to present with daytime sleepiness and have a significantly higher prevalence of hypersomnia compared to children with ADHD

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Sleep. 2020;43:A124.

NREM SLEEP EEG IN TYPICALLY DEVELOPING AND DRUG-NA+»VE ADHD ADOLESCENTS: DATA FROM A LONGITUDINAL STUDY.

Basishvili T, Eliozishvili M, Oniani T, et al.

Introduction: Structural MRI studies suggest delayed brain maturation in children with attention deficit hyperactivity disorder (ADHD). The steep adolescent decline in sleep slow wave EEG activity provides an opportunity to investigate brain electrophysiological evidence for this maturational delay. Most ADHD sleep EEG studies have been cross-sectional. Here we present data from an ongoing longitudinal study of the maturational trajectories of sleep EEG in drug-naïve ADHD and typically developing adolescents.
Methods: Nine children diagnosed with ADHD (combined subtype, DSM-V criteria, mean age 12.39-¦0.61 years), and nine typically developing controls (12.07-¦0.35 years) were recruited. Subjects underwent an adaptation night and all night polysomnography twice yearly at the Laboratory. Sleep EEG was analyzed using fast Fourier transform. NREM delta and theta EEG activity were compared across first two recordings.

Results: Group effects (ADHD vs. control) on all night delta and theta energy, and delta power were not significant (p>0.2 for all). All night theta power was lower (p=0.035) for the ADHD group, and all night NREM sleep duration trended (p=0.060) toward being lower for the ADHD group. Controlling for sleep duration differences by examining only the first 5 h of NREM sleep showed no group effect on delta power (p=0.77) and a trend toward lower theta power (p=0.057) for the ADHD group.
Conclusion: At age 12 to 13 years, NREM sleep delta EEG did not differ between ADHD and control subjects. Theta power, which declines at a younger age than delta, was lower in control subjects. The two recordings thus far differ only by 6 months. The entire study will provide 5 semiannual recordings and allow us to determine if the higher theta power in the ADHD group will hold and if delta power will be greater as well, and thus provide electrophysiological support for the delayed brain maturation suggested by MRI findings

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Sleep Biol Rhythms. 2020.
EFFECTS OF STIMULANT TREATMENT ON SLEEP IN ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).
Sanabra M, et al.
The main objective of this study is to assess the prevalence of sleep disorders in treatment-na+»ve children and adolescents with ADHD compared with healthy controls matched for age and gender; and, at the same time, to determine whether stimulant medication (methylphenidate) affects sleep in the same group of children and adolescents with ADHD (na+»ve) after a 3-month treatment. A total of 120 children and adolescents (60 newly diagnosed with ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV), and 60 gender- and age-matched controls) were evaluated through objective (actigraphy) and subjective (sleep diary) measures. Later, of those 60 newly diagnosed with ADHD, 30 started pharmacological treatment with methylphenidate with a mean daily dose of 0.58-ámg/kg. No significant differences in both measures within the ADHD group after following the 3-month pharmacological treatment with methylphenidate were found. There were neither any significant differences in sleep parameters through objective measures between the medication-na+»ve ADHD group and the control group, while significant differences were found through sleep diary (registered by parents) in latency and efficiency (p = < 0.05). These findings suggest that patients receiving a mean daily dose of 0.58-ámg/kg of methylphenidate for 3-ámonths did not experience sleep disturbances, based on objective (actigraphy) and subjective data. In addition, sleep problems in ADHD subjects may be overestimated by parents due to ADHD symptomatology

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Soc Psychiatry Psychiatr Epidemiol. 2020 Nov;55:1449-56.
DIFFERENCES IN PSYCHIATRIC CARE UTILISATION AMONG UNACCOMPANIED REFUGEE MINORS, ACCOMPANIED MIGRANT MINORS, AND SWEDISH-BORN MINORS.
Axelsson L, et al.
PURPOSE: To better understand underutilisation of psychiatric care among migrant children, we compared utilisation of psychiatric care among unaccompanied refugee minors and accompanied migrant minors, with Swedish-born minors.
METHODS: Using a large longitudinal database of linked national registers, we established a retrospective cohort of 1,328,397 people born 1984-1988 comparing minors born in Sweden to 2 Swedish-born parents (95.4%) to minors who had been arriving in Sweden between 2002 and 2011 with a permanent resident permit and were either unaccompanied refugee minors (0.4%), or accompanied migrant minors (4.0%). The outcome measures were different measures of psychiatric care including in- and outpatient care, and prescribed psychotropic medication.
RESULT: Compared with the Swedish-born minors the unaccompanied refugee minors had a higher likelihood of utilisation of all psychiatric care except ADHD medication. However, compared with

accompanied migrant minors, the Swedish-born minors had a higher likelihood of having utilised psychiatric care.
CONCLUSION: Our study shows that during the first years of living in Sweden, there seems to be fewer barriers to psychiatric care for unaccompanied refugee minors compared to the accompanied migrant minors. There are a number of possible reasons for this including stronger ties with the Swedish society

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Systematic Reviews in Pharmacy. 2020;11:618-26.
EFFECTIVENESS OF SMART BRAIN EXERCISE AND LOVING TOUCH THERAPY ON BEHAVIOR AMONG CHILDREN WITH ATTENTION DEFICIT HYPERACTIVE DISORDER (ADHD).
Sutarmi, Kistimbar S, Nuryanti E.
Background. The prevalence of ADHD in the world is estimated to be 3 - 10% among school-age children, and the number tends to increase annually. The number of ADHD in Indonesia is around 16.3% (3.5 million) of the total population. A comprehensive and integrative measure in addressing ADHD is needed, as well as education and communication.
Objective. This study aimed to determine the effectiveness of Smart Brain Exercise (SBE) and Loving Touch Therapy (LTT), as well as the combination of both (LTT & SBE) on behavior changes among children with ADHD.
Methods. This study was a true experimental study with pretest and post-test design. A total of 35 respondents were randomly selected based on class allocation, divided into four groups, including a control group. Behavior changes were assessed before and after intervention with the SNAP IV ADHD Score checklist; then, the data were analyzed using the Wilcoxon Test.
Results: The results of this study indicated that the intervention of SBE, LTT and the combination of both had a significant effect on improving ADHD behavior when compared to the control group. The combination of SBE and LTT intervention showed different effects on attentiveness behavior (p-value = 0.01).
Conclusion: It can be concluded that the SBE and LTT interventions are effective in changing the behavior of children with ADHD

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The American Journal of Psychiatry. 2020 Sep;177:855-66.
FROM RARE COPY NUMBER VARIANTS TO BIOLOGICAL PROCESSES IN ADHD.
Harich B, van der Voet M, Klein M, et al.
Objective: Attention deficit hyperactivity disorder (ADHD) is a highly heritable psychiatric disorder. The objective of this study was to define ADHD-associated candidate genes and their associated molecular modules and biological themes, based on the analysis of rare genetic variants.
Methods: The authors combined data from 11 published copy number variation studies in 6,176 individuals with ADHD and 25,026 control subjects and prioritized genes by applying an integrative strategy based on criteria including recurrence in individuals with ADHD, absence in control subjects, complete coverage in copy number gains, and presence in the minimal region common to overlapping copy number variants (CNVs), as well as on protein-protein interactions and information from cross-species genotype-phenotype annotation.
Results: The authors localized 2,241 eligible genes in the 1,532 reported CNVs, of which they classified 432 as high-priority ADHD candidate genes. The high-priority ADHD candidate genes were significantly coexpressed in the brain. A network of 66 genes was supported by ADHD-relevant phenotypes in the cross-species-database. Four significantly interconnected protein modules were found among the high-priority ADHD genes. A total of 26 genes were observed across all applied bioinformatic methods. Lookup in the latest genome-wide association study for ADHD showed that among those 26 genes, POLR3C and RBFOX1 were also supported by common genetic variants.
Conclusions: Integration of a stringent filtering procedure in CNV studies with suitable bioinformatics approaches can identify ADHD candidate genes at increased levels of credibility. The authors' analytic

pipeline provides additional insight into the molecular mechanisms underlying ADHD and allows prioritization of genes for functional validation in validated model organisms

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J Genet Psychol. 2020 Sep;181:391-404.

BEHAVIORS OF ADHD AND PEER RELATIONSHIP DIFFICULTIES IN CHINESE AND AMERICAN YOUTHS: ROLE OF CO-OCCURRING BEHAVIORS OF DEPRESSION AND ANXIETY.

Xing Tan T, Teng Y.

The co-occurrence of behaviors of attention-deficit/hyperactivity disorder (ADHD) with behaviors of anxiety or behaviors of depression is the norm, but little is known on how the co-occurrence accounted for youths' peer relations. The authors report results on difficult peer relations in relation to behaviors of ADHD, co-occurring behaviors of depression, and behaviors of anxiety from three studies on 862 youths in China and in the United States. Study 1 included 313 ethnically and socioeconomically diverse American youths; Study 2 included 250 youths who were adopted out of Chinese orphanages by American parents; and Study 3 included 299 youths from Beijing, China. Data on difficult peer relations and behaviors of ADHD, depression, and anxiety were collected with the third edition of Behavior Assessment System for Children-Self Report of Personality. In all three studies, each type of problems alone significantly predicted difficult peer relations, but behaviors of ADHD were not significant when co-occurring behaviors of depression or co-occurring behaviors of anxiety were considered. Despite that the youths in our study had different cultural and personal backgrounds, there was no evidence that behaviors of ADHD were detrimental to youths' peer relations when behaviors of depression or anxiety were considered. Implications for intervention were discussed

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Toxics. 2020;8:1-12.

PHTHALATES, PARA-HYDROXYBENZOIC ACIDS, BISPHENOL-A, AND GONADAL HORMONES' EFFECTS ON SUSCEPTIBILITY TO ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Tsai CS, Chou WJ, Lee SY, et al.

This study aimed to examine whether endocrine-disrupting chemicals (EDCs), such as phthalates, para-hydroxybenzoic acids, and bisphenol-A (BPA), affect gonadal hormones and further link to the susceptibility to attention-deficit/hyperactivity disorder (ADHD). We recruited 98 boys with ADHD, 32 girls with ADHD, 42 boys without ADHD and any other psychiatric disorders, and 26 girls without ADHD and any other psychiatric disorders. Urine levels of EDCs, including mono-methyl phthalate (MMP), monoethyl phthalate (MEP), mono-n-butyl phthalate (MnBP), monobenzyl phthalate (MBzP), monoethylhexyl phthalate (MEHP), methylparaben (MP), ethylparaben (EP), propylparaben (PP), butylparaben (BP), and bisphenol A (BPA), were examined. Endocrine systems were evaluated by using the serum levels of follicle-stimulating hormone (FSH), luteinizing hormone (LH), testosterone, free testosterone, estradiol, progesterone, sex hormone-binding globulin (SHBG), and prolactin. We found that boys with ADHD had higher levels of MnBP and EP than control boys. There were no significant differences regarding EDCs between the females with ADHD and control groups. No significant differences in testosterone, free testosterone, FSH, LH, estradiol, progesterone, or SHBG were found between the ADHD group and controls among either boys or girls. Among boys with ADHD, urine MBzP and MEHP levels were positively correlated with serum testosterone levels. Among girls, urine MEP levels were positively correlated with serum LH, testosterone, and free testosterone levels. The findings suggest that the possibility of an adverse impact of EDCs on gonadal hormones and neurodevelopment may exist. However, the results could be subject to potential selection bias, and the findings in this study should be interpreted with caution

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Transl Psychiatry. 2020;10.

EMOTIONAL FACE PROCESSING ACROSS NEURODEVELOPMENTAL DISORDERS: A DYNAMIC FACES STUDY IN CHILDREN WITH AUTISM SPECTRUM DISORDER, ATTENTION DEFICIT HYPERACTIVITY DISORDER AND OBSESSIVE-COMPULSIVE DISORDER.

Vandewouw MM, Choi EJ, Hammill C, et al.

Autism spectrum disorder (ASD) is classically associated with poor face processing skills, yet evidence suggests that those with obsessive-compulsive disorder (OCD) and attention deficit hyperactivity disorder (ADHD) also have difficulties understanding emotions. We determined the neural underpinnings of dynamic emotional face processing across these three clinical paediatric groups, including developmental trajectories, compared with typically developing (TD) controls. We studied 279 children, 5ΓÇô19 years of age but 57 were excluded due to excessive motion in fMRI, leaving 222: 87 ASD, 44 ADHD, 42 OCD and 49 TD. Groups were sex- and age-matched. Dynamic faces (happy, angry) and dynamic flowers were presented in 18 pseudo-randomized blocks while fMRI data were collected with a 3T MRI. Group-by-age interactions and group difference contrasts were analysed for the faces vs. flowers and between happy and angry faces. TD children demonstrated different activity patterns across the four contrasts; these patterns were more limited and distinct for the NDDs. Processing happy and angry faces compared to flowers yielded similar activation in occipital regions in the NDDs compared to TDs. Processing happy compared to angry faces showed an age by group interaction in the superior frontal gyrus, increasing with age for ASD and OCD, decreasing for TDs. Children with ASD, ADHD and OCD differentiated less between dynamic faces and dynamic flowers, with most of the effects seen in the occipital and temporal regions, suggesting that emotional difficulties shared in NDDs may be partly attributed to shared atypical visual information processing

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Transl Psychiatry. 2020;10.

ASSOCIATION BETWEEN DNA METHYLATION AND ADHD SYMPTOMS FROM BIRTH TO SCHOOL AGE: A PROSPECTIVE META-ANALYSIS.

Neumann A, Walton E, Alemany S, et al.

Attention-deficit and hyperactivity disorder (ADHD) is a common childhood disorder with a substantial genetic component. However, the extent to which epigenetic mechanisms play a role in the etiology of the disorder is unknown. We performed epigenome-wide association studies (EWAS) within the Pregnancy And Childhood Epigenetics (PACE) Consortium to identify DNA methylation sites associated with ADHD symptoms at two methylation assessment periods: birth and school age. We examined associations of both DNA methylation in cord blood with repeatedly assessed ADHD symptoms (age 4ΓÇô15 years) in 2477 children from 5 cohorts and of DNA methylation at school age with concurrent ADHD symptoms (age 7ΓÇô11 years) in 2374 children from 9 cohorts, with 3 cohorts participating at both timepoints. CpGs identified with nominal significance ($p < 0.05$) in either of the EWAS were correlated between timepoints (ü = 0.30), suggesting overlap in associations; however, top signals were very different. At birth, we identified nine CpGs that predicted later ADHD symptoms ($p < 1$ +ù 10-7), including ERC2 and CREB5. Peripheral blood DNA methylation at one of these CpGs (cg01271805 in the promoter region of ERC2, which regulates neurotransmitter release) was previously associated with brain methylation. Another (cg25520701) lies within the gene body of CREB5, which previously was associated with neurite outgrowth and an ADHD diagnosis. In contrast, at school age, no CpGs were associated with ADHD with $p < 1$ +ù 10-7. In conclusion, we found evidence in this study that DNA methylation at birth is associated with ADHD. Future studies are needed to confirm the utility of methylation variation as biomarker and its involvement in causal pathways

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Transl Psychiatry. 2020;10.

MITOCHONDRIAL DNA HAPLOGROUPS AND RISK OF ATTENTION DEFICIT AND HYPERACTIVITY DISORDER IN EUROPEAN AMERICANS.

Chang X, Liu Y, Mentch F, et al.

Although mitochondrial dysfunction has been implicated in the pathophysiology of attention deficit and hyperactivity disorder ADHD, the role of mitochondrial DNA (mtDNA) has not been extensively investigated. To determine whether mtDNA haplogroups influence risk of ADHD, we performed a case-control study comprising 2076 ADHD cases and 5078 healthy controls, all of whom were European decedents recruited from The Children's Hospital of Philadelphia (CHOP). Associations between eight major European mtDNA Haplogroups and ADHD risk were assessed in three independent European cohorts. Meta-analysis of the three studies indicated that mtDNA haplogroups K (odds ratio = 0.69, P = 2.24 +ù 10-4, Pcorrected = 1.79 +ù 10-3) and U (odds ratio = 0.77, P = 8.88 +ù 10-4, Pcorrected = 7.11 +ù 10-3) were significantly associated with reduced risk of ADHD. In contrast, haplogroup HHV* (odds ratio = 1.18, P = 2.32 +ù 10-3, Pcorrected = 0.019) was significantly associated with increased risk of ADHD. Our results provide novel insight into the genetic basis of ADHD, implicating mitochondrial mechanisms in the pathophysiology of this relatively common psychiatric disorder

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Z Kinder- Jugendpsychiatr Psychother. 2020;48:425-28.

TRANSITION PSYCHIATRY: ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Banaschewski T, Roth-Sackenheim C, Berg G, et al.

Attention deficit/hyperactivity disorder affects 5 % of all children and adolescents and 2-3 % of all adults. It is thus one of the most frequent neurodevelopmental disorders, frequently associated with comorbid disorders and multiple functional impairments. Administrative data indicate that many patients with ADHD are at a great risk for treatment discontinuation during the transition to adulthood despite persistent symptomatology and functional impairment. The article addresses potential consequences for optimizing ADHD treatment during this transition

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Restless Legs Syndrome in Children and Adolescents

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KEYWORDS

• Restless legs syndrome • Anxiety • Depression • ADHD • ODD • Sleep

KEY POINTS

- Restless legs syndrome (RLS) is a common and often underdiagnosed sleep disorder in children and adolescents.
- Children with psychiatric conditions may be at higher risk of RLS, especially children with attention-deficit/hyperactivity disorder.
- Many psychotropic medications, including antidepressants, sedating antihistamines, and antipsychotics, are associated with increased RLS or restless sleep.
- Both nonpharmacologic and pharmacologic therapies can be used in children with RLS.

RESTLESS LEGS SYNDROME

Restless legs syndrome (RLS), or Willis-Ekbom disease, is a neurologic disorder initially described by Sir Thomas Willis in 1685 and further defined by Ekbom in 1944; however, pediatric RLS was not described until 1994. Diagnostic criteria for pediatric-onset RLS, introduced in 2003 and updated in 2013, outline specific considerations for diagnosis in children and allow the use of age-related descriptive terms and words.[1] The recency of its recognition and limited education in sleep medicine by most clinicians have resulted in RLS still generally overlooked. This is true particularly in children who usually present with complaints related to bedtime refusal or insomnia, rather than with classic RLS symptoms. Additionally, children with RLS have been found to have an increased risk of comorbidities, in particular attention-deficit/hyperactivity disorder (ADHD). This article discusses clinical features of RLS, its treatment, and the association between RLS and ADHD and other comorbid psychiatric conditions.

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CLINICAL FEATURES

RLS is a clinical diagnosis and polysomnogram is not required for the diagnosis, although it can be useful in specific situations. The primary feature of RLS is the urge to move the legs, with or without accompanying leg sensations. If sensations are present, they invariably involve the legs, although the arms and other body parts sometimes are affected. Symptoms occur in the evening, when patients are settling for sleep and are relieved by movement. The discomfort associated with RLS can engender bedtime refusal and delayed sleep onset, which might be mistaken for behavioral insomnia in children.

RLS is relatively common in pediatrics, with an estimated prevalence of 2% to 4% in school-aged children and adolescents.[2] It often is misdiagnosed and generally is ignored by most pediatricians and general practitioners because of the mild and intermittent nature of the symptoms at younger ages or the inability of young children to characterize the sensations or discomfort in the legs. RLS is, however, usually progressive and can cause significant functional impairment.

A majority of children with RLS also report daytime leg discomfort. This differs from the typical increase during the evening or at night of adults and may be linked to the number of hours children spend sitting during the school day.[3]

The *International Classification of Sleep Disorders – Third Edition* (*ICSD-3*), states that "for children, the description of these symptoms should be in the child's own words." The interview questions should be phrased using words developmentally appropriate for the child. Language and cognitive development determine the applicability of the RLS diagnostic criteria, rather than age. As in adults, a significant impact on sleep, mood, cognition, and function is found. Impairment is manifest, however, more often in behavioral and educational domains.

Differentiating pediatric RLS from other conditions, or mimics, can be complicated.[4] Some of the common mimics of pediatric RLS are positional discomfort, sore leg muscles, ligament sprain/tendon strain, positional ischemia (numbness), dermatitis, bruises, growing pains, leg cramps, arthritis, peripheral neuropathy, radiculopathy, myelopathy, myopathy, fibromyalgia, and sickle cell disease.[5]

Patient Evaluation Overview

RLS is difficult to diagnose in children. The formal evaluation of children with RLS starts with a comprehensive history and physical examination. The sleep history must include a thorough bedtime routine, with particular attention to symptoms that occur while trying to fall asleep. Sensory symptoms are difficult for children to explain, so simple descriptions, such as a funny feeling, pain, hurting, tickling, bugs, spiders, ants, and goose bumps in the legs, can be clues alerting the clinician. Children may draw pins, needles, tiny sand particles, bugs, or a saw over their legs when asked to depict their symptoms. Walters and colleagues[6] initially described the presenting symptoms of children with RLS, which included, similarly to adults, nocturnal predominance of leg paresthesia or discomfort, and relief with movement. In younger children, other symptoms, such as delayed sleep onset, bedtime struggles, and parental concern of restlessness, were included as symptoms of pediatric RLS. In qualitative interviews, children expressed their symptoms as "have to move," "need to kick," "hurts," "bugs crawling," "weird feelings," and "tingling."[7] In this study, 48% of children expressed having similar feelings in their arms in addition to their legs, and 67% described experiencing the same symptoms during the day.[7] RLS-related pain in children typically occurs from both knees down and especially involves the calves, although symmetric or asymmetric thigh pain also may occur.

Family history is of utmost importance. Most early-onset cases (by definition with onset before age 35) are familial; approximately 40% to 92% of children with RLS have affected family members.[8] Several medical conditions, however, are associated with RLS symptoms. Causes of secondary RLS include peripheral neuropathy and uremia. In patients who are thought to have secondary RLS, screening for renal disease, thyroid dysfunction, vitamin B_{12}, and folic acid deficiency (peripheral neuropathy) should be considered.[9]

Periodic limb movements (PLMs) occur in approximately two-thirds of children with RLS and are considered an objective motor finding in RLS and supportive of an RLS diagnosis.[10] PLMs are brief extremity jerks that can be accompanied by transient arousals from sleep that are identified and measured by polysomnography. Often, a diagnosis of PLM disorder (PLMD) precedes the diagnosis of RLS in children under 6 years of age who do not yet have sufficiently well-developed language skills to describe the sensory component of RLS.[11] For this reason, although a sleep study is not indicated for RLS, a PLM during sleep (PLMS) index greater than 5 per hour in polysomnography could aid in the diagnosis.[6]

Finally, daytime symptoms are important to evaluate RLS. Children present with cognitive and academic difficulties in approximately half of cases and mood changes, irritability, or sadness in 58% of cases.[7]

Differential Diagnoses

Differential diagnoses should include mimics of RLS. Growing pains can occur intermittently in the evening and have a peak prevalence at 4 years to 6 years of age. Growing pains can be confused with RLS, but the urge to move the legs and the relief by movement differentiates RLS.[5] Furthermore, growing pains always are described as painful, whereas childhood RLS is considered painful only in 45% of cases.[12] In painful nocturnal leg cramps, there is no urge to move the legs and they do not necessarily occur in the evening prior to sleep.[13] Skin inspection during physical examination can rule out eczema. Examination and palpation of the legs also can exclude bruises, ligament tear, and tendon or muscle pain.

Offending Medications

Several classes of medications and common drugs can unmask or aggravate RLS, including selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants, metoclopramide, diphenhydramine, nicotine, caffeine, and alcohol.[9] For this reason, treating children with psychiatric disorders and RLS can be tricky. Objectively, it also has been shown that antidepressants or antipsychotics can cause an increase in PLMS, as a proxy for RLS.[14] Commonly used antidepressants, such as venlafaxine,[15] mirtazapine,[16] and tricyclic antidepressants,[17] can lead to an increase in PLMS. By contrast, drugs, such as levetiracetam, perampanel, or gabapentin, reduce PLMS[18,19]; valproic acid or carbamazepine have no effect on PLMS.[20,21] Considering the frequent association between PLMS and RLS in children[22] and the their presence since adolescence,[23,24] the choice of antidepressants for treating pediatric psychiatric disorders should seek to avoid possible drug-induced onset or worsening of PLMS.

PRESENTATION IN CHILDREN WITH PSYCHIATRIC COMORBIDITIES

Children with RLS have a higher incidence of ADHD, oppositional defiant disorder, anxiety disorders, and depression.[25] A retrospective study of 374 children with RLS found that 64% had 1 or more comorbid psychiatric conditions. ADHD was found in 25%, mood disturbances in 29%, and anxiety in 11.5% of children.[26] Work on children

with PLMS by DelRosso and colleagues[14] demonstrated that 21.6% also have a mood disorder/anxiety and 10% have ADHD. Unfortunately, there are scarce data on the link of pediatric depression and anxiety with RLS. The most commonly studied association is the one between ADHD and RLS although the directionality between the 2 conditions is unclear. Therefore, the remainder of this article discusses the link between ADHD and RLS in children.

Additionally, gender differences and possible iatrogenic factors might complicate the issue. A retrospective study showed that RLS was associated with ADHD in boys and mood disorders in girls and that there was a greater number of antidepressants prescribed in the same year of the diagnosis of RLS, possibly indicating a worsening of preexisting pathology by psychotropics.[26]

Both RLS and elevated PLMS are common in children with ADHD.[27] For instance, 93% of children with RLS and ADHD reported sleep problems whereas this concern was seen in only 56% of children without ADHD, even if the high comorbidity may be due to recruitment bias because the clinic at which the study was conducted specializes in ADHD and RLS. A study of 129 children (aged 6–17 years) with PLMS index greater than 5 per hour found that 91% were diagnosed with ADHD.[28] Other studies have shown that 26% to 64% of children with ADHD meet criteria for PLMD. Furthermore, an elevated PLMS index correlates with inattention/hyperactivity scores.[27,29] There is increased morbidity when the 2 conditions co-occur; children with PLMD and ADHD have more enuresis, nightmares, and difficulty initiating sleep than children with PLMD alone. ADHD, RLS, and PLMD have been postulated to result from reduced dopamine activity, potentially related to low iron stores, leading to the suggestion that improving ferritin levels also may improve ADHD symptoms.[27,29]

Pullen and colleagues[26] evaluated 374 children with RLS and found that 25% met criteria for ADHD; 29% had either a transient mood disturbance (eg, adjustment disorder) or a recurrent mood disturbance (ie, major depressive disorder or bipolar disorder); 11.5% had an anxiety disorder; and 11% had behavioral disturbances. Mood disturbances and anxiety disorders were more prevalent in girls and ADHD and behavioral disorders were more prevalent in boys. The study concluded that two-thirds of children with RLS had at least 1 psychiatric comorbidity, with 35% having more than 1. Picchietti and Stevens[25] studied 18 children with RLS and found that 13 had ADHD, 4 had oppositional defiant disorder, and 6 were diagnosed with anxiety and 5 with depression. Three children had both anxiety and depression. In all cases of anxiety and depression, the sleep disturbance occurred before the psychiatric diagnosis but the definite RLS diagnosis was given after the psychiatric condition was diagnosed, illustrating the common delay in RLS diagnosis. Oner and colleagues[30] studied 87 children with ADHD and found that 33% met criteria for RLS, and children with ADHD and RLS had lower ferritin levels than children without RLS. The impact of RLS on psychiatric comorbidities, however, has not been reported. The study also demonstrated that children and adolescents with RLS often present first for psychiatric evaluation rather than for sleep medicine evaluation. This dual relationship suggests both sleep-related symptoms and ADHD should be evaluated simultaneously. **Table 1** summarizes studies showing the increased prevalence of RLS in children with ADHD and the increased prevalence of ADHD symptoms in children with RLS.

TREATMENT

Treating pediatric RLS is important, because the associated sleep disturbances can lead to significant developmental, behavioral, and cardiovascular morbidities as well as impact on family well-being. **Table 2** summarizes the treatment options of RLS in

Table 1
Studies in children with attention-deficit/hyperactivity disorder and restless legs syndrome

Authors, Year of Publication	Method	Age (Mean [SD]), or Range	Sample Size	Findings
Liu et al,[31] 2019	AHQ	14.5 y (1.4 y)	11,831	RLS (OR 1.47; 95% CI, 1.02–2.11) was associated with subsequent symptoms of ADHD.
Castano-De la Mota et al,[32] 2017	SDSC questionnaire	6–18 y	73	RLS prevalence of 6.8% in children with ADHD
Kwon et al,[33] 2014	Questionnaire	10.8 y (2.3 y)	56	Family history of RLS (12.5%); symptoms of RLS in 24 patients (42.9%); probable or definite RLS (7.2%)
Pullen et al,[26] 2011	Diagnostic criteria	0–18 y	374	25% (94/374) of RLS patients met criteria for ADHD
Silvestri et al,[34] 2009	SDSC, Conners, video polysomnography	8.9 y (2.7 y)	45	RLS in 11.9%. IRLS severity scale average 18.6 (SD 8.6)
Picchietti and Stevens,[25] 2008	*DSM-IV, ICSD-3* criteria	0.2–17 y	18	ADHD was diagnosed in 13/18 children with RLS.
Oner et al,[30] 2007	Conners, RLS criteria	9.4 y (2.5 y)	87	33.3% of children with ADHD had RLS. Children with ADHD and RLS had lower ferritin levels.

Abbreviations: AHQ, Adolescent Health Questionnaire; Conners, Conners Parent Rating Scale; *DSM-IV*, *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition); SDSC, Sleep Disturbance Scale for Children.

children with psychiatric comorbidities while **Fig. 1** displays a recommended algorithm for their evaluation and management.

Nonpharmacologic Treatment Options

All children and parents should be educated on elements of sleep hygiene, including consistent bedtime routines, avoidance of electronics at bedtime/evening, and avoidance of caffeinated products. Caffeine consumption can exacerbate symptoms of RLS. Children should avoid not only coffee but also any other substances containing caffeine, including iced tea or chocolates.[35]

Other interventions include leg movements to alleviate the symptoms of RLS. These may include exercise in the afternoon or brief walks a few hours prior to bedtime.

Table 2
Treatment options of restless legs syndrome in children with psychiatric comorbidities

Intervention Modality	Recommendation	Concerning Side Effect
Antidepressant medication assessment	Treat underlying psychiatric condition. Consider using dopaminergic antidepressants (bupropion) when RLS present.	Worsening psychiatric symptoms if changing medications
Other medication assessment	Limit antihistaminic or other medications that can exacerbate RLS when possible.	
Avoid caffeine	Avoid chocolates, tea, coffee.	
Lifestyle modification	Exercise, massage, heating/cooling pads	
If ferritin <50 ng/mL	Oral iron supplementation (1–6 mg/kg/d) to a maximum of 65 mg/d	Constipation, teeth staining
If ferritin >50 ng/mL (off-label)	Clonazepam, 0.1–1 mg, at bedtime Gabapentin, 50–100 mg, at bedtime Clonidine, 0.05–0.1 mg, at bedtime Pramipexole, 0.03–0.25 mg/d	Drowsiness, suicidal ideation Depression, suicidal ideation Hypotension, depression Psychosis, impulse control disorders

Similarly, stretching, rubbing, or massaging the legs may provide relief.[36] Incidentally, some children find relief using cool or heating pads or weighted blankets. Parents can try these interventions one at the time for a few days and keep a sleep diary to assess effectiveness.

Avoiding or discontinuing medications that could aggravate RLS, that is, SSRIs, tricyclic antidepressants, metoclopramide, diphenhydramine, nicotine, caffeine, and alcohol, also may help.[9]

Pharmacologic Treatments

There currently are no Food and Drug Administration (FDA)-approved medications for RLS in children, and clinical guidelines and recommendations are sparse. Furthermore, the International Restless Legs Syndrome Study Group has published guidelines on treatment of RLS using iron supplementation in children, stating that evidence to recommend iron supplementation for children with RLS remains insufficient.[37] Iron supplementation, nevertheless, remains the first-line therapy for children with RLS in clinical care.[9,38]

Iron therapy

Serum ferritin is the best indicator of early iron deficiency . Saturation of peripheral iron stores typically occurs at ferritin levels of 80 ng/mL to 100 ng/mL. Current evidence suggests that achieving and maintaining serum ferritin above 50 ng/mL can be beneficial for RLS, PLMS, and ADHD.[39] The dopaminergic theory of RLS further supports

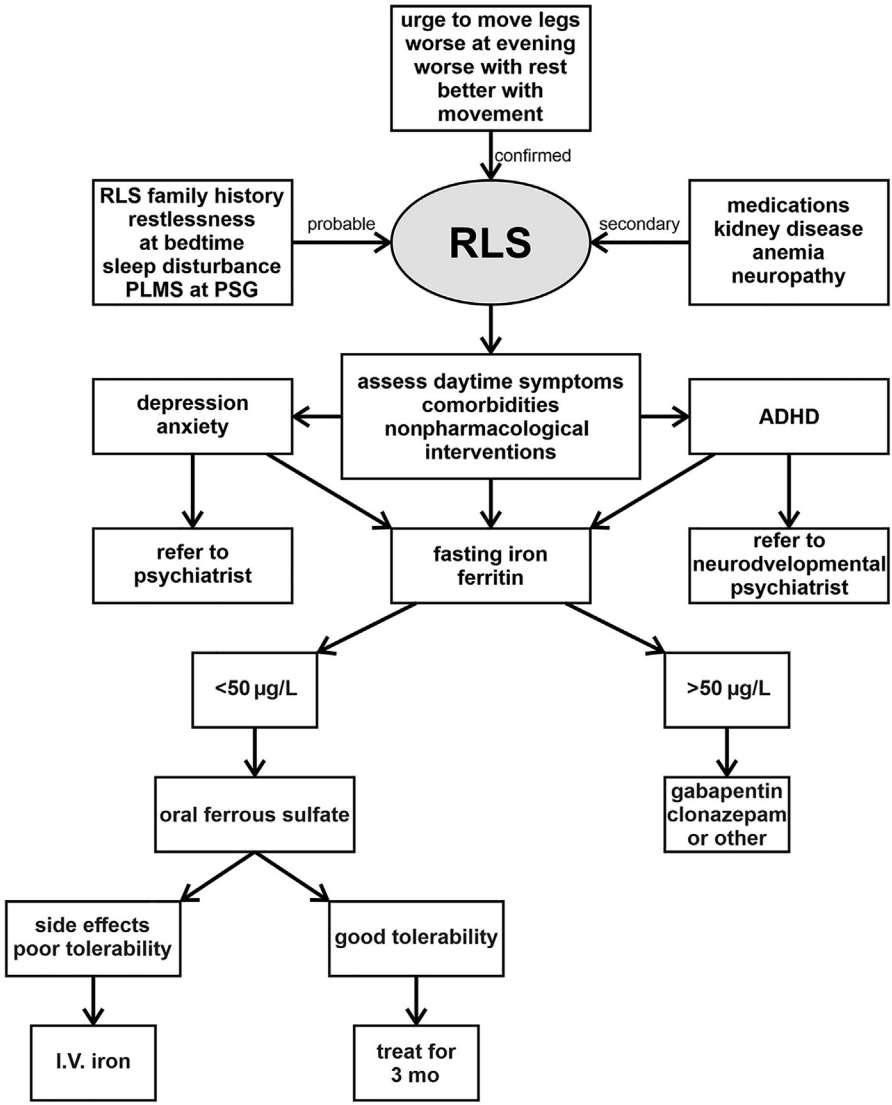

Fig. 1. Recommended algorithm for the evaluation and management of children with RLS and psychiatric comorbidities. I.V., intravenous.

the iron deficiency hypothesis, because iron is fundamental for the biosynthesis of dopamine and is necessary for tyrosine hydroxylation, which is the rate-limiting step for dopamine production.[40] The authors recommend checking fasting iron profile and ferritin levels prior to beginning oral iron supplementation. Iron is offered for patients with ferritin levels below 50 µg/Lng/mL, with dose ranges of 1 mg/kg/d to 6 mg/kg/d of ferrous sulfate at a dose of 50 mg to 65 mg of elemental iron.[9] To enhance absorption, iron ideally should be taken in the morning on an empty stomach with a source of vitamin C. It may take 3 months or more to improve iron levels and to demonstrate improvement of symptoms, based on a handful of studies.[35,41,42] In

addition to improving symptoms, iron therapy also may improve response to psychostimulant drugs,[43,44] an important consideration if correct management of iron status in children with RLS and psychiatric disorders allows the use of a lower antidepressant dose, with a lower probability of adverse effects. The most frequent adverse effects resulting from oral iron administration are constipation, nausea, and unpleasant taste[45]; these can reduce or prevent adherence. Moreover, not all patients respond to oral iron therapy; most responders show an improvement in ferritin levels after 2 months to 3 months of supplementation, with further improvement over time, whereas nonresponders maintain a low ferritin level, despite adherence.[45] When oral iron administration is not successful due to adverse effects or poor absorption, intravenous iron supplementation might be an alternative. Intravenous iron has been shown effective and safe in adults with RLS and some data appear to prove to support its efficacy for pediatric RLS and PLMD patients who do not tolerate or do not respond to oral iron; the most common adverse events reported are difficulty in positioning the intravenous access with risk of extravasation, changes in blood pressure, skin discoloration, and transient hypophosphatemia. A careful selection of candidates is needed because of possible allergic reaction, and caution should be considered in children from families with hemochromatosis, recent infections, or malaria.[46] Although various intravenous iron preparations have been tried in adults (iron dextran, iron gluconate, iron sucrose, ferumoxytol, iron isomaltoside, and ferric carboxymaltose), a single study using iron sucrose 1.2 mg/kg to 6.6 mg/kg, infused over 2 hours in 16 children aged 2 years to 16 years, showed improvement in sleep symptoms in 62.5% of them.[46]

Iron and psychotropic agents

Treatment of pediatric RLS always should include nonpharmacologic interventions, elimination of factors that worsen or precipitate RLS such as elimination of caffeine, and assessment of ferritin levels.[3,47] Because there are no FDA-approved medications for the management of RLS in children, any pharmacologic option used is off-label. When symptoms persist after iron supplementation, combination therapy with a second medication may be considered. In a study of 25 children with RLS and 28 controls, clonazepam (0.1–1 mg) or pramipexole (0.03–0.25 mg) was added to oral iron supplementation in children with persistent symptoms after 2 months.[48] Clonazepam is a long-acting benzodiazepine shown to improve sleep consolidation in patients with RLS albeit without reducing the motor or sensory manifestations of RLS.[49,50] Clonidine (0.05–0.1 mg) is used commonly in children to improve symptoms of insomnia. Clonidine is an α_2-adrenergic agonist that improves sleep onset in children with RLS and has been given in combination with iron supplementation.[51] Gabapentin is used commonly in adults with RLS to improve sleep-onset latency.[52] A small cohort of children treated with gabapentin (50–100 mg at bedtime) for RLS showed resolution of symptoms.[35] Gabapentin also can be combined with iron supplementation in refractory cases. The use of dopaminergic agonists should be restricted to the purview of pediatric sleep specialists. Consideration of side effects, risks, and benefits of each medication needs to be discussed with the family. **Table 3** lists treatment studies on children with ADHD and RLS.

Evaluation of Outcome and Long-Term Recommendations

Children with RLS should be evaluated periodically. If oral iron supplementation is initiated, side effects should be assessed within a couple of weeks. Side effects can be the limiting factor in treatment success for oral iron. Rapid identification of problems, such as bad taste or constipation, can delineate a strategy to address the side effects,

Table 3
Studies with treatment options for children with attention-deficit/hyperactivity disorder and restless legs syndrome

Authors, Year of Publication	Medication, Dose	Age (Mean [SD]) or Range	Sample Size	Conclusions
Baykal and Karakurt,[53] 2017	Atomoxetine, 0.8 mg/kg/d	9 y	1	Resolution of RLS symptoms
England et al,[54] 2011	Carbidopa/Levodopa, 25/100 controlled-release	9.3 (1.3) y	29	Levo-dopa improved RLS symptoms on international RLS severity scale. ADHD symptoms were worse in the non-RLS group and did not improve after treatment (Conners Parent Rating Scale)
Gagliano et al,[18] 2011	Levetiracetam, 10–20 mg/kg/d, up to 50–60 mg/kg/d	5–12 y	7	All showed significant improvement in the international RLS severity scale, quality of sleep, and daytime function. Behavioral symptoms improved although not overall ADHD.
Konofal et al,[55] 2005	Ferrous sulfate, 80 mg Ropinirole, 0.25 mg	6 y	1	Conners Parent Rating Scale improved from 30 to 21 after 3 mo of ferrous sulfate. After ropinirole, Conners Parent Rating Scale, oppositional behavior, attention, and sleep improved.

(*continued on next page*)

Table 3
(continued)

Authors, Year of Publication	Medication, Dose	Age (Mean [SD]) or Range	Sample Size	Conclusions
Walters et al,[39] 2000	L-dopa/carbidopa, CR 75/300–150/600 mg Pergolide, 0.4–1 mg daily	6–14 y	7	PLMS index improved from 72 to 15, the PLMS index decreased from 11.7 to 2.1. RLS symptoms improved. Conners Parent Rating Scale from 15.1 to 6.26. Significant improvement on oppositional defiant disorder scale and on Child Behavior Checklist

such as switching to a more palatable preparation or a sustained-release tablet and increasing fiber and liquid intake, among others. Discussion of alternative treatments should be done early to educate the family on potential risks, side effects, and alternatives to treatment. Studies on natural progression of RLS are lacking but, based on adult studies, a waxing and waning progression, with periods of exacerbation alternating with asymptomatic periods, can be expected. Education is key in identification of symptoms and prompt evaluation.

Treatment success can be assessed clinically by symptom relief. Questionnaires developed for symptom assessment have not been validated in children. If another sleep disorder, such as obstructive sleep apnea, is suspected or if symptoms are not improved, a sleep study may be indicated.

In summary, treatment of RLS should not be delayed in children with comorbid psychiatric conditions and both should be assessed and treated simultaneously to ensure improvement in quality of life and outcomes.

NEW DEVELOPMENTS

Recently, a new disorder has been proposed, restless sleep disorder (RSD).[40] Children with RSD do not have symptoms of RLS or leg movements on polysomnography but present with frequent movements and repositioning during sleep. The parent usually brings a child for evaluation with concerns of restless sleep and daytime symptoms which include, often, hyperactivity, daytime sleepiness, or behavioral problems. The proposed criteria include motor movements, involving large muscle groups, that occur during sleep and that persist all night and occur almost every night. The movements are evident on polysomnography and should be more than 5 per hour and cause clinically significant impairment in an area of functioning.[56] RSD has been shown to have a prevalence of 7.7% in patients referred to sleep centers and also is suspected to be associated with low iron stores in the brain.[57] Further studies are needed to assess the comorbidity of RSD with other neurodevelopmental, psychiatric, or neurologic conditions.

SUMMARY

RLS is a common and often overlooked disorder in children and adolescents. The relationship between RLS, ADHD, and psychiatric comorbidities is complex and bidirectional. Children with RLS have a significantly increased prevalence of symptoms of ADHD, anxiety, depression, and oppositional defiant disorder. But children diagnosed with ADHD also have an increased prevalence of RLS. This association calls for awareness of sleep disorders, in particular RLS, in children with ADHD and psychiatric disorders. Furthermore, commonly used psychotropic medications can exacerbate the symptoms of RLS. Patients with RLS present with difficulty with sleep onset, nocturnal awakenings, and daytime symptoms, such as behavioral problems. These symptoms can be masked by the presence of a comorbid conditions. Children often are referred to psychiatric evaluation before they are suspected of having RLS, and child psychiatrists should become familiar with clinical assessment and iron replacement therapy for RLS. The authors recommend concurrent evaluations, screening, and prompt treatment of RLS in children with ADHD or psychiatric diagnoses. The treatment of RLS improves both nighttime and daytime symptoms. Treatment options include behavioral interventions, iron supplementation, and combination therapy. For refractory cases of RLS, a referral to a pediatric sleep specialist is indicated.

Areas of future research include the impact of RLS treatment on symptoms of depression or anxiety in children and further assessment of RSD in the presence of comorbid ADHD or other psychiatric diagnoses. More studies are needed on pharmacologic treatment of RLS in children.

CLINICS CARE POINTS

- Screening of RLS and sleep disorders is recommended for all children referred for psychiatric evaluation.
- RLS often is associated with ADHD, anxiety, and depression.
- A diagnosis of RLS often is delayed in children with RLS and psychiatric comorbidities.
- Sleep problems, such as difficulty with sleep onset, are common in children with RLS and ADHD.
- Initial evaluation of children with RLS includes a thorough sleep history and physical examination.
- Fasting ferritin and iron profile should be obtained in all children with RLS.
- Iron supplementation is the first-line treatment in children with RLS.
- Nonpharmacologic treatment options include stretching exercises, cool or warm compresses, and weighted blankets.
- Common adverse effects of oral iron can limit adherence to treatment and need to be assessed early to find alternative treatments.
- There currently are no FDA-approved drugs for treating pediatric RLS; gabapentin and clonazepam often are used off-label as second-line treatment options.
- Concurrent evaluation and treatment of RLS and psychiatric comorbidities, especially ADHD, is recommended.

DISCLOSURE

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Impaired Motor Timing in Tourette Syndrome: Results From a Case–Control Study in Children

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Tourette syndrome (TS) is a neurodevelopmental disorder characterized by motor and vocal tics. Co-occurrence of attention-deficit/hyperactivity disorder (ADHD) or obsessive–compulsive disorder (OCD) is very frequent in the pediatric population as well as the presence of an impairment of the executive functions. The aim of our study was to investigate motor timing, that is, the temporal organization of motor behavior, in a pediatric population of Tourette patients. Thirty-seven Tourette patients (divided in 22 "pure" Tourette patients and 15 with ADHD) were compared with 22 healthy age- and gender-matched subjects. All subjects underwent a neuropsychiatric screening and were tested for their planning and decision-making abilities by using a standardized test, such as Tower of London (ToL). Two experimental paradigms were adopted: finger-tapping test (FTT), a free motor tapping task, and synchronization–continuation task. An accuracy index was calculated as measure of ability of synchronization. We found that "pure" TS as well as TS+ADHD showed lower scores in the FTT for the dominant and non-dominant hands than controls. Moreover, in the synchronization and continuation test, we observed an overall lack of accuracy in both TS groups in the continuation phase for 2,000 ms (supra-second interval), interestingly, with opposite direction of accuracy index. Thus, "pure" TS patients were classified as "behind the beat," whereas, TS+ADHD as "ahead of the beat." The performance in the finger tapping was inversely correlated to ToL total scores and execution time, whereas we did not find any correlation with the accuracy index of the synchronization and continuation test. In conclusion, here, we explored motor timing ability in a childhood cohort of Tourette patients, confirming that patients exhibit an impaired temporal control of motor behavior and these findings may be explained by the common underlying neurobiology of TS and motor timing.

Keywords: Tourette syndrome, ADHD, motor timing, synchronization ability, finger tapping, Tower of London

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INTRODUCTION

Tourette syndrome (TS) is a childhood-onset neurodevelopmental movement disorder clinically characterized by the presence of multiple motor tics and one or more phonic/vocal tics that last for more than 1 year (1). The age at onset of TS ranges from 2 to 21 years, and the mean age is 5–7 years, with males suffering more than females in a ratio of 3–4:1 (2). Pure TS patients, referring to

patients with TS without any other comorbid conditions, are relatively uncommon (3); attention-deficit/hyperactivity disorder (ADHD) or obsessive–compulsive disorder (OCD) is commonly associated (4), but other several clinical and subclinical conditions, such as explosive outbursts, conduct problems, anxiety, self-injurious behavior, and depression, could run the clinical course of the disease (5–7). Moreover, cognitive functions, and in particular, executive ones, including inhibition/attention, working memory, planning ability, and problem solving, have been reported to be impaired in TS (8), although with conflicting results (9, 10), probably because it is difficult to distinguish the role of comorbid conditions in this framework.

Time is an intriguing ability of humans and deserves several adaptive and behavioral responses to changing environment (11). Time processing is a multifaceted decoding ability of the brain depending on several factors including time intervals, reproduction of intervals, as well as estimation of a duration. Nevertheless, basic cognitive functions, such as working memory, attention, and decision making, deeply modulate and regulate time coding. Thus, although ultimate neural mechanisms are far to be completely elucidated, theories, widely accepted, on the psychological and anatomical components of interval timing are based on the neurobiological model of an "internal clock" (12), which consists of an internal pacemaker connected *via* a decision mechanism to previously important duration codes held in reference memory. Functional imaging studies in humans and lesional studies in animals pointed out the role of basal ganglia nuclei and cortico-striato-thalamo-cortical (CSTC) circuitry (13), as well as it seems that the model crucially depends on the striatal integration of oscillating cortical activity (14).

Despite its multifactorial and unknown etiology, recent studies suggest that a dysfunction of the CSTC circuits in TS leads to disinhibition and other dysfunctions in executive functioning (15, 16). Noteworthy, basal ganglia connection to the prefrontal cortex could be the neurobiological basis of impaired motor and non-motor inhibitory control, one of the key futures of TS as recently Morand-Bealieu et al. argued in a comprehensive meta-analysis (17). Distortion in motor and perceptual timing is present in many neurological and psychiatric conditions (18–21). Temporal processing has been studied also in movement disorders in both hypokinetic conditions, such as Parkinson's disease (22), as well as hyperkinetic disorders, including Huntington disease, essential tremor, and dystonia (23, 24). Findings clearly suggest that the basal ganglia network is involved in explicit motor and perceptual timing and implicit timing as well. TS has been investigated mainly for perceptual aspects of timing (23, 25, 26), meaning the ability to estimate temporal intervals measured by task of duration discrimination, duration estimation, and duration reproduction (27). Data show a reduction of accuracy on time reproduction tasks for supra-second intervals, with performance variability influenced by dopamine D2 receptor antagonists (23, 28). On the contrary, few studies have been conducted in children with TS elucidating mechanisms of motor timing. Motor timing, referring to the temporal organization of motor behavior, is a pivotal functional domain influencing the efficiency and the correctness to the context of any motor output (29). Recently, motor timing skills were investigated by Martino et al. in an adult cohort (29) and in 2011 by Avanzino et al. in a pediatric cohort (30). Nevertheless, in healthy infants, the existence of a primitive "sense" of time that changes and develops throughout childhood is well known (31), making difficult studying time in children but, likewise, even more appealing.

The ability to suppress tics, as well as to uncouple the premonitory urge sensation and tics, together with the possibility to train this capacity with appropriate techniques, reveals that motor timing plays an underestimated role in TS evaluation and management.

The aim of our study was to investigate motor timing processing in a cohort of children affected by TS with and without comorbidity compared with a healthy group of controls.

MATERIALS AND METHODS

Subjects

Thirty-seven patients with TS diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 criteria were prospectively recruited from the outpatient Movement Disorder Clinic of Bambino Gesù Children's Hospital of Rome. Inclusion criteria were (2) a defined diagnosis of TS, (3) age between 7 and 17 years old, and (4) no other neurological or general comorbidities. All TS patients were drug free from the previous 6 months before the study. Age- and sex-matched 26 healthy controls were enrolled by using a school-based recruitment call. Four of 26 healthy controls were excluded from the analysis because the neuropsychiatric screening resulted positive. The ethnicity of the entire sample was all Caucasian. Among the 37 TS patients, 15 subjects met the criteria of DSM-5 for ADHD; the remaining 22 subjects, on the other hand, had no DSM-5 diagnosis of ADHD. We consequently sub-grouped TS patients in two separate groups: TS+ADHD ($n = 15$) and "pure" TS ($n = 22$).

Procedure

Participants were tested individually in a quiet room in the Movement Disorder Clinic of the Department of Neuroscience; tests administration was performed with clinical feasibility to avoid fatigue, with frequent breaks and chats with the children along the evaluation, in order to make them feel more comfortable and increase the focus on the activities. Each session entirely lasted from 2 to 3 h. For the computer-based tests, we used a 17-inch laptop for the presentation of stimuli and recording the responses by the participants. The LCD screen had a resolution of 1,440 × 900 pixels and a refresh rate of 60 Hz. A standard Italian keyboard was used as response keys.

Abbreviations: ADHD, attention-deficit/hyperactivity disorder; OCD, obsessive–compulsive disorder; CBCL, Child Behavior Checklist; CPRS, Conners' Parent Rating Scale; CSTC, cortico-striato-thalamo-cortical; FTT, finger-tapping test; IQ, intelligence quotient; SD, standard deviation; SM, sensorimotor test; SMA, supplementary motor area; ToL, Tower of London; TS, Tourette syndrome; YGTSS, Yale Global Tic Severity Scale.

The background luminance of the screen was a mid-level gray measured at a viewing distance of 65 cm.

Measures Neuropsychiatric Screening

All subjects underwent a structured neuropsychological evaluation. They were tested by either a neuropsychologist or a child neuropsychiatrist. We performed a screening for neuropsychiatric comorbidities using parent report questionnaire to assess ADHD, obsessions and compulsions disorder, anxiety disorder, mood disorder, and conduct disorder (Child Behavior Checklist [CBCL] and Conners' Parent Rating Scale [CPRS]). Children's Yale–Brown Obsessive–Compulsive Scale (CY-BOCS) was used for obsessions and compulsions severity score. Furthermore, a structural neuropsychological evaluation including (2) a non-verbal cognitive test assessing fluid intelligence (*Raven's Progressive Matrices*) and (3) a spatial problem-solving and planning task (*Tower of London* [ToL] test) was performed. All TS patients were tested for tics severity and impairment using a questionnaire interview, the Yale Global Tic Severity Scale (YGTSS). For a detailed description of the tests, see **Supplementary Materials**.

Motor Timing Assessment

To assess motor timing, we used the finger-tapping test (FTT) and the sensorimotor test (SM), performed using the Inquisit 5.0 software (Millisecond®) downloaded on a laptop computer. Inquisit is a software widely used for experimental psychology (see www.millisecond.com for the latest research papers with Inquisit); in the Millisecond® website, a test library is provided with downloadable tests (and scripts) including those used for this study. For the SM tones at 500 Hz and 70 dB, sound pressure level (SPL) (duration 50 ms) were delivered through headphones. Subjects performed a single hand task.

Finger-Tapping Test

We used a script by Katja Borchert of Millisecond Software® (https://www.millisecond.com/download/library/v6/fingertapping/fingertapping/fingertapping.manual), adapted from the original Finger Tapping Oscillation Test part of Halstead's test battery of 1947 and later modified (32, 33). The FTT is a self-directed motor-speed test: participants have to tap with the index finger of both the dominant hand (DH) and the non-dominant hand (n-DH) as often they can within 10 s. Participants run through a mandatory number of 5 rounds (=blocks) of 10 s each. If the scores of these first 5 rounds were within 5 taps of each other, the final score was the mean of the number of taps of these 5 rounds (expressed as number of taps/10 s). On the other hand, if the scores of these 5 rounds were not within 5 taps of each other, an additional block was run, until 5 scores could be found that were within a 5-point range. The final score was the mean of these 5 scores for both the DH and the non-DH. The maximum number of rounds was 10. If no 5 scores could be found that are within a 5-point range from each other, the final score was the mean of all 10 tapping scores. After each round of testing, participants received feedback (number of taps) and got at least a 10-s rest period. After every 3 testing rounds, this resting period was increased to 60 s. We measured the final score for the DH and the final score for the non-DH.

Sensorimotor Synchronization Test

We used a script available from Millisecond Software® Library (https://www.millisecond.com/download/library/v6/timeestimation/pacedmotortiming/pacedmotortiming.manual) implementing a Paced Motor Timing procedure described by Wittmann et al. (19). In the SM test, the participant needed to synchronize responses with a series of 20 pacer signals (beeps, 500 Hz, 50 ms durations) for two stimuli, i.e., 1000 and 2000 ms (intertone intervals). The experimental procedure consisted of two different conditions (**Figure 1**): (a) in Condition A (synchronization subtest), the pacer signal was played for all test trials, and the participants had to synchronize their responses (spacebar press on the keyboard) with a steady series of the pacer signals. (b) In Condition B (continuation subtest), the pacer signals were played for the first 10 tones at the beginning of the trial; after 10 tones, the beat stopped, and the participants were asked to continue tapping (spacebar keyboard press) at the same rhythm until the end without the pacer signal. The continuation tapping was performed for 20 taps. The two conditions were tested in blocked format with Condition A running first. Stimuli were sampled randomly within each condition. Variables considered in the analysis were: *tap intervals (TI)* expressed as mean (±SD) of time intervals in ms between taps as measure of tapping speed for both Condition A and Condition B. For Condition A, we also considered the *invalid responses (IRs)* as the number of motor reactions (responses after 120 ms from the onset of tone) per trial as a further measure of synchronization ability. For Condition B, we considered *TI* expressed as mean (±SD) of time intervals in ms between taps. Additionally, for both Conditions A and B, we calculated an accuracy index (Δi) as follows: *subjective time* (*TI*)/*t* where subjective time was the *TI* produced experimentally by the subject, and *t* is the *objective time*, i.e., the base interval set (1000 or 2000 ms; Δi_{1000} and Δi_{2000}, respectively). This index provided the directionality of the tapping performance, being >0 if the subject was *behind the beat* and <0 if the subject is *ahead of the beat*; moreover, it was a direct measure of the magnitude of the error in reproducing the corresponding time interval. To complete the two subtests, it takes approximately 6 min. Δi was used in all statistical analysis performed.

Statistical Analysis

Results are reported as mean ± SD. Normal distribution was assessed by Shapiro–Wilk test and Levine test for normality. Differences between means were assessed using unpaired two-tailed *t* test (where appropriate) and analysis of covariance (ANCOVA) (considering "age" as covariate) with Bonferroni *post-hoc* test for comparison between the groups, at 95% CI. For finger-tapping results, we used a two-way ANOVA, in which GROUP was analyzed as between-subjects factor, and HAND (DH vs. n-DH) as within-subjects factor. *Post-hoc* comparisons were performed using the Bonferroni *post-hoc* test. Linear least-square regression and generalized linear model (GLM) analyses were used in the selection of predictors. GLM estimation was

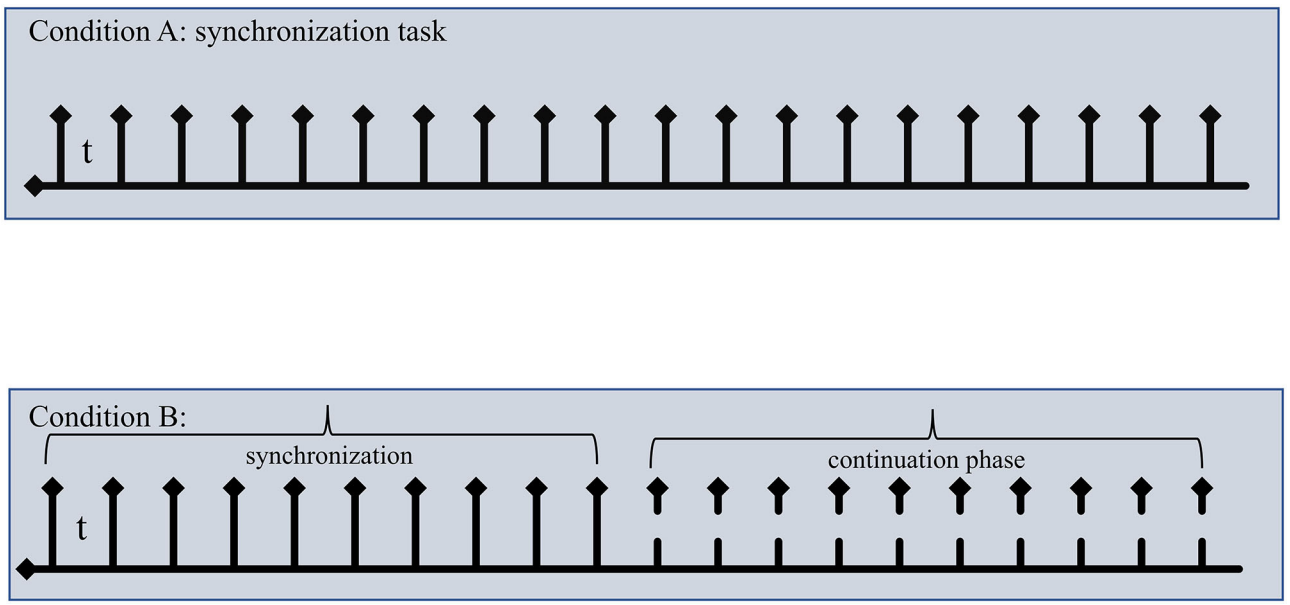

FIGURE 1 | A schematic representation of sensorimotor synchronization task. Top: In Condition A, subjects were asked to tap in synchrony to "beep. Bottom: in Condition B, subjects tapped in synchrony for the first 10 taps, then beeps stopped, and subjects continued to tap at same *tempo* in the so-called continuation phase (the last 10 taps). The last 10 taps for both conditions were used in the analysis. t: intertone interval 1000 ms or 2000 ms; solid arrow indicated taps in the synchronization phase; dashed arrows indicated when beep stopped.

performed by stepwise method with 95% CI. Significance was assigned for $p < 0.05$. All analyses were performed using SYSTAT software version 13.0 for Windows.

RESULTS

Demographic Characteristics

Twenty-two pediatric healthy controls and 37 TS patients were included in the analysis. In the patients' group, 60% had a diagnosis of TS without any comorbid condition (pure TS, $n = 22$) and 40% with ADHD comorbidity (TS+ADHD, $n = 15$). Male to female ratio was 3:1 in both groups. All patients and healthy controls did not take any medication. Participants' ages range between 8 and 14 years old, and no statistical significance was found between the groups (ANOVA-$F_{[2,56]} = 0.85$; $p = 0.43$). IQ levels were 108.3 ± 13.4 in the "pure" TS group, 110.1 ± 12.1 in the TS+ADHD group, and 114.5 ± 11.7 in the control group, showing no statistical significance between the groups (ANCOVA-$F_{[2,55]} = 1.77$; $p = 0.39$, corrected for age). Total mean score of the YGTSS rating scale for all TS was 41.3 ± 15.4 (maximum score 100). The two TS groups did not differ for YGTSS scores (40.9 ± 14.3 vs. 41.9 ± 17.4 for "pure" TS and TS+ADHD, respectively; $t = 0.182$, df 35; $p = 0.85$, 95% CI). Total mean score of the CY-BOCS rating scale for all TS patients was 8.6 ± 1.3 (maximum score 40); particularly, the range of severity of patients with obsessions and compulsions was subclinical in 32/37 (86.5%), mild in 2/37 (5.4%), moderate in 1/37 (2.7%), and severe in 2/37 (5.4%). CBCL and CPRS scores showed statistical differences between "pure" TS and TS+ADHD in several domains including those related to ADHD comorbidity. **Table 1** resumes all clinical characteristics of the population in the study.

Motor Timing

Finger-Tapping Test

In the FTT, DH as well as non-DH were tested. There was a statistical significance difference in mean number of taps (number of taps/trial) performed with DH between the three groups ($F_{[2,55]} = 6.849$; $p = 0.002$). In particular, we found a lower mean number of taps in both the Tourette groups, "pure" TS and TS+ADHD, respectively, 56.29 ± 5.78 (SD) ($p = 0.03$ *post-hoc* Bonferroni test) and 54.94 ± 7.03 (SD) ($p < 0.01$ *post-hoc* test) vs. controls, 63.28 ± 8.42 (SD). No statistical difference was found between "pure" TS and TS+ADHD. In non-DH trials, the "pure" TS group differed statistically from controls (respectively, 48.62 ± 13.31 vs. 55.81 ± 7.99; $p = 0.043$ *post-hoc* Bonferroni test), whereas no difference was found between controls and TS+ADHD (48.97 ± 8.70 vs. 55.81 ± 7.99). Considering in the model "HAND" as factor within each level (GROUP), we found that both controls and "pure" TS patients showed a statistically significant reduction with non-DH compared with DH (DH vs. non-DH, $p < 0.01$ *post-hoc* Bonferroni test). We did not find any difference in TS+ADHD between DH and non-DH.

Sensorimotor Test

In the SM task, we tested the ability of subjects to synchronize their taps with pacer signals with or without played beep (Conditions A and B, see Materials and Methods section for details). An accuracy index (Δi) was calculated as described in the Materials and Methods section to directly assess the accuracy

TABLE 1 | Demographic characteristics of the population in the study.

	Controls	Tourette	Tourette plus	*p* value
N	22	22	15	ns
Age (mean ± SD)	11.59 ± 2.26	10.86 ± 2.25	10.8 ± 1.78	ns
Male (N)	16	16	12	ns
Female (N)	6	6	3	ns
IQ (mean ± SD)	114.5 ± 11.71	108.31 ± 13.38	110.13 ± 12.05	ns
YGTSS (mean ± SD)	–	40.90 ± 14.3	41.86 ± 17.35	ns
CBCL-domain (%)				
Affective problems	–	5.10	60.00	$p < 0.001$
Anxiety	–	63.64	53.33	ns
Somatic complaints	–	27.27	26.67	ns
Attention and hyperactivity problems	–	4.55	33.33	$p < 0.001$
Oppositional defiant problems	–	4.55	40.00	$p < 0.001$
Conduct problems	–	9.09	66.67	$p < 0.001$
CPRS-domain (%)				
Oppositional defiant problems	–	9.09	33.33	$p < 0.001$
Attention/cognitive problems	–	4.55	60.00	$p < 0.001$
Hyperactivity	–	0.00	60.00	$p < 0.001$
Anxiety	–	31.82	46.67	ns
Perfectionism symptoms	–	18.18	26.67	ns
Social problems	–	27.27	33.33	ns
Somatic complaints	–	22.73	40.00	ns
Positive ADHD index	–	0.00	100.00	$p < 0.001$

CBCL and CPRS scores are reported as percentages of patients in each domain showing a threshold score T ≥ 70. Statistical comparison between the groups is reported with corresponding p value.

ADHD, attention-deficit/hyperactivity disorder; CBCL, Child Behavior Checklist; CPRS, Conners' Parent Rating Scale; IQ, intelligence quotient; N, number; ns, not significant; SD, standard deviation; YGTSS, Yale Global Tic Severity Scale.

of synchronization along with the directionality (earlier or later) of tapping. Additionally, in Condition A, we considered IRs as adjunctive measures of synchronization. In Condition A (*paced signals*) for the interval (t) tested, 1,000 ms, all groups did not differ in a statistical manner. $\Delta i_{1,000}$ values were 1.04 ± 0.04 for controls, 1.02 ± 0.05 for "pure" TS, and 1.02 ± 0.06 for TS+ADHD, indicating a good synchronization accuracy ($\Delta i = 1$). Mean number of IRs in each group per trial (reactions) confirmed the data. For the interval t, 2,000 ms, we did not find any statistical difference between the groups ($F_{[2,55]} = 0.65$; $p = 0.52$). Mean number of IRs confirmed the lack of difference between the groups. **Table 2** shows the results expressed as TI for each group. In Condition B (*unpaced signals*), $\Delta i_{1,000}$ did not differ significantly between the three groups ($F_{[2,55]} = 0.20$; $p = 0.55$). Conversely, in the task for 2,000 ms, both TS groups showed a statistical difference compared with controls ($\Delta i_{2,000} = 1.01 \pm 0.12$; $F_{[2,55]} = 14.2$; $p < 0.001$), adjusted for age; in particular, "pure" TS showed a $\Delta i_{2,000}$ value >1 (1.21 ± 0.25; $p = 0.035$ vs. controls; Bonferroni *post-hoc* test 95% CI), indicating a direction of synchronization "behind the beat," whereas TS+ADHD' $\Delta i_{2,000}$ was <1 (0.84 ± 0.22; $p = 0.035$ vs. controls; Bonferroni *post-hoc* test 95% CI), placing these patients significantly "ahead of the beat." A statistical significance was found comparing "pure" TS and TS+ADHD ($p < 0.001$). Data are summarized in **Table 2**, **Figure 2**.

Planning and Decision-Making Abilities

We measured planning and decision-making abilities using the standardized ToL test. Results are summarized in **Table 3**. Briefly, we considered the total score achieved, the mean solution time, the mean execution time, and the time of the first move (as measure of impulsivity). "Pure" TS and TS+ADHD differed from controls ($p < 0.001$) for the total score, with no effect of age in the model. As regards the total execution time, we found a statistical difference between the three groups. *Post-hoc* analysis showed a statistical significance between TS+ADHD and controls ($p < 0.001$), whereas no differences were found between "pure" TS and controls. Additionally, TS+ADHD patients showed statistically lower mean solution time values than controls ($p = 0.045$). No differences were found in the time of first move between the groups.

Correlation Analysis

Comparing the finger tapping scores with the IQ and tics severity (YGTSS), we did not find any correlation ($p > 0.05$), suggesting that tic severity did not impair *per se* motor performance. IQ and YGTSS did not correlate also with *accuracy index* for sensorimotor continuation test ($\Delta i_{2,000}$). We addressed the interplay between motor timing and ToL (planning and decision-making abilities). We used a GLM to statistically test this hypothesis. In the first model, we assigned as dependent variable the "mean of finger tapping" (DH) of FTT and as independent variables "groups" (controls, "pure" TS, and TS+ADHD), the mean execution time, the total score, and interactions between them (group × mean execution time; group × total score). We found that FTT scores were statistically correlated to group as expected, whereas in the "group × mean execution time" interaction, finger tapping scores and execution time were inversely related ($p < 0.001$). In the second model, we set as dependent variable the $\Delta i_{2,000}$ and as independent factors the mean execution time, the total score, and interactions between them. We did not find any significant correlation.

DISCUSSION

Here, we adopted two well-established experimental paradigms (32, 33), such as FTT and SM (synchronization and continuation), to study motor timing in two groups of TS patients, "pure" TS and TS+ADHD. While in free FTT, subjects tap in a freely chosen rhythm, in the synchronization and continuation task, the accuracy requires motor and perceptual timing fluctuation to replicate externally presented rhythm and memory-driven timing to continue tapping in the absence of the auditory cue (19).

TABLE 2 | Results of sensorimotor task.

Sensorimotor task				
	Controls	**TS only**	**TS plus**	***p* values**
Condition A/synchronization *t* = 1,000 ms				
TI (ms) (mean ± SD)	1041.56 ± 45.66	1015.07 ± 59.34	1023.31 ± 53.73	$p = 0.29$
Invalid responses (*N*) (mean N ± SD)	2.68 ± 3.58	2.95 ± 2.40	2.93 ± 1.15	$p = 0.90$
$\Delta i_{1,000}$	1.04 ± 0.04	1.02 ± 0.05	1.02 ± 0.06	$p = 0.50$
Condition A/synchronization *t* = 2,000 ms				
TI (ms) (mean ± SD)	2076.16 ± 213.98	2090.56 ± 254.96	2012.56 ± 104.17	$p = 0.50$
Invalid responses (*N*) (mean N ± SD)	4.22 ± 2.04	3.86 ± 1.89	3.33 ± 0.72	$p = 0.34$
$\Delta i_{2,000}$	1.04 ± 0.10	1.05 ± 0.12	1.01 ± 0.05	$p = 0.50$
Condition B/(synchronization and) continuation *t* = 1,000 ms				
TI (ms) (mean ± SD)	1039.18 ± 85.02	1135.43 ± 593.51	1128.07 ± 499.61	$p = 0.89$
$\Delta i_{1,000}$	1.04 ± 0.08	1.14 ± 0.59	1.13 ± 0.49	$p = 0.89$
Condition B/(synchronization and) continuation *t* = 2,000 ms				
TI (ms) (mean ± SD)	2013.02 ± 252.16	2415.12 ± 506.44	1689.57 ± 447.72	$p = 0.035$* $^{\dagger}p < 0.001$
$\Delta i_{2,000}$	1.01 ± 0.12	1.21 ± 0.25	0.84 ± 0.22	$p = 0.035$* $p < 0.001^{\dagger}$

Parameter for each Condition A and B and comparison between the groups are shown for each condition of the test.
TS, Tourette syndrome; TI, tap intervals; Δi, accuracy index; N, number; ms, milliseconds.
**TS only and TS plus vs. controls.*
†*TS only vs. TS plus Bonferroni post-hoc test 95% CI.*

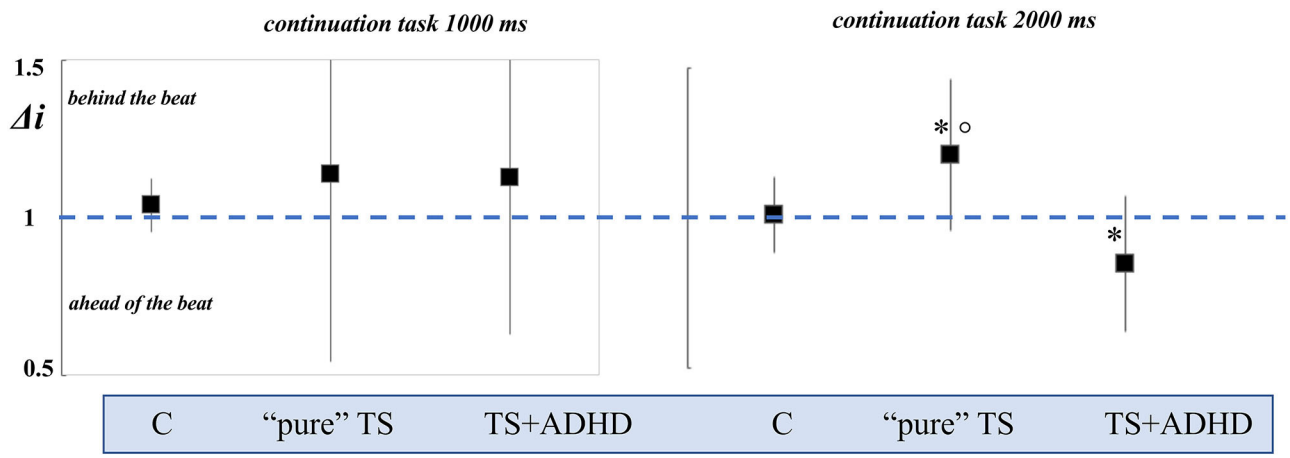

FIGURE 2 | Representation of accuracy index (Δi) in Condition B (synchronization and continuation task) for $t = 1{,}000$ ms and for $t = 2{,}000$ ms. The Δi value is 1 in the iso-synchrony performance (dashed blue line); values >1 or <1 indicate the direction of continuation tapping, "behind the beat" or" ahead of the beat," respectively. "Pure" TS and TS+ADHD patients showed a lack of accuracy in the continuation task for 2,000 ms, with opposite directions. "Pure" TS: Tourette syndrome only; TS+ADHD: Tourette syndrome plus; C: controls; *$p < 0.05$ Bonferroni *post-hoc* test with 95% CI vs. controls; °$p < 0.001$ Bonferroni *post-hoc* test with 95% CI "pure" TS vs. TS+ADHD.

In the FTT, we found that the control group scored better than both groups of TS patients when using their DH. Conversely, we found that controls scored better than "pure" TS patients also with non-DH, but not than the TS+ADHD group. In addition, controls and "pure" TS scored better with DH than with non-DH, and interestingly, this difference was not found in the TS+ADHD group. These findings deserve more clarification in light of existing data. Fine motor skills have been extensively

TABLE 3 | Results of performance in the tower of London test.

	Controls	"Pure" TS	TS+ADHD	*p* value
Total score	32.5 ± 2.15	26.90 ± 5.01	26.86 ± 5.51	**$p < 0.001$***
Solution time (s)	17.58 ± 5.79	21.58 ± 11	26.23 ± 10.8	**$p = 0.045$°**
Execution time (s)	6.71 ± 2.27	10.19 ± 4.28	13.94 ± 7.33	**$p < 0.001$§**
First move (s)	10.86 ± 4.6	12.10 ± 9.35	12.29 ± 5.4	$p = 0.85$

Data are expressed as mean ± SD. Comparison between the groups and relative p value are reported. Significant P values are displayed in bold.
ADHD, attention-deficit/hyperactivity disorder; TS, Tourette syndrome.
**Bonferroni post-hoc test with 95% CI $p < 0.001$ pure TS and TS+ADHD vs. controls.*
°*Bonferroni post-hoc test with 95% CI $p < 0.05$ TS+ADHD vs. controls.*
§*Bonferroni post-hoc test with 95% CI $p < 0.001$ TS+ADHD vs. controls.*

studied in TS with conflicting results depending on simple or more complex tasks adopted (34–38) as well as on confounding factors, such as age of the experimental cohort, tic severity, and not least comorbidities. The main aim of our study was different; thus, unfortunately, we did not clearly clarify these contradictory results. On one side, we confirm the evidence that an altered organization of motor behavior occurs in TS as well as that motor skills are impaired in TS (both pure or +ADHD) in a single-hand trial; on the other hand, as expected from motor lateralization studies (30), we found a symmetric performance between DH and n-DH only in TS+ADHD and not in pure TS. The symmetry between DH and n-DH in motor performance of TS has been explained by compensatory interhemispheric plasticity mechanisms in TS (30, 39, 40). The apparent inconsistency of our results could be explained by the nature of the task (single for each hand vs. bimanual) and by other factors contributing to the development of symmetry of motor performance, such as the younger age of the cohort (34, 35). Finally, the finding that the TS+ADHD group showed a more symmetrical (poorer) performance with both hands may imply that symmetrical compensatory mechanisms can establish earlier in TS patients with comorbidity than in "pure" TS.

The main result of our study is that obtained in the synchronization and continuation task. "Pure" TS and TS+ADHD showed a poor motor timing organization with opposite performance in the 2,000 ms continuation task (supra-seconds interval), classifying "pure" TS as "behind the beat" and TS+ADHD as "ahead of the beat," on the basis of their accuracy index. We also found that there is a lack of correlation between the timing accuracy and the tics severity scores (YGTSS), as well as with IQ scores. Martino et al. (29) recently reported motor timing performance in a cohort of adult TS patients, observing a reduced synchronization ability in the continuation condition for 2,000 ms interval. For the first time, our findings replicate this observation in a childhood cohort of "pure" TS. Furthermore, our study improves knowledge on motor timing in TS children, demonstrating that patients with comorbid ADHD scarcely synchronize as "pure" TS but with an opposite direction of accuracy (ahead of the beat) when compared with "pure" TS (see **Figure 2**).

ADHD comorbidity is considered a confounding factor generating conflicting results in TS studies (41). On the other hand, and strictly from a clinical point of view, ADHD accounts for at least 40% of the total comorbidity of TS patients (3, 42), and data are thought to be underestimated in several cases (43). Moreover, ADHD is one of the major components of clinical worsening of TS during lifespan (4, 44). Motor timing has been extensively studied in ADHD population with some diverging results, probably due to selection of the patients or due to different experimental conditions adopted (45–50). However, in a comprehensive review, Noreika et al. (27) concluded that both children and adults with ADHD tend to show premature responses and poor synchronization for sub-second and supra-second intervals, confirming a highly consistent pattern of motor timing abnormalities.

Motor timing is thought to be controlled by several cortical areas in conjunction with the basal ganglia and cerebellum, constituting the fronto-striato-cerebellar network (51). Additionally, functional MRI (fMRI) studies showed that sensorimotor synchronization is associated with the activation of cortical areas, such as dorsolateral frontal cortex (DLFC), inferior frontal cortex (IFC), medial frontal cortex (MFC), and supplementary motor area (SMA) [for a *review*, see (52)]. Moreover, Wiener et al. (53) found that bilateral anterior cingulate cortex (ACC), right SMA, dorsolateral prefrontal cortex (DLPFC), and inferior parietal cortex (IPC) were more involved in supra-second motor timing. After all, SMA plays a critical role in tics pathophysiology: SMA is strongly involved in tic generation in TS and also tic regulation during voluntary action (54–56). Ganos et al. (56) proposed that in TS, the right SMA seemed to act as a global inhibition mechanism in TS and was used to simultaneously stop tics and voluntary actions. Thus, SMA–striato-thalamo-cortical loop dysfunction could explain in "pure TS" patients their accuracy "behind the beat" in continuation tasks, as proposed also by Martino et al. (29). On the other hand, the opposite direction of accuracy index in TS+ADHD patients compared with pure TS leads to that other mechanisms occur. In TS+ADHD patients, it could be imagined that pre-frontal areas, such as ACC and DLPFC, may mediate the anticipatory performance for a lack of inhibitory control (impulsiveness) (49). Thus, our findings confirm once more that it is important to consider all endophenotypes in studying a puzzling complex syndrome as Tourette.

In addition, we tested patients (and controls) for their planning and decision-making abilities by performing a standardized task, such as ToL test, as measure of their "executive" function. We found that the pure TS and TS+ADHD groups compared with the control group showed lower scores in the total score, whereas the total execution time was lower in the TS+ADHD group. Planning skills refer to the capacity to organize cognitive and motor behavior in order to perform different steps needed to reach a goal (57). Termine et al. (58) showed in a small cohort of children that both pure TS and TS+ADHD patients show various impairments during the ToL test. Interestingly, we found an inverse correlation between finger tapping scores for DH and the total score and the mean execution time of the ToL test. These findings suggest, once more, that an impairment of "planning skills" in TS contributes

to an impairment of the organization of motor behavior in free tapping.

However, we did not find any correlation between continuation ability and ToL performance, suggesting that not all organization of motor timing is dependent from planning ability, and this is true for both groups independently from ADHD co-occurrence.

Finally, some limitations of the study need to be addressed. First, note the small sample size of our cohort and, in particular, of the TS+ADHD group. Second, as a pure ADHD group is lacking, our results cannot be readily transferred to ADHD patients. Finally, although all our efforts have been made to minimize confounding factors, we cannot exclude intrinsic (due to referral) bias in the selection of patients.

In conclusion, we demonstrated that children with TS show an impaired motor timing organization in the free tapping and in the continuation task (tempo synchronization). Moreover, findings in TS+ADHD confirm that, at least in part, TS groups differ, signifying that ADHD co-occurrence should be considered in all studies involving TS to not exclude possible confounding effect.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Bambino Gesù Local Ethical Committee. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

FG, CP, and AC contributed to the conception and design of the study. CP, FG, and LD organized the database. FG and AC performed the statistical analysis. FG wrote the first draft of the manuscript. FG, AC, PC, and FV wrote sections of the manuscript and critically discussed the final version. All authors contributed to manuscript revision, read and approved the submitted version.

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SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2020.552701/full#supplementary-material

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EDITORIAL

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Editorial: Two Centimeters More or Less. How Much Does It Matter to an Adolescent or a Young Adult With Attention-Deficit/Hyperactivity Disorder?

Sara Carucci, MD, PhD

Stimulants are the first-line medication for attention-deficit/hyperactivity disorder (ADHD), and methylphenidate (MPH) is the first choice in Europe, with good efficacy and acceptable tolerability in a short-term course during childhood and adolescence.[1] ADHD is, however a chronic condition, and patients can receive pharmacological treatment for a long period of time with understandable concerns related to long-term risks. Beside the well-known mild and transient adverse effects (ie, sleep disturbance, nervousness, anorexia, headache, and abdominal pain), in the last decade, emphasis has been placed on several less common, but potentially more serious, effects occurring with prolonged use, and in particular on a possible drug-related impact of medications on growth and pubertal maturation.

Several studies have monitored changes in height and weight associated with stimulant medications, without providing clear answers as to whether the observed changes are specifically drug-related and, eventually, whether they are clinically significant. Studies providing longitudinal data suggest that the height deficit can be clinically significant of about 1 cm per year during the first 3 years of treatment; other data suggest that these effects tend to attenuate over time, and that growth parameters in adulthood are generally not affected.[2,3] Considering the substantial variability at an individual level, with reports of significant growth suppression in some children, it is important, from a clinical point of view, to have standardized methods to assess this potential side effect in order to be able to manage it with the most appropriate strategies.

Following these lines, the study of Waxmonsky et al.[4] examined the impact of stimulants on growth in a sample of drug-naive children, aged 5 to 12 years, with ADHD, also testing the efficacy of 3 different weight recovery strategies. Within a well-structured research design, 230 children were randomized in a 4:1 ratio to either medication (MED, primarily osmotic release oral system-MPH) or behavioral therapy (BT). Any time after 6 months, MED or BT participants (as BT participants could cross to medication after month 6) evidencing a decline in body mass index (BMI) of >0.5 z-units were then randomized to 1 of the 3 weight recovery treatments (WRTs): (1) monthly monitoring of height/weight (MON, n = 24) and continuation of previous daily medication; (2) drug holidays (DH, n = 23), with medication limited to school days; or (3) daily caloric supplementation (CS, n = 24) with a 150-kcal supplement continuing previous daily medication.

From study entry to WRT entry, medication was associated with significant reductions in standardized weight and height (p values <.01) by comparing children entering WRT with participants never using medication, with differences amounting to about 0.66 cm and 3.7 kg.

By a comprehensive statistical approach, including a multi-level repeated-measures growth model by spline functions, the authors found a significant weight velocity increasing after WRT randomization ((β_2) = 0.271, SE = 0.027, p < .001), with no increase in height velocity. All WRT participants gained significantly more weight over a 10-month period: MON (+1.8 kg), DH (+3.4 kg), and CS (+3.0 kg). The magnitude of growth suppression associated with stimulants over the total 30 months of assessment in WRT participants was about 2.4 kg and 1.3 cm less than expected values. Never-medicated youths had an increase in standardized height and weight reflecting about +0.3 cm and +0.9 kg, respectively, whereas medicated youths who did not meet WRT criteria exhibited mean changes of −0.6 cm and −0.6 kg over a 12-month period.

This article provides an important contribution to the field by supporting previous findings[2] of a possible drug-related impact on height and weight of children medicated for ADHD.

The inclusion of a BT comparison group, thus excluding that the growth changes could be a consequence of the ADHD disorder itself, is one of the main strengths of the study. Accounting of the pubertal onset into the analysis by introducing a time-varying covariate overcomes another significant limitation of previous studies, allowing a more precise evaluation of the drug effect. Puberty is, in fact, the time that height velocity increases most, making only age stratification not adequate for an appropriate evaluation.

The effort to evaluate the effectiveness of specific strategies for the management of the potential adverse effects on growth represents the third main point of strength of this work. One of the recommended strategies to prevent a growth impact by stimulants is, in fact, to plan a break referred to as a "drug holiday," and another is to encourage a greater caloric intake[5]; no previous study compared these different strategies together. In fact, although DH and CS ensured the highest weight increases, monthly weight checks also appeared to be useful in promoting parental care regarding the problem, evidencing that a careful clinical monitoring with educational support can itself guarantee better management of ADHD, in terms of both core symptoms[6] and drug-related effects. Parents can feel reassured by frequent interaction with the clinician, and appear to be more able to manage the risks and benefits of the pharmacological therapy.

Although for most individuals the drug-related impact on growth is likely to have minimal clinical significance, changes can vary on an individual basis, and it could be matter of concern, especially for individuals with a height/weight Z score <2 DS at baseline; in the Waxmonsky *et al.* study, no significant correlation between baseline auxological parameters and the changes during WRTs was found.

The majority of studies in adult patients treated with psychostimulants as children suggest that final height may not be significantly impaired, although, in light of more recent publications, this hypothesis still remains uncertain. Swanson *et al.*[7] reported, in fact, that within the MTA study, after 16 years the ADHD group was 1.29 ± 0.55 cm shorter than the control group and that the impact on height was higher for the "constantly treated" subjects compared to the ADHD sample discontinuing medication.

How much, and in which way, a possible deficit in height or weight can affect the life of a growing individual is still an unclear clinical issue. At the moment, few studies report the characteristics of the more vulnerable subjects, individual data on drop-out, or the rating of clinical significance by physicians, parents, or patients; however, discontinuation of treatment because of losses in expected growth is generally rare with stimulant medications.

A few years ago, the European Commission funded a large research project on the long-term safety of methylphenidate: the Attention Deficit Hyperactivity Disorder Drugs Use Chronic Effects (ADDUCE; http://adhd-adduce.org).[8] The project included a systematic review,[9] confirming the results of previous detailed reviews and a 2-year prospective cohort study (total target population, 1,600 subjects) with appropriate control groups (non-medicated ADHD and normally developing subjects), finalized to addresses scientific questions on specific classes of potential long-term adverse effects of MPH including growth as well as neurological, psychiatric, and cardiovascular health, with height velocity, as a primary outcome. The final results of this large study will help to better define the longitudinal medication impact on growth trajectory in children, together with possible further accurate investigation on adult outcomes in reaching their target height.

In the meantime, it is important to adhere to the current clinical practice guidelines for monitoring of growth and pubertal maturation in children, with a careful assessment of the growth parameters before starting stimulants, and with periodic monitoring through repeated measurement by standardized growth charts. Particular caution should be taken in preschool children, in whom adverse effects are more likely.

Future progress in gene discovery and technical developments may facilitate the availability of genetic diagnosis as part of clinical care for patients on pharmacological treatment for a more personalized approach. At the moment, studies using a self-controlled case series design could be useful in giving more information about data at an individual level, to obtain a more precise indication for the management of possibly-more-vulnerable subjects in clinical practice.

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CASO CONTRIBUTIVO

SINDROME DI TOURETTE: ALLA FACCIA DELLA PANDAS!

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TOURETTE SYNDROME: A CASE REPORT

Key words
Tourette syndrome, Obsessive-compulsive disorder

Abstract
The paper describes the clinical case of a ten-year-old boy with Tourette's syndrome, initially classified as PANDAS. The persistence, the complexity of the symptoms and the comorbidity with obsessive-compulsive disorders (OCD) have framed the case as Tourette syndrome and OCD. Treatment with cognitive behavioural therapy and aripiprazole gave a good clinical response, with partial regression of the symptoms. In the light of clinical improvement, a good prognosis is expected in the long term.

RIASSUNTO

Viene descritto il caso clinico di un bambino di dieci anni affetto da sindrome di Tourette, inizialmente inquadrata come PANDAS. La persistenza, la complessità dei sintomi, la comorbidità con disturbi ossessivo-compulsivi hanno classificato il caso come sindrome di Tourette e DOC. Il trattamento con terapia cognitivo-comportamentale e con aripiprazolo ha dato una buona risposta clinica, con regressione parziale della sintomatologia. Alla luce del miglioramento clinico, si prospetta una buona prognosi a lungo termine.

CASO CLINICO

Bambino primogenito di anni 10, nato a termine, da parto spontaneo da gravidanza normodecorsa. Alla nascita Apgar 9-10, dati antropometrici adeguati all'età anagrafica, regolari le prime tappe dello sviluppo psicomotorio. Andatura sulle punte, piede equino con retrazione achillea, corretto chirurgicamente a 6 anni.

A 8 anni compaiono tic motori al volto (chiude le palpebre, muove la lingua, storce la bocca) e tic vocali. Dopo un mese dall'inizio dei sintomi la madre, spontaneamente, si affida alle cure di un neuropsichiatra infantile il quale, sulla base di un moderato incremento del TAS e degli anticorpi anti-DNAsi B (da lui richiesti e prescritti), pone diagnosi di PANDAS *(Paediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcus infections)* e propone cicli di antibioticoterapia con amoxicillina (15 giorni).

Finalmente vengo consultato, sconsiglio la terapia antibiotica e decido di rivalutare la situazione a breve.

Intanto i tic variano, da semplici diventano complessi, coinvolgono altri gruppi muscolari, diventano più frequenti, peggiorano quelli vocali; il bambino muove le spalle, cammina su e giù per la stanza, presenta ecolalia, è ossessionato dai calcoli e dagli stessi giochi.

Per la persistenza e l'aggravamento dei sintomi, nel sospetto di sindrome di Tourette associata a disturbo ossessivo-compulsivo (DOC), richiedo una visita neuropsichiatrica infantile e una consulenza psicologica che evidenziano un livello cognitivo nei limiti (alle scale di valutazione psicodiagnostica), ma rilevano rigidità cognitiva, pensiero ossessivo, fobie, comportamenti ripetitivi, tendenza a isolarsi.

Viene confermato il sospetto diagnostico di sindrome di Tourette in comorbidità con il disturbo ossessivo-compulsivo e avviata terapia cognitivo-comportamentale e aripiprazolo, neurolettico di terza generazione.

DISCUSSIONE

I tic sono movimenti o vocalizzazioni improvvisi, rapidi, ricorrenti, stereotipati, ma non involontari (possono infatti essere soppressi), aumentano in condizioni di stress, disagio psico-fisico, relax, diminuiscono quando è richiesta attenzione focalizzata.

I tic vanno distinti in:

- **motori semplici** (interessamento di un gruppo di muscoli smorfo-facciali, che determinano per esempio blefarospasmo o scatti del collo o della testa);
- **complessi** (interessamento di altri gruppi muscolari che generano movimenti rotatori o avanti e indietro ecc.);
- **vocali semplici** (tosse, emissioni di rumori provenienti dalla gola) **e complessi** (ecolalia, cioè ripetizione di suoni emessi da altri, e coprolalia, non comune).

La prevalenza dei tic nella popolazione pediatrica è di 1:10; l'età media di esordio è 9 anni (7-8 anni nella sindrome di Tourette, 5 anni nel DOC), il 25% dei tic cronici si associa alla sindrome di Tourette, che colpisce lo 0,3-1% della popolazione, rapporto M:F = 4:1[1,2].

Secondo il DSM-V, per la diagnosi di sindrome di Tourette devono essere presenti tic motori multipli e almeno uno vocale, più volte al giorno, ad accessi, quasi ogni giorno, per più di un anno; sede, tipo, frequenza e gravità dei tic variano. L'esordio deve avvenire prima dei 18 anni, in genere a 7 anni; il periodo di maggiore esacerbazione si ha tra 8 e 12 anni, con riduzione in adolescenza. Solo il 10% continua la psicoterapia in età adulta. Nell'80% dei casi si associano DOC e deficit di attenzione e iperattività (ADHD)[3,4].

In merito alla patogenesi della sindrome di Tourette, diverse teorie sono accreditate dalla letteratura internazionale:

- **Genetica** (poligenica multifattoriale) comprovata dalla concordanza fino al 94% nei gemelli monozigoti, il principale cromosoma coinvolto è il 13 e precisamente la regione 13q31.1, dove è presente il gene SLITRK1 implicato, attraverso la sintesi di una proteina transmembrana, nella crescita dei dendriti, dei neuroni e delle sinapsi nelle regioni dell'ippocampo; una mutazione di questo gene sarebbe alla base della sindrome di Tourette[5];
- Condizioni di **affaticamento, tensione** con successivo incremento di allopregnanolone, ormone dello stress prodotto dal cervello che accenderebbe i circuiti eccitatori[6];
- **Disordine ereditario della neurotrasmissione** che interesserebbe i circuiti dopaminergici, con una disinibizione di alcune zone in sede cortico-striato-talamico-corticale[4].

Alcuni Autori hanno cercato di chiarire il ruolo patogenetico delle disfunzioni della dopamina nella genesi della sindrome di Tourette, ipotizzando vari fattori quali: anomalia presinaptica neuronale del mediatore, alterazione nel trasporto, incremento della dopamina stessa con conseguente "iperinnervazione" e ipersensibilità degli stessi recettori dopaminergici. Sembrerebbe che proprio l'incremento della dopamina concorra al determinismo dell'*apprendimento* e dell'*azione* che porta alla genesi del tic stesso che, proprio perché appreso, si configura come disturbo reattivo a sensazioni che creano disagio[7,8].

Tali conoscenze fisiopatologiche fanno comprendere meglio l'efficacia dei farmaci anti-dopaminergici e della terapia cognitivo-comportamentale.

La diagnosi si avvale della valutazione dei sintomi attraverso lo *score* ottenuto dall'analisi di alcuni *item* che strutturano la scala di Yale che valuta la severità dei tic e la loro complessità[1,9].

Spesso l'*iter* diagnostico è complesso per la variabilità dei tic, per l'associazione con situazioni scatenanti, inoltre è necessario seguire i pazienti per almeno un anno ed escludere condizioni psicosociali, psichiatriche e neurologiche secondarie.

Un errore interpretativo in fase di diagnosi è quello di considerare il tourettico come un soggetto con problemi di adattamento, in quanto il soggetto vive la quotidianità in maniera del tutto peculiare, dimostrando una bassa tolleranza alle frustrazioni.

L'approccio terapeutico è prevalentemente cognitivo-comportamentale, le tecniche più efficaci sono l'esposizione con prevenzione della risposta e il *habit reversal training,* che prevede una risposta competitiva al movimento che genera il tic[1,4,9,10].

Si ricorre ai farmaci se il tic non risponde alla terapia o se coesiste un disturbo comportamentale.

I farmaci più utilizzati sono i neurolettici, prevalentemente anti-dopaminergici, quali:

- aloperidolo, scoperto negli anni '60;
- risperidone, inibitore completo del recettore della dopamina, utilizzato in presenza di comorbidità con atteggiamenti di aggressività;
- pimozide, un inibitore del recettore della dopamina;
- aripiprazolo, un neurolettico di ultima generazione, di grandi prospettive, utilizzato nei tic, nella sindrome di Tourette e nella sindrome bipolare, che agisce come agonista parziale della dopamina (quando la dopamina è bassa, attiva il recettore), come agonista ad alta efficacia dei recettori D2 dopaminergici e come antagonista dei recettori post-sinaptici della dopamina, come agonista parziale dei recettori serotoninergici 5TH1 e come antagonista dei 5TH2A; ha anche modesta azione regolatrice dei recettori dell'istamina;
- metilfenidato, viene utilizzato se è presente comorbidità con ADHD[9,11].

La valutazione del caso descritto e la PANDAS

Il caso in esame presenta peculiarità abbastanza tipiche della sindrome di Tourette (sintomi caratteristici, durata superiore a un anno, comorbidità con DOC); purtroppo frettolosamente era stata posta da uno specialista neuropsichiatra infantile, consultato dalla madre, diagnosi di PANDAS, entità clinica descritta da Swedo nel 1998, oggi spesso sovradiagnosticata. I criteri diagnostici nosografici della stessa PANDAS hanno subito in questi ultimi anni numerose critiche, che hanno di fatto sconfessato il diretto rapporto con la pregressa infezione da streptococco beta-emolitico di gruppo A (SBEGA). Oggi infatti si preferisce parlare di PANS *(Paediatric Acute-onset Neuropsychiatric Syndrome)*. I criteri clinici iniziali della PANDAS erano caratterizzati da presenza di DOC o tic, esordio prepuberale, comparsa improvvisa dei sintomi a decorso recidivante-remittente, associazione temporale fra infezione da SBEGA ed esordio o ricaduta sintomatologica, associazione con anomalie neurologiche (in particolare iperattività motoria e movimenti coreiformi)[12,13].

Le criticità maggiori che hanno di fatto ridimensionato la PANDAS riguardano i criteri diagnostici. Esistono infatti molti falsi negativi e positivi, in quanto il tempo di

osservazione fra infezione da SBEGA (molto frequente in età pediatrica) ed esordio della clinica non è ben codificato, non vi sono rapporti chiari fra nuove infezioni da SBEGA e riesacerbazione di sintomi riferibili alla PANDAS. Non esistono infine evidenze scientifiche dall'utilità della terapia con penicillina.

Il decorso del piccolo paziente è abbastanza buono, risponde bene alla terapia cognitivo-comportamentale e a quella farmacologica con aripiprazolo. Presenta infatti cospicua riduzione della sintomatologia ticcosa e dei disturbi ossessivi-compulsivi, è ben inserito a livello scolastico, non tende più all'isolamento, viene seguito presso un Centro di secondo livello con competenze specifiche per la sindrome di Tourette.

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Segreteria scientifica

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Iscrizione

Per iscriversi al corso è necessario inviare una mail a ***jessica.babboni@policlinico.mi.it*** indicando:

- *Nome*
- *Cognome*
- *Istituto di appartenenza (SOLO insegnanti)*

Riceverete una **mail** di conferma dell'iscrizione e in prossimità dell'incontro il **link** al quale collegarvi per partecipare.

Per ogni difficoltà di registrazione o iscrizione contattare la **segreteria organizzativa.**

Le iscrizioni al corso saranno aperte **fino ad esaurimento posti**.

La frequenza al corso è gratuita ed è aperta ai genitori e a tutti gli insegnanti di ogni ordine e grado.

Modalità del corso

ONLINE CON PIATTAFORMA ZOOM
PARTECIPAZIONE GRATUITA

Il corso è organizzato dal
Centro di Riferimento Regionale per il trattamento dell'ADHD

UONPIA
Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico – Milano

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FORMAZIONE

Riflettiamo insieme: ADHD, Disturbi del comportamento e didattica a distanza

18 Dicembre 2020
Ore 17:00 – 19:00

Convegno in modalità videoconferenza

Fondazione IRCCS Ca' Granda
Ospedale Maggiore Policlinico
Sistema Socio Sanitario
Regione Lombardia

Relatori

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Chi siamo?

L'Unità Operativa di Neuropsichiatria dell'Infanzia e dell'Adolescenza (UONPIA) è un servizio specialistico che svolge attività di prevenzione, diagnosi, cura e riabilitazione in ambito neurologico, psichiatrico e psicologico nella fascia d'età 0-18 anni. Il Polo Ospedaliero dispone di un servizio ambulatoriale ed effettua consulenze presso i reparti ed il Pronto Soccorso della Clinica Pediatrica De Marchi, per la gestione clinica di patologie neurologiche e psichiatriche. È questo il luogo presso cui si trova il Centro di Riferimento per il trattamento dell'ADHD.

Programma

ore 17:00
Inizio incontro

I disturbi del comportamento: impariamo a conoscerli

Un'ipotesi di percorso:
progetto regionale lombardo
E. Antonaci

Quali strategie possibili di intervento?

Breve descrizione dell'Intervento farmacologico, sulla famiglia (*Parent Training*) e sul bambino (*Child Training*)
E. Antonaci - C. Bissoli – J. Babboni - I. Cropanese

ADHD e scuola a distanza
E. Antonaci - I. Cropanese - C. Bissoli – J. Babboni

Tavola di discussione e domande

Obiettivi dell'incontro

Riflessione condivisa tra genitori, insegnanti e operatori sul Disturbo da Deficit di Attenzione con Iperattività e la Didattica a distanza: punti di forza, punti di debolezza, opportunità, ostacoli e strategie utili.

L'obiettivo è sviluppare un confronto utile per stimolare la collaborazione tra scuola e famiglie e valutare quali aspetti mantenere nel futuro.

Che cos'è l'ADHD

Alcuni bambini e ragazzi si distraggono facilmente, fanno fatica a concentrarsi, a portare a termine un'attività dall'inizio alla fine, a programmare ed a gestire il proprio tempo, ad aspettare il proprio turno nella conversazione e nel gioco, faticano a controllarsi ed a stringere amicizie.

Tutti i bambini ed i ragazzi possono mostrare, a volte, questi comportamenti, in particolare quando sono piccoli, ma il bambino-ragazzo con ADHD li manifesta più frequentemente e più intensamente degli altri, in un'età in cui in genere i coetanei li hanno superati.

Quando l'intensità con cui sono presenti i sintomi è tale da ripercuotersi in maniera negativa sulla qualità della vita dei ragazzi nei diversi contesti (casa, scuola, amici...) e diventare un ostacolo per la crescita e l'apprendimento, si parla di ADHD, *Attention Deficit Hyperactivity Disorder* ("Disturbo da Deficit di Attenzione ed Iperattività").

Non si tratta di cattiva educazione, né di cattivi ragazzi, non è colpa né della famiglia né della scuola, né dei ragazzi stessi, ma è necessario capire che tipo di difficoltà ci sono ed attivare una serie di interventi, tra cui prima di tutto degli adattamenti specifici dell'ambiente, che evitino il rischio di peggiorare le cose.

Per ricevere la newsletter iscriversi al seguente indirizzo:
http://www.adhd.marionegri.it/index.php/newsletter/iscrizione-newsletter

link per potersi cancellare dalla mailing list:
http://adhd.marionegri.it/index.php/newsletter/cancellazione-newsletter

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza
(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3798 del 08/05/2014, n. 778 del 05/02/2015, n. 5954 del 05/12/2016, N. 1077 del 02/02/2017 N. 1938 del 15/02/2019) Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia"
"*Percorsi diagnostico-terapeutici per l'ADHD*".

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