NEWSLETTER

INDICE:

BIBLIOGRAFIA ADHD FEBBRAIO 2021

Accid Anal Prev. 2021 Jan;149.

THE NATURE OF THE RISK FACED BY PEDESTRIANS WITH NEURODEVELOPMENTAL DISORDERS: A SYSTEMATIC REVIEW.

Wilmut K, Purcell C.

Pedestrians represent one of the most vulnerable road user groups worldwide. Children and adult pedestrians with neurodevelopmental disorders may be at greater risk due to deficits in a range of domains, such as attention, social communication, motor control and executive function. According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (American Psychological Association, 2013), neurodevelopmental disorders include individuals with a diagnosis of Autism Spectrum Disorders, Attention Deficit Hyperactivity Disorder, Specific Learning Disorder, Motor Difficulties, Communication Disorders and Intellectual Disabilities. The purpose of this systematic review and meta-analysis was to explore existing literature relating to determine the nature of the risk faced by pedestrians with neurodevelopmental disorders. Relevant databases including Web of Science, PhysInfo and CINAHL were searched up to July 2019. All peer reviewed journals that presented data focusing on neurodevelopmental disorders and some aspect of road crossing or roadside behaviour that included a control or comparison group were included. A total of 149 abstracts were assessed and 17 met the inclusion criteria. The identified papers could be grouped into four areas: (1) rate of injury; (2) assessment of risk; (3) eye gaze and understanding of road layout and (4) gap choice. No papers exploring the risk factors at the roadside for individuals with Specific Learning Disorders or Communication Disorders were identified. Overall, the review provide evidence for an elevated risk of injury for individuals with ADHD at the roadside, potentially as a consequence of poor temporal gap choice, although there was evidence that this risk could be mediated by executive dysfunction rather than ADHD symptomology. Furthermore, poor temporal gap choice was found in children with DCD but it remains unclear as to whether this risk translates to the roadside. Finally, both children and adults with ASD and children with ID were found to demonstrate differences in behaviour / understanding at the roadside. In general, co-occurrence between neurodevelopmental disorders has been largely ignored in the current literature relating to pedestrian risk and future research could consider this along with executive functioning

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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.

Acta Med Iran. 2020;58:637-48.

COMPARING THE EFFECTIVENESS OF THE TRANSCRANIAL ALTERNATING CURRENT STIMULATION (TACS) AND RITALIN ON SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN 7-14-YEAR-OLD CHILDREN.

Farokhzadi F, Mohamadi MR, Khajevand Khosli A, et al.

Several studies have been conducted on the effect of transcranial direct current stimulation on adult patients. But, in recent years, only a few studies have been carried out in children and teenagers because the aim of the present study was to compare the effectiveness of TACS and Ritalin in the treatment of attention deficit hyperactivity disorder (ADHD) symptoms. This interventional clinical trial study was performed on 62 children with ADHD who were referred to the private psychiatric clinic of children in Tehran. The children were randomly assigned to two coded groups based on a lottery so that they were enrolled in the TACS or the Ritalin group. A questionnaire child syndrome inventory (parental form) and integrated visual and auditory (IVA) test with a pretest and posttest design was used in this study. TACS therapy protocol was employed (3 days a week for eight weeks using alternating current stimulation at 10 Hz over two points on the prefrontal cortex: the anode centered over F3 [the left dorsolateral prefrontal cortex] and the cathode over F4[the right dorsolateral prefrontal cortex]). Results showed that the posttest scores of the TACS-treated group were higher than those of the Ritalin-treated group, and there was a significant difference between the areas of visual attention (visual vigilance, visual focus, Sustained attention visual) and response control visual and auditory prudence (P<0.05). Results indicated that TACS was more effective and more durable compared to Ritalin in reducing attention deficit, hyperactivity, and impulsivity

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Acta Psychiatr Scand. 2021.

PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN PEOPLE WITH MOOD DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Sandstrom A, Perroud N, Alda M, et al.

Objective: Attention-deficit/hyperactivity disorder (ADHD) in mood disorders is associated with unfavorable outcomes, including more frequent mood episodes, and increased risk of suicide. The reported prevalence of ADHD in individuals with mood disorders varies widely.

Methods: We searched PsycInfo and PubMed for articles published before September 21st, 2020, using search terms for ADHD and mood disorders. We included original data on the prevalence of ADHD in individuals with bipolar disorder (BD) or major depressive disorder (MDD). We estimated the prevalence of ADHD, by developmental period and disorder using random-effects meta-analyses. We also compared the rate of ADHD in people with MDD and BD, and with and without mood disorders.

Results: Based on 92 studies including 17089 individuals, prevalence of ADHD in BD is 73% (95% CI 66-79) in childhood, 43% (95% CI 35-50) in adolescence, and 17% (95% CI 14-20) in adulthood. Data from 52 studies with 16897 individuals indicated that prevalence of ADHD in MDD is 28% (95% CI 19-39) in childhood, 17% (95% CI 12-24) in adolescence, and 7% (95% CI 4ΓÇô11) in adulthood. ADHD was three times more common in people with mood disorders compared to those without and 1.7 times more common in BD compared to MDD.

Conclusion: People with mood disorders are at a significant risk for ADHD. ADHD should be assessed and treated in individuals with BD and MDD. Comprehensive assessment strategies are needed to address challenges of diagnosing ADHD alongside mood disorders

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Addictive Behaviors. 2021 Feb;113.

LOW PREVALENCE OF RISK DRINKING IN ADOLESCENTS AND YOUNG ADULTS WITH AUTISM SPECTRUM PROBLEMS.

Kaltenegger HC, Doering S, Gillberg C, et al.

Individuals with Autism Spectrum Disorder (ASD) have high rates of 'comorbidity'. Research on concurrent substance use (disorder) in ASD, however, is scarce and findings have been inconsistent. This study aims at assessing the prevalence of risk drinking in adolescent and young adult twins with and without autism spectrum problems. Data from a Swedish longitudinal nationwide twin study were analyzed. Across three

age groups of 15- (N = 10,050), 18- (N = 7,931) and 24-year-olds (N = 2,882) prevalence rates of risk drinking were compared between twins with and without an ASD proxy diagnosis and between different ASD subgroups based on comorbid proxies for attention-deficit/hyperactivity disorder (ADHD) and/or Learning Disorder (LD). ASD, ADHD, and LD were assessed using the Autism-Tics, ADHD, and other Comorbidities inventory (A-TAC), and risk drinking was captured by the Alcohol Use Disorders Identification Test (AUDIT; age 18 and 24) and another set of self-report questions (age 15). In each age group, the prevalence of risk drinking in ASD was lower than in individuals without ASD, yet increasing continuously with age. Exploratory subgroup ASD analyses showed a trend towards risk drinking being more common among individuals with co-existing ADHD or LD problems than among those without 'comorbidity', although sample sizes were too small to draw any certain conclusions. This study indicates low prevalence of risk drinking in adolescents and young adults with autism spectrum problems and highlights the need for further research on alcohol use in individuals with ASD and comorbid disorders

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Advances in Cognitive Science. 2020;21:1-11.

COMPARISON OF RAPID RESPONSE IMPULSIVITY AND CHOICE IMPULSIVITY BETWEEN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND NORMAL CHILDREN.

Bakhshipour A, Chalabianloo GR, Jahanbin F.

Introduction: Impulsivity is one of the features of attention-deficit/hyperactivity disorder. Rapid response impulsivity and choice impulsivity encompass two different structures of impulsivity, which take place due to the deficiency in response inhibition and inhibition of immediate execution of a strong desire, respectively. Studying the existing differences in these structures between two groups with and without this disorder is clinically crucial. Therefore, the present study aimed to compare the rapid response impulsivity and choice impulsivity between children with attention-deficit/hyperactivity disorder and normal children.

Methods: This research was conducted with a causal-comparative method on 19 children with attention-deficit/hyperactivity disorder and 19 normal children (at the age of 8 to 10 years) who selected, based on the purposive sampling method. The participants were evaluated using Structured Diagnostic Interview, Raven IQ test, and Conners' Parent and Teacher Rating Scales-revised (short form), and they were then grouped. The performance of the groups has determined using the second version of the Continuous Performance Test (CPT-II) and Real-time Discounting Task. Data have been analyzed using multivariate analysis of variance (MANOVA) and SPSS-20 software.

Results: The results obtained from the current research indicated a significant difference between groups in the rapid response impulsivity ($P < 0.017$), while there is no significant difference between groups in the choice impulsivity ($P > 0.017$). Based on the obtained results, children with attention-deficit/hyperactivity disorder performed poorly in the rapid response impulsivity task.

Conclusion: According to the results of this research, there is a significant difference in rapid response impulsivity between two groups but there is no significant difference in choice impulsivity between them. Thus, rapid response impulsivity may be more important than choice impulsivity in the attention-deficit/hyperactivity disorder

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Am J Epidemiol. 2020;189:1163-72.

THE ASSOCIATION OF PRENATAL TETANUS, DIPHTHERIA, AND ACELLULAR PERTUSSIS (TDAP) VACCINATION WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Becerra-Culqui TA, Getahun D, Chiu V, et al.

As prenatal vaccinations become more prevalent, it is important to assess potential safety events. In a retrospective cohort study of Kaiser Permanente Southern California (Pasadena, California) mother-child pairs with birth dates during January 1, 2011-December 31, 2014, we investigated the association between prenatal tetanus, diphtheria, and acellular pertussis (Tdap) vaccination and risk of attention-deficit/hyperactivity disorder (ADHD) in offspring. Information on Tdap vaccination during pregnancy was obtained from electronic medical records. ADHD was defined by International Classification of Diseases

codes (Ninth or Tenth Revision) and dispensed ADHD medication after age 3 years. Children were followed to the date of their first ADHD diagnosis, the end of Kaiser Permanente membership, or the end of follow-up (December 31, 2018). In Cox proportional hazards models, we estimated unadjusted and adjusted hazard ratios for the association between maternal Tdap vaccination and ADHD, with inverse probability of treatment weighting (IPTW) used to adjust for confounding. Of 128,756 eligible mother-child pairs, 85,607 were included in the final sample. The ADHD incidence rate was 3.41 per 1,000 person-years in the Tdap-vaccinated women and 3.93 per 1,000 person-years in the unvaccinated (hazard ratio = 1.01, 95% confidence interval: 0.88, 1.16). The IPTW-adjusted analyses showed no association between prenatal Tdap vaccination and ADHD in offspring (hazard ratio = 1.00, 95% confidence interval: 0.88, 1.14). In this study, prenatal Tdap vaccination was not associated with ADHD risk in offspring, supporting recommendations to vaccinate pregnant women

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Anadolu Psikiyatr Derg. 2021;22:7-11.

THE RELATIONSHIP BETWEEN THE THEORY OF MIND SKILLS AND DISORDER SEVERITY AMONG ADOLESCENTS WITH ADHD.

Kilincel S.

Objective: This study aimed to examine the sub-dimensions of the theory of mind (ToM) and to investigate the relationship between ToM skills and disorder severity by comparing adolescents with attention-deficit hyperactive disorder (ADHD) with healthy individuals.

Methods: The study included 42 adolescents with ADHD and educationand agematched 41 healthy volunteers. The Smarties test, ice cream truck test, faux pas recognition test, and eyes test were applied to all participants. Turgay Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-IV)-Based Child and Adolescent Disruptive Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S) was applied to the group with ADHD to measure the disorder severity.

Results: The group with ADHD was seen to have ToM skills impairment. There was a statistically significant difference between the groups in terms of the ice cream truck test, faux pas recognition test, and eyes test. A significant correlation was observed between the T-DSM-IV-S results and the eyes test results of the patients.

Conclusion: This study has shown that advanced ToM skills can be impaired in adolescents with ADHD and that impairment in skills is associated with disorder severity

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ANAE Approche Neuropsychol Apprentiss Enfant. 2020;32:647-56.

THE PSYCHOLOGICAL ASSESSMENT OF ADHD: WHAT PLACE FOR WISC-V?

Quartier V, Brodard F, Hanifi M, et al.

The assessment of ADHD arises many issues for the clinician. Beyond the diagnostic criteria, the psychological assessment remains a precious tool to assess cognitive and instrumental difficulties, but also resources and other coexisting conditions comorbid disorders. ADHD children often present WISC-V with a CPI lower than the GAI and difficulties in many subtests. Three clinical cases illustrate diff+®rent situations encountered in clinical practice

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An Pediatr. 2021.

THE IMPACT OF METHYLPHENIDATE TREATMENT ON THE FUNCTIONAL AND STRUCTURAL PROPERTIES OF THE LEFT VENTRICLE: A MEDIUM-TERM PROSPECTIVE STUDY.

Garcia Ron A, Rodriguez Mesa M, Arias Vivas E, et al.

Introduction: Although methylphenidate (MPH) used for treatment of Attention deficit hyperactivity disorder (ADHD) are considered safe in healthy children and adolescents in the short and medium term, there is a widespread concern about long-term cardiovascular safety.

Material and methods: Interventional, prospective, longitudinal and comparative study with a crossover design to evaluate the cardiovascular impact of the treatment with MPH in healthy children and adolescents diagnosed with ADHD. A protocol for the cardiovascular evaluation was established at a basal point, after the first and the second year of the beginning with treatment based on the monitoring of Blood pressure (BP) and echocardiographic follow-up of the systolic and diastolic functions, and structural cardiac properties.
Results: 73 patients completed the study, with an average age of 9 + /- 2.6 years, 75.3% were male and the majority were thin (64.4%). We found an increase in Systolic and Diastolic BP of 3.7 -¦ 9 mmHg (P).004) and 2 -¦ 11,5 mmHg respectively. There were no severe cardiovascular events. We didn't find any echocardiographic alterations namely on the structural properties or parameters of systolic function. Regarding diastolic function, a significant increase in the isovolumic relaxation time (IVRT) (P=.046) and deceleration time (P=.016) was observed. However, no significant alterations in the parameters related to distensibility of the LV neither in the early diastolic pressure were found.
Conclusion: Further studies are needed to evaluate the impact of psychostimulants as a modifiable long-term Cardiovascular Risk Factor

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Anesth Analg. 2021 Mar;132:e46-e47.
FURTHER STUDY NEEDED OF THE IMPACT OF EARLY-LIFE SURGERY WITH ASSOCIATED GENERAL ANESTHESIA ON THE RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.
Frisch M, Earp BD, Van Howe RS.

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Annals of Clinical and Analytical Medicine. 2021;12:69-73.
DETERMINATION OF DEPRESSION AND ANXIETY LEVELS AMONG PARENTS OF ADHD CHILDREN.
Oguzoncul AF, Kurt O, et al.
Aim: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common psychiatric disorders of childhood. The aim of this study is to compare the depression and anxiety levels of parents of children with ADHD with a healthy control group.
Material and Method: In this case-control study, cases were selected from the parents of patients aged 7-17 years who applied to Firat University Medical Faculty Child and Adolescent Psychiatry Outpatient Clinic, and the control group was selected from allied health personnel who had healthy children. A questionnaire consisting of questions investigating socio-demographic characteristics, the Beck Depression Inventory (BDI) and the Beck Anxiety Inventory (BAI) was applied to the participants.
Results: The mean BDI score of the mothers in the case group was found to be 15.61-¦10.301, and the mothers of the control group was found to be 8.56-¦6.973, and a statistically significant difference was determined between them (p=0.001). The mean BAI score of the mothers in the case group was 14.20-¦10.442, the mean scoreof the mothers of the control group was found to be 8.90-¦8.516 and the difference was statistically significant (p=0.001). The mean BAI score of the fathers of boys with ADHD was significantly higher than the fathers of girls with ADHD. It was found that the mean BDI score of mothers increased significantly when the diagnosis period of children with ADHD was increased (p=0.004). The mean BDI and BAI scores of the mothers in the study group were significantly higher than the mothers in the control group.
Discussion: In this study, no relationship was found between the ages of the mother and father and their level of depression and anxiety. In a study conducted by Ergin et al. with parents of disabled children, it was found that maternal age did not affect the level of depression [22]. In the study by +ûzdel et al., they did not find a relationship between age and depression level in university students

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Ann Gen Psychiatry. 2021;20.

PREDICTING THE NUMBER OF ARTICLE CITATIONS IN THE FIELD OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) WITH THE 100 TOP-CITED ARTICLES SINCE 2014: A BIBLIOMETRIC ANALYSIS.

Lin CH, Chien TW, Yan YH.

Background: Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in children or early adolescents with an estimated worldwide prevalence of 7.2%. Numerous articles related to ADHD have been published in the literature. However, which articles had ultimate influence is still unknown, and what factors affect the number of article citations remains unclear as well. This bibliometric analysis (1) visualizes the prominent entities with 1 picture using the top 100 most-cited articles, and (2) investigates whether medical subject headings (i.e., MeSH terms) can be used in predicting article citations.

Methods: By searching the PubMed Central-« (PMC) database, the top 100 most-cited abstracts relevant to ADHD since 2014 were downloaded. Citation rank analysis was performed to compare the dominant roles of article types and topic categories using the pyramid plot. Social network analysis (SNA) was performed to highlight prominent entities for providing a quick look at the study result. The authors examined the MeSH prediction effect on article citations using its correlation coefficients (CC).

Results: The most frequent article types and topic categories were research support by institutes (56%) and epidemiology (28%). The most productive countries were the United States (42%), followed by the United Kingdom (13%), Germany (9%), and the Netherlands (9%). Most articles were published in the Journal of the American Academy of Child and Adolescent Psychiatry (15%) and JAMA Psychiatry (9%). MeSH terms were evident in prediction power on the number of article citations (correlation coefficient = 0.39; t = 4.1; n = 94; 6 articles were excluded because they do not have MeSH terms).

Conclusions: The breakthrough was made by developing 1 dashboard to display 100 top-cited articles on ADHD. MeSH terms can be used in predicting article citations on ADHD. These visualizations of the top 100 most-cited articles could be applied to future academic pursuits and other academic disciplines

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Appl Neuropsychol Child. 2021 Jan;10:82-89.

MATERNAL SMOKING DURING PREGNANCY AND PHYSIOLOGICAL ANXIETY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Zambrano-Sánchez E, Martínez-Cortés J, Poblano A, et al.

Our objective was to explore the relationship between mother smoking during pregnancy and physiological anxiety of children with Attention deficit-hyperactivity disorder. Cognitive profile was evaluated by Wechsler Intelligence Scale for Children, physiological anxiety by Children's Manifest Anxiety Scale. Mother's smoking was evaluated by the Fagerström test for nicotine dependence. Ninety-seven children with Attention Deficit-Hyperactivity Disorder combined type, 70 inattentive, and 48 hyperactive-impulsive, and 130 controls were studied. We found a higher frequency of high smoking dependence in mothers of children with Attention Deficit-Hyperactivity Disorder-combined type, and Attention Deficit Hyperactivity Disorder-hyperactive type in the Fagerström test; and a significant correlation between physiological anxiety in children with Attention Deficit Hyperactivity Disorder-combined type, with high and moderate maternal smoking level during pregnancy. In conclusion, data suggests, with caution a brain alteration of infants, induced by nicotine exposure during pregnancy in children with Attention Deficit Hyperactivity Disorder-combined type, and Attention Deficit Hyperactivity Disorder-hyperactive type

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Arq Neuro-Psiquiatr. 2020;78:193-98.

COMBINING NEUROPSYCHOLOGICAL TESTS TO IMPROVE THE ASSESSMENT OF ARITHMETIC DIFFICULTIES IN CHILDREN WITH ADHD.

Rezende ART, Pacheco SP, Branco SCC, et al.

Objective: To compare the ways of evaluating arithmetic skills in Brazilian children with ADHD by combining three validated neuropsychological tests and determining whether they are sensitive to the methylphenidate treatment.

Methods: Forty-two children (9ΓÇô12 years old) participated in the present study: 20 were children with ADHD (DSM-IV) and 22 were age-matched controls. A classification criterion was used for each test separately and one, for their combination to detect the presence of arithmetic difficulties at two time points: baseline (time 1); and when children with ADHD were taking 0.3-0.5 mg/kg of methylphenidate (time 2). The study also assessed children's subtraction performance, combining parts of these tests.
Results: Separately, the tests were only sensitive to differences between groups without medication. However, by combining the three neuropsychological tests, we observed a difference and detected a reduction in arithmetic difficulties associated with the methylphenidate treatment. The same effects were found in subtraction exercises, which require a borrowing procedure.
Conclusions: The present study detected arithmetic difficulties in Brazilian children with ADHD and the effects of methylphenidate. Given this improvement in sensitivity, combining tests could be a promising alternative when working with limited samples

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Arts Psychother. 2021;73.

EFFECTIVENESS OF GROUP PSYCHODRAMA ON AGGRESSION AND SOCIAL ANXIETY OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED CLINICAL TRIAL.

Mojahed A, Zaheri Y, Firoozkoohi Moqaddam M.

This study aimed to determine the effects of psychodrama-based group therapy on reducing aggression, social anxiety, and attention-deficit/hyperactivity disorder (ADHD) symptoms in children. This clinical trial, with a pretest-posttest design and a two-month follow-up, involved 48 children (aged 8ΓÇô12) at two hospitals in Iran. The participants were selected by available sampling and randomly divided into experimental and control groups (each 24 participants). Group psychodrama in sessions of 2 h a week for 10 weeks was applied as an intervention for the experimental group, while the control group was assigned to a waiting list. The Child Behavior Checklist and Spence Children's Anxiety Scale were used for collecting the data. The mean and standard deviation were measured, and repeated measures ANOVA and Bonferroni correction tests were performed. We found that social anxiety, aggression, and ADHD symptoms significantly decreased in posttest in the psychodrama group, while there were no changes in these variables in the control group. Also, these results were persistent at the two-month follow-up. The present findings revealed that group psychodrama is effective in reducing aggression, social anxiety, and ADHD symptoms in children

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Asian J Psychiatr. 2021 Feb;56:102554.

IMPACT OF LOCKDOWN DUE TO COVID-19 PANDEMIC IN CHANGES OF PREVALENCE OF PREDICTIVE PSYCHIATRIC DISORDERS AMONG CHILDREN AND ADOLESCENTS IN BANGLADESH.

Mallik CI, Radwan RB.

Lockdown, isolation, quarantine and social distancing are proved to be only effective measures to prevent and tackle COVID-19 till date. Unfortunately, these measures have caused physical, economical and mental health problems. Children and adolescents are not immune to the adverse mental health effect due to the new changes. Research around the globe shows children and adolescents are suffering from an increased number of depressive symptoms, clinginess, inattention, irritability and worry. This cross-sectional online-based survey type study was aimed to get a snapshot of the prevalence of predictive psychiatric disorders in the child and adolescent population in Bangladesh before and during lockdown. Validated Bangla parent version of Strengths and Difficulties Questionnaire was used to assess the psychopathology among subjects. Total sample was 552 aged from 4-17 years. Boy-girl ratio was 1.3:1. Prevalence of any predictive psychiatric disorder before lockdown was 20.5 % and within lockdown was 39.7 % and the difference was highly significant ($P < 0.001$). Prevalence of emotional, conduct disorder and hyperactivity were also increased significantly during the lockdown period than before. Conduct disorder and hyperactivity were more prevalent among boys both before and within lockdown. In contrast, prevalence of emotional disorder was higher among girls before lockdown but within the lockdown period, the boy-girl prevalence was almost the same. This study shows the new extreme measures to tackle COVID-19 has a disaster impact on mental health of

children and adolescents. Subsequent studies and support should be developed to prevent conditions getting worse

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Asian J Psychiatry. 2021;57.

DRUG PRESCRIPTION FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER DRUGS IN PEDIATRIC OUTPATIENTS: A RETROSPECTIVE SURVEY OF JAPANESE ADMINISTRATIVE DATA (2012ΓÇô2018).

Kikuchi D, Obara T, Tokunaga M, et al.

We aimed to clarify the prescription trend of ADHD drugs in Japanese pediatric outpatients. From January 2012 to December 2018, we evaluated the trends of prescribing methylphenidate-osmotic-controlled release oral delivery system (OROS), atomoxetine, and guanfacine as monotherapy. In boys, methylphenidate-OROS and atomoxetine prescriptions decreased from 46.5 % to 37.2 % and 18.6 % to 15.6 %, respectively. Prescriptions of guanfacine increased from 0.0 % to 12.3 %. In girls, the methylphenidate-OROS prescriptions was not significantly different (37.0 % to 26.4 %); however, atomoxetine decreased from 23.1 % to 16.3 %, and guanfacine increased from 0.0 % to 12.8 %. Methylphenidate-OROS and atomoxetine prescriptions changed to guanfacine between 2012 and 2018

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Behav Genet. 2020;50:458.

TODDLER TEMPERAMENT MODESTLY PREDICTS MIDDLE CHILDHOOD MENTAL HEALTH PROFILES, VIA GENETIC PATHWAYS.

Hilton EC, Goldsmith HH.

Temperament provides a promising avenue for understanding childhood psychopathology risk, yet most studies only examine temperament links to single disorders. In contrast, we examine how broad temperament factors during toddlerhood predict empiricallyderived classes of psychopathology symptoms in middle childhood. Latent class analysis of symptoms at age 7 yielded 9 classes for each gender in a birth record-based twin sample (Vendlinski et al. 2014) Classes revealed pervasive symptom overlap. Using parent report on the Toddler Behavior Assessment Questionnaire (N = 1037), a linear mixed effects model with nesting within families showed the temperament factors were generally modestly but highly significantly associated with symptom classes. The low interest/attention and high negative affect/low control temperament factors predicted membership in more impaired/severe classes, which contained both internalizing and externalizing symptoms. Lower temperamental fear in toddlerhood predicted classes with moderate impulsivity. High interest/attention and low negative affect/high control predicted low and mild symptoms classes. Thus, toddler temperament factors were non-specific risk or protective factors for childhood symptoms. Bivariate Cholesky decompositions indicated that for the boys' low symptom class, the proportion of variance accounted for by genetic effects of high negative affect/low control was .35, but only .06 for a high symptom class with ADHD/conduct disorder features. For the same symptom classes, genetic effects attributable to the interest/attention factor were only .04 and .02. Genetic temperament symptoms paths were variable, with protective temperament factors showing greater genetic mediation

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Behav Genet. 2020;50:446.

UNDERSTANDING THE EFFECTS OF NEIGHBORHOOD DISADVANTAGE ON YOUTH PSYCHOPATHOLOGY.

Carroll SL, Klump KL, Burt SA.

In 1942, Shaw and McKay reported that disadvantaged neighborhoods predict youth psychopathology. In the decades since, dozens of papers have confirmed and extended these early results, convincingly demonstrating that disadvantaged neighborhoods predict elevated rates of both internalizing and externalizing disorders, and that they do so across childhood and adolescence. It is not yet clear, however, how neighborhood disadvantage increases psychopathology. The current study sought to fill this gap in the literature by examining the Area Deprivation Index (ADI), a composite measure of census tract disadvantage,

as an etiologic moderator of several common forms of psychopathology in two samples of school-aged twins (Total N = 11,130 twins in 5515 pairs), one of which was enriched for neighborhood disadvantage. Results indicated that, across both samples, additive genetic influences on attention-deficit hyperactivity problems were accentuated in the presence of marked disadvantage, while nonshared environmental contributions to callous-unemotional symptoms increased with increasing disadvantage. However, neighborhood disadvantage had little in the way of moderating effects on the etiology of internalizing symptoms. Such findings point to widespread influences of neighborhood disadvantage on psychiatric and psychological outcomes in childhood, while also suggesting that these effects are phenotype-specific. Implications and future research directions are discussed

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Behav Genet. 2020;50:466-67.

SEX DIFFERENCES IN PSYCHIATRIC POLYGENIC RISK IN CHILDREN WITH ADHD.

Martin J, Agha SS, Eyre O, et al.

Attention deficit hyperactivity disorder (ADHD) is more commonly diagnosed in males than females. It is frequently comorbid with and shares genetic risks with anxiety and depression, which are more common in females in the general population. We tested for sex differences in polygenic risk scores (PRS) for anxiety and depression in children with ADHD and examined possible sex differences in the association between anxiety and depression PRS with anxiety and depression symptoms in the context of ADHD. Exploratory analyses tested for sex differences in PRS for other psychiatric disorders. Children with ADHD were recruited from clinics and symptoms of anxiety (separation, social and generalised) and depression were assessed using a standardised diagnostic interview. We derived PRS based on large genetic studies of anxiety, major depressive disorders, ADHD, autism, bipolar disorder, and schizophrenia. In 885 children with ADHD (14% female), we found no sex differences in comorbid anxiety and depression symptoms or anxiety/ depression PRS. Exploratory analyses suggested higher PRS for bipolar disorder in females [OR(CIs) = 1.23 (1.00-1.51)] and this was replicated using an independent ADHD sample [OR(CIs) = 1.0 9(1.00-1.19)]. Anxiety PRS were associated with social [OR(CIs) = 1.54 (1.14-2.09)] and generalised anxiety symptoms [OR(CIs) = 1.46 (1.11-1.92)] in males but not females, with significant sex-by-PRS interactions. Depression PRS were not associated with depression symptoms. The results support the presence of sex differences in children with ADHD, indicating that the genetic link between ADHD and bipolar disorder may be stronger in females and that the aetiology of comorbid anxiety problems may differ in males and females with ADHD

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Behav Genet. 2020;50:459.

INTEGRATIVE MULTI-OMICS ANALYSIS OF EPIGENOMIC AND METABOLOMIC DATA FOR ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

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

Attention-deficit/hyperactivity disorder (ADHD) is a complex trait with a substantial heritability with other 'omics' e.g. epigenomics and metabolomics, influences on ADHD beginning to be explored. Multiomics is an evolving field which combines data from multiple 'omics' levels and provides methods for their simultaneous analyses to identify biological mechanisms and biomarkers for complex traits. This project applies an integrative multi-omics method, called DIABLO, based on multi-block Partial Least Squares Discriminant Analysis (PLS-DA) to build a predictive model for ADHD from metabolomics and epigenomics data. First-morning urine and buccal-cell samples were collected from 606 twins (N complete pairs = 275, mean age = 9.3 [SD = 0.63], male = 54.9%) who took part in Netherlands Twin Register ACTION project (Aggression in Children: Unraveling gene-environment interplay to inform Treatment and InterventiON strategies). Dichotomous ADHD status was based on the mother-rated Revised Conners' Parent Rating Scale (CPRS-R). First, in 20% of the data, the discriminative capacities of each 'omics' level and pair-wise cross-omics relationships were analysed with PLS-DA and PLS, respectively. Next, multi-block PLS-DA was applied to 50% of the data. The resulting model was used to predict the ADHD status in the remaining 30% of the data. The model selected metabolites and methylation probes involved in dopaminergic pathways and oxidative

stress, mechanisms that have previously been associated with ADHD. However, the predictive accuracy of the model was relatively low (Area under the curve = 0.449-0.588, p>0.10). Overall, the model seems promising and underlines the potential of a multi-omics approach in complex traits such as ADHD

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Biological Psychiatry: Cognitive Neuroscience and Neuroimaging. 2021.

DIRECT AND INDIRECT ASSOCIATIONS OF WIDESPREAD INDIVIDUAL DIFFERENCES IN BRAIN WHITE MATTER MICROSTRUCTURE WITH EXECUTIVE FUNCTIONING AND GENERAL AND SPECIFIC DIMENSIONS OF PSYCHOPATHOLOGY IN CHILDREN.

Cardenas-Iniguez C, Moore TM, Kaczkurkin AN, et al.

Background: Executive functions (EFs) are important partly because they are associated with risk for psychopathology and substance use problems. Because EFs have been linked to white matter microstructure, we tested the prediction that fractional anisotropy (FA) and mean diffusivity (MD) in white matter tracts are associated with EFs and dimensions of psychopathology in children younger than the age of widespread psychoactive substance use.

Methods: Parent symptom ratings, EF test scores, and diffusion tensor parameters from 8588 9- to 10-year-olds in the ABCD Study (Adolescent Brain Cognitive Development Study) were used.

Results: A latent factor derived from EF test scores was significantly associated with specific conduct problems and attention-deficit/hyperactivity disorder problems, with dimensions defined in a bifactor model. Furthermore, EFs were associated with FA and MD in 16 of 17 bilateral white matter tracts (range: +¦ =. 05; SE =. 17; through +¦ = ΓêÆ.31; SE =. 06). Neither FA nor MD was directly associated with psychopathology, but there were significant indirect associations via EFs of both FA (range: +¦ =. 01; SE =. 01; through +¦ = ΓêÆ.09; SE =. 02) and MD (range: +¦ =. 01; SE =. 01; through +¦ =. 09; SE =. 02) with both specific conduct problems and attention-deficit/hyperactivity disorder in all tracts except the forceps minor.

Conclusions: EFs in children are inversely associated with diffusion tensor imaging measures in nearly all tracts throughout the brain. Furthermore, variance in diffusion tensor measures that is shared with EFs is indirectly shared with attention-deficit/hyperactivity disorder and conduct problems

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BMJ Open. 2021;11.

CAUSAL MODELLING OF VARIATION IN CLINICAL PRACTICE AND LONG-TERM OUTCOMES OF ADHD USING NORWEGIAN REGISTRY DATA: THE ADHD CONTROVERSY PROJECT.

Mykletun A, Widding-Havneraas T, Chaulagain A, et al.

Introduction Attention-deficit/hyperactivity disorder (ADHD) is among the most common mental disorders in children and adolescents, and it is a strong risk factor for several adverse psychosocial outcomes over the lifespan. There are large between-country and within-country variations in diagnosis and medication rates. Due to ethical and practical considerations, a few studies have examined the effects of receiving a diagnosis, and there is a lack of research on effects of medication on long-term outcomes. Our project has four aims organised in four work packages: (WP1) To examine the prognosis of ADHD (with and without medication) compared with patients with other psychiatric diagnoses, patients in contact with public sector child and adolescent psychiatric outpatient clinics (without diagnosis) and the general population; (WP2) Examine within-country variation in ADHD diagnoses and medication rates by clinics' catchment area; and(WP3) Identify causal effects of being diagnosed with ADHD and (WP4) ADHD medication on long-term outcomes.

Method and analysis Our project links several nationwide Norwegian registries. The patient sample is all persons aged 5-18 years that were in contact with public sector child and adolescent psychiatric outpatient clinics in 2009-2011. Our comparative analysis of prognosis will be based on survival analysis and mixed-effects models. Our analysis of variation will apply mixed-effects models and generalised linear models. We have two identification strategies for the effect of being diagnosed with ADHD and of receiving medication on long-term outcomes. Both strategies rely on using preference-based instrumental variables, which in our project are based on provider preferences for ADHD diagnosis and medication.

Ethics and dissemination The project is approved by the Regional Ethics Committee, Norway (REC number 2017/2150/REC south-east D). All papers will be published in open-access journals and results will be presented in national and international conferences.
Trial registration numbers ISRCTN11573246 and ISRCTN11891971

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Brain Dev. 2021 Feb;43:280-87.

POSTOPERATIVE IMPROVEMENT OF EXECUTIVE FUNCTION AND ADAPTIVE BEHAVIOR IN CHILDREN WITH INTRACTABLE EPILEPSY.

Ueda R, Kaga Y, Kita Y, et al.

Introduction: An alteration in postoperative cognitive function varies according to the patients' background characteristics, such as etiology, focus, and seizure duration. Accurate prediction and assessment of postoperative cognitive function is difficult in each patient. Adaptive behavior could describe the typical performance of daily activities and represents the ability to translate cognitive potential into real-world skills. We examined the relationship between alterations of executive function (EF) and adaptive behavior in school children undergoing surgery for intractable epilepsy.
Methodology: We enrolled 31 children with focal resection or corpus callosotomy for intractable epilepsy [mean age at surgery, 12.5 years; 16 boys; mean intellectual quotient, 73.3]. We surveyed answered questionnaires on attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and adaptive behavior using the Vineland Adaptive Behavior Scale, 2nd edition (VABS-II), and performed continuous performance tests (CPTs) on children pre- and postoperatively.
Result: ADHD and ASD symptoms improved after epilepsy surgery. The omission error (OE) in the CPT variable improved after epilepsy surgery, especially in children with a shorter preoperative period. Improved ASD symptoms led to an increased score of the coping skills subdomain. The reduced OE observed after surgery also increased the score of the community skills subdomain.
Conclusion: Improvement in EF and ASD symptoms resulted in better adaptive behavior postoperatively. These results were important for the pre- and postoperative evaluation and re-evaluation of children with epilepsy requiring special education and related services

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Brain Sciences. 2020;10:1-9.

COMPUTERIZED EYE-TRACKING TRAINING IMPROVES THE SACCADIC EYE MOVEMENTS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Lee TL, Yeung MK, Sze SL, et al.

Abnormal saccadic eye movements, such as longer anti-saccade latency and lower pro-saccade accuracy, are common in children with attention-deficit/hyperactivity disorder (ADHD). The present study aimed to investigate the effectiveness of computerized eye-tracking training on improving saccadic eye movements in children with ADHD. Eighteen children with ADHD (mean age = 8.8 years, 10 males) were recruited and assigned to either the experimental (n = 9) or control group (n = 9). The experimental group underwent an accumulated 240 min of eye-tracking training within two weeks, whereas the control group engaged in web game playing for the same amount of time. Saccadic performances were assessed using the anti-and pro-saccade tasks before and after training. Compared to the baseline, only the children who underwent the eye-tracking training showed significant improvements in saccade latency and accuracy in the anti-and pro-saccade tasks, respectively. In contrast, the control group exhibited no significant changes. These preliminary findings support the use of eye-tracking training as a safe non-pharmacological intervention for improving the saccadic eye movements of children with ADHD

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Brain Sciences. 2021;11:1-12.

IMPULSIVITY AS EARLY EMERGING VULNERABILITY FACTOR–PREDICTION OF ADHD BY A PRESCHOOL NEUROPSYCHOLOGICAL MEASURE.

Pauli-Pott U, Becker K.

Impulsivity, comprising deviations of brain-based bottom-up and top-down control pro-cesses, has been regarded as a crucial, early emerging marker of a developmental pathway to attention-deficit/hyperactivity (ADHD) and externalizing disorders. In two independent studies (a cross-sectional study and a longitudinal study), we analyzed the concurrent and predictive validity of a task-based neuropsychological impulsivity measure for preschool children. The sample of Study 1 comprised 102 3ΓÇô5-year-old children (46% boys). In Study 2, 138 children (59% boys) with elevated ADHD symptoms were recruited and assessed at the ages of 4ΓÇô5 and 8 years. In both studies, preschool impulsivity was measured by a summary score of neuropsychological tasks on approach motivation and hot inhibitory control. For Study 1, the impulsivity measure was significantly associated with symptoms of ADHD and oppositional defiant disorder (ODD) (¤ç2 (1) = 9.8, p = 0.002; ¤ç2 (1) = 8.1, p = 0.004). In Study 2, the impulsivity measure predicted the 8-year-oldsΓÇÖ ADHD diagnoses over and above concurrent ADHD symptoms (¤ç2 (1) = 10.0, p = 0.002, OR = 5.0, 95% CI: 1.8ΓÇô14.0). The impulsivity measure showed good concurrent and predictive validity. The measure can be useful for the early identification of children at risk for developing ADHD and externalizing disorders

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Brain Sciences. 2021;11:1-16.

TRAUMATIC BRAIN INJURY-RELATED ATTENTION DEFICITS IN CHILDREN: A CONTROLLED TREATMENT TRIAL WITH LISDEXAMFETAMINE DIMESYLATE (VYVANSE).

Tramontana MG, Prokop JW, Williamson E, et al.

Attention deficits are among the most common and persistent impairments resulting from traumatic brain injury (TBI). This study was the first to examine the effects of lisdexamfetamine dimesylate (LDX, Vyvanse) in treating TBI-related attention deficits in children. It was an extension of a previous controlled trial with adults. This was a 12-week, randomized, double-blind, placebo-controlled, dose-titration, crossover trial. In addition to weekly safety monitoring, there were assessments on a broad range of neuropsychological and behavioral measures at baseline, 6-weeks, and 12-weeks. A total of 20 carefully selected children were enrolled, ranging from 10 to 16 years of age. The sample consisted of cases with mainly mild TBI (based on the known details regarding their injuries), but they had persisting attention deficits and other post-concussion symptoms lasting from 2 to 29 months by the time of enrollment. A total of 16 children completed the trial. One of the children withdrew due to a mild anxiety reaction while on LDX. There were no other adverse effects. Positive treatment results were found on both formal testing of sustained attention and in terms of parent ratings of attention, emotional status, behavioral controls, and various aspects of executive functioning. The findings also served to highlight broader insights into the nature of attention deficits and their treatment in children with TBI

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Brain Sciences. 2021;11:1-15.

ONE-YEAR FOLLOW-UP DIAGNOSTIC STABILITY OF AUTISM SPECTRUM DISORDER DIAGNOSIS IN A CLINICAL SAMPLE OF CHILDREN AND TODDLERS.

Benedetto L, Cucinotta F, Maggio R, et al.

Some studies show that the diagnosis of Autism Spectrum Disorder could be considered reliable and stable in children aged 18 to 24 months. Nevertheless, the diagnostic stability of early ASD diagnosis has not yet been fully demonstrated. This observational study examines the one-year diagnostic stability of autism spectrum disorder diagnosis in a clinical sample of 147 children diagnosed between 18 and 48 months of age. The ADOS-2 scores were used in order to stratify children in three levels of symptom severity: Autism (AD; comparison score 5-7), Autism Spectrum Disorder (ASD; comparison score 3ΓÇô4), and Sub-Threshold Symptoms; (STS; comparison score 1-2). Results: Overall, the largest part of children and toddlers

diagnosed with autism spectrum disorder between 18 and 48 months continued to show autistic symptoms at one-year follow-up evaluation. Neverthe-less, a significant percentage of children with higher ADOS severity scores exhibited a reduction of symptom severity and, therefore, moved towards a milder severity class one year later. Conversely, the number of subjects of the STS group meaningfully increased. Therefore, at one-year follow-up a statistically significant (2 (2) = 181.46, p < 0.0001) percentage of subjects (25.2% of the total) who had received a categorical diagnosis of Autistic Disorder or Autism Spectrum Disorder in baseline no longer met the criteria for a categorical diagnosis. Furthermore, children who no longer met the criteria for autism spectrum disorder continue to show delays in one or more neurodevelopmental areas, possibly related to the emergence of other neurodevelopmental/neuropsychiatric disorders. Overall, the comprehensive results of the study account for a high sensibility but a moderate stability of ASD early diagnosis

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Cephalalgia Reports. 2020;3:1.

COMPARISON OF PERCEPTIONS AND BELIEFS RELATED TO HEADACHE OF ADOLESSCENTS WITH EPISODIC MIGRAINE DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND GENERALIZED ANXIETY DISORDER.

Aksu GG, Kayar O, Tavas SD, et al.

Background: Psychiatric comorbidity often complicates headache treatment regardless of child, adolescent or adult and can lead to poor prognosis during the treatment process. Moreover, it is known that adult headaches begin to a great extent during childhood or adolescence. On the other hand, how individuals perceive their illness or what kind of beliefs they develop are determinant in the quality of life, quality of cognitive, emotional and behavioral response to treatment.

Method: Adolescents admitted to Mersin University Child and Adolescent Mental Health and Diseases outpatient clinic with the complaint of headache and was diagnosed as episodic migraine (EM) according to the diagnostic criteria of The International Classification of Headache Disorder 3rd edition betaversion by the neurologist were examined. Samples are between 12-18 years old and they had been chosen among 170 adolescents. By the psychiatric assessment performed by the child and adolescent psychiatrist by considering the DSM-V diagnostic criteria,19 adolescents with attention deficit hyperactivity disorder (ADHD) and 25 adolescents with generalized anxiety disorder (GAD) were included. In addition to the diagnosis of EM, it was intended to compare the perception for migraine and pain beliefs of adolescents with ADHD or GAD. In order to determine socio-demographic information and developmental/psychiatric features a 'Patient Assessment Form', 'Headache Questionnaire Form' to determine painrelated features, and 'Disease Perception Scale' to measure adolescents' perception of migraine and beliefs about headachewere performed

Results: Adolescents with GAD and EM perceive migraine as a more chronic, very serious and negative resulting emotionally damaging disease and try to identify and better understand their disease than adolescents with ADHD and EM. The perception of those with ADHD that they can control their headaches is more positive than adolescents with GAD.

Conclusion: In order to achieve more enlightening results, it is recommended to conduct studies examining various child and adolescent psychopathologies that commonly accompany migraine at different developmental stages and cognitive and emotional attitudes towards migraine in larger groups.

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Child Abuse Negl. 2021;114.

RISK FOR SUBSTANCE USE AMONG ADOLESCENTS AT-RISK FOR CHILDHOOD VICTIMIZATION: THE MODERATING ROLE OF ADHD.

Garcia BH, et al.

Background: Youth who are victimized by violence are at heightened risk for substance use (SU) during adolescence, a period characterized by elevated impulsivity and risk-taking behavior. This risk may be magnified by attention-deficit/hyperactivity disorder (ADHD).

Objective: To examine risk/protective factors for adolescent SU among adolescents at-risk for victimization and whether ADHD moderates these associations.
Participants and setting: Participants were 1058 caregiver-adolescent dyads in the U.S. who participated in the Longitudinal Studies of Child Abuse and Neglect (LONGSCAN). Method: Binary logistic regression analyses were conducted for each SU type. First-order effects of all variables were tested first and for each SU outcome, followed by tests of two-way interactions between ADHD group and each predictor, after controlling for first-order effects.
Results: More externalizing behavior (odds ratio [OR] = 1.38; 95 % confidence interval [CI]:1.12, 1.71) and less parental knowledge (OR = .75; 95 %CI: .60, .95) were associated with greater risk for subsequent tobacco use. Less positive peer affiliation was associated with greater risk for subsequent illicit SU (OR = .59; 95 %CI: .36, .96). More deviant peer affiliation were associated with greater risk for all forms of SU. ADHD moderated the association between deviant peer affiliation and marijuana use [b = .9, p < .05, 95 %CI: .03, 1.77), such that deviant peer affiliation was a significantly stronger predictor of marijuana use among adolescents with ADHD than those without.
Conclusions: Findings suggest risk and protective factors for SU are largely consistent for adolescents at-risk for victimization with and without ADHD, but at-risk adolescents with ADHD may be more susceptible to deviant peer influences

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Child Adolesc Psychiatry Ment Health. 2021;15.

GENDER DIFFERENCES IN EXTERNALIZING AND INTERNALIZING PROBLEMS IN SINGAPOREAN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Lau TWI, Lim CG, Acharryya S, et al.

Background: Studies on gender differences in attention-deficit/hyperactivity disorder (ADHD) comorbidities in the Asian populations have been limited and previous studies have shown inconclusive findings. Singapore is a city-state country in Southeast Asia with a population of 5.7-ámillion. This study examined gender differences in internalizing and externalizing problems in Singaporean children and adolescents with ADHD. The plausible social factors underlying the gender differences were discussed.
Methods: A total of 773 participants (aged 6 to 18, 88% males) newly diagnosed with ADHD were recruited from the largest public child and adolescent psychiatric center in Singapore. Their internalizing and externalizing problems were assessed using the Child Behavioral Checklist and Teacher's Report Form by parents and teachers respectively. Demographics and relevant social factors were collected using parent questionnaires.
Results: Females with ADHD were reported to have less delinquent and aggressive behavior but more depressive symptoms than their male counterparts, similar to findings in the Western literature. Gender remained a significant predictor of externalizing problem after controlling for other factors. Lower socioeconomic status and parental use of physical punishment were significant predictors of both internalizing and externalizing problems.
Conclusions: Gender differences in ADHD comorbidities do exist in the Asian clinical population. The lack of externalizing symptoms in females with ADHD has made timely referral and diagnosis challenging. More research is needed in understanding the gender differences in ADHD and the biopsychosocial mechanism underlying the differences in order to improve the detection of ADHD in females

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Child Neuropsychol. 2021.

COGNITIVE MECHANISMS OF METHYLPHENIDATE IN ADHD: DO IMPROVEMENTS IN SUSTAINED ATTENTION MEDIATE BEHAVIORAL IMPROVEMENTS IN THE NATURAL ENVIRONMENT?

Merrill BM, Raiker JS, Evans SW, et al.

The relation between sustained attention in the laboratory and behaviors exhibited in naturalistic settings among children with Attention Deficit/Hyperactivity Disorder (ADHD) remains unclear. Additionally, research on stimulant medication effects in these areas and their association with one another remains scarce.

Twenty-one children with ADHD and 21 children without ADHD completed a novel continuous performance test (CPT) involving high cognitive demands (e.g., visual search). Participants with ADHD also attended a Summer Treatment Program and received three doses of stimulant medication (placebo, low, and high). Their behavior in classroom and peer settings was observed and recorded, and they completed the CPT in each medication condition. The CPT measures of bias and sensitivity were used in analyses. Results indicated that children with ADHD had impaired overall performance and worse bias during the second half of the task compared to controls. Methylphenidate improved both naturalistic behavior and overall CPT performance but did not specifically improve the sustained attention deficit. Despite improvements in overall CPT performance, medication-related improvement in CPT performance did not mediate medication-related improvement in observed behavior in classroom or recreational settings. As such, our findings suggest that although children with ADHD do demonstrate a sustained attention deficit, salutary psychostimulant effects on CPT performance are not indicative of, or causally linked to, psychostimulant effects on presenting problems in naturalistic settings

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Child Neuropsychol. 2021.

ACTIVITIES OF DAILY LIVING AND WORKING MEMORY IN PEDIATRIC ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Irwin LN, Soto EF, Chan ESM, et al.

Most children with ADHD have impaired working memory abilities. These working memory deficits predict impairments in activities of daily living (ADLs) for adults with ADHD. However, our understanding of the relation between pediatric ADHD and ADLs is limited. Thus, this study aimed to examine (1) the extent to which pediatric ADHD is associated with ADL difficulties; and if so (2) the extent to which these difficulties are related to their well-documented working memory difficulties and/or core ADHD inattentive and hyperactive/impulsive symptom domains. A well-characterized, clinically evaluated sample of 141 children ages 8ΓÇô13-áyears (M =-á10.36, SD-á=-á1.46; 51 girls; 70% White/non-Hispanic) were administered a battery of well-validated working memory tests and assessed for ADHD symptoms (teacher-ratings) and ADL difficulties (parent-ratings); cross-informant reports were used to control for mono-informant bias. Children with ADHD exhibited medium magnitude difficulties with ADLs (d =-á0.61, p <0.005, 38% impaired). Results of the bias-corrected, bootstrapped conditional effects model indicated that lower working memory predicted reduced performance of age-expected ADLs (+¦-á=0.28) and greater ADHD inattentive (+¦-á=-áΓêÆ0.40) and hyperactive/impulsive symptoms (+¦-á=-áΓêÆ0.16). Greater inattentive, but not hyperactive/impulsive, symptoms predicted greater ADL difficulties (+¦-á=-áΓêÆ0.36) even after controlling for working memory. Interestingly, working memory exerted a significant indirect effect on ADLs via inattentive (indirect effect: +¦-á=0.15, effect ratio-á=0.54) but not hyperactive/impulsive symptoms. These findings implicate ADHD inattentive symptoms as a potential mechanism underlying ADL difficulties for children with ADHD, both independently and via working memoryΓÇÖs role in regulating attention

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Child Neuropsychol. 2021.

BRIEF REPORT: EVALUATION OF WORKING MEMORY DEFICITS IN CHILDREN WITH ADHD USING THE NIH LIST SORTING WORKING MEMORY TASK.

Jusko ML, Raiker JS, Campez M, et al.

Variability in working memory (WM) task selection likely contributes to heterogeneity in effect size estimates of deficiencies in youth with attention-deficit/hyperactivity disorder (ADHD). This has resulted in the development of brief, easy to administer assessments such as the NIH List Sorting Working Memory (LSWM) task from the NIH Cognitive Toolbox in hopes of standardizing measurement of this construct. Unfortunately, substantial questions persist regarding the specific constructs being evaluated by this task (e.g., visuospatial [VS] or phonological [PH] WM) as well as the ability of this task to detect WM deficits in previously identified impaired groups (e.g., ADHD). The current study examines the extent to which the LSWM task is associated with VS and PHWM performance as well as symptoms of ADHD. Additionally, we examined the magnitude

of differences between ADHD and Typically Developing (TD) youth on this task relative to empirically derived WM tasks utilized in the past. Forty-six children (25 ADHD, 21 TD) completed multiple WM tasks. The LSWM task was moderately associated with PHWM and demonstrated relatively weaker associations with VSWM. Symptoms of inattention and hyperactivity/impulsivity were unrelated to the LSWM task; whereas tasks assessing PH and VSWM were moderately associated with inattention and weakly associated with hyperactivity (VSWM only). No significant between-group differences in performance emerged on the LSWM task; however, significant large-magnitude group differences were observed on both the PH and VSWM tasks. These findings suggest that the LSWM task may lack the ability to detect WM difficulties in youth with ADHD

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Child Neuropsychol. 2021 Feb;27:165-89.

DIMENSIONAL STRUCTURE OF THE BRIEF2 AND ITS RELATIONS WITH ADHD SYMPTOMS AND TASK PERFORMANCE ON EXECUTIVE FUNCTIONS IN CHINESE CHILDREN.

Shum KK-M, Zheng Q, Chak GS, et al.

This study examined the dimensional structure of the Behavior Rating Inventory of Executive Function, Second Edition (BRIEF2) in a Chinese sample of children with attention-deficit/hyperactivity disorder (ADHD)-related concerns and the correlations of the BRIEF2 with the children's ADHD symptoms and their performance on executive function (EF) tasks. Participants were 339 Chinese children aged 6–15 (M = 9.18 years, SD = 2.33; boys: 78.2%) recruited from 35 schools in Hong Kong. The results from confirmatory factor analyses revealed the best fit for a three-factor nine-scale model compared to a two-factor or single-factor model. Significant correlations were found between the BRIEF2 parent and teacher forms for the Behavioral Regulation Index and Cognitive Regulation Index, but not for the Emotion Regulation Index. Associations between performance on an EF task and the rating of the corresponding subscale on the BRIEF2 purportedly measuring the same EF construct were not consistently observed. Lastly, the BRIEF2 showed good convergent validity with the ratings of ADHD symptoms on the Swanson, Nolan, and Pelham Rating Scale Version IV (SNAP-IV). This study provided plausibly the first evidence on the dimensional structure of the BRIEF2 Parent and Teacher Forms in an Asian sample and confirmed the factorial validity of the Chinese version of the BRIEF2

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Child Psychiatry Hum Dev. 2021 Feb;52:96-103.

THE VISUO-MOTOR ATTENTION TEST IN BOYS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): METHYLPHENIDATE—PLACEBO RANDOMIZED CONTROLLED TRIAL.

Hadar Y, Hocherman S, Lamm O, et al.

To assess the visuomotor attention ability in children with ADHD and controls and their response to placebo and Methylphenidate (MPH) treatment. 36 boys with ADHD and 36 age matched typical controls were administered the visuomotor attention test (VMAT) as a baseline and following a week of MPH(IR) or placebo administered to the study group, in a randomized crossover design. A significant difference between the study and control groups was found on several VMAT measures. No performance difference between ADHD dimensional sub-types was observed at the baseline assessment. Under MPH treatment a significant improvement in VMAT measures was observed and particularly in the combined and predominantly hyperactive (C\HI) type. The VMAT results obtained in the present study are consistent with previous findings. ADHD subtypes appear similarly short of visuomotor attention resources; a visuomotor test can be used in the assessment of gains derived from MPH treatment

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Child Health Care. 2021.

ASSESSING MENTAL HEALTH IN CHILDREN AND ADOLESCENT WITH MTHFR POLYMORPHISMS: PSYCHIATRIC DISORDERS, EXECUTIVE FUNCTIONING, AND SYMPTOM PROFILE IN A TURKISH CLINICAL SAMPLE.

Poyraz Fidik OT, Murat D, et al.

This study investigated behavioral phenotype, executive functions profile, and the existence of comorbid psychiatric disorders in children and adolescents with methylenetetrahydrofolate reductase (MTHFR) polymorphisms admitted to pediatric metabolism outpatient clinic. Internalizing problems, especially somatic complaints were common in patients with MTHFR. More than half of the cases had emotional control and initiating problems as executive function deficits. Attention-deficit/hyperactivity disorder was the most common psychiatric diagnosis, followed by anxiety disorder. Current findings emphasize that health care providers should be aware of the mental health needs of cases with MTHFR polymorphism in order to make plans of integrative physical and mental health care

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Clin Neuropharmacol. 2021 Jan;44:37-38.

METHYLPHENIDATE-INDUCED ENURESIS: 3 CASE REPORTS.

Uzun N, Akinci MA, Karatoprak S.

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder in children and adolescents. Methylphenidate (MPH) is one of the most widely used drugs in the treatment of ADHD. Enuresis can occur comorbidly with ADHD. However, enuresis is sometimes seen in patients with ADHD as an adverse effect of MPH treatment. In contrast, in some cases, MPH reportedly improves enuresis in patients with ADHD comorbid with enuresis. The literature is contradictory with regard to the relationship between MPH and enuresis. This report presents the cases of 3 children with ADHD who displayed enuresis during MPH treatment

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Clin Neurophysiol. 2021;132:699-707.

SCAFFOLDING THE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BRAIN USING TRANSCRANIAL DIRECT CURRENT AND RANDOM NOISE STIMULATION: A RANDOMIZED CONTROLLED TRIAL .

Berger I, Dakwar-Kawar O, Grossman ES, et al.

Objective: Improving symptomology and cognitive deficits in neurodevelopmental disorders is a crucial challenge. We examined whether neurostimulation protocols, which have been shown to yield long-term effects when combined with cognitive training, could benefit children with Attention-deficit/hyperactivity-disorder (ADHD), the most common neurodevelopmental disorder in childhood.

Methods: We used a randomized double-blind active-controlled crossover study of 19 unmedicated children with ADHD, who received either anodal transcranial direct current stimulation (tDCS) over the left dorsolateral prefrontal cortex (dlPFC) or random noise stimulation (tRNS) over the bilateral dlPFC, while completing executive functions training.

Results: For our primary outcome, tRNS yielded a clinical improvement as indicated by the reduced ADHD rating-scale score from baseline, and in comparison to the changes observed in tDCS. The effect of brain stimulation one week after completion of treatment yielded further improvement, suggesting a neuroplasticity-related effect. Finally, tRNS improved working memory compared to tDCS, and a larger tRNS effect on ADHD rating-scale was predicted for those who showed the greatest improvement in working memory.

Conclusions: We found that our intervention can have a lasting effect, rather than a merely immediate effect as was shown for in previous medical interventions in ADHD.

Significance: Our results provide a promising direction toward a novel intervention in ADHD

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Clinical Schizophrenia and Related Psychoses. 2020;14.

ASSESSING RISK FACTORS OF AUTISM SPECTRUM DISORDERS (ASD) AND ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AMONG SAUDI MOTHERS: A RETROSPECTIVE STUDY.

Khalil AI, Almutairi MS, Ahmed ME.

Background: Autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) are both lifelong neurological and developmental disorders that affect children at an earlier age. The etiology of both disorders is complex.

Aim: was to assess the risk factors associated with pregnancy, delivery, and postpartum periods among mothers having Autism spectrum disorders (ASD) and Attention deficit hyperactivity (ADHD) children retrospectively.

Methods: A cross-sectional survey-retrospective study design was used to recruit 134 Saudi mothers having autistic and ADHD children from 3 settings located at Jeddah, Saudi Arabia. Three tools were used to collect data which are The Quick Environmental Exposure and Sensitivity Inventory (QEESI), risk factors questionnaires, and demographic characteristics of the participants. Validity, reliability, and piloting of the tools were done and ensured.

Results: Mothers ages range between 23 years and 65 years. The mean of maternal age was 27.6 -¦ 6.1 SD, mothers gravidity was computed at 3.6, while parity was 0.55. The distribution of mothers according to the diagnosis of their children, 36.6% of mothers had children with ADHD, and 35.1% of them had a diagnosis result of ASD, while 28.3% of mothers had a child diagnosis of ASD with ADHD features. All mothers who stated disabling symptoms when exposed to Gasoline and Paint were found to had ASD with ADHD features, indicating the strong association between these two variables. Allergies reaction was found to be significant with diagnosis results. 60.0% of mothers with disabling symptoms of allergies reaction have had a result of ASD with ADHD features. The association between diagnosis outcome and the risk factors during the postpartum period, gestational weight percentile was significantly associated with the diagnosis result of children. A significant difference between diagnosis outcomes was found based on the women's gravidity, the lowest values of gravity were associated with having ASD+ADHD diagnosis.

Conclusion and implication: The findings concluded that none of the risk factors during labor were correlated with the result of child diagnosis. ASD children with ADHD features had no clear association with the risk factors during pregnancy, delivery, or postnatal period. Lowest gravid numbers are associated with a significantly increased risk of low birth weight, preterm births, and the ADHD children's diagnosis among the study participants. Therefore, careful monitoring, attention to nutritional sufficiency, psychological and emotional support, and avoidance of stressful events for these mothers which may lead to improve the outcomes of their pregnancies, labor, and postpartum

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CNS Spectr. 2021.

A CLINICIAN'S GUIDE FOR NAVIGATING THE WORLD OF ADHD MEDICATIONS.

Mattingly GW, Young J.

Once considered a condition of hyperactive boys, our knowledge and understanding of attention deficit hyperactivity disorder (ADHD) and has dramatically evolved. Landmark studies by Biederman, Kessler, Faraone and others have changed and deepened our understanding of ADHD to include a condition which not only affects boys but quite often affects girls1,The evolution of symptoms across the lifespan and the concomitant neurologic changes which underlie this symptomatic expression has similarly evolved.Studies by Dalsgaard and others have brought to light the significantly increased morbidity and mortality associated with preschoolers, children and adults struggling with ADHD and associated conditions

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Complementary Medicine Research. 2021.

THE EFFICACY OF ACUPUNCTURE TREATMENT FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Chen YC, Wu LK, Lee MS, et al.

Background: This study aimed to assess the efficacy of acupuncture for treating attention deficit hyperactivity disorder (ADHD) in children and adolescents.

Patients and Methods: Systematic review and meta-analysis including randomized controlled trials that compared the effects of acupuncture treatment (AT) with pharmacotherapy (methylphenidate hydrochloride, MPH) among patients with ADHD. A total of 12 electronic databases were searched from inception until February 3, 2020. The main outcomes were the effective rate and post-treatment hyperactivity scores. We also assessed the incidence of adverse events and follow-up course.

Results: A total of 10 studies involving 876 patients were included in this study. The meta-analysis revealed that AT yielded a significantly higher effective rate than MPH (odds ratio 2.239, 95% CI 1.438-3.487, $p < 0.001$, 8 studies), and that AT can reduce the hyperactivity scores to a lesser degree than MPH (standardized mean difference = -0.882, 95% CI -1.295 to -0.469, $p < 0.001$, 3 studies). Two studies reported no adverse events in the AT group, while one study suggested that AT can reduce adverse drug reactions. Furthermore, 3 studies concluded that the effects of AT were maintained, even after completion of treatment.

Conclusion: This study suggests that AT may be more beneficial than MPH therapy for ADHD patients. However, the evidence may be highly limited, especially considering the outcome of hyperactivity scores with the high risk of bias, very low GRADE, and small number of studies. Thus, further studies of rigorous design and high quality are needed to confirm and strengthen the results, especially in the Western part of the world. Additionally, well-designed randomized controlled trials that evaluate adverse events and include a long-term follow-up should be conducted to determine the efficacy, safety, and side effects of AT for ADHD in children and adolescents

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Cortex. 2021;136:77-88.

DEVELOPMENT OF LATERAL PULVINAR RESTING STATE FUNCTIONAL CONNECTIVITY AND ITS ROLE IN ATTENTION.

Huang AW, Barber AD.

Objective: The lateral pulvinar nucleus (LPN) has a well-established role in visual attention. Oscillatory activity of the LPN is critical for cortico-cortical communication within and among occipital and temporal visual processing regions. However, the functional development of the LPN and its role in attention deficits is not understood. This study examined the development of thalamic functional connectivity and its relation to attention abilities.

Method: Resting state functional Magnetic Resonance Imaging images from 950 participants (ages 8-21) in the Philadelphia Neurodevelopmental Cohort (PNC) were used to examine age effects. Follow-up General Linear Models were performed to examine brain-behavior effects with Attention Deficit Hyperactivity Disorder (ADHD) symptom ratings and D-prime scores from the Penn Continuous Performance Task, a behavioral measure of selective attention.

Results: LPN functional connectivity with ventral visual stream regions of the occipital and temporal cortices decreased with age, while LPN functional connectivity with the supplementary motor area increased with age. Weaker LPN connectivity in the inferior parietal lobule, supramarginal gyrus, posterior insula, and inferior frontal gyrus was associated with more ADHD symptoms; stronger pulvinar-cerebellar connectivity was also associated with more ADHD symptoms. Better D-prime scores were associated with greater connectivity between the pulvinar and superior parietal gyrus; better D-prime scores were associated with weaker pulvinar connectivity with striatal, middle temporal gyrus, and medial prefrontal cortex regions.

Conclusion: These findings implicate the LPN in the development of the ventral visual processing stream between late childhood and early adulthood and suggest that LPN connectivity with higher order attention networks is important for attention abilities

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Dev Cognitive Neurosci. 2021;48.

BEHAVIORAL AND COGNITIVE CORRELATES OF THE APERIODIC (1/F-LIKE) EXPONENT OF THE EEG POWER SPECTRUM IN ADOLESCENTS WITH AND WITHOUT ADHD.

Ostlund BD, Alperin BR, Drew T, et al.

Efficient information processing facilitates cognition and may be disrupted in a number of neurodevelopmental conditions. And yet, the role of inefficient information processing and its neural underpinnings remains poorly understood. In the current study, we examined the cognitive and behavioral correlates of the aperiodic exponent of the electroencephalogram (EEG) power spectrum, a putative marker of disrupted, inefficient neural communication, in a sample of adolescents with and without ADHD (n = 184 nADHD = 87; Mage = 13.95 years, SD = 1.36). Exponents were calculated via FOOOF (Donoghue et al., 2020a) from EEG data recorded during an 8-minute baseline episode. Reaction time speed and variability, as well as drift diffusion parameters (including the drift rate parameter, a cognitive parameter directly related to inefficient information processing) were calculated. Adolescents with ADHD had smaller aperiodic exponents (a flattened EEG power spectrum) relative to their typically-developing peers. After controlling for ADHD, aperiodic exponents were related to reaction time variability and the drift rate parameter, but not in the expected direction. Our findings lend support for the aperiodic exponent as a neural correlate of disrupted information processing, and provide insight into the role of cortical excitation/inhibition imbalance in the pathophysiology of ADHD

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Dev Med Child Neurol. 2020;62:48-49.

EATING ISSUES AFFECT CHILDREN WITH ADHD IN MORE THAN ONE WAY.

Senroy CH.

Introduction: Children with Attention Deficit Hyperactivity Disorder (ADHD) are known to have adverse reactions to food and also their eating behaviour. Dietary practices are only one of many facets of regular life influenced by ADHD, which might not receive due importance in clinical practice. The main aim of this study is to find out if there is any particular dietary issues that affect the study cohort of the ADHD children.

Patients and Methods: A general questionnaire is prepared which consists of four domains like food habits, eating behaviour or patterns, psychological aspects related to food and sensory perspective of food. This questionnaire is then used to interview parents of both the ADHD children and the control participants (feedback), and then evaluate participants' food habits (clinical). For this, 50 children with ADHD (mean age: 6y) and 50 healthy children as the control group (mean age: 6y) were recruited. After that, we analysed any difference between the two participant groups.

Results: Compared to the control group of children, children with ADHD demonstrated an interesting mix of food related issues in most domains evaluated. The correlation with the severity of ADHD clinical symptoms and food habits was also an interesting finding.

Conclusion: ADHD children and healthy controls have different dietary food habits and eating behaviour, which may play a role in the pathophysiology of ADHD. Clinicians should routinely consider dietary patterns and specific eating behaviour in the routine assessment of children with ADHD more robustly than before

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Dev Med Child Neurol. 2020;62:52.

PERSONAL FACTORS IN ICF CORE SETS MAY BE CODABLE NOT ONLY IN CP, BUT ALSO IN OTHER DISORDERS LIKE ADHD AND ASD.

Sahu R.

Introduction: Personal factors are the background of an individual's life, and comprise features of the individual that are not part of a health condition or health state.

Patients and Methods: A follow up pilot study to postulate suitability of coding of Personal Factors (PF) for children in newly developed core sets for ADHD and ASD, as well as CP using the ICF (Core Set). We first collated and stratified PFs using the ICF Core set coding of children with CP, ASD and ADHD Core Sets (ICF) for clinical usage. We coded ICF Core Sets in 10 children each in CP, ASD and ADHD using Common

Brief ICF Core Sets for each condition. The researchers, who coded the Common Brief Core Sets (Researcher 2a, 2b and 2c) were blinded against the researcher who coded all 30 children's PF (Researcher 1) separately. Researcher 3 reviewed the impact of PFs on ICF of these children and was thus not blinded.
Results: After analyzing the PF in ICF core sets of CP, ASD and ADHD, we found 399 (total of 3) Facilitators and 761 (total of 3) Barriers.
Conclusion: Coding of PFs in ADHD and ASD as well as CP is possible, important, and useful, and can lead to the determining and influencing appropriate interventions in a biopsychosocial environment of children with disability. PFs are important determinants for CP, ADHD and ASD both in clinical assessments and outcomes

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Dev Neurorehabilitation. 2021.
READY FOR A LEARNER'S PERMIT? CLINICAL NEUROPSYCHOLOGICAL OFF-ROAD TESTS AND DRIVING BEHAVIORS IN A SIMULATOR AMONG ADOLESCENTS WITH ADHD AND ASD.
Selander H, Strand N, Almberg M, et al.
A simulator driving test (SDT) and two neuropsychological tests, the Useful Field of View (UFOV) test and the Test of Variables of Attention (TOVA) were evaluated with regard to validity for fitness to drive on 51 young clients diagnosed with attention deficit hyperactivity disorder (ADHD), 33 of whom also had autism spectrum disorder (ASD), and 38 adolescents without a neurodevelopmental diagnosis. The results show generally much greater variability and significantly poorer performance in the SDT and the TOVA for clients with ADHD/ASD compared with the control group. The SDT results were strongly intratest correlated, but had no interest correlation with either the UFOV test or the TOVA. The greater variability among clients with ADHD/ASD suggests greater effort and susceptibility to motivational issues and decline in sustained attention over several tests. In conclusion, the SDT is sensitive and has good face validity, and the TOVA is sensitive to neuropsychological aspects of safe driving. The SDT and the TOVA thus complement each other, and discrepancy between test scores calls for special consideration

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Epidemiol Psychiatr Sci. 2020.
ASSOCIATION OF PSYCHIATRIC COMORBIDITIES WITH THE RISK OF TRANSPORT ACCIDENTS IN ADHD AND MPH.
Liu YC, Chen VCH, Yang YH, et al.
Aims Although the relationship between attention-deficit/hyperactivity disorder (ADHD) and transport accidents has been shown, there is limited information on the relationship between medication and dose-response effects and transport accident risk. This study aims to determine whether young people with ADHD, including adolescents, are more prone to transport accidents than those without, and the extent to which methylphenidate (MPH) prescription in these patients reduces the risk.
Methods We identified 114 486 patients diagnosed with ADHD from Taiwan's National Health Insurance Research Database from 1997 to 2013. Using a Cox regression model, we compared the risk of transport accidents between ADHD and non-ADHD groups and estimated the effect of MPH on accidents. Furthermore, we applied a self-control case-series analysis to compare the risk of accidents during the medication periods with the same patients' non-medication periods.
Results Male ADHD patients had a higher risk of transport accidents than non-ADHD individuals (adjusted hazard ratio [aHR] = 1.24, [95% confidence interval (CI) 1.10-1.39]), especially for those comorbid with epilepsy, oppositional defiant disorder/conduct disorder (ODD/CD), and intellectual disabilities (ID). Female ADHD patients showed no relationship, except for comorbid with autism spectrum disorder (ASD) or ID. We found a reduced risk of transport accidents in patients with ADHD with MPH medication than those without MPH, with a plausible dose-response relationship (aHR of 0.23 to 0.07). A similar pattern was found in self-controlled case-series analysis.

Conclusions Male patients with ADHD, especially those comorbid with epilepsy, ODD/CD, or ID, were at high risk of transport accidents. Female patients, when comorbid with ASD or ID, also exhibited a higher risk of accidents. MPH treatment lowered the accident risk with a dose-response relationship

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Epilepsia. 2021.

PRENATAL VALPROATE EXPOSURE AND ADVERSE NEURODEVELOPMENTAL OUTCOMES: DOES SEX MATTER?

Honybun E, Thwaites R, Malpas CB, et al.

Objective: Prenatal exposure to the antiepileptic drug (AED) valproic acid (VPA) is associated with an increased risk of impaired postnatal neurodevelopment, including autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD). We aimed to evaluate the influence of sex and drug dosage on the association between prenatal VPA exposure and postnatal behavioral outcomes.

Methods: The Australian Pregnancy Register of AEDs was interrogated to identify children aged 4-11 years prenatally exposed to AEDs. Parents reported on their child's behavior using the Autism Spectrum Quotient-Children's Version and the National Institute for Children's Health Quality Vanderbilt Assessment Scale for ADHD. General linear mixed-effects models were used to investigate the relationship between clinicodemographic variables and psychometric scores.

Results: A total of 121 children were studied: 54 prenatally exposed to VPA (28 males, 26 females; mean dose -¦ SD: 644-á-¦-á310-ámg/day) and 67 exposed to other AEDs. There was a main effect of sex showing higher ASD scores in males compared to females (p-á=.006). An interaction between sex and VPA exposure revealed that males had higher ASD symptoms among children exposed to AEDs other than VPA (p-á=.01); however, this typical sex dynamic was not evident in VPA-exposed children. There was no evidence of any dose-response relationship between VPA exposure and ASD symptoms. Males had higher ADHD scores compared to females, but there was no evidence for a link between ADHD symptoms and VPA exposure.

Significance: Prenatal VPA exposure seems to negate the usual male sex-related predominance in the incidence of ASD. These initial findings deepen the concept of VPA as a "behavioral teratogen" by indicating that its effect might be influenced by sex, with females appearing particularly sensitive to the effects of VPA. No association between VPA doses and adverse postnatal behavioral outcomes was detected, possibly related to the low VPA doses used in this study

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Epitheorese Klinikes Farmakologias kai Farmakokinetikes. 2020;38:171-86.

ATTENTION DEFICIT HYPERACTIVITY DISORDER: PHARMACEUTICAL TREATMENT.

Liantzi DM, Konstantinidis GS, Tzouveleki MM.

SUMMARY. The aim of our review is to present the pharmaceutical therapy to treat attention deficit disruption and hyperactivity disorder. Initially, a reference is made to the definition of the syndrome, its etiology as well as structural and biochemical differences in the brain of the disorder. Symptoms, diagnosis, separation of Attention Deficit Hyperactivity Disorder in subtypes according to the DSM-IV criteria and its course over the years are presented. This review is emphasizing in the treatment of the disorder. Non-pharmaceutical interventions (behavioral and educational) are briefly presented and the main categories of drugs administered to children with ADHD, including stimulants, antidepressants and selective stimulants, are presented extensively. In addition, their individual substances are displayed, their activity and their unwanted effects are determined. Finally, they are compared in terms of their effectiveness in addressing ADHD

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Ethnicity and Disease. 2021;31:67-76.

DISPARITIES IN ADHD DIAGNOSIS AND TREATMENT BY RACE/ETHNICITY IN YOUTH RECEIVING KENTUCKY MEDICAID IN 2017.

Davis DW, Jawad K, Feygin Y, et al.

Background: Kentucky has among the highest rate of attention deficit/hyperactivity disorder (ADHD) and stimulant use in the United States. Little is known about this use by race/ethnicity and geography. This article describes patterns of diagnosis of ADHD and receipt of stimulants and psychosocial interventions for children aged 6-17 years receiving Kentucky Medicaid in 2017 and identifies factors associated with diagnosis and treatment.

Methods: Using Medicaid claims, children with and without ADHD (ICD-10 codes F90.0, F90.1, F90.2, F90.8, and F90.9) were compared and predictors of diagnosis and treatment type were examined. Psychosocial interventions were defined as having at least one relevant CPT code. Chi-squared tests and logistic regression models were used for univariate and multivariable analysis, respectively.

Results: The rates of ADHD, stimulant use, and psychosocial interventions in our study population exceeded the national average (14% vs 9%; 75% vs 65.5%; and 51% vs 46.5%, respectively). The distributions varied by sex, race/ethnicity, sex among race/ethnicities, and population density. In general, race/ethnicity predicted ADHD diagnosis, stimulant use, and receipt of psychosocial interventions with non-Hispanic White children being more likely to receive diagnosis and medication, but less likely to receive psychosocial therapy than other children. Differences were also shown for rural compared with urban residence, sex, and sex within racial/ethnic groups.

Conclusions: Diagnosis and treatment modalities differed for children by race/ ethnicity, population density, and sex. More data are needed to better understand whether differences are due to provider bias, child characteristics, or cultural variations impacting the utilization of different treatment options

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Eur Child Adolesc Psychiatry. 2021.

PARENT TRAINING IN NON-VIOLENT RESISTANCE FOR CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CONTROLLED OUTCOME STUDY.

Schorr-Sapir I, Gershy N, Apter A, et al.

Current forms of parent training for childhood attention deficit hyperactivity disorder (ADHD) are often insufficient. Many families drop out of the training, and treatment gains are often not maintained. Nonviolent resistance parent training (NVR) focuses on helping parents resist the child's negative behaviors without escalating the problem. NVR helps parents to fulfill an anchoring function, supporting the child through presence, self-regulation, structure, and support network. This study is a randomized controlled trial designed to assess the efficacy of NVR in the treatment of childhood ADHD. Participants were Israeli parents of children with primary ADHD diagnosis (N = 101; 5-13 years old; 79% male participants) randomly assigned to either 12-session NVR (N = 50) or waiting list (N = 51). Measures were administered before and after treatment and at a 4-month follow-up. ADHD outcomes included the Conners and Child Behavior Checklist. Parenting outcomes included parental helplessness, emotional regulation, anchoring function, and family chaos. Participants in the NVR condition reported significant improvements in the child's internalizing, externalizing, and ADHD symptoms, as well as improvement in paternal and maternal helplessness and anchoring. Participants in the control condition did not report changes in the child's symptoms or the parents condition. The results at follow-up revealed maintenance of change in the child's externalizing and internalizing symptoms, but failure to maintain gains in ADHD core symptoms. Maternal helplessness and anchoring, as well as family chaos continued to improve at follow-up. Dropout rates in the treatment group were low (5%), and fathers engagement was close to 100%. NVR is an efficient treatment for childhood ADHD, with benefits extending beyond the child's symptoms to the entire family. NVR's special focus on parental distress may have contributed to low dropout, high paternal engagement, and maintenance of change

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Eur Child Adolesc Psychiatry. 2021;30:143-53.

DIFFERENTIAL UTILITY OF TEACHER AND PARENTΓÇÔTEACHER COMBINED INFORMATION IN THE ASSESSMENT OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS.

Garcia-Rosales A, Vitoratou S, Faraone SV, et al.

Background: Consistent research findings indicate that parents and teachers observe genuinely different Attention Deficit/Hyperactivity Disorder (ADHD) behaviours in their respective settings. Objective: To evaluate the utility of information provided by teacher informant assessments (INFAs) of ADHD symptoms, and the implications of aggregation algorithms in combing parents information, i.e. using or-rule (endorsement by either one informant) versus and-rule (endorsement by both informants).

Method: Teacher ratings on Conners scales and clinical data from parental accounts on 1383 probands and their siblings from the IMAGE study were analysed. The psychometric properties of teacher and combined ratings using the item response theory model (IRT) are presented. Kappa coefficients, intraclass correlations and linear regression were employed.

Results: First, teacher endorsement of symptoms is located in a narrow part of the trait continuum close to the average levels. Symptoms exhibit comparable perception in the measurement of the trait(s) with similar discrimination ability and information (reliability). Second, the IRT properties of the or-rule ratings are predominantly influenced by parent-INFAs; and the and-rule ratings predominantly by teacher-INFAs ratings. Third, parent-teacher INFAs agreement was low, both for individual items (+¦ = 0.01-0.15) and for dimensional scores (r = 0.12-0.16). The or-rule captured milder expressions of ADHD symptoms, whereas the and-rule indexed greater severity of ADHD.

Conclusions: Parent and teacher-INFAs provide different kinds of information, while both are useful. Teacher-INFA and the and-rule provide a more accurate index of severity than an additive symptom count. Parent-INFA and the or-rule are more sensitive for detecting cases with milder ADHD

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Eur Child Adolesc Psychiatry. 2021.

ACUTE MYOCARDIAL INFARCTION DUE TO SPONTANEOUS CORONARY ARTERY DISSECTION IN A 6-YEAR-OLD BOY WITH ADHD ON THE THIRD DAY OF TREATMENT WITH METHYLPHENIDATE.

Stammschulte T, Pitzer M, Rascher W, et al.

Methylphenidate (MPH) is an indirect-acting sympathomimetic drug and structurally related to amphetamine. It is widely used to treat children aged 6-áyears and older, as well as adolescents who have attention-deficit/hyperactivity disorder (ADHD). We report on a 6-year-old boy who presented with typical angina symptoms occurring several hours after intake of an increased dose of MPH, which had been initiated for ADHD treatment 2-ádays earlier. Despite typical angina symptoms, the diagnosis of myocardial infarction due to spontaneous coronary artery dissection of the right coronary artery was delayed. Most epidemiological studies could not detect an increased risk for cardiovascular events in association with ADHD medications. However, the direct temporal relationship in our case indicates the possibility that MPH may trigger spontaneous coronary artery dissection in predisposed patients. Since myocardial infarction in children is rare but comprises various etiologies, awareness of this possible catastrophic event among medical staff may be lower and may delay immediate life-saving diagnostic and therapeutic measures

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Eur Child Adolesc Psychiatry. 2021.

A NOVEL SCHOOL-BASED APPROACH TO SCREENING FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Coghill D, Du Y, Jiang W, et al.

Current approaches to screening for ADHD result in high rates of false positives. A proof of concept study to investigate the added benefits in the school-based detection of ADHD of adding a standardised teacher to teacher interview to traditional parent and teacher report questionnaires. A school-based study of diagnostic accuracy of ADHD using a novel 2-stage screening process. Participants were all 1026 pupils enrolled in grades 1 to 6 (ages 6-12 years) of a school in Hunan Province, China. The primary outcome was a diagnosis of ADHD on the Kiddie Schedule for Affective Disorders and Schizophrenia Present Lifetime version. 230

(22.4%) of the 1026 students screened positive at Stage 1 (parent and teacher questionnaires) (Sensitivity 0.86 [95% CI, 0.75 to 0.96], specificity 0.80 [95% CI, 0.78-0.83], false positive rate 0.20 (95% CI, 0.18 to 0.23), false negative rate was 0.14 (95% CI, 0.12 to 0.16). 65 remained screen-positive at the Stage 2 screen (teacher to teacher SNAP-IV interview). 36/65 (55.4%) of these Stage 2 screen positive participants and 1/144 (0.7%) of the screen negative subjects met DSM-IV criteria for ADHD (sensitivity 0.83 [95% CI, 0.71-0.95]; specificity of 0.97 [95% CI, 0.96-0.98]; false positive rate 0.03 [95% CI, 0.01 to 0.04], false negative rate 0.16 [95% CI, 0.15 to 0.19]. Adding teacher to teacher interviews to traditional questionnaire-based screening has the potential to improve the clinical utility of school-based screening for ADHD reducing the proportion of false positives, without a negative impact on sensitivity

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Eur Neuropsychopharmacol. 2020;40:S27-S28.

P.042 MENTAL HEALTH AND QUALITY OF LIFE AMONG CAREGIVERS OF ADHD CHILDREN IN AN URBAN COMMUNITY IN SOUTH KOREA.

Kim SI.

Introduction: The purpose of this study was to investigate the mental health, quality of life, and family characteristics of the caregiver of ADHD children and adolescents referred to the ADHD problem in Yangcheon-gu Mental Health Welfare Center and to investigate the effects of socio-demographic variables and mental health on the caregiver's quality of life.

Methods: Two hundred and seven children and adolescents (ages 5Γê+18) and 207 caregivers who were referred to the Yangcheon-gu Mental Health Welfare Center for ADHD related problems from 2015 to 2018 were included. Children and adolescents with ADHD were assessed by the K-ARS (Korean ADHD Rating Scale) as the first test, the CAT (Comprehensive Attention Test) and CBCL (Child Behavior Checklist) as the second test, comprehensive psychological test as the third test. The caregivers were asked about the questionnaire on demographic and social characteristics, and mental health such as the Global Assessment of Recent Stress (GARS), the Center for Epidemiological Studies-Depression Scale (CES-D), the State-Trait Anxiety Inventory (STAI), Barratt Impulsiveness Scale (BIS), World Health Organization Quality of Life Assessment Instrument (WHOQOL), Social Support Scale (SS), Family Adaptation and Cohesion Evaluation Scale, and the Connor-Davidson Resilience Scale (CDRS).

Results: Among the 207 children, 162 (78.3%) were male and 44 (21.3%) were female. By age, 10 (4.8%) were 6-7years old, 69 (33.4%) were 8-10 years old, 88 (42.5%) were 11-13 years old, and 40 (19.3%) were 14-19 years old. As a result of caregivers analysis, among the sociodemographic factors, the household structure was 127 (61.4%) for married families, 19 (9.2%) for single-parent families, 8 (3.8%) for multicultural families, and 5 (2.4%) for remarried families. The K-ARS score showed a significant correlation with caregivers stress, depressed mood, and anxiety even after adjusting for their sociodemographic characteristics such as age, education, occupation, religion and income level, but not with other mental health including quality of life. In the multiple linear regression model, stress (+f=-0.182, p=0.035), depressed mood (+f=-0.226, p=0.009), impulsivity (+f=-0.296, p<0.001) and resilience (+f=0.189, p=0.009) showed statistical significance with QOL in caregivers and these four features accounted for 27.6% of the variation in the group.

Conclusions: Negative, excessive, and impulsive behaviour of ADHD children not only increase parental mental health problems and life difficulties, but also lead to poor parental quality of life. [1] The K-ARS scores of the children and adolescents did not directly affect QOL of caregivers, but they did affect caregivers stress and depressed mood, which negatively affected QOL. Therefore, it is necessary to evaluate and treat the caregiver's stress and depressed mood. In addition, impulsivity and resilience are also reported to be related to the QOL of the caregiver. Programs and support systems should be developed to restore their stress, depressed mood, and impulsivity to improve the QOL of life of caregivers [2]. No conflict of interest

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Eur Neuropsychopharmacol. 2020;40:S118-S119.

P.204 BEHAVIOURAL AND NEURAL CORRELATES OF RESPONSE INHIBITION IN DISRUPTIVE BEHAVIOUR DISORDERS.

Saracaydin G, van Rooij D, Buitelaar J, et al.

Background: Disruptive behavior disorders (DBDs) are among the most commonly diagnosed disorders in childhood and adolescence with a prevalence ranging of 1% to 11% [1]. Attention-deficit/hyperactivity disorder (ADHD) is frequently comorbid with DBDs, with reported comorbidity rates ranging up to 30% [2,3]. While impaired response inhibition has been regarded as a primary deficit specific to ADHD [4-8], the relationship between response inhibition and DBDs independent from ADHD is less well established [4,5,9-11]. Here, we investigated the behavioral and neural correlates of response inhibition in children and adolescents with DBD without comorbid ADHD (DBD ADHD) and DBD with comorbid ADHD (DBD+ADHD) in comparison with healthy controls (HC).

Method: Event-related fMRI were available for 83 subjects with DBDs (8-18 years old, 16 females and 67 males, 58 with DBD ADHD and 25 with DBD+ADHD), and 65 age-matched HC (26 females and 39 males) while performing a performance-adjusted stop-signal task [12]. The fMRI data were preprocessed following ICA-AROMA protocol [13] and the subject-level analyses were conducted using a general linear model in FSL FEAT [14]. In the group-level analysis, F-test was conducted to determine possible between-group differences while controlling for sex, age, IQ, and scanning site by using an FDR-corrected cluster significance threshold of p=0.05 with Z>2.3. For every participant, the mean parameter estimates for all clusters showing significant group differences were extracted, and pairwise comparisons were carried out in R [15]. The task outcomes of the stop-signal task between the groups were compared by ANCOVAs, with sex, age, IQ, and scanning site as covariates, in R. To control family-wise type I error rate, Bonferroni-Holm correction [16] was applied to all pairwise comparisons.

Results: Compared to the controls, the DBD-groups showed greater variability in mean reaction time and the DBD ADHD also made more omission errors during go trials, while the groups did not differ in terms of speed of inhibitory control. During successful inhibition versus go trials, the DBD+ADHD group demonstrated increased activation in the right superior parietal regions compared to the other two groups. During successful versus failed inhibition, relative to controls, right frontal hyperactivation was shared by the DBD-groups while the DBD+ADHD group showed increased activation in the right parietal and left superior parietal regions compared to the other two groups. Further, bilateral parietal activation in DBDs were found to be correlated with ADHD symptom counts.

Conclusion: Given that the groups did not differ in terms of response inhibition-related behavioral performance, right frontal hyperactivation shared by the DBD-groups could be associated with deficient higher-order processing of sensory information mediating stimulus selection and attention in the DBD population. Moreover, bilateral parietal hyperactivation in the DBD+ADHD group and positive correlations between these activations and ADHD symptom counts in DBDs suggest the recruitment of more attentional resources to maintain task performance at the same level as the other groups. Therefore, considering additional hyperactivation observed in the participants with DBD and comorbid ADHD, it is crucial to screen for comorbid conditions and take into account ADHD comorbidity in treatment of DBDs [2-11]. No conflict of interest

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Eur Neuropsychopharmacol. 2020;40:S460-S461.

P.829 CLINICAL CHARACTERISTICS OF SCHIZOPHRENIA OFFSPRING, CHILDREN DIAGNOSED WITH ATTENTION DEFICIT HIPERACTIVITY DISORDER AND HEALTHY CONTROLS.

la Serna ED, Camprodon-Boadas P, Sugranyes G, et al.

Child and adolescent offspring of patients with schizophrenia (SZoff). Attention Deficit Hyperactivity Disorder (ADHD) is the most prevalent psychopathology in SZoff (Sanchez-Gistau, et al., 2015). The high prevalence of ADHD observed in SZoff can conceal the vulnerability characteristics specific to schizophrenia. The aim of this study is to analyze the clinical and cognitive characteristics of a sample of child and adolescent SZoff diagnosed with ADHD (SZoff-ADHD) compared to a sample of children with ADHD without a family history of psychotic disorders and a sample of healthy controls. We hypothesize that SZoff-ADHD will show more psychopathology and more prodromal psychotic symptoms than the other two groups. Methods: we studied a sample of 22 SZoff-ADHD children, 15 children with ADHD with no familiar history of psychotic disorders

and 40 healthy controls (HC) between 6 and 17 years old and we conducted a complete clinical assessment which included: Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS), Young Mania Rating Scale (YMRS), Hamilton Depression Rating Scale (HDRS), Structured interview for Prodromal Symptoms (SOPS) and Global Assessment Functioning (GAF). In order to detect significant differences between groups, multilevel mixed-effect logistic regression models (categorical variables) or multilevel mixed-effect linear regression models (continuous variables) were performed with group as the fixed factor and the fact of having a sibling in the same study (identified by the family number) as the random variable. Results: significant differences between groups were found in socio-economic status which was lower in the SZoff-ADHD group than in the other two groups (F=15.886; p<0.001). Moreover the SZoff-ADHD also showed a higher percentage of males (90.9%) compared with the ADHD group (62.5%) and the HC (45%) (F=12.647; p=0.002). No significant age differences between groups were detected. Regarding clinical assessments, the SZoff-ADHD group showed a higher percentage of conduct disorders (F=3.720; p=0.039) than the ADHD group. No significant differences were observed in other psychopathological diagnoses. Furthermore the SZoff-ADHD group also obtained higher scores than the HC group on the following scales: YMRS, positive, negative, general and total sub-scales of the SOPS and lower scores in the GAF. The ADHD group obtained significantly higher scores than the HC group in the sub-scale of SOPS general prodromal symptoms and lower scores on the GAF. Significant differences were detected between SZoff-ADHD and ADHD in the YMRS and the positive and negative sub-scales of the SOPS where the SZoff-ADHD group showed higher scores than the ADHD group. Conclusions: Compared with the HC group, the SZoff-ADHD displayed more manic, prodromal psychotic symptoms and worse psychosocial functioning. The ADHD group showed an intermediate pattern between the SZoff-ADHD and the HC group, with more general prodromal symptoms and lower psychosocial functioning than the HC group but lower scores than the SZoff-ADHD in the psychotic prodromal symptoms interview [1ΓÇô3]. No conflict of interest

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Eur Neuropsychopharmacol. 2020;40:S355-S356.

P.632 A WITHIN-SAMPLE COMPARISON OF TWO INNOVATIVE NEUROPSYCHOLOGICAL TESTS FOR DIAGNOSING ADHD.

Baader A, Kiani B, Brunkhorst-Kanaan N, et al.

Continuous performance tests measure the key symptoms of ADHD and can be used to supplement the diagnostic process. Although neuropsychological testing is currently not explicitly recommended by clinical guidelines, recent findings give rise to believe that a multidimensional approach using neuropsychological tests in combination with clinical assessment may improve the prediction of adult ADHD diagnoses [1]. A precise diagnosis is needed for accurate treatment. Two commercially available continuous performance tests were used to measure the core symptoms of ADHD. As the accuracy of continuous performance tests concerning sensitivity and specificity has been criticised [2], the utilized tests were chosen due to their outstanding technology. The current study aims to compare two continuous performance tests with regard to their compatibility with clinical rating scales and a personality-based measure. Nesplora Aquarium is implemented with a virtual-reality-headset, while the Qb-Test detects head movements with an infrared camera. Several studies have compared continuous performance tests before, however a direct comparison of these innovative tests within the same sample is so far lacking. Nesplora Aquarium and the Qb-Test were evaluated in a clinical sample of 29 adult patients presenting to our ADHD outpatient clinic. Testing order was randomized across the sample. In order to enable a direct comparison between previously described components of the Qb-Test with the measures of Nesplora Aquarium, a principal component analysis was calculated for Nesplora Aquarium. To assess the compatibility of both tests with clinical features, correlational analyses were performed between neuropsychological data, clinical rating scales and a personality-based measure. Inattention was found to positively correlate between the two tests in a moderate way (r= 0.49, p= 0.01). Despite the overlap between both tests, no relationship between inattention and clinical measures was found. Hyperactivity did not correlate between both tests. However, current ADHD symptoms have shown to be positively associated with Nesplora Aquarium (r= 0.52 to 0.61, p< 0.05) and the Qb-Test (r= 0.52 to 0.71, p< 0.05), while the Qb-Test additionally correlated with childhood ADHD symptoms (r= 0.50, p= 0.04). Impulsivity, mainly driven by commission errors, was not correlated between the two tests. Still there was a negative correlation found between impulsivity in the Qb-Test and urgency (r= -0.49, p= 0.046), a subscale

of the Impulsive Behaviour Scale. Conclusively, the overall comparability of the tests was limited. Although inattention has shown to link both tests, it fails to predict clinical features of ADHD. In line with recent findings [3] the current results suggest that hyperactivity measured in neuropsychological testing represents the most accurate correlate of ADHD symptoms. The inconsistent measurement of impulsivity throughout both tests as well as the poor association with clinical or personality-based measures supports the finding that behavioural and self-reported components of impulsivity are largely independent [4]. The overall insufficient link between subjective and objective measures of ADHD need to be addressed by further research. No conflict of interest

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Eur Neuropsychopharmacol. 2021;44:66-78.

MATERNAL ADHD MEDICATION USE DURING PREGNANCY AND THE RISK OF ADHD IN CHILDREN: IMPORTANCE OF GENETIC PREDISPOSITIONS AND IMPACT OF USING A SIBLING ANALYSIS.

Lemelin M, Sheehy O, Zhao JP, et al.

Attention deficit with hyperactivity disorder (ADHD) medications in pregnancy would be associated with ADHD in children, however, estimates can be confounded by genetic predispositions and environmental factors related to the mother-child pair. We aim to quantify the risk of ADHD in children associated with ADHD medication exposures during pregnancy. A prospective cohort study and sibling analysis conducted within The Quebec Pregnancy/Child Cohort (QPC). All full-term singleton live births covered by the provincial prescription drug insurance in Quebec from 1998 to 2015 were included. ADHD medication exposure during pregnancy was defined according to trimester of use and class-specific medication. ADHD in children was defined as having at least one diagnosis or one prescription filled for an ADHD medication. Cox proportional hazards regression models were used to calculate crude and adjusted hazard ratios (aHR) with 95% confidence intervals (CIs) in the overall cohort, the sub-cohort and the sibling analysis. Of 166,047 full-term singleton live births included, 25,454 (15.3%) had ADHD. In the overall cohort, maternal exposure to ADHD medication during pregnancy was associated with ADHD in children (aHR= 1.96, 95% CI 1.22ΓÇô3.15). In the ADHD pregnant women sub-cohort (aHR= 1.56; 95% CI 0.93ΓÇô2.62) and the sibling control analysis (aHR= 1.14; 95% CI 0.62ΓÇô1.98), ADHD medications during pregnancy was not associated with an increased risk of ADHD in children. Our findings suggest that in utero exposure to ADHD medications was not associated with an increased risk of ADHD in children. This suggests that the association is due to genetic and/or family environmental factors

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Evidence-Based Practice in Child and Adolescent Mental Health. 2021.

SEX-SPECIFIC NORMS FOR DIAGNOSING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDHOOD: A RECEIVER OPERATING CHARACTERISTIC (ROC) ANALYSIS.

Babinski D, Shroff DM, Cao VT, et al.

This study employed Receiver Operating Characteristic (ROC) analyses to identify optimal symptom count cutoffs for girls and boys with attention-deficit/hyperactivity disorder (ADHD). A nationally representative sample of parents of 1050 children (51.5% boys; 78.8% white; 84.2% non-Hispanic) ages 5-áto-á12-áyears old (M =-á8.42, SD-á=-á2.31) completed ratings of their childrenΓÇÖs ADHD symptoms, impairment and internalizing (i.e., depression and anxiety) and externalizing (i.e., oppositional defiant disorder and conduct disorder) problems. Results provided evidence for a sex-specific ADHD symptom cutoff for girls that was lower than the current symptom threshold required by the Diagnostic and Statistical Manual, Fifth Edition (DSM-5). Girls with four or more symptoms of inattention and/or hyperactivity/impulsivity experienced greater co-occurring psychopathology, including internalizing (i.e., depression, and anxiety) and externalizing (i.e., oppositional defiant disorder and conduct disorder) problems, compared to girls with average levels of ADHD. Compared to girls and boys with ADHD defined using DSM-5 symptom count criteria, girls in the sex-specific ADHD group manifested lower levels of internalizing and externalizing problems, although there was also some evidence for similar levels of oppositional defiant disorder and depression among these three groups. In contrast, the symptom cutoff identified using ROC analysis among boys was consistent with existing DSM-

5 guidelines. These findings add to the growing evidence supporting the use of sex-specific norms in the diagnosis of ADHD in girls. Future work should seek to extend these results using a multi-method approach to the assessment of ADHD

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Frontiers in Pediatrics. 2020;8.

ADOLESCENTS WITH ADHD DO NOT TAKE LONGER TO RECOVER FROM CONCUSSION.

Cook NE, Iverson GL, Maxwell B, et al.

The objective of this study was to determine whether adolescents with attention-deficit/hyperactivity disorder (ADHD) have prolonged return to school and sports following concussion compared to those without ADHD and whether medication status or concussion history is associated with recovery time. We hypothesized that having ADHD would not be associated with longer recovery time. This prospective observational cohort study, conducted between 2014 and 2019, examined concussion recovery among school sponsored athletics throughout Maine, USA. The sample included 623 adolescents, aged 14ΓÇô19 years (mean = 16.3, standard deviation = 1.3 years), 43.8% girls, and 90 (14.4%) reported having ADHD. Concussions were identified by certified athletic trainers. We computed days to return to school (full time without accommodations) and days to return to sports (completed return to play protocol) following concussion. Adolescents with ADHD [median days = 7, interquartile range (IQR) = 3ΓÇô13, range = 0ΓÇô45] did not take longer than those without ADHD (median days = 7, IQR = 3ΓÇô13, range = 0ΓÇô231) to return to school (U = 22,642.0, p = 0.81, r = 0.01; log rank: (Formula presented.) = 0.059, p = 0.81). Adolescents with ADHD (median days = 14, IQR = 10ΓÇô20, range = 2ΓÇô80) did not take longer than those without ADHD (median days = 15, IQR = 10ΓÇô21, range = 1ΓÇô210) to return to sports (U = 20,295.0, p = 0.38, r = 0.04; log rank: (Formula presented.) = 0.511, p = 0.48). Medication status and concussion history were not associated with longer recovery times. Adolescents with ADHD did not take longer to functionally recover following concussion. Recovery times did not differ based on whether adolescents with ADHD reported taking medication to treat their ADHD or whether they reported a prior history of concussion

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Front Psychiatry. 2020;11.

USE OF VIRTUAL REALITY WORKING MEMORY TASK AND FUNCTIONAL NEAR-INFRARED SPECTROSCOPY TO ASSESS BRAIN HEMODYNAMIC RESPONSES TO METHYLPHENIDATE IN ADHD CHILDREN.

Jang S, Choi J, Oh J, et al.

Virtual reality (VR) neuropsychological tests have emerged as a method to explore drug effects in real-life contexts in attention deficit hyperactivity disorder (ADHD) children. Functional near-infrared spectroscopy (fNIRS) is a useful tool to measure brain activity during VR tasks in ADHD children with motor restlessness. The present study aimed to explore the acute effects of methylphenidate (MPH) on behavioral performance and brain activity during a VR-based working memory task simulating real-life classroom settings in ADHD children. In total, 23 children with ADHD performed a VR n-back task before and 2 h after MPH administration concurrent with measurements of oxygenated hemoglobin signal changes with fNIRS. Altogether, 12 healthy control (HC) subjects participated in the same task but did not receive MPH treatment. Reaction time (RT) was shortened after MPH treatment in the 1-back condition, but changes in brain activation were not observed. In the 2-back condition, activation of the left dorsolateral prefrontal cortex (DLPFC) and bilateral medial prefrontal cortex (mPFC) was decreased alongside behavioral changes such as shorter RT, lower RT variability, and higher accuracy after MPH administration. Bilateral mPFC activation in the 2-back condition inversely correlated with task accuracy in the pre-MPH condition; this inverse correlation was not observed after MPH administration. In ADHD children, deactivation of the default mode network mediated by mPFC reduced during high working memory load, which was restored through MPH treatment. Our results suggest that the combination of VR classroom tasks and fNIRS examination makes it easy to assess drug effects on brain activity in ADHD children in settings simulating real-life

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Front Psychiatry. 2020;11.

BALANCE TRAINING AS AN ADJUNCT TO METHYLPHENIDATE: A RANDOMIZED CONTROLLED PILOT STUDY OF BEHAVIORAL IMPROVEMENT AMONG CHILDREN WITH ADHD IN CHINA.

Feng L, Ren Y, Cheng J, et al.

Objective: This study aimed to compare the therapeutic effects of two different approaches to attention deficit hyperactivity disorder (ADHD): (1) methylphenidate (MPH) treatment combined with balance training, and (2) MPH monotherapy.

Methods: The study was based on a randomized, single-blind trial involving 27 ADHD patients. An experimental group received the treatment combining MPH and balance training, while a control group were administered just MPH. After 40 sessions of training at the 6-month mark, patients' improvement as observed in their core symptoms and behavioral problems were compared between the experimental and control group.

Results: A total of 27 patients underwent randomization, with 13 assigned to the experimental group and 14 to the control group. After the 6-month trial, the experimental group outperformed the control group in terms of teachers' scores for inattention on the ADHD-RS-IV (19.38 ± 2.96 vs. 23.21 ± 3.91, t = -2.854, P = 0.009). The experimental group also showed greater improvement on the items involving behavior (3.14 ± 1.46 vs. 5.24 ± 1.04, t = 1.463, P = 0.026) and hyperactivity (1.92 ± 1.19 vs. 3.86 ± 2.32, t = -2.697, P = 0.012).

Conclusion: In children with ADHD, the experimental group displayed a significant improvement in the symptoms and behavior associated with inattention than did the group whose treatment consisted of only MPH

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Front Psychiatry. 2020;11.

METHYLPHENIDATE FOR ATTENTION-DEFICIT AND HYPERACTIVITY DISORDER IN ADULT PATIENTS WITH SUBSTANCE USE DISORDERS: GOOD CLINICAL PRACTICE.

Chamakalayil S, Strasser J, Vogel M, et al.

Attention-deficit and hyperactivity disorder (ADHD) is a widespread neurodevelopmental disorder in children and adolescents, persisting into adulthood in a majority of them. ADHD and substance use disorders (SUDs) commonly co-occur in the clinical adult population. The higher-than-normal prevalence rates of SUDs in people with ADHD indicate increased risk for developing SUD. This narrative review deals with the question of whether or not adults with both disorders should be treated with methylphenidate (MPH), addressing specific issues surrounding this form of treatment. MPH is considered as first-line pharmacotherapy for ADHD. However, because of its stimulant-like reinforcing properties, MPH has a significant addictive potential to which persons with SUDs are especially susceptible. Appropriate treatment is therefore complex. Because of concerns about misuse and diversion of MPH medication, clinicians may be reluctant to use MPH to manage ADHD symptoms in these patients. However, it is essential to diagnose and treat ADHD adequately as appropriate therapy reduces the impairments, as well as the risk of developing comorbid disorders and poor treatment response. MPH should not be deprived of these patients because of the risk for misuse, especially as several strategies can be applied to minimize this risk. To conclude, carefully applied guideline-based diagnostics to clarify the potential presence of ADHD as well as a responsible prescription practice in a well-defined therapeutic setting with reliable monitoring of medication intake and regular consultations are essential conditions for a safe and proficient MPH treatment of ADHD in patients with SUD

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International Journal of Developmental Disabilities. 2021.

THE MODERATING EFFECT OF TYPES OF CHILD'S NEURODEVELOPMENTAL DISORDER ON THE RELATIONSHIP BETWEEN INDONESIAN MOTHERS PERCEPTION OF CHILD'S MALADAPTIVE BEHAVIOUR AND MATERNAL PARENTING STRESS.

Daulay N.

This study aimed to examine the effect of mother’s perception of child’s maladaptive behaviour and types of child’s neurodevelopment disorder on maternal parenting stress, and examine the role of types of child’s neurodevelopmental disorder in moderating the relationship between mother perception of child’s

maladaptive behaviours and maternal parenting stress. The mother perception of child's maladaptive behaviours tested included internalizing and externalizing maladaptive behaviours, while the types of child's neurodevelopmental disorder included intellectual disability (ID), attention-deficit/hyperactivity disorder (ADHD), and autism spectrum disorder (ASD). A total of 163 mothers of children with different types of neurodevelopmental disorders were included in this study. The data were analysed with regression analysis, t-test, and ANOVA. The results showed that 1) there is an influence of the mother's perception of child's maladaptive behaviours and types of neurodevelopmental disorders on parenting stress; 2) types of child neurodevelopmental disorders moderate the relationship between the mother's perception of child's maladaptive behaviour and maternal parenting stress; 3) mothers of children with ASD experience higher levels parenting stress than mothers of children with ADHD and ID

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Int J Environ Res Public Health. 2021;18:1-7.

INCREASED ALOPECIA AREATA RISK IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND THE IMPACT OF METHYLPHENIDATE USE: A NATIONWIDE POPULATION-BASED COHORT STUDY.

Ho HY, Wong CK, Wu SY, et al.

Alopecia areata (AA) is an autoimmune disease that causes sudden hair loss. Although few studies have reported the association between AA and attention-deficit/hyperactivity disorder (ADHD), the impact of methylphenidate (MPH) on AA has not been examined. This study examined whether AA risk is higher in children with ADHD than in those without ADHD as well as the impact of MPH use on AA risk in children with ADHD. From the Taiwan Maternal and Child Health Database, we enrolled all 1,750,456 newborns from 2004 to 2017 in Taiwan. Of them, 90,016 children received a diagnosis of ADHD whereas the remaining 1,660,440 did not. To compare AA risk in ADHD and the impact of MPH treatment on it, multiple Cox regression with adjustments for covariates (i.e., age, sex, and psychiatric comorbidities) was performed. The results indicated that 88 (0.098%) children with ADHD and 1191 (0.072%) children without ADHD had AA. Nevertheless, after adjustment for the covariates, AA risk was higher in children with ADHD than in those without ADHD (adjusted hazard ratio [aHR]: 1.30, 95% confidence interval [CI]: 1.04-1.64). Our data indicated a considerable reduction in AA risk (aHR: 0.64) among children with ADHD who received MPH than among those who did not receive MPH; however, this difference was nonsignificant, indicated by a wide 95% CI (0.32-1.25). In conclusion, ADHD and AA may share some underlying mechanisms

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Int J Environ Res Public Health. 2021;18:1-11.

STRESS/IMMUNE BIOMARKERS IN SALIVA AMONG CHILDREN WITH ADHD STATUS .

Krahel A, Paszynska E, Slopien A, et al.

Background. This cross-sectional study aimed to evaluate stress and immune biomarkers in saliva samples of attention-deficit/hyperactivity disorder ADHD compared to healthy non-ADHD children.

Material and methods. A total of 132 children under 11 years old (8.5 -¦ 1.1) enrolled in a cross-sectional study: with confirmed ADHD (n = 60) and healthy controls (n = 72). The clinical evaluation included physical measurements (height, waist, hip circumference, body weight, body mass index BMI, BMI z-score) and unstimulated saliva collection and measurements of free cortisol, salivary alpha-amylase (sAA), and secreted immunoglobulins (sIgA, IgG, and IgM) with quantitative assay (ELISA) analysis. Unpaired t-test, Welch test, or Mann-Whitney U test were applied for group comparisons when appropriate, and the correlation between variables was analyzed with Spearman's rank coefficient. Results were considered significant at $p < 0.05$.

Results. In the ADHD group, body weight (p 0.01), BMI (p 0.009), and hip circumference (p 0.001) significantly differed, while waist size and BMI z-score did not ($p > 0.05$). Significant elevation of the salivary sAA ($p = 0.03$), sIgA ($p = 0.02$), and IgM (p 0.001) biomarkers were detected, without differences in the morning cortisol ($p > 0.05$). Significant correlations between cortisol and BMI, hip size, and IgA, as well as between IgG and sAA and IgA were obtained.

Conclusions. Saliva can be used to monitor ADHD status with regard to biomarkers indicating the hypothalamusΓÇôpituitary-adrenal axis, as HPA axis, and sympathetic activity. The results indicate that

morning collection of saliva in contrast to unchanged salivary cortisol, may evaluate mentioned above system dysregulations by measurements of sAA and immunoglobulins among ADHD children

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Int J Environ Res Public Health. 2021;18:1-18.

THE ASSOCIATION BETWEEN LOW BLOOD PRESSURE AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) OBSERVED IN CHILDREN/ADOLESCENTS DOES NOT PERSIST INTO YOUNG ADULTHOOD. A POPULATION-BASED TEN-YEAR FOLLOW-UP STUDY.

Schulz J, Huber F, Schlack R, et al.

Background: Attention-deficit hyperactivity disorder (ADHD) is one of the most common behavioral disorders in childhood and adolescence associated with relevant psychosocial impair-ments. The basic pathophysiology of ADHD may be related, at least partly, to a deficit in autonomic arousal processes, which not only influence core symptoms of the disorder, but may also lead to blood pressure (BP) deviations due to altered arousal regulation.

Objectives: This study examined long-term changes in BP in children and adolescents with ADHD up to young adulthood. Methods: In children and adolescents aged between 7 and 17 years at baseline, we compared BP recordings in subjects with (n = 1219, 11.1%) and without (n = 9741, 88.9%) ADHD over a 10-year follow-up using data from the nationwide German Health Survey for Children and Adolescents (KiGGS). Propensity score matching was used to improve the comparability between children in the ADHD and control groups with now n = 1.190 in each group.

Results: The results of these matched samples revealed that study participants with ADHD showed significantly lower systolic BP (107.6 -¦ 10.7 mmHg vs. 109.5 -¦ 10.9 mmHg, p < 0.001, Cohen's d = 0.17) and diastolic BP (64.6 -¦ 7.5 mmHg vs. 65.8 -¦ 7.4 mmHg, p < 0.001, CohenΓÇÖs d = 0.16) at baseline. In a sensitivity analysis with a smaller (n = 272) and more stringently diagnosed ADHD group, the significant differences remained stable with somewhat higher Cohen's d; i.e., 0.25 and 0.27, respectively. However, these differences did not persist after 10-year follow-up in a smaller matched longitudinal sub-group (ADHD n = 273; control n = 323), as subjects with and without ADHD had similar levels of systolic (123.4 -¦ 10.65 vs. 123.78 -¦ 11.1 mmHg, p = 0.675, Cohen's d = 0.15) and diastolic BP (71.86 -¦ 6.84 vs. 71.85 -¦ 7.06 mmHg, p = 0.992, Cohen's d = 0.16).

Conclusions: At baseline, children and adolescents with ADHD had significantly lower BP (of small effect sizes) compared to the non-ADHD group, whereas this difference was no longer detectable at follow-up ten years later. These developmental alterations in BP from adolescence to early adulthood may reflect changes in the state of autonomic arousal, probably modulating the pathophysiology of ADHD

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Int J Environ Res Public Health. 2021;18:1-14.

POSTURAL CONTROL IN CHILDHOOD: INVESTIGATING THE NEURODEVELOPMENTAL GRADIENT HYPOTHESIS.

Zoccante L, Ciceri ML, Chamitava L, et al.

Neurodevelopmental disorders (NDDs) have been suggested to lie on a gradient con-tinuum, all resulting from common brain disturbances, but with different degrees of impairment severity. This case-control study aimed to assess postural stability against such hypothesis in 104 chil-dren/adolescents aged 5ΓÇô17, of whom 81 had NDDs and 23 were healthy controls. Compared to healthy controls, Autism Spectrum Disorder (ASD) resulted in the most severely impaired neurode-velopmental condition, followed by Attention Deficit Hyperactive Disorder (ADHD) and Tourette Syndrome (TS). In particular, while ASD children/adolescents performed worse than healthy controls in a number of sensory conditions across all parameters, ADHD children/adolescents performed worse than healthy controls only in the sway area for the most complex sensory conditions, when their vision and somatosensory functions were both compromised, and performance in Tourette Syndrome (TS) was roughly indistinguishable from that of healthy controls. Finally, differences were also observed between clinical groups, with ASD children/adolescents, and to a much lesser extent ADHD children/adolescents, performing worse than TS children/adolescents, especially when sensory systems were not operationally accurate. Evidence from this study indicates that poor postural control may

be a useful biomarker for risk assessment during neurodevelopment, in line with predictions from the gradient hypothesis

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Int J Environ Res Public Health. 2021;18:1-10.

PROPOSING AND VALIDATING THE DIAGNOSIS SCALE FOR INTERNET GAMING DISORDER IN TAIWANESE ADHD ADOLESCENTS: LIKERT SCALE METHOD BASED ON THE DSM-5.

Chang YC, Tzang RF.

The paper aims to adjust the Taiwanese version of Internet gaming disorder-short form Likert scale with Likert (IGD-SF-T-L) based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria to a Likert scale model and test its psychometric property among children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD). Confirmatory factor analysis (CFA) was conducted for validity and the CronbachΓÇÖs +¦ for reliability of IGD-SF-T-L. The ROC (receiver operating curves) was used to propose the cut-off point for assessing the instrumentΓÇÖs psychometric properties and its corresponding indices for the diagnostic accuracy. In total, 102 children and adolescents with ADHD were recruited. The construct validity of IGD-SF-T by CFA was model well fitted with excellent reliability (CronbachΓÇÖs +¦ = 0.918). The ROC using the ChenΓÇÖs CIAS > 56 as the state variable for IGD diagnosis showed the AUC (areas under the curves) was 0.918. The cut-off point proposed for IGD-SF-T-L to indicate a diagnosis of IGD was ΓëÑ 10. The corresponding indices of accuracy: sensitivity, specificity, LR (likelihood ratio) +, LR-, and AUC were 0.893, 0.826, 5.134, 0.130, and 0.859, respectively. The proposed IGD-SF-T-L is an adequate, standardized psychomet-rical measurement for diagnosing IGD among Taiwanese adolescents with ADHD. More attention should be paid toward recent ADHD youth with Internet gaming disorder and their family

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Int J Epidemiol. 2021;49:857-75.

MATERNAL PRE-PREGNANCY OVERWEIGHT/OBESITY AND THE RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN OFFSPRING: A SYSTEMATIC REVIEW, METAANALYSIS AND QUASI-EXPERIMENTAL FAMILY-BASED STUDY.

Li L, Lagerberg T, Chang Z, et al.

Background: Previous studies are inconclusive concerning the association between maternal pre-pregnancy overweight/obesity and risk of attention-deficit/hyperactivity disorder (ADHD) in offspring. We therefore conducted a systematic review and meta-analysis to clarify this association. To address the variation in confounding adjustment between studies, especially inadequate adjustment of unmeasured familial confounding in most studies, we further performed cousin and sibling comparisons in a nationwide population-based cohort in Sweden.

Methods: We searched PubMed, Embase and PsycINFO during 1975-2018. We used random-effects models to calculate pooled risk ratios (RRs) with 95% confidence interval. In the population-based study, Cox proportional hazard models were used to calculate the unadjusted hazard ratios (HRs) and HRs adjusted for all confounders identified in previous studies. Stratified Cox models were applied to data on full cousins and full siblings to further control for unmeasured familial confounding.

Results: Eight cohorts with a total of 784 804 mother-child pairs were included in the meta-analysis. Maternal overweight [RRoverweight= 1.31 (1.25-1.38), I2=6.80%] and obesity [RRobesity= 1.92 (1.84-2.00), I2= 0.00%] were both associated with an increased risk of ADHD in offspring. In the population-based cohort of 971 501 individuals born between 1992 and 2004, unadjusted Cox models revealed similar associations [HRoverweight= 1.30 (1.28-1.34), HRobesity=1.92 (1.87-1.98)]. These associations gradually attenuated towards the null when adjusted for measured confounders [HRoverweight= 1.21 (1.19-1.25), HRobesity=1.60 (1.55-1.65)], unmeasured factors shared by cousins [HRoverweight= 1.10 (0.98-1.23), HRobesity= 1.44 (1.22-1.70)] and unmeasured factors shared by siblings [HRoverweight= 1.01 (0.92-1.11), HRobesity = 1.10 (0.94-1.27)].

Conclusion: Pre-pregnancy overweight/obesity is associated with an increased risk of ADHD in offspring. The observed association is largely due to unmeasured familial confounding

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Iranian Journal of Pharmaceutical Sciences. 2017;13:70-71.

EVALUATION OF CYPROHEPTADINE ADMINISTRATION IN PREVENTION OF SLEEP DISORDERS INDUCED BY METHYLPHENIDATE IN ATTENTION DEFICIT HYPERACTIVITY DISORDER CHILDREN.

Kadkhodamezerji F, Elyasi S.

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in childhood. Stimulants are first line therapy for this disorder. Methylphenidate which is the best choice for therapy has a few side effects (1). The most common one is loss of appetite. The adverse effects may limit optimal dosing and pateints+ó compliance and lead to treatment discontinuation. This research evaluated the effects of cyproheptadine on appetite problems induced by methylphenidate in children with ADHD (2).

Methods: During this pilot, randomized, double-blinded, placebo-controlled clinical trial, the effect of cyproheptadine 4mg daily in two divided doses for eight weeks, on loss of appetite occurrence induced by methylphenidate was assessed. Forty patients, that fulfilled the inclusion criteria assigned to the cyproheptadine or placebo group. Patient+ó weight and ADHD rating scale scores were recorded at baseline and weekly during these 8weeks. Rate of growth was evaluated weekly for each patient.

Results: There were no significant differences between cyproheptadine and placebo groups regarding weight and rate of growth in weekly assessments. In addition, there were no significant differences between two groups in response to therapy based on ADHD rating scale scores.

Conclusion: Cyproheptadine does not have considerable effect on appetite problems induced by methylphenidate in ADHD children. Moreover, cyproheptadine has no negative impact on patients+ó response to methyphenidate

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JAMA Pediatr. 2021;175:191-92.

DIAGNOSIS, EVALUATION, AND TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Loe IM, Kakar PA, Sanders LM.

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JAMA Pediatr. 2021;175.

ASSOCIATION OF MATERNAL AUTOIMMUNE DISEASE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN.

Nielsen TC, Nassar N, Shand AW, et al.

Importance: Maternal autoimmune disease has been associated with increased risk of neurodevelopmental disorders in offspring, but few studies have assessed the association with attention-deficit/hyperactivity disorder (ADHD).

Objective: To examine the association between maternal autoimmune disease and ADHD within a population-based cohort and combine results in a subsequent systematic review and meta-analysis.

Design, Setting, and Participants: A cohort study was conducted of singleton children born at term gestation (37-41 weeks) in New South Wales, Australia, from July 1, 2000, to December 31, 2010, and followed up until the end of 2014; and a systematic review evaluated articles from the MEDLINE, Embase, and Web of Science databases to identify all studies published before November 20, 2019. A total of 12610 children exposed to maternal autoimmune disease were propensity score matched (1:4) to 50440 unexposed children, for a total cohort of 63050. A child was considered to have ADHD if they had (1) an authorization or filled prescription for stimulant treatment for ADHD or (2) a hospital diagnosis of ADHD. Children linked to a first ADHD event before 3 years of age were excluded. Data were analyzed from January 13 to April 20, 2020.

Exposures: One or more maternal autoimmune diagnoses in linked hospital admission records between July 1, 2000, and December 31, 2012. Thirty-five conditions were considered together and individually.
Main Outcomes and Measures: The main outcome was child ADHD identified from stimulant authorization or prescription data and diagnoses in linked hospital admission records. Multivariable Cox regression was used to assess the association between maternal autoimmune disease and ADHD adjusted for child sex. Pooled hazard ratios (HRs) were calculated using random-effects meta-analysis with inverse-variance weights for each exposure reported by 2 or more studies.
Results: In the population-based cohort analysis, 831718 singleton, term infants born to 831718 mothers (mean [SD] age, 29.8 [5.6] years) were assessed. Of 12767 infants (1.5%) who were linked to a maternal autoimmune diagnosis, 12610 were propensity score matched to 50440 control infants, for a total study cohort of 63050 infants. In this cohort, any autoimmune disease was associated with ADHD in offspring (HR, 1.30; 95% CI 1.15-1.46), as was type 1 diabetes (HR, 2.23; 95% CI, 1.66-3.00), psoriasis (HR, 1.66; 95% CI, 1.02-2.70), and rheumatic fever or rheumatic carditis (HR, 1.75; 95% CI, 1.06-2.89). Five studies (including the present study) were included in the meta-analysis. Any autoimmune disease (2 studies: HR, 1.20; 95% CI, 1.03-1.38), type 1 diabetes (4 studies: HR, 1.53; 95% CI, 1.27-1.85), hyperthyroidism (3 studies: HR, 1.15; 95% CI, 1.06-1.26), and psoriasis (2 studies: HR, 1.31; 95% CI, 1.10-1.56) were associated with ADHD.
Conclusions and Relevance: In this cohort study, maternal autoimmune diseases were associated with increased ADHD among children. These findings suggest possible shared genetic vulnerability between autoimmune disease and ADHD or a potential role for maternal immune activation in the expression of neurodevelopmental disorders in children. Future studies measuring disease activity, modifiers, and medication use are required to better understand the mechanisms underlying this association.

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J Adolesc Health. 2021;68:284-91.
ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: ADVERSE BEHAVIORS AND COMORBIDITY.
Sultan RS, Liu SM, Hacker KA, et al.
Purpose and Objective: There is growing evidence that adolescents with ADHD develop long-term impairments and adverse outcomes, yet less is known about their adverse behaviors. To quantify rates of mental health comorbidities in adolescents with ADHD and compare the risks of adverse behaviors among adolescents with and without ADHD.
Methods: We performed a cohort analysis of 6,483 youth from the National Comorbidity Survey Adolescent Supplement (NCS-A), a nationally representative in-person structured diagnostic interview of adolescents aged 14-18 years focusing on mental, emotional, and behavioral disorders.
Main Outcomes: (1) Percentages with comorbid anxiety, mood, disruptive behavior, and substance use disorders. (2) Strength of associations of ADHD with several adverse behaviors, including suicidal symptoms, aggression, behavior regulation, life events, education, and substance use. Odds ratios were adjusted for age, sex, and race.
Results: Among the sample of 6,483 adolescents, overall, 9.5% met the criteria for ADHD. Most (69.5%) of adolescents with ADHD had at least one comorbid mental health condition. As compared to adolescents without ADHD, those with ADHD were significantly more likely to have had a suicide attempt (aOR 2.9, 95% CI = 1.3-6.6) and to have had perpetrated physical aggression (aOR 2.3, 95% CI = 1.7-3.2). Adolescents with ADHD were also more likely to have been expelled from school or fired from a job (aOR 3.3, 95% CI = 1.7 −6.5) and to have had problems related to drinking alcohol (95% CI = 1.2-2.9).
Conclusions: ADHD in adolescents is a complicated disorder with elevated risks for a wide range of adverse behaviors

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J Allergy Clin Immunol. 2021;147:AB43.

INFANT RHINORRHEA AND WATERY EYES AND ADOLESCENT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Perzanowski M, Rauh V, Ramphal B, et al.

Rationale: Comorbidity between asthma and attention deficit hyperreactivity disorder (ADHD) is well documented. Parasympathetic nervous system (PNS) activity is a known but less well-acknowledged underlying mechanism of asthma and ADHD, with differing risks observed among boys and girls. We previously reported associations between infant rhinorrhea and watery eyes without a cold (RWWC), and school age asthma morbidity with evidence of underlying PNS dysregulation. Increased PNS activity has been associated with ADHD Inattentive but not Hyperactive-Impulsive symptoms. We hypothesized that infant RWWC would predict adolescent ADHD symptoms.

Methods: With Columbia's Center for Children's Environmental Health birth cohort, mothers were queried about their child's RWWC and wheeze symptoms every 3 months in the first year of life and ADHD symptoms at age 8-14 years (DuPaul ADHD-Rating Scale). ADHD Total score in the highest quartile for sex was the primary outcome measure. Separate models evaluated Inattentive and Hyperactive-Impulsive subscale scores.

Results: Among children with complete data (n=311), in a model adjusting for sex, age, race/ethnicity, maternal asthma, material hardship, environmental tobacco smoke, RWWC in infancy predicted higher total AHDH scores (Relative Risk (RR) =1.66, P=0.019). The association was observed among girls (RR=2.7, P=0.002) but not boys (RR=1.2, P=0.54; Pinteraction=0.066). RWWC predicted higher Inattention (RR=1.7, P=0.007), but not Hyperactive-Impulsive symptoms (RR=1.4, P=0.14).

Conclusions: Girls with increased PNS responses in infancy (RWWC) had higher ADHD risk at age 8-14. The increased PNS response associated with one ADHD subtype. Altered PNS activity may thus represent a shared biological pathway leading to asthma and risk for ADHD Inattentive-subtype

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J Autism Dev Disord. 2021.

EXECUTIVE FUNCTION IN AUTISM: ASSOCIATION WITH ADHD AND ASD SYMPTOMS.

Lee RR, Ward AR, Lane DM, et al.

There is substantial comorbidity between autism spectrum disorder (ASD) and attention deficit/hyperactivity disorder (ADHD), and there are well-documented executive functioning (EF) deficits in both populations. An important question concerns whether EF deficits in children with ASD are related to severity of ASD, ADHD, or both. We examined ADHD and ASD symptoms in relation to ratings of EF in the home and classroom. The sample comprised 64 children (55 males) diagnosed with ASD (mean age = 9.26 years; mean FSIQ = 92). Analyses indicated that parent and teacher ratings of EF (except Shift and Emotional Control) were consistently related to ADHD symptom severity, but not to ASD severity. Thus, functioning in the domains of Shift and Emotional control appear relatively spared, whereas performance in all other EF was impaired in relation to ADHD symptoms

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J Child Neurol. 2021.

READING COMPREHENSION IMPAIRMENT IN CHILDREN WITH NEUROFIBROMATOSIS TYPE 1 (NF1): THE NEED OF MULTIMODAL ASSESSMENT OF ATTENTION.

Biotteau M, Tournay E, Baudou E, et al.

Attention span, which has been shown to have an impact on reading quality in many other conditions, is one of the main cognitive disorders of neurofibromatosis type 1 (NF1). The aim of this work is to observe the impact of attention on reading comprehension, in NF1 and non-NF1 children. A multicenter, cross-sectional study was conducted on 150 children (8-12 years old) with or without NF1 (75 NF1 vs 75 non-NF1; 72 female, 78 male), matched for age, sex, handedness, and reading level, thus forming a continuum from good to poor readers in both NF1 and non-NF1 groups. Children with intellectual deficiency or neurologic or psychiatric disorder were excluded. Attentional skills were assessed by combining a parent questionnaire (Child Behavior CheckList) and a performance-based assessment (Conner's Continuous Performance Test-

Second Edition). Reading comprehension was assessed through a standardized reading comprehension test (ORLEC Lobrot). The performance-based attention scores were associated with text and sentence comprehension ability (P =.0235 and P =.0164, respectively), while indirect questionnaire attention scores were only associated with sentence comprehension (P =.0263). For both groups, the correlations between questionnaire and performance-based measures were low. We have shown that reading comprehension is greatly influenced by attention in NF1 and non-NF1, even if predictors of good reading comprehension also include IQ score and reading accuracy. Indirect observer-rated questionnaires and direct performance-based measures of attention do not assess the same variables, are linked to different components of reading skills, and are not interchangeable assessments of attention difficulties. Both assessments are complementary and must be used simultaneously, leading to recommendations that support multimodal assessment of attention

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J Child Psychol Psychiatry. 2020 Dec;61:1309-16.

VOLITIONAL EYE MOVEMENT CONTROL AND ADHD TRAITS: A TWIN STUDY .

Sanchez MS, Falck-Ytter T, Kennedy DP, et al.

Background: Top-down volitional command of eye movements may serve as a candidate endophenotype of ADHD, an important function underlying goal-directed action in everyday life. In this twin study, we examined the relation between performance on a response inhibition eye-tracking paradigm and parent-rated ADHD traits in a population-based twin sample. We hypothesized that altered eye movement control is associated with the severity of ADHD traits and that this association is attributable to genetic factors.

Methods: A total of 640 twins (320 pairs, 50% monozygotic) aged 9–14 years) from the Child and Adolescent Twin Study in Sweden (CATSS) participated. Twins performed the antisaccade task indexing inhibitory alterations as either direction errors (following exogenous cues rather than instructions) or premature anticipatory eye movements (failure to wait for cues). We calculated the associations of eye movement control and ADHD traits using linear regression mixed-effects models and genetic and environmental influences with multivariate twin models.

Results: Premature anticipatory eye movements were positively associated with inattentive traits (ß = .17; 95% CI: 0.04, 0.31), while controlling for hyperactive behaviors and other covariates. Both premature anticipatory eye movements and inattention were heritable (h^2 = 0.40, 95% CI: 0.22, 0.56; h^2 = 0.55; 95% CI: 0.42, 0.65; respectively), and their genetic correlation was small but statistically significant (r = .19, 95% CI: 0.02, 0.36). However, the genetic correlation did not remain significant after adjusting for covariates (age, sex, hyperactivity traits, IQ). No link was found between direction errors and ADHD traits.

Conclusions: This study indicates that there is a specific, genetically influenced, relation between top-down eye movement control and the inattentive traits typical of ADHD

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J Child Psychol Psychiatry. 2021 Feb;62:232-43.

DEVELOPMENTAL PROFILES OF CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND IRRITABILITY: ASSOCIATION WITH ADOLESCENT MENTAL HEALTH, FUNCTIONAL IMPAIRMENT, AND SUICIDAL OUTCOMES.

Galera C, Orri M, Vergunst F, et al.

Background: Irritability is frequently comorbid with ADHD. Although irritability alone has been linked to deleterious mental health and adaptive issues, the joint developmental course of ADHD and irritability symptoms during childhood as well as its association with later mental health and suicidal outcomes is not fully understood. We aimed to describe the developmental trajectories of childhood ADHD and irritability symptoms and to quantify their association with adolescent mental health and suicidal outcomes.

Methods: The Quebec Longitudinal Study of Child Development (QLSCD) included 1407 participants from the general population followed up from age 5 months to 17 years. We used a multitrajectory approach to identify developmental trajectories of childhood (6–12 years) ADHD and irritability symptoms. Outcome measures were adolescent (13–17 years) mental health (psychiatric symptoms/functional impairment) and suicidal outcomes.

Results: We identified distinct developmental profiles: combined absent or very low ADHD and absent or very low irritability (940 [66.8%]; reference group), moderately high irritability and low ADHD (158 [11.2%]), moderately high ADHD and low irritability (198 [14.1%]), and combined high ADHD and high irritability (111 [7.9%]). Multivariate modeling showed that, compared to children in the reference group, those in the combined high ADHD and high irritability profile showed higher levels of ADHD continuity (d ranges = 0.40–0.50), externalizing (d ranges = 0.25–0.59), internalizing (d ranges = 0.20–0.29), and functional impairments (d ranges = 0.17–0.48) and suicidal behaviors (odds ratio (OR) = 2.12, confidence interval (CI) = 1.47–3.06) in adolescence.
Conclusions: The presence of persistently high levels of irritability along with ADHD symptoms during childhood significantly predicts adolescent ADHD continuity, externalizing, internalizing, and suicidal outcomes. Systematic consideration of irritability when assessing and treating ADHD may improve long-term mental health outcomes

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Journal of Medical Internet Research. 2020;22.

INTERNET-BASED SUPPORT AND COACHING WITH COMPLEMENTARY CLINIC VISITS FOR YOUNG PEOPLE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND AUTISM: CONTROLLED FEASIBILITY STUDY.

Sehlin H, et al.

Background: Individuals with attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) can experience obstacles in traditional health care situations due to difficulties associated with their impairment.
Objective: This controlled study aims to investigate the feasibility of an internet-based support and coaching intervention (IBSC), including 2 weekly chat sessions and 2 complementary clinic visits with coaches over the course of 8 weeks, for adolescents and young adults with ADHD and/or ASD in 2 naturalistic routine care settings.
Methods: Individuals with ADHD and/or ASD aged 15-32 years were recruited in 2 clinical settings, where they received either IBSC (n=24) or treatment as usual (TAU; n=20). Outcome measures included self-report questionnaires assessing quality of life (Manchester Short Assessment for Quality of Life), sense of coherence (Sense Of Coherence 29), self-esteem (Rosenberg Self-Esteem Scale), and anxiety and depressive symptoms (Hospital Anxiety and Depression Scale [HADS] and Montgomery-+àsberg Depression Rating Scale-Self-reported, respectively).
Results: Significant between-group effects were observed in measures of anxiety (HADS) at postintervention (P=.02) as well as at the 6-month follow-up (P=.004). Significant between-group effects were also noted for depressive symptoms (HADS) postintervention (P=.04). The between-group effects were partially explained by a deterioration in the TAU group. A significant increase in self-esteem (P=.04) as well as a decrease in anxiety (P=.003) at the 6-month follow-up was observed in the intervention group following IBSC. Findings from a qualitative study of the intervention are consistent with the results.
Conclusions: The findings from this study suggest that IBSC holds promise as a feasible complement or alternative to traditional face-to-face health care meetings

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J Neural Transm. 2021 Jan;128:115-20.

ALTERED URINARY TETRAHYDROISOQUINOLINE DERIVATIVES IN PATIENTS WITH TOURETTE SYNDROME: REFLECTION OF DOPAMINERGIC HYPERACTIVITY?

Capetian P, Roessner V, Korte C, et al.

Tetrahydroisoquinolines (TIQs) such as salsolinol (SAL), norsalsolinol (NSAL) and their methylated derivatives N-methyl-norsalsolinol (NMNSAL) and N-methyl-salsolinol (NMSAL), modulate dopaminergic neurotransmission and metabolism in the central nervous system. Dopaminergic neurotransmission is thought to play an important role in the pathophysiology of chronic tic disorders, such as Tourette syndrome (TS). Therefore, the urinary concentrations of these TIQ derivatives were measured in patients with TS and patients with comorbid attention-deficit/hyperactivity disorder (TS + ADHD) compared with controls.

Seventeen patients with TS, 12 with TS and ADHD, and 19 age-matched healthy controls with no medication took part in this study. Free levels of NSAL, NMNSAL, SAL, and NMSAL in urine were measured by a two-phase chromatographic approach. Furthermore, individual TIQ concentrations in TS patients were used in receiver-operating characteristics (ROC) curve analysis to examine the diagnostic value. NSAL concentrations were elevated significantly in TS [434.67 ± 55.4 nmol/l (standard error of mean = S.E.M.), two-way ANOVA, $p < 0.0001$] and TS + ADHD patients [605.18 ± 170.21 nmol/l (S.E.M.), two-way ANOVA, $p < 0.0001$] compared with controls [107.02 ± 33.18 nmol/l (S.E.M.), two-way ANOVA, $p < 0.0001$] and NSAL levels in TS + ADHD patients were elevated significantly in comparison with TS patients (two-way ANOVA, $p = 0.017$). NSAL demonstrated an AUC of 0.93 ± 0.046 (S.E.M) the highest diagnostic value of all metabolites for the diagnosis of TS. Our results suggest a dopaminergic hyperactivity underlying the pathophysiology of TS and ADHD. In addition, NSAL concentrations in urine may be a potential diagnostic biomarker of TS

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J Pediatr Neurol. 2021;19:36-39.

MUTATION IN KCNJ2 GENE IN A BOY WITH ATYPICAL FEATURES OF ANDERSEN-TAWIL SYNDROME, ADHD, AND ASD: AN EXPANDING PHENOTYPE.

Fadilah A, Mordekar SR, Matthai S.

Andersen-Tawil syndrome, a potassium ion channelopathy, is caused by mutations in the KCNJ2 gene, and accounts for approximately 10% of channelopathies. Phenotype is variable. An 11-year-old boy presented with periodic paralysis without localizing neurological signs, associated in only two of three occasions with hypokalemia, on a background of a diagnosis of attention deficit hyperactivity disorder and autism spectrum disorder. There was a history of syncope and palpitations. This was a matter of diagnostic uncertainty due to the difficulty in interpreting his neurological signs, and inconsistency of abnormal potassium levels. In children/young people with recurrent episodes of weakness without localizing signs on physical examination, and syncope, the possibility of a channelopathy should be considered, even in the absence of serum electrolyte abnormalities. There is a possible link between KCNJ2 mutations and difficulties in attention and a specific neurocognitive profile

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Journal of Pediatric Neurosciences. 2020;15:402-08.

SERUM LEVELS OF INTERLEUKIN-6 AND TUMOR NECROSIS FACTOR ALPHA IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Elsadek AE, Al-shokary AH, Abdelghani WE, et al.

Background: Attention-deficit hyperactivity disorder (ADHD) is a common disorder in children, but its etiology and pathogenesis are still unclear. Aims: The aims of this study were to measure the level of serum interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF-+¦) as markers of immune system involvement in children with ADHD, and to study their correlation with symptoms severity of ADHD.

Materials and Methods: The study was conducted on 80 children diagnosed as ADHD based on the criteria adapted from the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Eighty healthy children of matched age and sex served as a control group. All children enrolled in the study were subjected to history taking, clinical examination, and psychometric tests. Assay for serum IL-6 and TNF-+¦ for all patients and controls was performed using enzyme-linked immunosorbent assay.

Results: The mean serum level of IL-6 was 26.11 -¦ 11.14 and 6.23 -¦ 2.52 in children with ADHD and controls, respectively. Children with ADHD showed significantly higher serum IL-6 levels than the control group ($P = 0.001$). Serum IL-6 showed no significant correlation with the intelligence quotient (IQ) or the Abbreviated Conners' Rating Scale scores for parents. However, TNF-+¦ showed no significant differences between the two groups and no significant correlation with the IQ or the Abbreviated Conners' Rating Scale scores for parents.

Conclusion: Serum IL-6 levels were significantly higher in children with ADHD compared to controls; however, the IL-6 levels did not correlate with ADHD symptoms severity. Increased IL-6 levels may contribute to the etiology of ADHD

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J Psychiatry Neurosci. 2021;46:E14-E33.

NONINVASIVE BRAIN STIMULATION IN CHILDREN AND ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Westwood SJ, Radua J, Rubia K.

Background: Repetitive transcranial magnetic stimulation (rTMS) or transcranial direct current stimulation (tDCS) could provide treatment alternatives to stimulant medication for attention-deficit/hyperactivity disorder (ADHD), given some evidence for improvements in cognition and clinical symptoms. However, despite a lack of solid evidence for their use, rTMS and tDCS are already offered clinically and commercially in ADHD. This systematic review and meta-analysis aimed to critically appraise rTMS and tDCS studies in ADHD to inform good research and clinical practice.

Methods: A systematic search (up to February 2019) identified 18 studies (rTMS 4, tDCS 14; 311 children and adults with ADHD) stimulating mainly the dorsolateral prefrontal cortex (dlPFC). We included 12 anodal tDCS studies (232 children and adults with ADHD) in 3 random-effects meta-analyses of cognitive measures of attention, inhibition and processing speed.

Results: The review of rTMS and tDCS showed positive effects in some functions but not others, and little evidence for clinical improvement. The meta-analyses of 1 to 5 sessions of anodal tDCS over mainly the left or bilateral dlPFC showed trend-level improvements in inhibition and processing speed, but not in attention. Limitations: Heterogeneity in stimulation parameters, patient age and outcome measures limited the interpretation of findings.

Conclusion: The review and meta-analysis showed limited evidence that 1 to 5 sessions of rTMS and tDCS, mostly of the dlPFC, improved clinical or cognitive measures of ADHD. These findings did not support using rTMS or tDCS of the dlPFC as an alternative neurotherapy for ADHD as yet. Larger, multi-session stimulation studies identifying more optimal sites and stimulation parameters in combination with cognitive training could achieve larger effects

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J Psychopathol Behav Assess. 2021.

DO CHILDHOOD EMOTIONAL LABILITY AND ADHD SYMPTOMS HAVE SHARED NEUROPSYCHOLOGICAL ROOTS?

Van Liefferinge D, Sonuga-Barke EJS, Danckaerts M, et al.

Emotional Lability (EL) is a source of impairment in multiple mental disorders of children, including attention-deficit/hyperactivity disorder (ADHD). It has been proposed that the overlap between EL and ADHD symptoms is the result of common neuropsychological deficits. The aim of the present study was to test this hypothesis by using a multi-method approach. In a mixed sample of 61 children (49 community sample and 12 children with an ADHD diagnosis) aged between 8 and 12-áyears, we examined the relationship between parental reports of ADHD and EL, real-time children's emotional expressions in an experimental context, children's performance on neuropsychological tasks and parental ratings of neuropsychological functioning. Parental EL ratings were significantly predicted by task-based reaction time variability and by questionnaire measures of Self-Direction & Organization and Arousal Regulation. Parental EL ratings were also significantly related to both ADHD symptom dimensions. After controlling for shared neuropsychological factors, ADHD symptoms no longer predicted parental EL ratings. Neuropsychological task performance was not significantly related to real time emotional expressions. However, positive emotional expressions were significantly predicted by higher parental ratings of Cognition and negative emotional expressions by parental ratings of low Effort engagement accounting for some of the correlation with ADHD symptoms.

The current results highlight the plausible role of cognitive energetic processes in explaining the EL and ADHD symptom association

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J Am Acad Child Adolesc Psychiatry. 2020;59:S152.

5.10 EFFICACY AND SAFETY OF AN EXTENDED-RELEASE, ORALLY DISINTEGRATING METHYLPHENIDATE TABLET IN CHILDREN 6-12 YEARS OF AGE BASED ON ADHD RATING SCALE-IV SCORE AT BASELINE.

Ann CC, Kollins SH, Cutler AJ, et al.

Objectives: The objective of this presentation is to show results on the efficacy and safety of methylphenidate extended-release orally disintegrating tablets (MPH XR-ODT) for the treatment of ADHD during the open-label phase of a laboratory classroom study in children based on ADHD symptom severity at baseline (NCT01835548).

Methods: Children (6-12 years old) diagnosed with ADHD were enrolled. Treatment was initiated with MPH XR-ODT 20 mg/day. Doses were adjusted by 10 to 20 mg/day each week during the 4-week dose optimization period until a dose that balanced safety, tolerability, and efficacy was reached. This optimal dose was maintained during the 1-week stabilization period. Efficacy was assessed using the ADHD Rating Scale-IV (ADHD-RS-IV) total score. Adverse events (AEs) were recorded throughout the study. A secondary analysis of subgroups by baseline ADHD-RS-IV score was performed (<42 for moderate symptom severity vs 42 for marked symptom severity).

Results: Of the 87 participants enrolled in the study, 50 had a baseline ADHD-RS-IV score <42 and 37 had a baseline score 42. The mean (SD) final optimized MPH XR-ODT dose was significantly lower for participants with a baseline score <42 (37.1 [14.7] mg) compared with a baseline score 42 (48.1 [11.9] mg). The percent of participants who achieved 50% change in ADHD-RS-IV total score from baseline was numerically higher in participants with a score 42 compared with participants with a score <42 (62.2% vs 59.2%). The least squares mean (SD) ADHD-RS-IV total score decreased progressively with dose optimization and was similar at visit 6 in both groups (16.0 [1.6] for participants with a score 42 vs 18.8 [1.3] for a score <42). Treatment-emergent AEs (TEAE) were experienced by 34 (68.0%) participants with a score <42 and 28 (75.7%) with a score 42. Common TEAEs (5% of participants) in both groups were mild/moderate and included decreased appetite, upper abdominal pain, headache, and insomnia.

Conclusions: Treatment with an optimized dose of MPH-XR ODT was safe, well tolerated, and associated with a reduction in ADHD symptoms. These data suggest that among children aged 6 to 12 years with higher baseline ADHD-RS-IV scores, higher dosing within labeling guidelines may provide greater symptom improvement. STIM, SAC, ADHD

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J Am Acad Child Adolesc Psychiatry. 2021;60:236-51.

STEPPED TREATMENT FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND AGGRESSIVE BEHAVIOR: A RANDOMIZED, CONTROLLED TRIAL OF ADJUNCTIVE RISPERIDONE, DIVALPROEX SODIUM, OR PLACEBO AFTER STIMULANT MEDICATION OPTIMIZATION.

Blader JC, Pliszka SR, Kafantaris V, et al.

Objective: Stimulant medications are the most prevalent first-line pharmacotherapy for attention-deficit/hyperactivity disorder, but children with aggressive behavior often receive multiagent treatment. There is sparse evidence for the benefits of adjunctive medications when stimulant monotherapy provides inadequate benefit for aggressive behavior, yet the adverse effects of common adjuncts are well established. This study compared the efficacy in reducing aggressive behavior of risperidone (RISP), divalproex sodium (DVPX), and placebo (PBO) added to stimulant medication among childrenwhose symptoms persisted after individually optimized stimulant treatment.

Method: This trial enrolled 6- to 12-year-old with attention-deficit/hyperactivity disorder, a disruptive disorder, significant aggressive behavior, and prior stimulant treatment. Open, systematically titrated stimulant treatment identified patients with inadequate reductions in aggressive behavior, who were then randomly assigned to receive adjunctive RISP, DVPX, or PBO under double-blinded conditions for 8 weeks. Family-

based behavioral treatment was offered throughout the trial. The primary outcome was the parent-completed Retrospective Modified Overt Aggression Scale.
Results: Participants included 175 children (mean [SD] age 9.48 [2.04] years, 19% female). Of participants, 151 completed the stimulant optimization phase, with aggression remitting among 96 (63%), and 45 were randomly assigned to adjunctive treatment groups. The adjunctive RISP group showed greater reductions in aggression ratings than the PBO group (least squares means difference [SM], 2.33; 95% CI, 3.83 to 0.82; effect size [ES], 1.32), as did the DVPX group (SM, 1.60; 95% CI, 3.18 to 0.03; ES, 0.91). Mean standardized body mass index scores increased more among RISP-treated participants than participants receiving PBO (SM, 1.54; 95% CI, 0.68 to 2.40; ES, 0.58).
Conclusion: High response rate during the trial's open stimulant optimization phase suggests that rigorous titration of stimulant medication and concurrent behavioral therapy may avert the need for additional medications. Among nonremitters, RISP and DVPX were efficacious adjunctive treatments, although RISP was associated with weight gain.
Clinical trial registration information: Effectiveness of Combined Medication Treatment for Aggression in Children With Attention Deficit With Hyperactivity Disorder (The SPICY Study); https://www.clinicaltrials.gov; NCT00794625

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J Am Acad Child Adolesc Psychiatry. 2021.
SYSTEMATIC REVIEW: EDUCATIONAL ACCOMMODATIONS FOR CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Lovett BJ, Nelson JM.
Objective: Children and adolescents with attention-deficit/hyperactivity disorder (ADHD) often receive instruction and take tests using educational accommodations. This review aims to summarize and integrate the research literature on accommodations for this specific population.
Method: Electronic databases in medicine (MEDLINE), psychology (PsycINFO), and education (ERIC) were systematically searched (last update January 13, 2020), with inclusion criteria selecting any document with a focus on accommodations in educational settings or on academic tasks for children or adolescents with ADHD. The search yielded 497 unique documents. Additional searches yielded 13 more documents. Of the 510 total potentially useful documents, 68 met criteria for topical relevance and age range, to be discussed in the narrative review. The wide range of document types led to a qualitative synthesis.
Results: Accommodations are by far the most common response to ADHD in educational settings, with testing accommodations such as extended time being particularly prevalent. However, most accommodations fail to show evidence of benefits that are specific to students with ADHD, and many of the more common accommodations have few or no experimental studies supporting them. An exception is read-aloud accommodations, which have two randomized experiments finding specific benefits for younger students with ADHD. Students and those who work with them often express ambivalence and dissatisfaction over the accommodations process.
Conclusion: More empirical research is needed to examine the effects of these extremely common supports. In the absence of supportive evidence, health professionals should be hesitant to recommend accommodations immediately after a diagnosis. Even when such evidence exists, educational accommodations should only be provided along with evidence-based interventions, or after interventions have failed, as suggested by the life course model of managing ADHD

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J Am Acad Child Adolesc Psychiatry. 2021;60:222-35.
SYSTEMATIC REVIEW: MEDICATION EFFECTS ON BRAIN INTRINSIC FUNCTIONAL CONNECTIVITY IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Pereira-Sanchez V, Franco AR, Vieira D, et al.
Objective: Resting-state functional magnetic resonance imaging (R-fMRI) studies of the neural correlates of medication treatment in attention-deficit/hyperactivity disorder (ADHD) have not been systematically

reviewed. Our objective was to systematically identify, assess and summarize within-subject R-fMRI studies of pharmacological-induced changes in patients with ADHD. We critically appraised strengths and limitations, and provide recommendations for future research.
Method: Systematic review of published original reports in English meeting criteria in pediatric and adult patients with ADHD up to July 1, 2020. A thorough search preceded selection of studies matching prespecified criteria. Strengths and limitations of selected studies, regarding design and reporting, were identified based on current best practices.
Results: We identified and reviewed 9 studies (5 pediatric and 4 adult studies). Sample sizes were small-medium (16ΓÇô38 patients), and included few female participants. Medications were methylphenidate, amphetamines, and atomoxetine. Wide heterogeneity was observed in designs, analyses and results, which could not be combined quantitatively. Qualitatively, the multiplicity of brain regions and networks identified, some of which correlated with clinical improvements, do not support a coherent mechanistic hypothesis of medication effects. Overall, reports did not meet current standards to ensure reproducibility.
Conclusion: In this emerging field, the few studies using R-fMRI to analyze the neural correlates of medications in patients with ADHD suggest a potential modulatory effect of stimulants and atomoxetine on several intrinsic brain activity metrics. However, methodological heterogeneity and reporting issues need to be addressed in future research to validate findings which may contribute to clinical care. Such a goal is not yet at hand

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J Can Acad Child Adolesc Psychiatry. 2020;29:260-61.
Comparison of Shame in Adolescents with ADHD and Without ADHD Poster.
Yee C, Roberts N.
Our aim is to examine the prevalence of Shame in youth diagnosed with ADHD, and to compare results of the shame questionnaire in ADHD with Non-ADHD youth from an urgent consult clinic. Adult literature shows an association between shame and ADHD; we expect to find similar results in our youth.;
Methods: Adolescents =>13 years routinely complete the ADHD questionnaire (SNAP-26) and the Brief Shame and Guilt Questionnaire (BSGQ) at their initial assessment in the clinic. At the end of each assessment the forms will be marked ADHD or other (any other diagnosis). This is all secondary data, where identifying information on the questionnaires will be removed, except for age, gender and diagnosis. These questionnaires will be reviewed only at the end of the study period. Data analysis will be conducted using frequencies, percentages, means and standard deviations to describe age, gender and Diagnosis. Chi square and OR will be used for Group comparison.
Results: We expect to have data from at least 60 patients with ADHD and an equal number for other diagnoses. We will report the prevalence of Shame amongst ADHD group by gender. Further results from the comparison of shame questionnaire scores between ADHD with Non ADHD will be reported.
Conclusion: The results of this pilot study will inform the development of a larger longer length prospective study on Shame as a variable in Adolescents presenting with different mental health disorders, being a potential factor to address to improve treatment compliance

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Journal of the Korean Medical Association. 2021;64:49-56.
PHARMACOLOGICAL TREATMENT FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER IN ADULTS.
Kweon K.
Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by attention deficits, hyperactivity, and impulsivity. In the past, ADHD was considered to be limited to children and adolescents. However, ADHD has now been reconceptualized as a lifelong disorder, and two-thirds of ADHD patients continue to have core symptoms and dysfunction in adulthood. Currently, the public and clinicians' interest in adult ADHD is rapidly increasing in Korea. In addition to interviews with patients for an adult ADHD diagnosis, interviews with family members, existing school records, and neuropsychological tests help clinicians to make a diagnosis. It is necessary to check whether the core symptoms of ADHD were expressed

in childhood. Since adults' symptom patterns differ from those of children, a self-report tool designed for adult ADHD is useful. The medications currently approved for ADHD in adults by the Ministry of Food and Drug Safety of Korea are long-acting methylphenidate and atomoxetine. Both methylphenidate and atomoxetine improve the core symptoms of ADHD as well as daily function. Methylphenidate and atomoxetine can be used safely as first-line treatments, and the overall adverse effects are tolerable. However, attention should be paid to possible cardiovascular adverse events and misuse. Bupropion, modafinil, alpha2-agonist, and tricyclic antidepressants can also be used off-label

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Medicine (Baltimore). 2021 Feb;100:e23953.

EFFICACY AND SAFETY OF ACUPUNCTURE ON CHILDHOOD ATTENTION DEFICIT HYPERACTIVITY DISORDER: A PROTOCOL FOR SYSTEMATIC REVIEW AND META-ANALYSIS.

Lin Y, Jin H, Huang B, et al.

INTRODUCTION: The purpose of this paper is to evaluate the efficacy and safety of acupuncture in the treatment of childhood attention deficit hyperactivity disorder (ADHD).

METHODS AND ANALYSIS: We will electronically search PubMed, Medline, Embase, Web of Science, the Cochrane Central Register of Controlled Trial, China National Knowledge Infrastructure, China Biomedical Literature Database, China Science Journal Database, and Wan-fang Database from their inception. Also, we will manually retrieve other resources, including reference lists of identified publications, conference articles, and grey literature. The clinical randomized controlled trials or quasi-randomized controlled trials related to acupuncture treating pediatric ADHD will be included in the study. The language is limited to Chinese and English. Research selection, data extraction, and research quality assessment will be independently completed by 2 researchers. Data were synthesized by using a fixed effect model or random effect model depend on the heterogeneity test. The scores of Revised Conners' Parent Rating Scale (CPRS-R), Conners Teacher Rating Scale (CTRS-R), and Child Behavior Checklist (CBCL) will be the primary outcomes. Besides, the scores of the Conners Continuous Performance Test, Internal Restlessness Scale, and Behavior Assessment System for Children (BASC), and the possible adverse events will also be assessed as secondary outcomes. RevMan V.5.3 statistical software will be used for meta-analysis, and the level of evidence will be assessed by Grading of Recommendations Assessment, Development, and Evaluation (GRADE). Continuous data will be expressed in the form of weighted mean difference or standardized mean difference with 95% confidence intervals (CIs), while dichotomous data will be expressed in the form of relative risk with 95% CIs.

ETHICS AND DISSEMINATION: The protocol of this systematic review (SR) does not require ethical approval because it does not involve humans. We will publish this article in peer-reviewed journals and presented at relevant conferences.

SYSTEMATIC REVIEW REGISTRATION: OSF Registries, DOI: 10.17605/OSF.IO/XVYP9 (https://osf.io/xvyp9)

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Nature Communications. 2021;12.

RISK VARIANTS AND POLYGENIC ARCHITECTURE OF DISRUPTIVE BEHAVIOR DISORDERS IN THE CONTEXT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Demontis D, Walters RK, Rajagopal VM, et al.

Attention-Deficit/Hyperactivity Disorder (ADHD) is a childhood psychiatric disorder often comorbid with disruptive behavior disorders (DBDs). Here, we report a GWAS meta-analysis of ADHD comorbid with DBDs (ADHD + DBDs) including 3802 cases and 31,305 controls. We identify three genome-wide significant loci on chromosomes 1, 7, and 11. A meta-analysis including a Chinese cohort supports that the locus on chromosome 11 is a strong risk locus for ADHD + DBDs across European and Chinese ancestries (rs7118422, P = 3.15+ù10-10, OR = 1.17). We find a higher SNP heritability for ADHD + DBDs (h2SNP = 0.34) when compared to ADHD without DBDs (h2SNP = 0.20), high genetic correlations between ADHD + DBDs and aggressive (rg = 0.81) and anti-social behaviors (rg = 0.82), and an increased burden (polygenic

score) of variants associated with ADHD and aggression in ADHD + DBDs compared to ADHD without DBDs. Our results suggest an increased load of common risk variants in ADHD + DBDs compared to ADHD without DBDs, which in part can be explained by variants associated with aggressive behavior

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NeuroImage. 2021;229.

CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SPEND MORE TIME IN HYPERCONNECTED NETWORK STATES AND LESS TIME IN SEGREGATED NETWORK STATES AS REVEALED BY DYNAMIC CONNECTIVITY ANALYSIS.

Shappell HM, Duffy KA, Rosch KS, et al.

Previous studies in children with attention-deficit/hyperactivity disorder (ADHD) have observed functional brain network disruption on a whole-brain level, as well as on a sub-network level, particularly as related to the default mode network, attention-related networks, and cognitive control-related networks. Given behavioral findings that children with ADHD have more difficulty sustaining attention and more extreme moment-to-moment fluctuations in behavior than typically developing (TD) children, recently developed methods to assess changes in connectivity over shorter time periods (i.e., dynamic functional connectivity), may provide unique insight into dysfunctional network organization in ADHD. Thus, we performed a dynamic functional connectivity (FC) analysis on resting state fMRI data from 38 children with ADHD and 79 TD children. We used Hidden semi-Markov models (HSMMs) to estimate six network states, as well as the most probable sequence of states for each participant. We quantified the dwell time, sojourn time, and transition probabilities across states. We found that children with ADHD spent less total time in, and switched more quickly out of, anticorrelated states involving the default mode network and task-relevant networks as compared to TD children. Moreover, children with ADHD spent more time in a hyperconnected state as compared to TD children. These results provide novel evidence that underlying dynamics may drive the differences in static FC patterns that have been observed in ADHD and imply that disrupted FC dynamics may be a mechanism underlying the behavioral symptoms and cognitive deficits commonly observed in children with ADHD

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Neuropsychiatr Dis Treat. 2021;17:19-32.

THE IMPACT OF METHYLPHENIDATE ON QBTEST PERFORMANCE OF CHILDREN WITH ADHD: A RETROSPECTIVE CLINICAL STUDY.

Knez R, Stevanovic D, Nasic S, et al.

Introduction: The Quantified behavior Test (QbTest), which combines a continuous performance task (CPT) and motion tracking, provides data for the core signs of attention-deficit/hyperactivity disorder (ADHD): attention, hyperactivity, and impulsivity. This study aimed to evaluate the performance of children and adolescents with ADHD on the QbTest before and after a single methylphenidate (MPH) dose. Subjects and **Methods**: This retrospective chart review study included data from 149 children and 215 adolescents who completed the QbTest. A summary index of the CPT and motion capture data on the QbTest is provided by three cardinal parameters: QbActivity, QbImpulsivity, and QbInattention. The test was performed twice on the same day, before and up to three hours after MPH intake. A decrease by 0.5 in a cardinal parameter score was considered an improvement, whereas an increase by ΓëÑ 0.5 a deterioration.

Results: QbActivity improvement after MPH intake was present in 71.7% and 76.2% of the children and adolescents, respectively. QbImpulsivity improvement was observed in 50.4% of the children and 44.7% of the adolescents, and QbInattention improvement in 85.1% and 91.1% of the children and adolescents, respectively. All three parameters improved simulta-neously in 27.7% of the children and 28.7% of the adolescents. The likelihood that one parameter deteriorated after MPH use was greater if that parameter was within the normal range before medication. This was most pronounced for QbImpulsivity. Among male adolescents, QbInattention improvement was often accompanied by QbImpulsivity deterioration.

Conclusion: The QbTest inattention and motor activity parameters improved markedly after a single MPH dose in children and adolescents with ADHD, while less so for impulsivity. Improvement of one parameter is not necessarily associated with improvement of the other two, and deterioration, especially regarding

impulsivity, may occur. If confirmed, these results highlight the need for optimization and individualization of MPH treatment, while monitoring all aspects of the ADHD symptomatology based on the QbTest performance

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Neuropsychiatr Dis Treat. 2021;17:229-37.

RELIABILITY AND VALIDITY OF THE CHEN ADHD SCALE (C-ADHDS).

Chen YL, Chen VCH, Gossop M.

Purpose: This study aimed to establish the Chen ADHD Scale and to examine its reliability and validity.

Patients and Methods: We recruited 114 individuals diagnosed with attention- deficit/hyperactivity disorder (ADHD) and 39 non-ADHD controls aged between 5 and 18 years. Their parents completed the Chen ADHD Scale, Chinese versions of the SNAP-IV, and Strengths and Difficulties Questionnaire (SDQ). We examined the psychometric proper- ties of Chen ADHD Scale, including test-retest reliability, internal consistency, construct validity, convergent and divergent validity.

Results: Receiver operating characteristic analysis was performed to calculate the area under the curve (AUC), sensitivity, and specificity of the Chen ADHD Scale for predicting ADHD. The Chen ADHD Scale demonstrated satisfactory test-retest reliability (intraclass correlation = 0.916), internal consistency (alpha = 0.966 to 0.978), a good model fit for a two-factor structure (inattention and hyperactivity-impulsivity) and good convergent and divergent validity with SNAP-IV and SDQ. The AUC of Chen ADHD Scale for predicting ADHD was 0.944. The optimal cut-off value of Chen ADHD Scale with impairment requirement for predicting ADHD was 37 with a sensitivity of 0.87 and a specificity of 0.97.

Conclusion: The Chen ADHD Scale is a reliable and valid instrument for screening ADHD symptoms in clinical settings in Taiwan

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Neuropsychopharmacology. 2020;45:82-83.

IMPACT OF DAILY CAFFEINE ON ACTIGRAPHICALLY-MEASURED SLEEP DURATION AMONG ADOLESCENTS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Lunsford-Avery J, Wang K, Engelhard M, et al.

Background: Caffeine use is increasingly ubiquitous among adolescents and may interfere with sleep health. Specifically, greater caffeine consumption has been associated with shorter sleep duration in this age group, and research from adult studies suggests that timing of caffeine intake (morning versus evening) may affect the extent to which sleep duration is impacted. Clarifying the relationship between caffeine and sleep may be particularly critical for adolescents with attention-deficit/hyperactivity disorder (ADHD), who have been shown to have greater sleep disturbances as well as elevated caffeine intake compared to typically developing youth. A recent study of adolescents with ADHD suggested associations between afternoon and evening caffeine use and self-reported, but not actigraphically-measured, sleep health. However, that study used a self-report measure of caffeine use that aggregated intake over the past 30 days, which may not be sensitive enough to capture the effect of daily caffeine intake on subsequent sleep duration. The current study had two primary aims: (1) to evaluate the impact of daily caffeine intake on subsequent actigraphically-measured sleep duration in adolescents, and moreover, to determine whether this relationship is dependent on the timing of caffeine use, and (2) to examine whether the relationship between caffeine intake and objectively assessed sleep duration differs among youth with ADHD versus those without.

Methods: Eighty-nine adolescents aged 11-17 (mean age = 14.08 (SD = 1.78), 45.6% female) were recruited from the community as well as the Duke ADHD Program. Twenty-one youth had a prior diagnosis of ADHD, any presentation type, and sixty-eight did not have prior psychiatric history. Exclusion criteria included occult sleep disorders (i.e., obstructive sleep apnea, periodic leg movement syndrome), current use of prescribed or over-the-counter sleep aids (e.g., sedatives, melatonin), and diagnosis of an acute or chronic medical illness or other medication use that may interfere with sleep as determined by the research team. Following study intake, participants were instructed to wear an actigraph watch for seven consecutive days and nights on their non-dominant wrist. Each morning of the study, participants completed a daily electronic sleep diary

that queried about sleep the prior night. The daily diary also queried the number of caffeinated drinks (e.g., coffee, tea, soda) consumed during the prior day, separately by the time of day (i.e., morning (before noon), afternoon, evening (after 6 pm)). Linear mixed models controlling for the prior night's TST assessed associations between daily caffeine intake and subsequent sleep duration (total sleep time; TST) that night as well as group differences in these relationships.

Results: Total daily caffeine use was associated with reduced TST in the full sample (+¦ = -.18, t=-2.53, p = .01). A coefficient of -0.18 suggests that with every additional caffeinated drink taken in a day, a particular participant could experience on average 0.18 hours (Γê+11 mins) less TST that night. When examined separately by timing of caffeine use, evening caffeine intake was associated with reduced subsequent TST in the full sample (+¦ = .38, t= -3.01, p = .002), while morning and afternoon caffeine use were not (p's > .05). ADHD youth did not report greater caffeine intake than non-ADHD adolescents (p = .17); however, there was an ADHD by caffeine interaction on TST (+¦ = -.77, t=- 2.28, p = .005), such that greater caffeine intake in the afternoon contributed to shorter TST among youth with ADHD, but not youth without ADHD.

Conclusions: Results suggest that daily caffeine intake reduces subsequent actigraphically-measured sleep duration inadolescents. Moreover, this is the first study to use a daily measure of caffeine to demonstrate that (1) similar to the adult literature, the timing of caffeine intake is critical to its impact on objectively assessed sleep duration in adolescents, and (2) the relationship of caffeine intake to sleep differs between adolescents with and without ADHD. Although a prior study using an aggregated measure of caffeine use suggested associations between afternoon/ evening caffeine intake and self-reported sleep health among adolescents with ADHD, that study failed to find associations with actigraphy. By utilizing a more sensitive (daily) measure of caffeine, the current study builds on prior work to show relationships between caffeine intake - especially afternoon use - with subsequent sleep duration in adolescents with ADHD. This finding highlights the importance of assessing caffeine use among adolescents with ADHD, as eliminating or reducing intake - particularly later in the day - may represent one avenue for improving sleep in this population. Future studies may utilize experimental methods and standardized doses/timing of caffeine intake to clarify further the relationships between caffeine intake and timing with sleep health among adolescents with ADHD. In addition, further clarification of types of caffeine used (e.g., coffee, sodas, energy drinks) and the motivation for afternoon/evening intake (e.g., to improve focus) among adolescents with ADHD may further inform interventions aimed at improving sleep in this population

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Neuropsychopharmacology. 2021.

AN EXAMINATION OF THE RELATIONSHIPS BETWEEN ATTENTION/DEFICIT HYPERACTIVITY DISORDER SYMPTOMS AND FUNCTIONAL CONNECTIVITY OVER TIME.

Norman LJ, Sudre G, Bouyssi-Kobar M, et al.

Previous cross-sectional work has demonstrated resting-state connectivity abnormalities in children and adolescents with attention/deficit hyperactivity disorder (ADHD) relative to typically developing controls. However, it is unclear to what extent these neural abnormalities confer risk for later symptoms of the disorder, or represent the downstream effects of symptoms on functional connectivity. Here, we studied 167 children and adolescents (mean age at baseline = 10.74 years (SD = 2.54); mean age at follow-up = 13.3 years (SD = 2.48); 56 females) with varying levels of ADHD symptoms, all of whom underwent resting-state functional magnetic resonance imaging and ADHD symptom assessments on two occasions during development. Resting-state functional connectivity was quantified using eigenvector centrality mapping. Using voxelwise cross-lag modeling, we found that less connectivity at baseline within right inferior frontal gyrus was associated with more follow-up symptoms of inattention (significant at an uncorrected cluster-forming threshold of p 0.001 and a cluster-level familywise error corrected threshold of p < 0.05). Findings suggest that previously reported cross-sectional abnormalities in functional connectivity within inferior frontal gyrus in patients with ADHD may represent a longitudinal risk factor for the disorder, in line with efforts to target this region with novel therapeutic methods

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Neuropsychopharmacology. 2021.

ASSOCIATION OF GRAY MATTER VOLUMES WITH GENERAL AND SPECIFIC DIMENSIONS OF PSYCHOPATHOLOGY IN CHILDREN.

Durham EL, Jeong HJ, Moore TM, et al.

Childhood is an important time for the manifestation of psychopathology. Psychopathology is characterized by considerable comorbidity which is mirrored in the underlying neural correlates of psychopathology. Both common and dissociable variations in brain volume have been found across multiple mental disorders in adult and youth samples. However, the majority of these studies used samples with broad age ranges which may obscure developmental differences. The current study examines associations between regional gray matter volumes (GMV) and psychopathology in a large sample of children with a narrowly defined age range. We used data from 9607 children 9ΓÇô10 years of age collected as part of the Adolescent Brain Cognitive DevelopmentSM Study (ABCD Study-«). A bifactor model identified a general psychopathology factor that reflects common variance across disorders and specific factors representing internalizing symptoms, ADHD symptoms, and conduct problems. Brain volume was acquired using 3T MRI. After correction for multiple testing, structural equation modeling revealed nearly global inverse associations between regional GMVs and general psychopathology and conduct problems, with associations also found for ADHD symptoms (pfdr-values 0.048). Age, sex, and race were included as covariates. Sensitivity analyses including total GMV or intracranial volume (ICV) as covariates support this global association, as a large majority of region-specific results became nonsignificant. Sensitivity analyses including income, parental education, and medication use as additional covariates demonstrate largely convergent results. These findings suggest that globally smaller GMVs are a nonspecific risk factor for general psychopathology, and possibly for conduct problems and ADHD as well

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Neurosci Biobehav Rev. 2021;124:63-77.

PARENTAL ADHD IN PREGNANCY AND THE POSTPARTUM PERIOD. A SYSTEMATIC REVIEW.

Kittel-Schneider S, Quednow BB, Leutritz AL, et al.

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders worldwide, and in the majority of patients persists into adulthood. However, it remains unclear how maternal ADHD could affect pregnancy and birth as well as early mother-(father)-child interaction. There are several studies investigating the effect of depressed or anxious parents on parent-child-interactions in early infancy, but data about the influence of parental ADHD is lacking although it is a common mental disorder in parents. Additionally, the prescription of stimulant and other ADHD medication for adult ADHD patients is rising due to improved diagnostic procedures and a greater awareness of this disorder in adulthood among psychiatrists and psychologists. However, this leads to increased numbers of treated ADHD women that wish to have children or experience unplanned pregnancies while taking stimulant medication. In our systematic review we aimed at analysing the current evidence for the association of maternal ADHD with pregnancy and birth outcomes, pregnancy risks and health behaviour in pregnancy, as well as the association of parental ADHD with early parent-child interaction and early child development in the first 3 years. Furthermore, we reviewed recent evidence on the risks of stimulant and non-stimulant treatment for ADHD in pregnancy and lactation

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Nord J Psychiatry. 2020.

SELF ESTEEM AND CLINICAL FEATURES IN A CLINICAL SAMPLE OF CHILDREN WITH ADHD AND SOCIAL ANXIETY DISORDER.

Celebi F, et al.

Objective: In this study, we aimed to investigate self-esteem and clinical features in clinically referred children and adolescents with attention-deficit/hyperactivity disorder (ADHD) and comorbid Social Anxiety Disorder (SAD) and compare these to children and adolescents without SAD.

Methods: One hundred and twenty child and adolescent drug-na+»ve outpatients (6-15 years of age) with a primary diagnosis of ADHD were included. Schedule for Affective Disorders and Schizophrenia for School

Age Children-Present and Lifetime Version (K-SADS-PL), was used to evaluate ADHD and comorbidities. Parents filled in clinical and sociodemographic data form, Conners Parent Rating Scale (CPRS) and patients filled in Rosenberg Self-esteem Scale (RSES) and apa Social Phobia Scale for children and adolescents (ESF).
Results: Forty-six of the 120 (38.3%) children had comorbid SAD. Forty-six patients with SAD (ADHD + SAD group) and 74 patients without SAD (ADHD without SAD group) were compared in terms of the sociodemographic and clinical features, rate of psychiatric comorbidities, and rating scale scores. The rate of inattentive subtype of ADHD ($p = 0.009$), and social anxiety symptom scores ($p < 0.001$) were higher and self-esteem was lower ($p < 0.001$) in the ADHD + SAD group. Additionally, there was a statistically significant correlation between ESF scores and CPRS anxiety subscale scores ($r = 0.300$, $p = 0.001$), and also Rosenberg self-esteem scale scores ($r = 0.470$, $p < 0.001$).
Conclusion: Children and adolescents with ADHD who had comorbid SAD may differ from ADHD patients without SAD in terms of ADHD subtype, clinical features and self-esteem

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Nutrients. 2021;13:1-16.

THE USE OF LOWER OR HIGHER THAN RECOMMENDED DOSES OF FOLIC ACID SUPPLEMENTS DURING PREGNANCY IS ASSOCIATED WITH CHILD ATTENTIONAL DYSFUNCTION AT 4-5 YEARS OF AGE IN THE INMA PROJECT.

Compan Gabucio LM, et al.

We assessed the association between the use of lower- and higher-than-recommended doses of folic acid supplements (FAs) during pregnancy and attentional function in boys and girls at age of 4-5. We analyzed data from 1329 mother-child pairs from the mother-child cohort INfancia y Medio Ambiente Project (INMA) study. Information on FAs use during pregnancy was collected in personal interviews at weeks 12 and 30, and categorized in <400, 400-999 (recommended dose), and ≥1000 µg/day. Child attentional function was assessed by Conners' Kiddie Continuous Performance Test. Multivariable regression analyses were used to estimate incidence rate ratios (IRR) and beta coefficients with 95% confidence intervals (CI). Compared to recommended FAs doses, the periconceptional use of <400 and ≥1000 µg/day was associated with higher risk of omission errors-IRR = 1.14 (95% CI: 1.01; 1.29) and IRR = 1.16 (95% CI: 1.02; 1.33), respectively. The use of FAs < 400 µg/day and ≥1000 µg/day was significantly associated with deficits of attentional function only in boys. FAs use < 400 µg/day was associated with higher omission errors with IRR = 1.22 and increased hit reaction time (HRT) β = 34.36, and FAs use ≥ 1000 µg/day was associated with increased HRT β = 33.18 and HRT standard error β = 3.31. The periconceptional use of FAs below or above the recommended doses is associated with deficits of attentional function in children at age of 4-5, particularly in boys

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Pakistan Journal of Medical and Health Sciences. 2020;14:731-33.

PREVALENCE AND ASSESSMENT OF ATTENTION DEFICIT HYPERACTIVE DISORDER IN SCHOOL GOING CHILDREN OF GRADE 1 TO GRADE 5 IN SWAT.

Ali H, Hussain A, Haq SU, et al.

Aim: To assess the frequency of gender ratio and the related psychosocial factors among the school going children of ADHD in Swat.
Methods: This cross-sectional study was done using a non-probability convenient sampling technique at the psychiatry department of Saidu Medical College, Swat, from July 2019 to December 2019. The sample size was 553. Children from grade 1 to 5 studying in schools and living in Swat's residential area were included. All children whose parents refused to participate in the study were excluded. All children were accessed through their teachers and parents. The behavior rate scale questionnaire was filled to grade the tendency of ADHD.
Results: Of the total 553 respondents, the suspected children were 131. Out of those 131 children, 111 had a score of 20-29 on the behavior rating scale, and 20 had a score of 30 and onwards. On the basis of gender, there were 89 males out of 319 total males (27.8%), and there were 42 females out of a total of 234 females

(17.9%) who were screened out. This made a total of 131 students who were screened from 553 students making up 23.6% of students who showed a strong tendency towards ADHD.
Conclusion: Children with ADHD are frequently encountered in the primary care setting. They should be diagnosed by primary care providers based on procedures supported by evidence from empirical investigations. Clinics should use ADHD-specific rating scales completed by caregivers and teachers in their efforts to identify highly suspected children for ADHD

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PharmacoEconomics. 2021.
GLOBAL ECONOMIC BURDEN OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW.
Chhibber A, Watanabe AH, Chaisai C, et al.
Background: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common mental disorders affecting children and adults. Previous systematic reviews have provided estimates of ADHD-associated costs but were limited to the USA and Europe.
Objectives: This study aimed to systematically summarise all global evidence on the economic burden of ADHD.
Methods: A systematic search for published studies on costs of ADHD was conducted in EconLit, EMBASE, PubMed, ERIC, and PsycINFO. Additional literature was identified by searching the reference lists of eligible studies. The quality of the studies was assessed using the Larg and Moss checklist.
Results: This review included 44 studies. All studies were conducted in high-income countries and were limited to North America and Europe except for four studies: two in Asia and two in Australia. Most studies were retrospective and undertook a prevalence-based study design. Analysis revealed a substantial economic impact associated with ADHD. Estimates based on total costs ranged from $US831.38 to 20,538 for per person estimates and from $US356 million to 20.27 billion for national estimates. Estimates based on marginal costs ranged from $US244.15 to 18,751.00 for per person estimates and from $US12.18 million to 141.33 billion for national estimates. Studies that calculated economic burden across multiple domains of direct, indirect, and education and justice system costs for both children and adults with ADHD reported higher costs and translated gross domestic product than did studies that captured only a single domain or age group.
Conclusions: Despite the wide variation in methodologies in studies reviewed, the literature suggests that ADHD imposes a substantial economic burden on society. There is a dire need for cost-of-illness research in low- and middle-income countries to better inform the treatment and management of ADHD in these countries. In addition, guidelines on the conduct and reporting of economic burden studies are needed as they may improve standardisation of cost-of-illness studies

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Pharmacoepidemiol Drug Saf. 2020;29:276.
METHYLPHENIDATE ADHERENCE AND LOSS TO FOLLOW-UP IN ADHD CHILDREN IN A TERTIARY CARE PSYCHIATRIC HOSPITAL.
Kunacharoensuk N, Kamjak T, Kamduang N, et al.
Background: Methylphenidate is a common and effective medication treatment for ADHD in children. Little is known about long-term methylphenidate adherence and loss to follow up in this population. Objectives: To determine the rates of methylphenidate adherence and loss-to-follow-up 3 years after the initiation of the treatment and factors associated with methylphenidate adherence.
Methods: We conducted a cross-sectional descriptive study using patient chart review. Children 6-12 years diagnosed with ADHD receiving methylphenidate treatment at a tertiary care psychiatric hospital in Thailand during January 2008-July 2012 were included. Methylphenidate was grouped by immediate-release or extendedrelease formulation. Adherence, using medication possession ratio (MPR), was measured using 80% cut-off in year 1 to 3. We collected data and tested whether age, gender, IQ, type of health insurance, distance from hospital, and care giver's relationship with the child, marital status, and education were

associated with methylphenidate adherence using a binomial logistic regression model. Loss to follow-up of methylphenidate treatment was measured if no hospital visit over 6 months in one year was present.
Results: The study samples (n= 197) was male (84.3%) and diagnosed with ADHD at the age of 6-7 years (57.9%). Most patients were prescribed immediate-release methylphenidate (88.8%). First, second, and third year methylphenidate adherence rates (MPR.80%) decreased over time (66.5%, 48.7%, and 45.2%, respectively). ADHD patients with care giver with higher education were more likely to adhere to methylphenidate than patients with care giver with less education (4.44, 95% CI, 1.02-19.34). Cumulative loss to follow-up rates were 21.8%, 24.4%, and 37.6% in 3 years.
Conclusions: Methylphenidate adherence in children was suboptimal and declined over 3 years after receiving the treatment. Care giver's education was associated with methylphenidate adherence in the first year of the treatment

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Pharmacoepidemiol Drug Saf. 2020;29:515.

PRENATAL EXPOSURE TO NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER DIAGNOSIS AND SYMPTOMS: A FOLLOW-UP IN THE NORWEGIAN MOTHER, FATHER AND CHILD COHORT STUDY.

Hjorth S, Lupattelli A, Handal M, et al.

Background: Non-steroidal anti-inflammatory drugs (NSAIDs) are used in 5-15% of pregnancies despite that first and third trimester use is associated with risk of negative birth outcomes. Few studies have investigated neurodevelopment in children exposed to NSAIDs in utero and none have followed the children up to school age.
Objectives: To investigate the association between timing and duration of prenatal exposure to NSAIDs and risk of attention deficit hyperactivity disorder (ADHD) diagnosis and symptoms.
Methods: This study was based on the Norwegian Mother, Father and Child Cohort Study linked to the Medical Birth Registry of Norway. The study sample was restricted to women reporting indications for NSAID use (N=76 385). Prenatal NSAID exposure was identified by maternal report during pregnancy and post-partum. The primary outcome, child ADHD, was identified as an ICD-10 diagnosis from the Norwegian Patient Registry and/or ADHD medication fills from the Norwegian Prescription Database. The secondary outcome, child ADHD symptoms at age 5 years, was measured using Conners' Parent Rating Scale-Revised. To account for time-varying exposure and confounders, marginal structural models were fitted to estimate hazard ratios and mean difference in z-scores. Missing data were handled via multiple imputation. Several sensitivity analyses were done to investigate potential misclassification of exposure and outcome, residual confounding by disease severity, and model misspecifications.
Results: The analyses on ADHD diagnoses included 56 340 children. The average age at follow-up was 10 years. The analyses on ADHD symptoms included 34 961 children. There was no increased risk of ADHD diagnosis in children exposed to NSAIDs in utero regardless of timing of exposure (first trimester: HR 1.12 [95% CI 0.86;1.45], second trimester: HR 0.98 [0.69;1.38], third trimester: HR 0.68 [0.31; 1.46]). ADHD symptoms scores were also similar in exposed and unexposed (first trimester: mean difference 0.03 [95% CI-0.03;0.09], second trimester: mean difference 0.03 [-0.04;0.11], third trimester: mean difference 0.11 [-0.03; 0.25]). There was no duration-response relationship. The results were stable in sensitivity analyses.
Conclusions: The findings are reassuring and suggest no substantially increased risk of ADHD diagnosis or symptoms in children exposed to NSAIDs in utero, regardless of timing or duration, though nondifferential misclassification of the exposure may have attenuated results

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Pharmacoepidemiol Drug Saf. 2020;29:67-68.

THREATENED ABORTION AND RISK OF EPILEPSY, CEREBRAL PALSY AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN OFFSPRING: A REGISTRYBASED COHORT STUDY IN DENMARK.

Dudukina E, Horvath-Puho E, Toft Sorensen H, et al.

Background: Children born following a pregnancy complicated by threatened abortion (TAB) are at increased risk of autism spectrum disorders. It is unknown whether TAB is associated with other neurologic and behavioral disorders.

Objectives: To examine incidence rate (IR), incidence rate difference (IRD), and hazard ratio (HR) of epilepsy, cerebral palsy, and attentiondeficit/ hyperactivity disorder (ADHD) in offspring born from a pregnancy affected with TAB as compared with offspring born from a pregnancy unaffected with TAB.

Methods: In this cohort study, we included singletons live-born in Denmark, 1979-2010. The exposed cohort included children born from a TAB-affected pregnancy before 20th gestational week. The comparison cohort included children born in the same calendar period from a TABunaffected pregnancy. The three study outcomes were hospital diagnosis of epilepsy, cerebral palsy, and hospital ADHD diagnosis or use of ADHD drugs. We applied a sibling comparison design to estimate HRs of the outcomes in pairs of discordantly exposed full siblings born in 1991-2010. We followed the children from birth until the earliest of each of the outcomes, 16th birthday, emigration, death, or December 31, 2016. For each outcome, we computed crude IR and IRD (per 1000 person-years). Using Cox proportional hazards regression, we computed HRs with 95% confidence intervals (CIs) while adjusting for the calendar year, birth order, parental age, maternal pre-pregnancy somatic, psychiatric and neurologic morbidity, medication use, employment, education, and income.

Results: In the total population (N=1 864 221), 59 134 (3.2%) offspring were in TAB cohort and 1 805 087 offspring were in the comparison cohort. The population of full siblings included 20 091 discordantly exposed pairs. In the TAB cohort of the total population, the IRs of epilepsy, cerebral palsy, and ADHD were 1.6 (1.5-1.7), 0.4 (0.3-0.4), and 3.2 (3.0-3.4), respectively. The IRD with the comparison cohort was small (0.4 for epilepsy, 0.1 for cerebral palsy, and 0.8 for ADHD). In the total population, the offspring from TAB cohort was at 1.2-fold (1.2-1.3) increased hazard of epilepsy, at 1.4-fold (1.2-1.6) increased hazard of cerebral palsy, and at 1.2-fold (1.1-1.3) increased hazard of ADHD. In the sibling analyses, all associations were attenuated: HR=1.0 (0.9-1.2) for epilepsy, HR=1.2 (0.8-1.6) for cerebral palsy and HR=1.1 (0.9-1.2) for ADHD.

Conclusions: We found a weak association between TAB and offspring's subsequent risk of the neurological and behavioral outcomes of interest

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Phytother Res. 2021.

COMPLEMENTARY EFFECTS OF PINE BARK EXTRACT SUPPLEMENTATION ON INATTENTION, IMPULSIVITY, AND ANTIOXIDATIVE STATUS IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A DOUBLE-BLINDED RANDOMIZED PLACEBO-CONTROLLED CROSS-OVER STUDY.

Hsu CD, Hsieh LH, Chen YL, et al.

The purpose of this study was to investigate the complementary effects of polyphenolic compounds from pine bark extract (PE) as a strong antioxidative substrate on the symptoms of inattention and impulsivity in children with attention-deficit hyperactivity disorder (ADHD). This was a randomized, double-blind, crossover, placebo-controlled study that included two experimental units (4 weeks with PE supplementation and 4 weeks with placebo supplementation) separated by a 2-week washout period. ADHD participants were supplemented with 25 mg or 50 mg PE. We recruited 20 participants (17 boys and 3 girls) with a mean age of 10.0 -¦ 2.1 years. PE supplementation caused a significant reduction in the inattention and hyperactivity-impulsivity items of SNAP-IV. During the period of PE supplementation, the item of commissions in the Continuous Performance Test III (CPT III) significantly decreased, which was used to evaluate the symptoms of inattention and impulsivity. In addition, the erythrocytic reduced glutathione/oxidized glutathione ratio significantly increased, and the plasma TBARs level significantly decreased after 4 weeks of PE supplementation. However, there was no significant correlation between CPT III (commission) and

antioxidative status indictors. PE supplementation may have potential effects of ameliorating inattention and impulsivity, and elevating the antioxidative status in children with ADHD

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PLoS ONE. 2020;15.

DIURNAL VARIATION OF MOTOR ACTIVITY IN ADULT ADHD PATIENTS ANALYZED WITH METHODS FROM GRAPH THEORY.

Fasmer OB, Fasmer EE, Mjeldheim K, et al.

Attention-deficit /hyperactivity disorder (ADHD) is a common neurodevelopmental syndrome characterized by age-inappropriate levels of motor activity, impulsivity and attention. The aim of the present study was to study diurnal variation of motor activity in adult ADHD patients, compared to healthy controls and clinical controls with mood and anxiety disorders. Wrist-worn actigraphs were used to record motor activity in a sample of 81 patients and 30 healthy controls. Time series from registrations in the morning and evening were analyzed using measures of variability, complexity and a newly developed method, the similarity algorithm, based on transforming time series into graphs. In healthy controls the evening registrations showed higher variability and lower complexity compared to morning registrations, however this was evident only in the female controls. In the two patient groups the same measures were not significantly different, with one exception, the graph measure bridges. This was the measure that most clearly separated morning and evening registrations and was significantly different both in healthy controls and in patients with a diagnosis of ADHD. These findings suggest that actigraph registrations, combined with mathematical methods based on graph theory, may be used to elucidate the mechanisms responsible for the diurnal regulation of motor activity

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PLoS ONE. 2021;16.

GUIDELINE ADHERENCE IN THE MANAGEMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN: AN AUDIT OF SELECTED MEDICAL RECORDS IN THREE AUSTRALIAN STATES.

Ellis LA, Blakely B, Hazell P, et al.

Objective To assess General Practitioner (GP) and pediatrician adherence to clinical practice guidelines (CPGs) for diagnosis, treatment and management of attention deficit hyperactivity disorder (ADHD).

Method Medical records for 306 children aged Γëñ15 years from 46 GP clinics and 20 pediatric practices in Australia were reviewed against 34 indicators derived from CPG recommendations. At indicator level, adherence was estimated as the percentage of indicators with 'Yes' or 'No' responses for adherence, which were scored 'Yes'. This was done separately for GPs, pediatricians and overall; and weighted to adjust for sampling processes.

Results Adherence with guidelines was high at 83.6% (95% CI: 77.7-88.5) with pediatricians (90.1%; 95% CI: 73.0-98.1) higher than GPs (68.3%; 95% CI: 46.0-85.8; p = 0.02). Appropriate assessment for children presenting with signs or symptoms of ADHD was undertaken with 95.2% adherence (95% CI: 76.6-99.9), however ongoing reviews for children with ADHD prescribed stimulant medication was markedly lower for both pediatricians (51.1%; 95% CI: 9.6-91.4) and GPs (18.7%; 95% CI: 4.1-45.5).

Conclusion Adherence to CPGs for ADHD by pediatricians was generally high. Adherence by GPs was lower across most domains; timely recognition of medication side effects is a particular area for improvement.

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Psychiatry Res. 2021;297.

DIGITAL HEALTH INTERVENTIONS (DHI) FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN - A COMPARATIVE REVIEW OF LITERATURE AMONG VARIOUS TREATMENT AND DHI.

Pandian GSB, Jain A, Raza Q, et al.

The objective of this study is to compare game-based digital therapeutic device and other DHI like (smartphone apps, wearable technologies) for ADHD with the current pharmacological and behavior therapy. The FDA has approved a game-based digital therapeutic device - EndeavorRx, for the treatment of ADHD in pediatric patients belonging to the age group of 8-12 years old. This has been primarily recommended for the treatment of inattentive or combined-type ADHD who have demonstrated an attention issue. This is the first game-based therapeutic device to be approved by the FDA for any type of condition. According to the FDA, this has been shown to improve attention which is measured by computer-based testing. Objective: The objective of this study is to compare a game-based digital therapeutic device and other DHI (smartphone apps, wearable technologies) with the current pharmacological and behavior therapy used in the treatment of ADHD

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Psychiatry Res. 2021;298.

REWARD AND PUNISHMENT SENSITIVITY ARE ASSOCIATED WITH CROSS-DISORDER TRAITS.

Portengen CM, Sprooten E, Zwiers MP, et al.

Reversal learning deficits following reward and punishment processing are observed across disruptive behaviors (DB) and attention-deficit/hyperactivity disorder (ADHD), and have been associated with callous-unemotional (CU) traits. However, it remains unknown to what extent these altered reinforcement sensitivities are linked to the co-occurrence of oppositional traits, ADHD symptoms, and CU traits. Reward and punishment sensitivity and perseverative behavior were therefore derived from a probabilistic reversal learning task to investigate reinforcement sensitivity in participants with DB (n=183, ODD=62, CD=10, combined=57, age-range 8-18), ADHD (n=144, age-range 11-28), and controls (n=191, age-range 8-26). The SNAP-IV and Conners rating scales were used to assess oppositional and ADHD traits. The Inventory of CU traits was used to assess CU traits. Decreased reward sensitivity was associated with ADHD symptom severity (p=0.018) if corrected for oppositional symptoms. ADHD symptomatology interacted with oppositional behavior on perseveration (p=0.019), with the former aggravating the effect of oppositional behavior on perseveration and vice versa. Within a pooled sample, reversal learning alterations were associated with the severity of ADHD symptoms, underpinned by hyposensitivity to reward and increased perseveration. These results show ADHD traits, as opposed to oppositional behavior and CU traits, is associated with decreased reward-based learning in adolescents and adults

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Psychiatry Res. 2021;298.

THE ROLE OF TRYPTOPHAN METABOLIC PATHWAY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER WITH AND WITHOUT COMORBID OPPOSITIONAL DEFIANT DISORDER AND CONDUCT DISORDER.

Saglam E, et al.

Accumulating data presented that tryptophan metabolic pathway (TMP) may play a role in attention-deficit/hyperactivity disorder (ADHD). However, no study have investigated potential role of TMP in disruptive behavior disorders coexisting with ADHD. This study compared serum levels of tryptophan, kynurenine, kynurenic acid, 3-hydroxykynurenine and 3-hydroxyantranilic acid in medication-free children with ADHD combined presentation (ADHD-C), with ADHD-C and oppositional defiant disorder (ODD), and with ADHD-C and conduct disorder (CD) versus healthy controls. The study also compared several ratios that are previously suggested to reflect the activities of the KP enzymes (kynurenine/tryptophan, kynurenic acid/kynurenine, 3-hydroxykynurenine/kynurenine) or neuroprotective activity (kynurenic acid/3-hydroxykynurenine) among groups. A total of 122 patients were enrolled: 46 children with ADHD-C alone, 43 children with ADHD-C+ODD, 33 children with ADHD-C+CD and 50 healthy controls. Targeted biochemical molecules were assessed by liquid chromatography-mass spectrometry/mass spectrometry. Compared to

control group, serum kynurenine levels were significantly higher in the ADHD-C group, serum 3-hydroxykynurenine levels were significantly lower in the ADHD-C and ADHD-C+ODD groups, the serum kynurenic acid/kynurenine ratio was significantly higher in the ADHD-C, ADHD-C+ODD and ADHD-C+CD groups, and the serum 3-hydroxykynurenine/kynurenine ratio was significantly lower in the ADHD-C group. These findings suggest that TMP may play a role in the pathophysiology of ADHD-C

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Reproductive Toxicology. 2020;97:8.

INCREASING INTEREST IN MEDICATIONS USED FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER DURING PREGNANCY AND BREAST-FEEDING.

Ellfolk MA, Reponen J, Malm H.

Introduction: The use of Attention Deficit Hyperactivity Disorder (ADHD) medications has increased over the years. According to the Finnish Statistics on Medicines, the number of patients receiving reimbursement for ADHD medications increased almost five-fold from around 6,000 in 2007 to nearly 29,000 in 2017. We wanted to investigate if this increase was also reflected in the calls to the Finnish Teratology Information Service (FIN-TIS). While recent studies have not confirmed a teratogenic risk, there are no data on long term neurocognitive development in prenatally exposed children.

Methods: We searched the call database at Finnish TIS between Jan 1st 2007 - Dec 31st 2019 for calls during preconception, pregnancy and during breastfeeding about drugs indicated for use in ADHD and including atomoxetine, dexamphetamine, guanfacine, lisdexamphetamine and methylphenidate.

Results: Of the total 74,628 calls, 244 (0.3%) concerned ADHD medications; of these, 135 calls (56%) concerned use during preconception or the first trimester and 79 calls (32%) concerned breastfeeding. Methyphenidate was the most commonly used ADHD medication (201 calls), followed by lisdexamphetamine (27 calls, starting since 2016), atomoxetine (14 calls) and dexamphetamine (3 calls). There were no inquiries about guanfacine. In the beginning of our study period only methylphenidate was on the market and the calls received concerning ADHD medication were stable, around 10 calls/year (0.2% of calls). An increase in the calls occurred in 2013 (16 calls; 0.3%) when methylphenidate was granted reimbursement status for adults above 25 years. The number of calls concerning ADHD medication increased further to 42 (0.8%) in 2019. The first calls regarding atomoxetine in the database were recorded in 2014, and for dexamphetamine and lisdexamphetamine in 2016, coinciding with the timing of approved reimbursement status.

Conclusions: The interest in using ADHD medications during pregnancy and breastfeeding is increasing, warranting more research on the short- and long-term safety of these drugs

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Res Autism Spectr Disord. 2021;82.

ANXIETY RELATES TO CLASSROOM EXECUTIVE FUNCTION PROBLEMS IN STUDENTS WITH ASD, BUT NOT ADHD.

Dieckhaus MFS, Hardy KK, Gutermuth Anthony L, et al.

Background: Anxiety occurs at elevated rates in developmental disorders and has been linked to executive functioning (EF) deficits. EF is strongly related to academic outcomes, but the relationship between anxiety and EF in the classroom has not been examined.

Method: We explored this relationship in two neurodevelopmental disorders, autism spectrum disorders (ASD) and attention-deficit/hyperactivity disorder (ADHD), in order to evaluate the specificity of associations between parent-reported anxiety and teacher-reported EF deficits in the classroom setting.

Results: Greater anxiety was associated with more classroom EF-related problems in the ASD group, but not in the ADHD group. Item-level analysis of classroom EF problems in the ASD group revealed associations between anxiety and difficulties with task initiation, attention, and completion. Anxiety was not related to total or item-level teacher-reported EF problems in the ADHD group.

Conclusion: Further investigation into disorder-specific mechanisms that lead to the manifestation of anxiety symptoms may pave the way for more effective treatment and favorable academic outcome. Anxiety is related to poor EF in the classroom for students with ASD, which has implications for treating anxiety to promote positive academic outcomes and incorporating EF supports and training into treatment models for

anxiety. The lack of association between anxiety and EF for students with ADHD was unexpected and warrants further exploration

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Res Dev Disabil. 2021;111.

PERCEIVED SOCIAL SUPPORT IN CHILDREN AND ADOLESCENTS WITH ADHD.

Emser TS, Christiansen H.

Background: Social support is crucial to healthy development, serving as an important protective factor. Aims: This study is the first to evaluate the psychometric properties of the German version of the Child and Adolescent Social Support Scale (CASSS). We further investigated differences between children and adolescents with and without ADHD.

Methods: Our total sample of N = 525 consisted of clinical participants diagnosed with ADHD (28.8 %) and healthy controls (71.2 %). We investigated item properties, factorial validity and reliability of the CASSS and performed a group comparison between patients with ADHD and healthy controls.

Results: Factor analyses confirmed a four-factor structure corresponding to different sources of social support. All scales showed very good internal consistency. Results revealed that patients with ADHD perceived less overall support compared to the healthy controls.

Conclusions: The German version of the CASSS is a reliable and valid instrument for the assessment of perceived social support in children and adolescents. As children with ADHD perceived less social support in comparison to healthy controls, the identification and promotion of social skills should be an integral part of the treatment of ADHD

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Res Dev Disabil. 2021;111.

ADHD SEVERITY AS A PREDICTOR OF COGNITIVE TASK PERFORMANCE IN CHILDREN WITH AUTISM SPECTRUM DISORDER (ASD).

Mansour R, Ward AR, Lane DM, et al.

Background: In recent years, a number of studies have begun to explore the nature of Attention-Deficit/Hyperactivity Disorder (ADHD) in children with Autism Spectrum Disorder (ASD). In this study, we examined the relationship between both symptoms of ADHD and symptoms of ASD on cognitive task performance in a sample of higher-functioning children and adolescents with ASD. Participants completed cognitive tasks tapping aspects of attention, impulsivity/inhibition, and immediate memory.

Aims: We hypothesized that children with ASD who had higher levels of ADHD symptom severity would be at higher risk for poorer sustained attention and selective attention, greater impulsivity/disinhibition, and weaker memory.

Methods and procedures: The sample included 92 children (73 males) diagnosed with ASD (Mean Age = 9.41 years; Mean Full Scale IQ = 84.2). Outcomes and results: Using regression analyses, more severe ADHD symptomatology was found to be significantly related to weaker performance on tasks measuring attention, immediate memory, and response inhibition. In contrast, increasing severity of ASD symptomatology was not associated with higher risk of poorer performance on any of the cognitive tasks assessed.

Conclusions and implications: These results suggest that children with ASD who have more severe ADHD symptoms are at higher risk for impairments in tasks assessing attention, immediate memory, and response inhibition-similar to ADHD-related impairments seen in the general pediatric population. As such, clinicians should assess various aspects of cognition in pediatric patients with ASD in order to facilitate optimal interventional and educational planning

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Res Dev Disabil. 2021;112.

THE CO-OCCURRENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND MATHEMATICAL DIFFICULTIES: AN INVESTIGATION OF THE ROLE OF BASIC NUMERICAL SKILLS.

von Wirth E, Kujath K, Ostrowski L, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) and dyscalculia, also called mathematics disorder, frequently co-occur, yet the etiology of this comorbidity is poorly understood.
Aims: This study investigated whether impairments in the understanding of numbers and magnitudes (basic numerical skills) are a unique risk factor for mathematical difficulties (MD) or a shared risk factor that could help to explain the association between ADHD and MD.
Methods and procedures: Basic numerical skills were assessed with eight subtests in children (age 6ΓÇô10 years, N = 86) with clinically significant ADHD symptoms and/or MD and typically developing children (control group). This double dissociation design allowed to test for main and interaction effects of ADHD and MD using both classical and Bayesian analysis of variance (ANOVA).
Outcomes and results: Children with MD were impaired in transcoding, complex number and magnitude comparison, and arithmetic fact retrieval. They were not impaired in tasks assessing core markers of numeracy, which might be explained by the sample including children with mathematical difficulties instead of a diagnosed dyscalculia. ADHD was not associated with deficits in any of the tasks. The evidence for an additive combination of cognitive profiles was weak.
Conclusions and implications: Impairments in basic numerical skills are uniquely associated with MD and do not represent a shared risk factor for ADHD symptoms and MD

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Research on Child and Adolescent Psychopathology. 2021 Jan;49:39-62.

INHIBITORY CONTROL DEFICITS IN CHILDREN WITH OPPOSITIONAL DEFIANT DISORDER AND CONDUCT DISORDER COMPARED TO ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Bonham MD, Shanley DC, Waters AM, et al.

Inhibitory control deficits are known to be characteristic of Oppositional Defiant Disorder (ODD), Conduct Disorder (CD), and Attention-Deficit/Hyperactivity Disorder (ADHD); but it is unclear whether children with ODD/CD have inhibitory control problems independent of ADHD comorbidity. Previous reviews of inhibitory control and ODD/CD have only focused on one type of measure of inhibitory control or used non-clinical samples. The current meta-analysis explored inhibitory control problems of children with ODD/CD by systematically reviewing studies where children have a diagnosis of ODD and/or CD. Comparisons were made across 25 studies between children with ODD/CD, ODD/CD + ADHD, ADHD, and healthy controls (HC) on various measures of inhibitory control and ADHD symptomatology to explore impacts of ADHD comorbidity. A small significant effect ($g = -0.58$, $p < .001$) suggested children with ODD/CD are likely to have more difficulties with inhibitory control than healthy children. However, comparisons between clinical groups suggested this effect may be due to ADHD symptomatology present in each group. As difficulties with inhibitory control are similar, across clinical groups, a dimensional approach to understanding ODD/CD and ADHD may be more useful to consider in future diagnostic criteria. Similarities across clinical groups highlight that therapeutic approaches that assist children with disruptive behaviours could benefit from teaching children and their families how to cope with inhibitory control deficits

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Research on Child and Adolescent Psychopathology. 2021 Feb;49:185-96.

IRRITABILITY PREDICTS HYPERACTIVE/IMPULSIVE SYMPTOMS ACROSS ADOLESCENCE FOR FEMALES.

Kahle S, Mukherjee P, Dixon JF, et al.

Irritability is common in Attention-Deficit Hyperactivity Disorder (ADHD), but little is known about whether irritability predicts the course of ADHD symptoms over time. Adolescence is a dynamic period of emotional development as well as shifts in ADHD symptoms; an important goal is to identify youth at risk of increasing or persisting symptoms. We examined irritability as a longitudinal predictor of change in adolescents' ADHD symptoms, as well as how this link may differ in females versus males. The sample included 108 youth (72

males) age 12–16 years (M = 14.21 years, SD = 1.44 years), 62 of whom met criteria for ADHD. Approximately 18 months later, 80 participants (48 males) were followed up at Time 2. A dimensional approach was used to examine changes over time in parent-reported inattentive and hyperactive/impulsive symptoms. Longitudinal path analysis revealed that irritability at Time 1 predicted higher relative hyperactive/impulsive symptoms at Time 2 after controlling for age and longitudinal stability in all variables. A multiple-group analysis examining moderation by sex/gender revealed that this association was significant only for females. These results suggest that irritability may play a key role in the persistence and worsening of hyperactive/impulsive symptoms across adolescence for females, with potential implications for the diagnosis and treatment of females with ADHD

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Revista Ecuatoriana de Neurologia. 2021;29:31-39.

PSYCHOMETRIC PROPERTIES OF THE CABI INVENTORY IN THE DETERMINATION OF ADHD.

Pinochet-Quiroz P, Belmar-Mellado M, Lagos-Luciano J, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most frequent mental health issues among children and adolescents worldwide. Current literature shows that ADHD could affect both academic and work performances of those who present it. The aim of the present study was to analyze the psychometric properties of the Child and Adolescence Behavior Inventory (CABI) through an exploratory study, based on the report of 350 Chilean parents. Results indicated a three-dimensional model (sluggish cognitive tempo, inattention and hyperactivity) with adequate fit of the data (RMSEA=0.065; CFI= 0.954; TLI=0.941; PL=207) that explained 61.76% of the total variance with an Alpha of 0.961. Results show that the subscales analyzed have acceptable psychometric properties, an adequate internal consistency and that their indicators have a correct discriminatory power. Therefore, according to these preliminary results, CABI can be considered a useful assessment tool for the diagnosis of ADHD. Implications for practice, policy and future research are discussed

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Sci Total Environ. 2021;773.

THE ASSOCIATIONS AMONG ORGANOPHOSPHATE PESTICIDE EXPOSURE, OXIDATIVE STRESS, AND GENETIC POLYMORPHISMS OF PARAOXONASES IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Chang CH, Yu CJ, Du JC, et al.

This study will help to clarify the relationship between organophosphate pesticides (OPs) and attention deficit/hyperactivity disorder (ADHD) related to oxidative stress and paraoxonases (PON) polymorphisms to further characterize the gene-environment interaction. This case-control study enrolled 85 children with ADHD and 96 control subjects. Urinary OP levels were analyzed by using gas chromatographyΓÇômass spectrometry (GC-MS). Oxidative stress biomarkers, such as 8-hydroxy-2-deoxyguanosine (8-OHdG), 8-nitroguanine (8-NO2-Gua), 8-iso-prostaglandin F2+¦ (8-iso-PGF2+¦), and 4-hydroxy-2-nonenoic acid-mercapturic acid (HNE-MA), were analyzed by using liquid chromatography-tandem mass spectrometry (LC-MS/MS). The relative excess risk due to interaction (RERI), attributable proportion due to interaction (AP), and synergy index (S) were calculated to evaluate the additive interactions between OP exposure and PON genetic polymorphism on ADHD. A causal mediation analysis was conducted to clarify the mediation effects of oxidative stress due to OP exposure on ADHD. Children with ADHD had significantly higher DMP (238.95 nmol/g cre. vs. 164.83 nmol/g cre., p value = 0.01) and HNE-MA (30.75 ++g/g cre. vs. 18.41 ++g/g cre., p value<0.01) concentrations than control children. Children who carried the PON1 GG genotype (rs705379) had low urinary DMP levels, and the level increased with increasing numbers of allele variants. The risk for developing ADHD reached 2.06-fold (OR = 2.06, 95% CI:1.23-3.44) and 1.43-fold (OR = 1.45, 95% CI:1.04-2.03) when the DMP and HNE-MA levels increased by 1 natural log of the concentration, respectively. The estimated AP value was 0.66 (95% CI: 0.17-1.15), indicating that 66% of ADHD cases in DMP-exposed children with the PON1 CT/TT (rs705381) genotype were due to gene-environment interactions. No significant mediation of HNE-MA was observed between DMP exposure and the risk of ADHD. The estimated

proportion mediated was only 7.0% (95% CI: 0.08-0.46). This research suggests the role of OP exposure in the occurrence of ADHD after adjusting for covariates

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Sleep Med. 2021;80:171-75.

LONGITUDINAL ASSESSMENT OF NREM SLEEP EEG IN TYPICALLY DEVELOPING AND MEDICATION-FREE ADHD ADOLESCENTS: FIRST YEAR RESULTS.

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

Objective: Clinical observation and structural MRI studies suggest that delayed brain maturation is a major cause of attention deficit hyperactivity disorder (ADHD). Sleep electroencephalogram (EEG) which exhibits major changes across adolescence provides an opportunity to investigate brain electrophysiology evidence for maturational delay. We present data from an ongoing longitudinal study of sleep EEG in medication-free ADHD and typically developing adolescents to investigate brain electrophysiological evidence for this maturational delay.

Methods: Nine adolescents diagnosed with ADHD (combined presentation, DSM-V criteria, mean age 12.39 -¦ 0.61 years, 2 females), and nine typically developing controls (12.08 -¦ 0.35 years, 4 females) were recruited. Subjects underwent an adaptation night and all night polysomnography twice yearly at the Laboratory.

Results: Basic sleep structure did not differ between the ADHD and control groups. In addition, we found no group differences on delta power ($p = 0.77$), but found a possible trend toward higher theta power ($p = 0.057$) for the ADHD group. The decline of standardized delta power across the 4 non-rapid eye movement (NREM) periods differed by group ($p < 0.05$) with the percent delta power in the first NREM period being lower in the ADHD group.

Conclusions: Our data support the preponderant evidence that basic sleep structure is unaltered with ADHD. Our data do suggest altered sleep homeostatic recuperative processes in ADHD. The theta findings from the first two recordings are suggestive of a maturational delay associated with ADHD, but follow-up data-points are needed

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Sleep Medicine: X. 2021;3.

SENSITIVITY OF THE CHILD BEHAVIOUR CHECKLIST SLEEP ITEMS AND CONVERGENT VALIDITY WITH THE SLEEP DISORDERS SCALE FOR CHILDREN IN A PAEDIATRIC ADHD SAMPLE.

Mancini VO, Pearcy BTD.

Objective: The Child Behavior Checklist (CBCL) is a commonly used measure of child and adolescent functioning, which includes seven items that can be aggregated to provide a purportedly valid measure of sleep functioning. The objective of this study was to examine the convergent validity of the CBCL in a paediatric ADHD population and to evaluate the sensitivity of the instrument when benchmarked against the Sleep Disorders Scale for Children (SDSC).

Methods: The parents of 215 individuals (ages 6ΓÇô17 years, 86% male) completed the CBCL and SDSC as part of a battery of measured administered as part of a specialised ADHD service located in Perth, Western Australia. All participants had a diagnosis of ADHD confirmed by a paediatrician or psychiatrist prior to attending the service.

Results: The CBCL Sleep Composite Scale was strongly correlated with the SDSC, but reported below adequate internal reliability. Receiver Operating Characteristic (ROC) suggests that a cut-off score of 4 may have good diagnostic accuracy compared to SDSC.

Conclusions: The CBCL Sleep Composite Scale may be reasonable to use if no purpose-developed sleep screening tool is available. The CBCL sleep items demonstrated good convergent validity, however, did not otherwise demonstrate acceptable psychometric properties that would endorse its use in an ADHD sample. The development of a specific measure of sleep in children with ADHD children is recommended

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Soc Sci Med. 2021;272.

PARENTAL INTERVENTION IN SCHOOL, ACADEMIC PRESSURE, AND CHILDHOOD DIAGNOSES OF ADHD.

Owens J.

Childhood diagnoses of attention-deficit/hyperactivity disorder (ADHD) have increased dramatically in the U.S. in recent decades. Prior research has alluded to the possibility that high levels of parental intervention in school are associated with increased diagnoses of ADHD, but this relationship remains understudied. This study investigates: 1) whether the children of intervening parents are more likely to be diagnosed with ADHD, and; 2) whether parental intervention moderates the extent to which children's pre-diagnosis behavioral problems and exposure to strict educational accountability policies predict ADHD diagnosis. Analyses of longitudinal, population-level data from the Early Childhood Longitudinal Study-Kindergarten Cohort of 1998-99 (n = 9,750) reveal that a standard deviation increase above the mean on parental intervention in school is associated with a 20% increase in the odds of ADHD diagnosis among elementary school children. This relationship is robust to differences in children's pre-diagnosis behavioral problems, academic achievement, parental knowledge of/exposure to ADHD, and school selection, and can arise because parents who intervene in school on average exhibit heightened sensitivity to behavioral problems and academic pressure from accountability-based educational policies. In light of prior work establishing both social class and racial/ethnic differences in parental intervention in school, this positive relationship between parental intervention in school and children's diagnoses of ADHD may carry important implications for the production of inequality in children's mental health and educational opportunities

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S Afr J Psychiatry. 2020;26:1-7.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN SCHOOL-AGE CHILDREN IN GABORONE, BOTSWANA: COMORBIDITY AND RISK FACTORS.

Olashore AA, Paruk S, Ogunjumo JA, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders in children. Its occurrence and pattern of presentation are unknown in Botswana. Aim: To determine the prevalence of attention-deficit hyperactivity disorder (ADHD), associated comorbid conditions and risk factors amongst school-age children in Botswana.

Setting: Primary schools in Gaborone, Botswana.

Methods: This study used a cross-sectional design. A two-stage random sampling technique was utilised to select learners from 25 out of the 29 public schools in the city. The Vanderbilt ADHD Diagnostic Rating Scale (VADRS), teacher and parent versions, was administered.

Results: Of the 1737 children, 50.9% (n = 884) were male, and their mean age was 9.53 years (s.d. = 1.97). The prevalence of ADHD was 12.3% (n = 213). The most prevalent presentation was the predominantly inattentive, 7.2% (n = 125). A family history of mental illness (odds ratio [OR] = 6.59, 95% CI: 1.36-32.0) and perinatal complications (OR = 2.16, 95% CI: 1.08-4.29) emerged as the independent predictors of ADHD.

Conclusions: The prevalence of ADHD in Botswana is slightly higher than that reported in the literature, but the pattern of presentations and comorbidities is similar. A positive family history of mental illness and perinatal complications independently predicted ADHD. Mental health screening amongst families of the affected individuals and improved perinatal care should be considered as health care priorities in Botswana

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S Afr J Psychiatry. 2020;26:1-7.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND BEHAVIOURAL PLANNING DEFICIENCIES IN SOUTH AFRICAN PRIMARY SCHOOL CHILDREN.

Boshomane TT, Pillay BJ, Meyer A.

Background: Attention-deficit/hyperactivity disorder (ADHD) is defined as a cognitive or behavioural developmental disorder. Inattentiveness, overactivity and impulsivity are regarded as the main clinical symptoms of ADHD. These symptoms may occur together or separately resulting in three recognised presentations: predominantly inattentive, predominantly hyperactive-impulsive and combined presentations.

Aim: This study investigated deficiencies in behavioural planning in South African primary school children with and without ADHD. Setting: Tzaneen area in Limpopo province, South Africa.
Methods: A total of 156 children (78 with ADHD and 78 matched controls without ADHD) of both genders, who were medication naïve and aged 6ΓÇô15 years, participated in the study. The performance of the two groups was compared on a test of planning and problem-solving, the Tower of London (ToL) task. The results were analysed as a function of gender, age and ADHD presentation.
Results: Children with ADHD especially ADHD-PI and ADHD-C used significantly more moves and took a longer time to complete the task than the controls ($p < 0.001$). There were no significant differences in the number of moves and time taken by the predominantly hyperactive-impulsive presentations of ADHD when compared to the controls. Gender and age did not influence the performance.
Conclusion: The results showed that children with ADHD showed significantly more deficits mainly the ADHD-PI and ADHD-C presentations, which indicates that inattention is mainly responsible for deficiencies in behaviour planning. The ADHD-HI presentations and the control group were not affected

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Taiwanese Journal of Obstetrics and Gynecology. 2021.

PRIMARY DYSMENORRHEA IN ADOLESCENTS: ASSOCIATION WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND PSYCHOLOGICAL SYMPTOMS.

Kabukcu C, et al.

Objective: No prior study has investigated the relation of primary dysmenorrhea (PD) with attention deficit hyperactivity disorder (ADHD) symptoms in adolescent age groups. This study aimed to investigate the relationship of PD with ADHD and psychological symptoms among adolescents. Another objective was to examine the PD related non-psychogenic factors and sleep quality.
Materials and methods: Two hundred nine adolescent girls who applied to policlinics for various reasons were enrolled. All participants completed self-report questionnaires. Questionnaire for sociodemographic data, menstrual pattern and dysmenorrhea in adolescents, Visual analog scale, Pittsburgh Sleep Quality Index, DSM-5 Level 2 Sleep Disorders Scale, Brief Symptom Inventory, and the Turgay Diagnostic and Statistical Manual of Mental Disorders, 4th edition-Based Child and Adolescent Disruptive Behavior Disorders Screening and Rating Scale were used to measure outcomes.
Results: A hundred and four (49.8%) adolescents reported having pain that affects daily activities during menstruation. These adolescents had worse sleep quality, more inattention and hyperactivity-impulsivity problems, and other psychological symptoms of anxiety, depression, somatization, negative self-perception, and hostility in comparison to others ($P < 0.05$). The menstrual pain severity, measured by VAS, was positively correlated with ADHD symptoms and all other psychological parameters ($P < 0.05$).
Conclusion: PD affecting daily-activities may be related to ADHD symptoms and psychiatric distress. Future studies are needed to support the association between ADHD and PD. Assessing the psychiatric problems of adolescents with dysmenorrhea is important

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Transl Psychiatry. 2021;11.

INTEGRATIVE ANALYSIS OF GENOME-WIDE ASSOCIATION STUDIES IDENTIFIES NOVEL LOCI ASSOCIATED WITH NEUROPSYCHIATRIC DISORDERS.

Yao X, Glessner JT, Li J, et al.

Neuropsychiatric disorders, such as autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), schizophrenia (SCZ), bipolar disorder (BIP), and major depressive disorder (MDD) share common clinical presentations, suggesting etiologic overlap. A substantial proportion of SNP-based heritability for neuropsychiatric disorders is attributable to genetic components, and genome-wide association studies (GWASs) focusing on individual diseases have identified multiple genetic loci shared between these diseases. Here, we aimed at identifying novel genetic loci associated with individual neuropsychiatric diseases and genetic loci shared by neuropsychiatric diseases. We performed multi-trait joint analyses and meta-analysis across five neuropsychiatric disorders based on their summary statistics from the Psychiatric

Genomics Consortium (PGC), and further carried out a replication study of ADHD among 2726 cases and 16299 controls in an independent pediatric cohort. In the multi-trait joint analyses, we found five novel genome-wide significant loci for ADHD, one novel locus for BIP, and ten novel loci for MDD. We further achieved modest replication in our independent pediatric dataset. We conducted fine-mapping and functional annotation through an integrative multi-omics approach and identified causal variants and potential target genes at each novel locus. Gene expression profile and gene-set enrichment analysis further suggested early developmental stage expression pattern and postsynaptic membrane compartment enrichment of candidate genes at the genome-wide significant loci of these neuropsychiatric disorders. Therefore, through a multi-omics approach, we identified novel genetic loci associated with the five neuropsychiatric disorders which may help to better understand the underlying molecular mechanism of neuropsychiatric diseases

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Transl Psychiatry. 2021;11.

EVIDENCE FOR SIMILAR STRUCTURAL BRAIN ANOMALIES IN YOUTH AND ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A MACHINE LEARNING ANALYSIS.

Zhang-James Y, Helminen EC, Liu J, et al.

Attention-deficit/hyperactivity disorder (ADHD) affects 5% of children world-wide. Of these, two-thirds continue to have impairing symptoms of ADHD into adulthood. Although a large literature implicates structural brain differences of the disorder, it is not clear if adults with ADHD have similar neuroanatomical differences as those seen in children with recent reports from the large ENIGMA-ADHD consortium finding structural differences for children but not for adults. This paper uses deep learning neural network classification models to determine if there are neuroanatomical changes in the brains of children with ADHD that are also observed for adult ADHD, and vice versa. We found that structural MRI data can significantly separate ADHD from control participants for both children and adults. Consistent with the prior reports from ENIGMA-ADHD, prediction performance and effect sizes were better for the child than the adult samples. The model trained on adult samples significantly predicted ADHD in the child sample, suggesting that our model learned anatomical features that are common to ADHD in childhood and adulthood. These results support the continuity of ADHDΓÇÖs brain differences from childhood to adulthood. In addition, our work demonstrates a novel use of neural network classification models to test hypotheses about developmental continuity

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GENETIC AND CLINICAL ANALYSES OF PSYCHOSIS SPECTRUM SYMPTOMS IN A LARGE MULTIETHNIC YOUTH COHORT REVEAL SIGNIFICANT LINK WITH ADHD.

Olde Loohuis LM, Mennigen E, Ori APS, et al.

Psychotic symptoms are not only an important feature of severe neuropsychiatric disorders, but are also common in the general population, especially in youth. The genetic etiology of psychosis symptoms in youth remains poorly understood. To characterize genetic risk for psychosis spectrum symptoms (PS), we leverage a community-based multiethnic sample of children and adolescents aged 8ΓÇô22 years, the Philadelphia Neurodevelopmental Cohort (n = 7225, 20% PS). Using an elastic net regression model, we aim to classify PS status using polygenic scores (PGS) based on a range of heritable psychiatric and brain-related traits in a multi-PGS model. We also perform univariate PGS associations and evaluate age-specific effects. The multi-PGS analyses do not improve prediction of PS status over univariate models, but reveal that the attention deficit hyperactivity disorder (ADHD) PGS is robustly and uniquely associated with PS (OR 1.12 (1.05, 1.18) P = 0.0003). This association is driven by subjects of European ancestry (OR = 1.23 (1.14, 1.34), P = 4.15 +ù 10-7) but is not observed in African American subjects (P = 0.65). We find a significant interaction of ADHD PGS with age (P = 0.01), with a stronger association in younger children. The association is independent of phenotypic overlap between ADHD and PS, not indirectly driven by substance use or childhood trauma, and appears to be specific to PS rather than reflecting general psychopathology in youth. In an independent sample, we replicate an increased ADHD PGS in 328 youth at clinical high risk for psychosis, compared to 216 unaffected controls (OR 1.06, CI(1.01, 1.11), P = 0.02). Our findings suggest

that PS in youth may reflect a different genetic etiology than psychotic symptoms in adulthood, one more akin to ADHD, and shed light on how genetic risk can be investigated across early disease trajectories

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Zhongguo Dang Dai Er Ke Za Zhi. 2021 Feb;23:148-52.

INTELLECTUAL CHARACTERISTICS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND DEVELOPMENTAL DYSLEXIA.

Yu ZZ, Yang BR, Zhang SH, et al.

OBJECTIVE: To study the intellectual characteristics of children with attention deficit hyperactivity disorder (ADHD) and developmental dyslexia (DD).

METHODS: A total of 55 children with ADHD and DD (ADHD+DD group), 150 children with ADHD alone (ADHD group), and 22 children with DD alone (DD group) were enrolled as subjects. Wechsler Intelligence Scale for Children-Fourth Edition (WISC-IV) was used to evaluate and compare intellectual characteristics among the three groups.

RESULTS: There were significant differences in the scores of full-scale intelligence quotient (FSIQ), verbal comprehension index, perceptual reasoning index, and working memory index among the three groups ($P < 0.05$):the ADHD+DD group had significantly lower scores of FSIQ, verbal comprehension index, perceptual reasoning index, and working memory index than the ADHD group, as well as a significantly lower FSIQ score than the DD group. A comparison of the 10 core subtests in WISC-IV showed that compared with the ADHD group, the ADHD+DD group had significantly lower scores of similarities, vocabulary, comprehension, recitation, picture concepts, matrix reasoning, and letter-number sequencing ($P < 0.05$). Compared with the DD group, the ADHD+DD group had significantly lower scores of vocabulary, similarities, picture concepts, matrix reasoning, and recitation ($P < 0.05$).

CONCLUSIONS: Compared with the children with ADHD alone, the children with ADHD and DD have more severe impairment of FSIQ, verbal comprehension, perceptual reasoning, and working memory, and therefore, it is suggested to enhance the training on similarities, vocabulary, matrix reasoning, picture concepts, and recitation for children with ADHD and DD in clinical practice

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MDPI

Article

One-Year Follow-Up Diagnostic Stability of Autism Spectrum Disorder Diagnosis in a Clinical Sample of Children and Toddlers

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Abstract: Some studies show that the diagnosis of Autism Spectrum Disorder could be considered reliable and stable in children aged 18 to 24 months. Nevertheless, the diagnostic stability of early ASD diagnosis has not yet been fully demonstrated. This observational study examines the one-year diagnostic stability of autism spectrum disorder diagnosis in a clinical sample of 147 children diagnosed between 18 and 48 months of age. The ADOS-2 scores were used in order to stratify children in three levels of symptom severity: Autism (AD; comparison score 5–7), Autism Spectrum Disorder (ASD; comparison score 3–4), and Sub-Threshold Symptoms; (STS; comparison score 1–2). Results: Overall, the largest part of children and toddlers diagnosed with autism spectrum disorder between 18 and 48 months continued to show autistic symptoms at one-year follow-up evaluation. Nevertheless, a significant percentage of children with higher ADOS severity scores exhibited a reduction of symptom severity and, therefore, moved towards a milder severity class one year later. Conversely, the number of subjects of the STS group meaningfully increased. Therefore, at one-year follow-up a statistically significant ($\chi^2(2) = 181.46$, $p < 0.0001$) percentage of subjects (25.2% of the total) who had received a categorical diagnosis of Autistic Disorder or Autism Spectrum Disorder in baseline no longer met the criteria for a categorical diagnosis. Furthermore, children who no longer met the criteria for autism spectrum disorder continue to show delays in one or more neurodevelopmental areas, possibly related to the emergence of other neurodevelopmental/neuropsychiatric disorders. Overall, the comprehensive results of the study account for a high sensibility but a moderate stability of ASD early diagnosis.

Keywords: autism spectrum disorder; behavioral treatment; diagnostic stability; follow-up

1. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that describes a range of etiologies and clinical presentations [1]. The symptoms of ASD include early-onset difficulties in social communication and unusually restricted, repetitive behaviors and

interests [2] with a great phenotypic heterogeneity that encompasses numerous comorbidities [3,4] and that reflects a complex multifactorial etiology [5]. The prevalence of ASD has dramatically increased in the last decades, reaching estimates of 1 subject in 59 as reported by the Centre for Disease, Control, and Prevention in the US [6]. This phenomenon is partly related to changes in diagnosis reporting practices [7] and partly due to the environmental factors potentially involved in the pathogenesis [8]. The early onset and lifelong social and adaptive impairments resulting from ASD remain a significant cause of morbidity in society [9].

Since ASD has been considered a severe and chronic disability for decades, several studies have demonstrated that early intervention can improve both short- and long-term outcomes of children with ASD [10–16]. Researchers agree that the early identification of ASD and its subsequent treatment can ultimately lead to better outcomes and quality of life [17–22] and to a significant decrease of long-term societal costs [23]. The most rapid gains in development and the greatest reduction in symptom severity appear to occur in the first two years of intervention, most notably in the first year [11,24,25]. Rate of learning in the early stages of intervention predicts later gains [26,27]. Thus, early identification of autism is viewed as vital to prognosis, since numerous studies have consistently shown that children who receive treatment at a younger age have better outcomes [28].

Current diagnosis of ASD can be reliably made as early as two years of age [29] based on a combination of the standardized diagnostic assessment data for infants and toddlers (e.g., Autism Diagnostic Observation Schedule-Toddler—ADOS-T; [30]) and expert clinical opinion [31]. However, some studies showed that the diagnosis could be considered reliable and stable in children aged 18 to 24 months [32–36]. The months surrounding the first birthday are considered a remarkable time for a toddler's development [37]. At this age, toddlers learn to walk, speak their first words, and engage in a range of joint social attention behaviors, such as pointing and showing objects to others to share social attentional focus [38].

Although the awareness of early signs of autism may be increasing along with the prevalence of ASD and many children with ASD show developmental concerns in their educational and/or health records prior to age three, for example most balance-influencing parameters mature with age but not in ASD children [39], currently as few as 42% of children with autism at age eight have received their first comprehensive evaluation before their third birthdays, with median age of diagnosis at 40–53 months [6,40,41].

This diagnostic delay could be due, at least in part, to a series of unsolved questions regarding the early-age diagnostic stability, the age of clinical symptom onset and the overlap of early-age clinical symptoms between ASD and other disorders (e.g., language disorders or global developmental delay).

A meta-analysis of studies based on DSM-IV criteria had reported a significant stability (overall stability rate of 86.3%) of ASD diagnosis over time in children diagnosed before 36 months [42]. In addition, a systematic review of 10 studies conclude that diagnostic stability of ASD diagnosis is higher in toddlers diagnosed before age three [43]. New studies conducted after the DSM-5 modification of ASD inclusion criteria largely confirmed the stability of the early ASD diagnosis. For example, a recent study [44] aimed to prospectively follow 96 children, initially assessed for suspected ASD at an average age of 2.9 years and found that 76 met full criteria for ASD after two years of follow-up. Interestingly, the children who did not meet the criteria for ASD at T2 had symptoms of or met the criteria for other neurodevelopmental/neuropsychiatric disorders in combination with marked autistic traits.

However, clinicians and researchers have expressed concerns about the impact of the new DSM-5 criteria on the diagnosis of ASD in a population whose symptomatology may be emerging because the strict nature of the criteria is unsuitable for an early diagnosis model [45]. Moreover, enquiries about the permanence of ASD diagnosis have been emphasized by empirical reports of children who have lost the ASD diagnosis in middle or later childhood [46,47]. Concerns about the possibility to produce false positives are

largely shared in the scientific community, and there are initial doubts about the stability of diagnosis for children identified before 36 months. Furthermore, both clinicians and researchers raised important questions about the youngest age at which a reliable diagnosis could be made, given the costs of early autism treatment [48].

Overall, the diagnostic stability of ASD diagnosis has not yet been fully demonstrated, even though much previous research supports the stability of ASD diagnosis even in very young children [33–35]. The present observational study aims to explore the one-year diagnostic stability of diagnosis in a clinical sample of toddlers and children diagnosed with ASD between 18 and 48 months of age. The purpose of the study is to evaluate if children would differ in diagnostic stability on the basis of the interaction between two variables: age of diagnosis and symptom severity.

2. Materials and Methods

2.1. Research Design and Procedure

We implemented a longitudinal prospective observational cohort study: first diagnostic evaluation (T0) and a follow-up evaluation (T1) at 12 months after the diagnosis. We recruited patients at their first neuropsychiatric consultation. This study was overseen by the Institutional Review Board of Intercompany Ethics Committee of the province of Messina, which approved the data collection and analysis (protocol number 56/13, 15 October 2013). Informed consent was obtained from both parents to data collection before the study enrollment, the patient names were removed from our spreadsheets to protect their identities. A multidisciplinary team (child neuropsychiatrists, psychologists, and speech/language therapists) with experience in ASD diagnosis conducted an extensive neuropsychiatric diagnostic assessment based on clinical observation and standardized measures. Parent clinical interviews about child's developmental delays and/or problems (including play, social interaction, communication, and atypical behaviors) were carried out. A trained clinical psychologist conducted the evaluation of ASD severity symptoms and child's developmental functioning with standardized measures (see below, Measures section). All the patients underwent the same assessment performed by the same professional team who collected standardized measures on child's functioning and ASD severity at T0 and T1.

A complete diagnosis was assigned based on the clinical judgment of experienced clinicians in according to DSM-5 diagnostic criteria (APA 2013), throughout this longitudinal project, in order to maintain the same reliability. An extensive battery of clinical laboratory tests (EEG, auditory evoked potentials, genetic endocrine-metabolic, and immunological exams) was performed in order to exclude the association with known medical or genetic conditions or environmental factors, such as seizures and epilepsy, significant hearing and visual sensory deficits, traumatic brain injury or other significant genetic disorders (e.g., fragile X syndrome). At the conclusion of each evaluation, caregivers were provided with feedback regarding the assessment, which included the diagnosis and recommendations for intervention.

2.2. Participants

The inclusion criteria were patients aged between 18 and 48 months at their first neuropsychiatric consultation, availability of both Autism Diagnostic Observation Schedule (ADOS) baseline and follow-up scores. Children who presented other significant medical conditions (e.g., epilepsy, significant hearing and visual sensory deficits, traumatic brain injury, or other significant genetic disorders) were excluded.

We recruited 215 outpatients at their first neuropsychiatric consultation, aged between 18 and 48 months (M = 27.92, SD = 6.17), consecutively followed for ASD symptoms at the ambulatory of Child and Adolescent Psychiatry Unit of AOU Policlinico "G. Martino" of Messina, between June 2016 and January 2018. For 23 children (10.6%) a neurological, genetic, or metabolic disorder was found. Among the remaining 192 children, 25 (13%)

dropped out for various reasons. Moreover, we excluded 20 children for whom the database was not completed.

Thus, the final research sample was of 147 children (117 males and 30 females). For a large percentage of children (38.1%), parents themselves directly requested a neuropsychiatric evaluation for concerns about their children's social/communicative deficits, language delay and atypical/repetitive behaviors. A similar number of children (35.4%) was recruited by our unit after a primary care evaluation by the pediatrician and after a positive screening at the Modified Checklist for Autism in Toddlers (M-CHAT) [49] and another 23.1% was recruited after a specialist visit by an infant neuropsychiatrist and/or a neonatal neurologist. In 3.4% of the sample, parents were encouraged for accurate assessment by nursery educators/teachers who observed children's impairments (i.e., social/communicative interactions, repetitive play, or restricted interests) in nursery/kindergarten settings. Children were Caucasians except for one child of African origins and all completed ADOS-2 assessment (see below) both at the first clinical diagnosis (T0) and at a follow-up assessment one year later (T1), (360 ±3 average days for participant).

To examine the stability of the clinical diagnosis related to the age of children, all participants were age-matched in months and divided into three classes: 18–24 months, 25–36 months, and 37–48 months

At baseline assessment (T0), all participants were grouped into three severity classes based on the ADOS-2 comparison score inferred from the appropriate comparison table provided in the ADOS-2 manual:

- Group 1 (n = 8) Sub-Threshold Symptoms (STS): children with isolated symptoms or very mild symptoms, not fully consistent with the criteria for the disorder (ADOS severity score between 1 and 2).
- Group 2 (n = 68) Autism Spectrum Disorder (ASD): children that still met the DSM-5 criteria for ASD but with mild symptom severity (ADOS severity score between 3 and 4).
- Group 3 (n = 71) Autistic Disorder (AD): children with the highest symptom severity that fully met the DSM-5 criteria for ASD (ADOS severity score between 5 and 7).

All children started the treatment within 3 weeks from the diagnosis. They received a usual intervention program specifically aimed to target ASD symptoms throughout the period between T0 and T1. All of them received the treatment as usual (TAU), available from local child neuropsychiatric services of their living area, for a mean of 6 (±1) h per week. TAU can be placed within a continuum ranging from highly structured behavioral approaches to approaches that follow the interests of the child in a naturalistic setting, mainly based on staff expertise rather than manualized treatment protocols. It also includes speech therapies for children and monthly parent coaching sessions. Overall, the type and the frequency of treatment were highly homogenous among the enrolled children.

2.3. Measures

Autism Severity

The Autism Diagnostic Observation Schedule—Second Edition (ADOS-2; [50]) is a semi-structured observation tool measuring ASD symptoms in children. A standard set of interactional examiner–child (or caregiver) activities was administered to assess social communication, play, repetitive, and restricted behaviors. It provides a measure of the severity of ASD symptoms, supporting clinical observation and decision about ASD diagnosis. Furthermore, it measures separately two main aspects: social affect (SA), restricted, repetitive behaviors (RRBs). It uses an algorithm composed by numeric score ranges from 0 to 2, with higher score indicating more severe deficits; the total score of SA and RRB can be transformed into a standardized severity score to compare ASD severity directly across modules.

In this study, the ADOS-2 scores were used in order to stratify children in three levels of symptom severity: Autism (AD; comparison score 5–7), Autism Spectrum Disorder (ASD; comparison score 3–4), and Risk for Autism (Sub-Threshold Symptoms; comparison

score 1–2). The ADOS-2 consists of different modules with an activity program designed for children with different levels of language development. Noteworthy, ADOS was created for diagnostic purposes, and thus it was not specifically designed to facilitate longitudinal and cross-sectional data comparisons. In our study, we have used the ADOS as a diagnostic instrument, even though the total scores provided a common stand-in for a measure of autism severity.

In the present study Toddler Module (12–30 months) and Module 1 (31 months or older) were used for diagnosis at T0, whereas Module 1 and 2 (for verbally fluent children under three years) were administered at follow up (T1) according to the language level reached by the child. All modules were administered by trained examiners meeting the standard requirements for research reliability.

2.4. Statistical Approach

As first step, to test diagnostic stability we compared participant proportions within each severity class at T0 vs. T1 by chi-square test, using T0 proportions as expected values at T1.

Secondly, we distinguished four different patterns of stability: a stable positive diagnosis consisting of ASD or AD (true positives [TP]), a stable negative diagnosis (true negatives [TN]), and two unstable diagnostic groups including patients who met the ASD or AD criteria only at the first time point (false positives [FP]), and conversely patients who failed to meet the ASD or AD criteria at the first time point but received a diagnosis at the follow-up evaluation (false negatives [FN]). The McNemar's test served to test these patterns of stability. Then, we computed sensitivity (as $TP/(TP + FN) \times 100$), specificity (as $TN/(TN + FP) \times 100$), positive predictive value (PPV as $TP/(TP + FP) \times 100$), and negative predictive value (NPV as $TN/(TN + FN) \times 100$). Differences in sensitivity and specificity between age groups were tested using the equiprobability chi-square test.

Moreover, we compared T0 and T1 ADOS-2 scores for each age class with the non-parametric Wilcoxon Signed Rank Test, because data did not approximate the characteristics of the normal distribution.

Statistical analyses were performed using the IBM Statistical Package for Social Science (SPSS), version 19.0.

3. Results

3.1. Severity Class Distribution at Baseline vs. Follow-Up (T0 vs. T1)

Table 1a,b shows the participants' distribution within the three severity groups as function of the first neuropsychiatric consultation age at baseline (48.3% AD, 46.3% ASD; 5.4% STS) and at 1-year follow-up (32.7% AD, 36.7% ASD; 30.6% STS). The main result is the reduction of the percentage of subjects in the highest severity class from 48.3% to 32.7% (Figure 1). It does mean that 32.4% of the subjects with AD (23/71) moved towards a mild severity class one year later. In addition, the group with ASD had a slight percentage reduction. Conversely, the number of subjects of the STS group (children with isolated symptoms or very mild symptoms, not fully consistent with the criteria for the disorder) meaningfully (566.7%) increased from 5.4% to 30.6% of the total. Therefore, at one-year follow-up a statistically significant ($\chi^2(2) = 181.46$, $p < 0.0001$) percentage of subjects (25.2% of the total) who had received a categorical diagnosis of Autistic Disorder or Autism Spectrum Disorder in baseline no longer met the criteria for a categorical diagnosis.

Table 1. Baseline (T_0) and follow-up (T_1) diagnosis categories by age classes.

a. (T_0)			**Age Classes**			**Total**
			18–24 Months	**25–36 Months**	**37–48 Months**	
Baseline Diagnosis	**STS**	Counting	2	5	1	8
		T_0-diagnosis %	25.0%	62.5%	12.5%	100.0%
		Age classes %	4.0%	5.8%	9.1%	5.4%
		Total %	1.4%	3.4%	0.7%	5.4%
	ASD	Counting	33	31	4	68
		T_0-diagnosis %	48.5%	45.6%	5.9%	100.0%
		Age classes %	66.0%	36.0%	36.4%	46.3%
		Total %	22.4%	21.1%	2.7%	46.3%
	AD	Counting	15	50	6	71
		T_0-diagnosis %	21.1%	70.4%	8.5%	100.0%
		Age classes %	30.0%	58.1%	54.5%	48.3%
		Total %	10.2%	34.0%	4.1%	48.3%
b. (T_1)						
Follow up Diagnosis	**STS**	Counting	19	22	4	45
		T_1-diagnosis %	42.2%	48.9%	8.9%	100.0%
		Age classes %	38.0%	25.6%	36.4%	30.6%
		Total %	12.9%	15.0%	2.7%	30.6%
	ASD	Counting	17	34	3	54
		T_1-diagnosis %	31.5%	63.0%	5.6%	100.0%
		Age classes %	34.0%	39.5%	27.3%	36.7%
		Total %	11.6%	23.1%	2.0%	36.7%
	AD	Counting	14	30	4	48
		T_1-diagnosis %	29.2%	62.5%	8.3%	100.0%
		Age classes %	28.0%	34.9%	36.4%	32.7%
		Total %	9.5%	20.4%	2.7%	32.7%
Total		Counting	50	86	11	147
		Age classes %	100.0%	100.0%	100.0%	100.0%
		Total %	34.0%	58.5%	7.5%	100.0%

Note: T_0 = Time 0 (Baseline data collection), T_1 = Time 1 (1-year follow-up data collection), AD = Autistic Disorder, ASD = Autism Spectrum Disorder, STS = Sub-Threshold Symptoms.

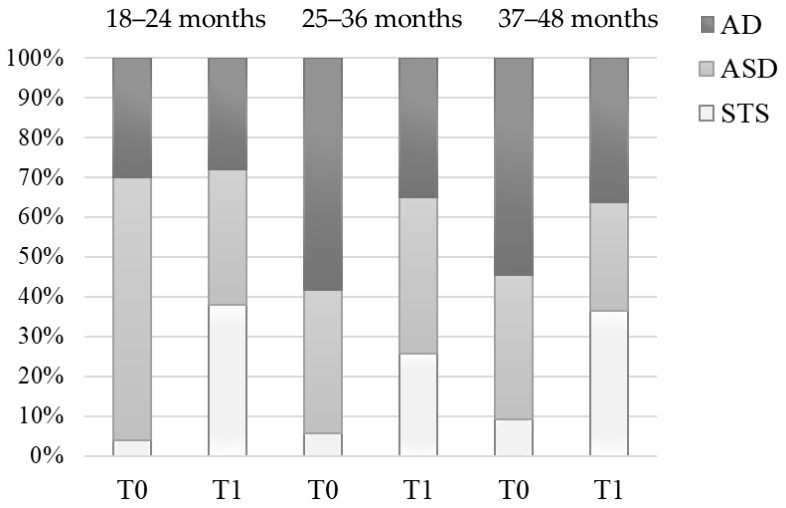

Figure 1. Participants' distribution within the three severity groups as function of the age at baseline and follow-up visits.

The participants' distribution within the three severity groups significantly changed from baseline to follow-up visit for each first-consultation-age group: 18–24 months,

$\chi^2(2) = 152.32$, $p < 0.0001$; 25–36 months, $\chi^2(2) = 66.09$, $p < 0.0001$; 37–48 months, $\chi^2(2) = 9.92$, $p < 0.007$. In particular, in the first age class (18–24 months) we observed a significant enlargement of the STS group from 4.0% to 38.0% ($\chi^2(1) = 17.25$, $p < 0.0001$) and, conversely, a marked reduction from 66.0% to 34.0% of ASD group ($\chi^2(1) = 10.14$, $p = 0.0015$); in contrast to these two clusters, AD cluster undergoes minimal variations ($\chi^2(1) = 0.05$, $p = 0.83$).

3.2. Stability and Diagnostic Parameters (T0 vs. T1)

Table 2 shows the diagnostic trends from T0 to T1. Grouping AD and ASD participants into an "autistic class" (A) regardless of the age at the first consultation, we considered the four different patterns of stability: true positives (TP), true negatives (TN), false positives (FP), and, conversely, false negatives (FN) (see Table 3).

Table 2. Trend over time of the three diagnostic classes.

	T_0	T_1		
		AD	**ASD**	**STS**
AD	71	32		
			28	
				11
ASD	68	15		
			23	
				30
STS	8	1		
			3	
				4
Total	147	48	54	45

Note: T_0 = Time 0 (Baseline data collection), T_1 = Time 1 (1-year follow-up data collection), AD = Autistic Disorder, ASD = Autism Spectrum Disorder, STS = Sub-Threshold Symptoms.

Table 3. Outcome classification.

T_0	T_1	Total	Classification
A	A	98 (66.7%)	True positives
A	STS	41(27.9%)	False positives
STS	A	4 (2.7%)	False negatives
STS	STS	4 (2.7%)	True negatives
Total		147	

Note: T_0 = Time 0 (Baseline data collection), T_1 = Time 1 (1-year follow-up data collection), A = Autistic Disorder plus Autism Spectrum Disorder, STS = Sub-Threshold Symptoms.

We estimated the same parameters along the three age groups and, from them, Sensitivity, Specificity, Positive Predicted Value (PPV), and Negative Predicted Value (NPV). These diagnostic parameters are summarized in Table 4 for participants taken as a whole, and in Table 5 for the age groups. The high sensitivity values contrast with the clearly lower specificity values; this reflects the small number of true negatives detected in the whole sample.

Table 4. Diagnostic reliability on the whole sample.

Diagnostic Parameters	
Sensitivity	96.08%
Specificity	8.89%
Positive Predictive Value	70.50%
Negative Predictive Value	50%

Note: Sensitivity is calculated as TP/(TP + FN) × 100; Specificity is calculated as TN/(TN + FP) × 100; PPV is calculated as TP/(TP + FP) × 100; NPV is calculated as TN/(TN + FN) × 100.

In Table 5 the 36–48 months stability rates were not reported because of the small sample size. Although sensitivity was almost the same between the two groups, there was a small increase in specificity from 18 months (5.26%) to 25 months (9.09%) and also in positive predictive values from 18 months (62.50%) to 25 months (75.30%). These proportion differences were not significant (all $p > 0.05$).

Table 5. Stability and diagnostic classification parameters at different ages.

	True Positive (n = 98)	False Positive (n = 41)	False Negative (n = 4)	True Negative (n = 4)	Sensitivity	Specificity	Positive Predicted Value	Negative Predicted Value
18–24 months (n = 50)	30	18	1	1	96.77%	5.26%	62.50%	50%
25–35 months (n = 86)	61	20	3	2	95.31%	9.09%	75.30%	40%
36–48 months (n = 11)	7	3	0	1	–	–	–	–

Note: TP = True Positive, FP = False Positive, FN = False Negative, TN = True Negative; sensitivity is calculated as TP/(TP + FN) × 100; specificity is calculated as TN/(TN + FP) × 100; Positive Predicted Value (PPV) is calculated as TP/(TP + FP) × 100; Negative Predicted Value (NPV) is calculated as TN/(TN + FN) × 100.

3.3. ADOS-2 Subscales at Baseline vs. Follow-Up (T0 vs. T1)

We compared follow-up outcomes after one year of follow up. From T0 to T1 all ADOS-2 total and sub-scale scores (Social Affect (SA) and Restricted and Repetitive Behavior (RRB)) decreased. Reductions were significant for SA scores of the two youngest age classes and for RRB scores in the oldest age class (see Tables 6 and 7, and Figure 2). A significant reduction of symptoms was found in SA scores for the two youngest age classes and of RRB score symptoms in the oldest age class.

Table 6. T_0 and T_1 descriptive statistics of ADOS-2 sub-scales and total score as a function of the three age classes (18–24, 25–36, and 37–48 months at the first consultation).

ADOS-2 Scales	T_0		T_1	
	18–24 Months (n = 50)			
	M	**SD**	**M**	**SD**
Social Affect	13.22	3.65	8.68	5.20
Restricted and Repetitive Behavior	2.76	1.70	2.42	1.80
Total Score	16.10	4.51	11.14	6.16
	25–36 Months (n = 86)			
Social Affect	12.52	4.57	9.57	5.37
Restricted and Repetitive Behavior	3.02	1.75	2.87	2.03
Total Score	15.53	5.50	12.33	6.37
	37–48 Months (n = 11)			
Social Affect	10.00	4.49	7.91	4.11
Restricted and Repetitive Behavior	3.09	1.58	2.00	1.41
Total Score	13.45	5.47	9.91	5.32

Note: ADOS-2 = Autism Diagnostic Observation Schedule—Second Edition, T_0 = Time 0 (Baseline data collection), T_1 = Time 1 (1-year follow-up data collection).

Table 7. Wilcoxon Signed Ranks Test applied to ADOS-2 SA and RRB sub-scores at T_0 and T_1 for each age class (18–24, 25–36, and 37–48 months at the first consultation).

18–24 Months	ADOS-2–SA T_1–T_0	ADOS-2–RRB T_1–T_0
Z	−4.384 [a]	−0.783 [a]
p (2-tailed)	< 0.001	0.646
25–36 months		
Z	−5.624 [a]	−0.631 [a]
p (2-tailed)	<0.001	0.528
37–48 months		
Z	−1.637 [a]	−2.154 [a]
p (2-tailed)	0.102	0.031

Note: ADOS-2 = Autism Diagnostic Observation Schedule—Second Edition, SA = Social Affect, RRB = Restricted and Repetitive Behavior, T_0 = Time 0 (Baseline data collection), T_1 = Time 1 (1-year follow-up data collection). [a] Based on positive ranks.

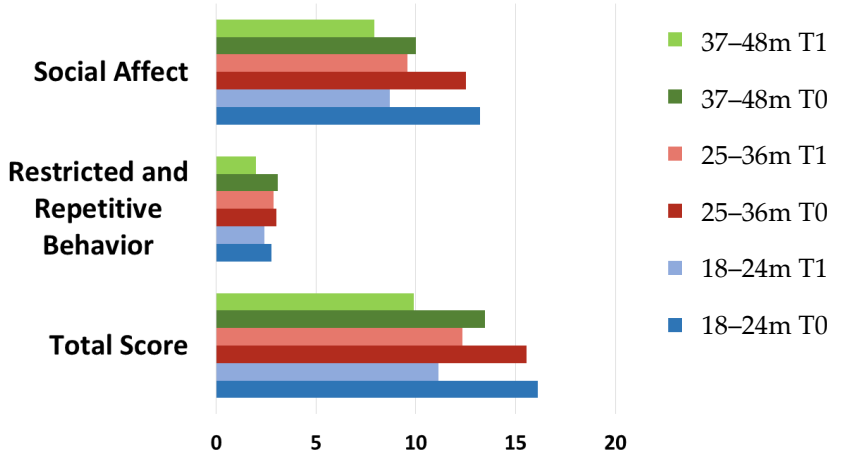

Figure 2. Age class and sub-scales (Social Affect, Restricted and Repetitive Behaviors, and Total) ADOS-2 scores at baseline and at 1-years follow-up. ADOS-2 = Autism Diagnostic Observation Scheme 0. = 1-year follow-up data collection.

4. Discussion

The purpose of the present study was to examine the diagnostic stability of early autism diagnosis over twelve months. Overall, the largest part of children and toddlers diagnosed with autism spectrum disorder between 18 and 48 months continued to show autistic symptoms at one-year follow-up evaluation. Nevertheless, the participants' distribution within the three severity groups significantly changed. In particular, the percentage of subjects in the highest severity class (AD) had a significant reduction. This means that a significant percentage of children with the ADOS highest severity score exhibited a reduction of symptom severity and, therefore, moved towards a mild severity class one year later. At the same time, the children with moderate symptom severity (ASD) had a slight percentage reduction. Conversely, the number of subjects of the STS group (children with isolated symptoms or very mild symptoms, not fully consistent with the criteria for the disorder) meaningfully increased from 5.4% to 30.6% of the total. Therefore, at one-year follow-up a statistically significant percentage of subjects who had received a categorical diagnosis of Autistic Disorder or Autism Spectrum Disorder in baseline no longer met the criteria for a categorical diagnosis.

This result is partially consistent with the previous literature evidence showing that early diagnosis of ASD is relatively stable and reliable, even when formulated between 18 and 36 months of life [35–38,40]. A more recent study [51] reports an overall ASD

diagnostic stability of 0.84 (95% CI, 0.80–0.87) after 12 months, in a very large cohort of toddlers with a median age at the first evaluation of 17.6 months. The study also reports that the diagnostic stability of ASD within the youngest age band (12–13 months) was lowest at 0.50 (95% CI, 0.32–0.69) but increased to 0.79 by 14 months and 0.83 by 16 months, suggesting that an ASD diagnosis becomes stable starting at 14 months of age.

Inconsistent results across the studies could be related to different diagnostic tools and/or to the parameters used to evaluate the stability. However, the majority of studies underline that an accurate diagnosis in toddlers allows clinicians to start early treatments as a fundamental resource for achieving a better outcome in autism spectrum disorder. A very recent review [52] addressing the outcomes of young children with ASD who started early interventions at a range of ages, a strong evidence that "earlier is better" with regard to interventions for young children with ASD.

4.1. Diagnostic Stability in Function of Different Age Classes Compared to Different Severity Levels

Although previous research demonstrated stability of ASD diagnosis even in very young children, very few studies assessed the ASD diagnostic stability in relation to different age classes compared to different severity levels. Our longitudinal study provides a more detailed description of the outcome analyzing the differences between the three age classes and the three severity levels of symptoms.

In the youngest age class (18–24 months), a significant percentage of children lost the diagnosis of ASD, as it is possible to infer by the enlargement of the STS group and the reduction of ASD group. Conversely, the AD group maintained exactly the same amplitude. This could support the hypothesis that those who showed very severe autistic symptoms at a very young age maintained at the follow-up evaluation the same severity level of symptoms and, therefore, the diagnosis of Autism. The high degree of symptom stability in this severity class provides further support to the legitimacy of assigning the autism spectrum diagnosis to children aged between 18 and 24 months when they show a severe symptom level. Conversely, the percentage of children between 18 and 24 months showing milder symptoms (ASD diagnosis) has dropped by half at the follow-up evaluation. Thus, the validity of early autism diagnoses for the children with a lower symptom severity level (defined here as ADOS severity score between 3 and 4) seems to be weaker compared to those formulated for children showing clear autistic features with higher symptom severity ab initio. We argue that some behaviors could be abnormal because of the occurrence of different neurodevelopment disorders (e.g., ADHD, language disorder, ID) which are not easily distinguishable from autism in very young children. For instance, some authors suggest [53] that restricted and repetitive behaviors (RRBs) are common in children with Intellectual Disability (ID), leading to potential invalid autism diagnoses. Other authors [54] endorse the intellectual disability as a confounding factor that could potentially affect the validity of ASD diagnosis. The children of our sample losing the diagnosis of ASD at follow-up evaluation could have kept neurodevelopmental delay symptoms, as revealed by the enlargement of STS group (from 4.1% to 13.6%). These symptoms could be revealed by ADOS even if unreliable with a specific autistic phenotype. This is consistent with some authors' description of autistic behaviors that may suggest a disease different from "classical" autism [55] and with most of the neurodevelopmental disorders sharing common features in cognitive, adaptive, social symptoms and stereotyped activities. According to some researchers' hypothesis [56] the ASD diagnosis may be a "preliminary diagnosis" that will be changed as the child matures and more testing is done. A 2012 study, led by a government epidemiologist [57], found that 4% of children lost their diagnosis by age 8.2 and that almost all of them had at least another diagnosis, such as Attention-Deficit Hyperactivity Disorder (ADHD), developmental delay, or language delay. This kind of outcome could be more likely when the early ASD diagnosis is based on a milder presentation of symptoms. Therefore, below 24 months of age caution should be paid in formulating the ASD diagnosis in children presenting mild symptoms.

Another noteworthy point arises from the comparison between the outcomes of the children diagnosed between 18 and 24 months and the outcomes of children diagnosed later. In the second age class (25–36 months), both the STS and ASD groups increased, whereas the AD group significantly decreased. Actually, around one-third of subjects diagnosed between 25 and 48 months that met the full ASD criteria moved to a milder or subthreshold phenotype one year later. Therefore, the diagnostic stability of autism diagnosis seems to diminish with age increasing. This result may appear unexpected. However, many cultural campaigns focused on autism, and directed to pediatricians and general population, consistently reduced the average age at referral bringing it below 24 months. It appears to be plausible that the children of this group were probably later followed and diagnosed by a specialist. In particular, higher IQ scores and better verbal and communicative abilities would have led both parents and pediatricians to have fewer early concerns, even in presence of clear autistic symptoms. This hypothesis could explain the better outcomes and would be consistent with the large number of researches outlining that starting to speak at a younger age and having higher IQ facilitate the recovery [46,58,59]. At the same time, it must be stated, that ASD symptoms, usually clearly evident at two years of age, in one-third of children appear around 24 months, with a regression of the first acquired skills [18]. Children with this onset patterns do not appear to present different behavioral phenotypes from children with earlier onset of symptoms [60].

Regarding the oldest age class (37–48 months) of our sample since both the STS and ASD groups increased, whereas the AD group significantly decreased. Noteworthy, the sample of this age class is very small due to the low probability that the first ASD diagnosis is done at this age in our region. Therefore, the results of our study are not fully consistent with the previous reports supporting that children diagnosed with ASD at 30 months or younger were more likely to have a change in classification from ASD to non-ASD than children diagnosed with an ASD at 31 months or older [57]. However, the paucity of the oldest age class sample suggests considering this last evidence with caution.

4.2. Diagnostic Reliability in Relation to Different Age Classes

Our study also evaluated some parameters concerning the diagnostic reliability between different age classes. Consistently with previous literature evidence [48], our results show a good sensitivity of the early diagnosis. We found four different patterns in the three diagnostic classes (see Table 2): the first two patterns describe subjects with very clear diagnostic features (true positive or true negative). Conversely, the two other patterns describe children with unstable diagnosis: those who meet the ASD or AD criteria only at the first time point (false positives) or only at follow-up evaluation (false negatives) (see Table 3). Starting from these results and analyzing the sensitivity (the percentage of those diagnosed at the second time point who were identified at the earlier visit) and the specificity (the percentage of those without a diagnosis at the second time point who were correctly identified as STS at the first visit), we calculated a Positive Predicted Value. This value can be considered a more reliable parameter of the stability of the diagnosis since it describes the percentage of those identified with AD and ASD at the earlier visit who maintain the diagnosis at the second time point. Secularly, the Negative Predicted Value represents the percentage of those identified as STS at the first visit and failed to meet ASD criteria at the second time point (Table 4). Interestingly, the number of true negatives in the whole sample was very small. This could explain the high sensitivity and the relatively low specificity that we found. Finally, we found that the diagnostic sensitivity in relation to the age groups was very similar between the two youngest age classes, with only a slight advantage (not statistically significant) for the specificity and the positive predictive value for the children aged between 18 and 24 months. This result refers to age-dependent differences in the diagnostic stability of ASD/AD diagnosis with a favorite window for the identification between 18 and 24 months.

4.3. Follow-Up Outcomes Assessed by the ADOS-2 Subscale Scores at Baseline and Follow-Up

A second level of information provided by our study regards the follow-up outcomes assessed by the ADOS-2 subscale scores (Social Affect (SA) and Restricted and Repetitive Behaviors (RRB]) at baseline and follow-up. The focus on the symptom domains rather than on the overall symptom severity allows us to describe the diagnostic stability from a different perspective. In the two youngest age classes (18–24 and 25–36 months), the reduction of ASD total score was due exclusively to a reduction of SA scores. Conversely, Restricted and Repetitive Behaviors persisted at the same level. The opposite condition has been observed n the oldest age class (37–48 months), where the social affect domain does not further improve and only the RRB symptoms show a slight decrease.

Our results seem to be consistent with the conclusions of a recent review [61] aimed to examine the temporal stability of autism spectrum disorder and the longitudinal trajectories of autism core symptom severity. In fact, most of the included studies showed minor but statistically significant changes in ADOS total raw scores but no improvements in restricted and repetitive behaviors over time. At the same time minor improvements in social affect over time were described. These results could be related to the emphasis that the current early start treatment programs for ASD children have on the development of social competences, currently seen as the pivotal developmental domain. Most of the recent developed toddler interventions are delivered in naturalistic and interactive social contexts, and there is evidence that naturalistic interventions promote the social development in that they typically involve interactive exchanges between the child and an adult or typically developing peers [62,63].

By comparing the different diagnostic subgroups, we also identified the clinical characteristics that could help clinicians to outline the early diagnosis outcome. In particular, the earlier predicted factors for positive outcomes seem to be the symptom severity, fewer symptoms in RBBs domains, and stronger early social and communications skills.

5. Limitations and Future Directions

There are several limitations to the current study. First, the relatively small sample size of the enrolled subjects (mainly the 37–48 months group) limited the statistical power. Furthermore, the few amount of true negatives allowed a limited qualitative analysis. A second important limitation is that we cannot exclude some potential influences due to the qualitive differences of treatments received by children between T0 and T1. Moreover, our follow-up maximum age (48 months) limits our ability to assess children's later outcomes. Future more prolonged studies, analyzing a larger group of children, with more homogeneous and manualized treatments, should give more information about the factors that could improve the diagnostic stability of ASD children.

6. Conclusions

The comprehensive results of the study account for a high sensibility but a moderate stability of ASD early diagnosis. One out of four children lost the diagnosis of ASD at one-year follow-up. Furthermore, children who no longer met the criteria for autism spectrum disorder continued to show delays in one or more neurodevelopmental areas, possibly related to the emergence of other neurodevelopmental/neuropsychiatric disorders.

Even if the stability of ASD diagnosis is moderately strong, clinicians ought to consider the early diagnosis and the access to an early treatment the strongest factor influencing the outcome.

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Postural Control in Childhood: Investigating the Neurodevelopmental Gradient Hypothesis

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Abstract: Neurodevelopmental disorders (NDDs) have been suggested to lie on a gradient continuum, all resulting from common brain disturbances, but with different degrees of impairment severity. This case-control study aimed to assess postural stability against such hypothesis in 104 children/adolescents aged 5–17, of whom 81 had NDDs and 23 were healthy controls. Compared to healthy controls, Autism Spectrum Disorder (ASD) resulted in the most severely impaired neurodevelopmental condition, followed by Attention Deficit Hyperactive Disorder (ADHD) and Tourette Syndrome (TS). In particular, while ASD children/adolescents performed worse than healthy controls in a number of sensory conditions across all parameters, ADHD children/adolescents performed worse than healthy controls only in the sway area for the most complex sensory conditions, when their vision and somatosensory functions were both compromised, and performance in Tourette Syndrome (TS) was roughly indistinguishable from that of healthy controls. Finally, differences were also observed between clinical groups, with ASD children/adolescents, and to a much lesser extent ADHD children/adolescents, performing worse than TS children/adolescents, especially when sensory systems were not operationally accurate. Evidence from this study indicates that poor postural control may be a useful biomarker for risk assessment during neurodevelopment, in line with predictions from the gradient hypothesis.

Keywords: autism spectrum disorder; attention deficit hyperactivity disorder; Tourette disorder; transdiagnostic approach; mental health prevention

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1. Introduction

Since the 1960s, a rising prevalence of childhood disabilities has been documented, largely because of an increase in the prevalence of mental and behavioral conditions such as Autism Spectrum Disorder (ASD), Attention Deficit Hyperactive Disorder (ADHD), and Tourette Syndrome (TS), whereas the prevalence of any other developmental delay such as cerebral palsy, hearing loss, and seizures, declined over time [1]. ASD, ADHD, and TS share common symptomatic features [2], such as impairments in the fields of general development [3], communication and language [3,4], social inter-relatedness [3,5–7], motor coordination [8], attention [9], activity [10,11], behavior, mood [7,12,13], and sleep [7,14–16]. However, it is also important to recognize that although symptoms may overlap, this does

not always imply the same presentation of symptoms or the same response to treatment efforts. Thus, from a phenotypic perspective, similar behavioral manifestations may exist across conditions and similar behaviors may manifest differently within a condition [17]. In light of such extensive difficulties, these conditions can affect individuals' personal (e.g., impaired executive functions), social, and school skills (e.g., impaired learning), with implications for future working abilities [2]. This is of paramount importance, considering that interpersonal skills may per se be less proficient among individuals with neurodevelopmental conditions, making it difficult to infer directionality of effects. It is plausible that individuals with neurodevelopmental conditions may be differentially susceptible to a variety of environmental factors with negative effects on their preexisting behavioral difficulties [18].

Despite evidence of comorbidity [5,10,19], ASD, ADHD, and TS were previously considered different from each other [20]. Only recently have they been grouped into the single diagnostic category of neurodevelopmental disorders (NDDs) [3] because of substantial overlapping not only at the clinical [5,6,21,22] but also at the neurobiological level [23–27]. This has led to the hypothesis that NDDs, including those that typically emerge in late adolescence and early adulthood such as affective and non-affective psychoses, should be seen as lying on an etiological and neurodevelopmental gradient continuum, all resulting from the commonality of disrupted or deviant brain development [28], but with different degrees of neurodevelopmental impairment severity [20]. According to the neurodevelopmental gradient hypothesis, the earlier the age of onset and the higher the severity and persistence of the psychopathological, cognitive, genetic, and sensorimotor impairment, the greater the overall neurodevelopmental impairment [20]. In line with this, when such impairments are compared across disorders, the rates are in decreasing severity from ASD to late-onset NDD [20].

Motor abnormalities are core features of ASD (e.g., stereotypic movements), ADHD (e.g., hyperactivity), and TS (e.g., tics), and have been suggested to represent a transdiagnostic domain putatively sharing neurobiological mechanisms of neurodevelopmental origin [29]. Motor difficulties, especially in the coordination domain, have also been reported in typically developing children, potentially reflecting age-dependent reversible developmental traits [30]. However, their persistence in late childhood is suggestive of a disrupted sensory integration, thus affecting the sequencing of complex motor acts [31,32], and seem to be related with poor cognitive performance [8] in predicting the manifestation of an NDD [8,29]. Further, a developmental coordination disorder, the most severe phenotype of coordination impairment, once defined as "dyspraxia" or "motor clumsiness", is frequently diagnosed in children with an NDD [33–35].

Abnormal sensory responsivity has been implicated in atypical neurodevelopment, independently of concomitant motor difficulties [36]. Research evidence indicates that sensory feedback and movement are intrinsically connected [37], as a variety of sensory information from the environment needs to be integrated in order to plan and execute movement effectively [36]. Studies conducted over the last decade have started to explore the contribution of aberrant sensorimotor integration, defined as an impairment in the pathway involving motor activity triggered by sensory stimuli, to the development and maintenance of NDDs [38].

Sensorimotor integration deficits among individuals with neurodevelopmental [39,40] and other developmental [41] conditions may affect postural control in both static and dynamic conditions. Standing balance requires the ability to integrate sensory inputs from visual, somatosensory, and vestibular systems [42]. Briefly, as we interact with our environment, the central vestibular system receives regular afferent fibers transmitting detailed information about head rotations through precise spike-timing as well as irregular afferents responding to high-frequency features exclusively through changes in the firing rate. Then, the brain combines vestibular and extra-vestibular cues, such as visual and proprioceptive information, at the earliest stages of central vestibular processing to construct an estimate of self-motion. Finally, vestibular processing is shaped as a function of context during

reflex behavior as well as more complex voluntary behaviors. Thus, disturbances in the multisensory integration by the brain may disrupt the accurate control of behavior in everyday life, including posture and balance [43]. Both preclinical and clinical studies converge on the evidence that efficient multisensory integration depends on intact feedback and feedforward neuronal loops between cortical regions, including primary sensory regions as well as multisensory areas such as the superior temporal sulcus and motor regions, and subcortical regions such as the thalamus. These cortico-cortical and cortico-subcortical transmissions have been suggested to serve a central integrative mechanism where visual, somatosensory, and vestibular inputs converge to support postural stability [44].

Experimental perturbation of sensory inputs can help in examining how individuals suffering from different conditions utilize combinations of that sensory feedback to maintain an upright stance [45]. In line with the National Institute of Mental Health (NIMH) Research Domain Criteria (RDoC) project, which promotes a framework for translational research on functional neurobehavioral dimensions across different disorder categories, sensorimotor systems may well represent a domain of function to be studied in neurodevelopment [46]. However, although previous studies have examined balance performances in developmental disorders [39–41], sensorimotor integration processes across different NDDs have not been systematically assessed. The present study attempted to fill this gap by performing a case-control analysis of postural stability under normal and altered sensory conditions in NDDs (ASD, ADHD, and TS) as compared to healthy controls. We hypothesized that, compared to healthy controls, children/adolescents with an NDD would present with decreasing postural balance impairment from ASD to ADHD and TS, in line with predictions from the gradient hypothesis.

2. Materials and Methods

2.1. Participants

Volunteers were enrolled in a case-control study through convenience sampling, based on their willingness to participate, at the Veneto Autism Spectrum Disorder Regional Centre, Integrated University Hospital of Verona, Italy. Participants aged 5 to 17 were assessed for the presence of a neurodevelopmental disorder (NDD) and recruited if they fulfilled the Diagnostic and Statistical Manual of Mental Disorders, fifth edition, (DSM-5) criteria for one of the following conditions: (a) Autism Spectrum Disorder (ASD), (b) Attention Deficit Hyperactivity Disorder (ADHD), (c) Tourette Syndrome (TS). Patients were excluded if presenting with (a) a formal comorbid neurodevelopmental condition, i.e., satisfying DSM-5 diagnostic criteria for more than one neurodevelopmental condition (e.g., receiving diagnosis of both ASD and TS); (b) a formal comorbid neuropsychiatric condition, i.e., satisfying DSM-5 diagnostic criteria for another neuropsychiatric condition such as psychosis-related disorders, depression-related disorders, anxiety-related disorders, and obsessive–compulsive-related disorders (e.g., receiving diagnosis of both ADHD and major depressive disorder); (c) a clinically relevant medical condition, particularly a neurological (receiving diagnosis of cerebral palsy, epilepsy, or otherwise-classified motor handicap) or orthopedic (receiving diagnosis of fracture or severe injury) condition; (d) a genetic syndrome (receiving diagnosis of chromosomal abnormalities); (e) a severe form of atypical neurodevelopment rendering it difficult to satisfactorily perform the study (all ASD children/adolescents included in the study had a diagnosis ranked severity level 1, which is the least severe form in terms of needed support, according to the DSM-5 three-level severity classification). Such exclusion criteria were applied in order to reduce the implications of "spurious comorbidity", which is the higher co-occurrence of disorders in clinically ascertained samples than in population-based samples, possibly due to such patients presenting with comorbid conditions being more likely to seek medical care and receive a diagnostic evaluation.

Healthy peers were recruited outside of the hospital facility and enrolled into the study with the support of several primary and secondary schools and the Hospital Pediatric Unit of Verona. Children/adolescents who wanted to participate in the study were recruited

only if presenting with good overall health. They were excluded if presenting with (a) a neurodevelopmental condition; (b) a neuropsychiatric condition; (c) a clinically relevant medical condition; (d) a genetic syndrome.

2.2. General Assessment

Socio-demographic information, such as age and gender, were obtained from all study participants. All volunteers were extensively visited by expert clinicians. Assessments included: (a) Review of clinical records, (b) in-depth physical exam, (c) medical history, (d) rating scales. Socio-demographic and clinical characteristics of the study sample, including cognitive performance as well as developmental motor and coordination abilities have been extensively described before [8]. Briefly, children/adolescents with an NDD presented with a lower range intelligence quotient, less proficient movement skills when compared with healthy peers' normative data, and coordination performance indicative of potential developmental coordination difficulties [8]. The present report focuses on stabilometric data.

2.3. Postural Control

In order to assess postural control, all participants underwent stabilometry, the methods of which have already been reported in detail [45]. Briefly, stabilometric assessments were performed in a standing position on an electronic monoaxial platform known as the TecnoBody® Platform (PK200WL, Prokin Tecnobody, Dalmine (BG), Italy). Participants' age, height, and weight were entered into the software in order for results to be consistent with such anthropometric information. The placement of each participants' feet on the platform was standardized with the medial malleolus at the rotation axis, as indicated by a V-shape, keeping a distance of 3 cm between the two malleoli, and extra-rotating 12° the medial borders of the feet.

Stabilometric performance was evaluated according to the Sensory Organization Test (SOT) [47], a protocol whose reliability and validity have been well established, also in pediatric populations with NDDs [48–51]. The SOT protocol allows quantifying subjects' ability to effectively use visual, vestibular, and proprioceptive inputs, as well as suppress inexact sensory information while standing. It consists of six sensory conditions: (i) Eyes open and with fixed support (SOT1-EO); (ii) eyes closed and with fixed support (SOT2-EC); (iii) sway-referenced vision and with fixed support (SOT3-SV); (iv) eyes open and with sway-referenced support (SOT4-EOSS); (v) eyes closed and with sway-referenced support (SOT5-ECSS); and (vi) sway-referenced vision and sway-referenced support (SOT6-SVSS) [52] (Figure 1). For each condition, four distinct parameters were measured to describe postural control: (i) The sway area (mm^2; area), that is the space covered due to body oscillations during the test; (ii) the length of the Center of Pressure (CoP) trajectory (mm; perimeter), that is the length of the route recorded due to body oscillations during the test; (iii) the mean velocity of the CoP displacement in the anteroposterior direction (mm/s; Anterior–Posterior Average Velocity (APAV)); and (iv) the mean velocity of the CoP displacement in the mediolateral direction (mm/s; Lateral Average Velocity (LAV)).

Two practice trials for each condition were conducted before the recording began. The test protocol consisted of three trials of each condition. Children/adolescents stood for 30 s for each condition.

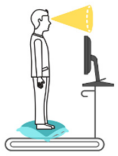
CONDITION	REGISTRATION SETTING	SENSORY SYSTEMS		DESCRIPTION
SOT1-EO		✓	VISUAL INPUT	This is the baseline measure of postural stability; all three sensory systems are operationally accurate.
			VESTIBULAR INPUT	
		✓	SOMATOSENSORY INPUT	
SOT2-EC		✗	VISUAL INPUT	Similar to the SOT1-EO condition, except that the child's eyes are closed.
			VESTIBULAR INPUT	
		✓	SOMATOSENSORY INPUT	
SOT3-SV		!	VISUAL INPUT	Similar to the SOT1-EO condition, except that the visual surround moves to track the child's sway, which provides inaccurate visual orientation cues.
			VESTIBULAR INPUT	
		✓	SOMATOSENSORY INPUT	
SOT4-EOSS		✓	VISUAL INPUT	The child stands with his/her eyes open, the visual surround is fixed, and the platform moves in response to the child's sway.
			VESTIBULAR INPUT	
		!	SOMATOSENSORY INPUT	
SOT5-ECSS		✗	VISUAL INPUT	Identical to the SOT4-EOSS condition, except that the child's eyes are now closed such that only the vestibular system is completely operative.
			VESTIBULAR INPUT	
		!	SOMATOSENSORY INPUT	
SOT6-SVSS		!	VISUAL INPUT	Identical to the SOT4-EOSS condition, except that the visual surround moves in response to the child's sway, such that only the vestibular system is a reliable source of sensory input.
			VESTIBULAR INPUT	
		!	SOMATOSENSORY INPUT	

Figure 1. SOT: Sensory Organization Test; EO: Eyes Open; EC: Eyes Closed; SV: Sway-referenced Vision; EOSS: Eyes Open Sway-referenced Support; ECSS: Eyes Closed Sway-referenced Support; SVSS: Sway-referenced Vision Sway-referenced Support. Visual input is the sensation of any change in the visual environment. Vestibular input is the sensation of any change in position, direction, or movement of the head. Somatosensory input is the sensation of any change in, but not limited to, touch, temperature, posture, and limb position. ✓ Normal sensory input; ✗ absent sensory input; ! sway-referenced input.

2.4. Statistical Analyses

The descriptive statistics were presented as means and standard deviations (SD) for normally distributed continuous variables, and as medians and interquartile ranges (IQR) for continuous variables that failed the normality test (Shapiro–Wilk tests). Frequencies and percentages were used to describe categorical variables. To take into account the non-

normal distributions of the data, for each of the four outcomes (area, perimeter, APAV, and LAV) and each of the six sensory conditions (SOT1-EO, SOT2-EC, SOT3-SV, SOT4-EOSS, SOT5-ECSS, and SOT6-SVSS), the comparison between cases and controls was performed through quantile regression models adjusted for gender and age. The threshold level selected for statistical significance was $p < 0.05$. All pairwise comparisons of adjusted medians were conducted and Bonferroni correction was applied to account for multiple testing. All calculated probabilities are presented as adjusted p-value after Bonferroni correction. The statistical analyses were performed with the statistical software Stata 16.1 (https://www.stata.com (accessed on 9 February 2021)).

2.5. Ethics

The research ethics committee at the Integrated University Hospital of Verona approved all protocols and procedures which led to the current study (CESC 2242 and CESC 2243). Parents and guardians of all study participants were offered an extensive description of the study and then consented to their inclusion in the study by signing an informed written consent. Consent was also obtained with reference to the publication of the collected research data.

3. Results

3.1. Socio-Demographic Information and Clinical Characteristics

Data were obtained on 104 participants, 81 of whom had a neurodevelopmental disorder (NDD) and 23 were healthy peers. As expected, there was a male-biased representation among children/adolescents with NDDs. Descriptive statistics of the study participants are reported in Table 1.

Table 1. Socio-demographic and clinical characteristics of the study participants.

	ASD	ADHD	TS	Healthy Controls
N (%)				
Participants	20 (19.2)	31 (29.8)	30 (28.9)	23 (22.1)
Gender (male)	16 (80.0)	26 (83.9)	27 (90.0)	10 (43.5)
M (SD)				
Age (years)	10.7 (2.0)	10.0 (2.4)	10.4 (2.2)	12.3 (2.6)
[range]	[7.2–14.6]	[5.7–15]	[7.4–16]	[8.3–16.9]
Total IQ	94.1 (15.9) ^	97.0 (16.5)	93.9 (16.7) ^^	105.2 (15.5) ^
[range]	[65–115]	[60–141]	[45–120]	[65–132]

ASD, Autism Spectrum Disorder; ADHD, Attention Deficit Hyperactivity Disorder; TS, Tourette Syndrome; M, mean; SD, standard deviation; IQ, Intelligence Quotient; ^, 1 missing value; ^^, 2 missing values.

3.2. Postural Control

Medians of raw data for NDD as a whole group (ASD+ADHD+TS) and for each neurodevelopmental condition as well as for healthy controls are reported in Supplementary Tables S1–S5.

3.2.1. Area

Medians adjusted for gender and age for the four groups (ASD, ADHD, TS, and healthy controls) are reported in Table 2. A graphical representation of such data is also presented in Supplementary Figure S1. After Bonferroni correction for multiple comparisons, there were statistically significant differences in the median area for the SOT1-EO ($p = 0.025$) and SOT6-SVSS ($p = 0.003$) conditions as well as a difference approaching significance for the SOT2-EC condition ($p = 0.057$) between ASD children/adolescents and healthy controls. Moreover, the median area for the SOT6-SVSS condition was significantly larger in ADHD children/adolescents as compared to healthy controls ($p = 0.009$).

Table 2. Performance in the area parameter among neurodevelopmental disorder (NDD) conditions and controls.

Conditions	ASD	ADHD	TS	Controls
	Adjusted Median * (95% CI)			
SOT1-EO	115 (82–147)	80 (53–106)	63 (36–90)	44 (11–78)
SOT2-EC	234 (163–306)	148 (89–207)	94 (34–154)	93 (18–168)
SOT3-SV	204 (130–279)	202 (141–264)	143 (80–205)	85 (7–163)
SOT4-EOSS	148 (92–204)	132 (86–178)	118 (71–165)	90 (31–149)
SOT5-ECSS	423 (288–559)	429 (318–541)	268 (156–381)	232 (90–373)
SOT6-SVSS	573 (442–704)	521 (413–629)	331 (222–440)	216 (79–354)

NDD, Neurodevelopmental Disorder; ASD, Autism Spectrum Disorder; ADHD, Attention Deficit Hyperactivity Disorder; TS, Tourette Syndrome; *, adjusted for gender and age; CI, Confidence Interval; SOT, Sensory Organization Test; EO, Eyes Open; EC, Eyes Closed; SV, Sway-referenced Vision; EOSS, Eyes Open Sway-referenced Support; ECSS, Eyes Closed Sway-referenced Support; SVSS, Sway-referenced Vision Sway-referenced Support.

Further, there was a difference approaching significance in the median area for the SOT1-EO condition ($p = 0.099$) as well as statistically significant differences for the SOT2-EC ($p = 0.023$) and SOT6-SVSS ($p = 0.037$) conditions between ASD children/adolescents and TS children/adolescents. Finally, there was a difference approaching significance in the median area for the SOT6-SVSS condition between ADHD and TS children/adolescents ($p = 0.090$).

3.2.2. Perimeter

Medians adjusted for gender and age for the four groups (ASD, ADHD, TS, and healthy controls) are reported in Table 3. A graphical representation of such data is also presented in Supplementary Figure S2. After Bonferroni correction for multiple comparisons, the median Perimeter for the SOT2-EC condition was significantly longer in ASD children/adolescents as compared to healthy controls ($p = 0.017$).

Table 3. Performance in the perimeter parameter among NDD conditions and controls.

Conditions	ASD	ADHD	TS	Controls
	Adjusted Median * (95% CI)			
SOT1-EO	178 (152–204)	146 (125–167)	145 (123–166)	134 (107–161)
SOT2-EC	276 (234–318)	224 (190–258)	207 (172–241)	181 (137–225)
SOT3-SV	240 (196–283)	215 (179–251)	178 (142–215)	181 (135–227)
SOT4-EOSS	236 (199–273)	245 (214–275)	207 (176–238)	219 (180–258)
SOT5-ECSS	433 (369–496)	426 (374–478)	351 (298–403)	359 (293–425)
SOT6-SVSS	429 (352–506)	392 (328–455)	339 (275–404)	354 (273–435)

NDD, Neurodevelopmental Disorder; ASD, Autism Spectrum Disorder; ADHD, Attention Deficit Hyperactivity Disorder; TS, Tourette Syndrome; *, adjusted for gender and age; CI, Confidence Interval; SOT, Sensory Organization Test; EO, Eyes Open; EC, Eyes Closed; SV, Sway-referenced Vision; EOSS, Eyes Open Sway-referenced Support; ECSS, Eyes Closed Sway-referenced Support; SVSS, Sway-referenced Vision Sway-referenced Support.

Further, there was a difference approaching significance in the median Perimeter for the SOT2-EC condition between ASD and TS children/adolescents ($p = 0.078$).

3.2.3. Anterior–Posterior Average Velocity

Medians adjusted for gender and age for the four groups (ASD, ADHD, TS, and healthy controls) are reported in Table 4. A graphical representation of such data is also presented in Supplementary Figure S3. After Bonferroni correction for multiple comparisons, the median Anterior–Posterior Average Velocity (APAV) for the SOT2-EC condition was significantly higher in ASD children/adolescents as compared to healthy controls ($p = 0.003$).

Table 4. Performance in the Anterior–Posterior Average Velocity (APAV) parameter among NDD conditions and controls.

Conditions	ASD	ADHD	TS	Controls
		Adjusted Median * (95% CI)		
SOT1-EO	5 (4–6)	4 (3–5)	4 (3–5)	4 (4–5)
SOT2-EC	9 (7–10)	7 (5–8)	6 (5–7)	5 (4–7)
SOT3-SV	6 (5–8)	6 (5–7)	5 (4–6)	5 (4–6)
SOT4-EOSS	6 (5–7)	7 (6–8)	5 (4–6)	6 (5–7)
SOT5-ECSS	12 (11–14)	12 (10–13)	9 (8–11)	11 (9–12)
SOT6-SVSS	11 (9–13)	11 (10–13)	9 (7–10)	10 (8–12)

APAV, Anterior–Posterior Average Velocity; NDD, Neurodevelopmental Disorder; ASD, Autism Spectrum Disorder; ADHD, Attention Deficit Hyperactivity Disorder; TS, Tourette Syndrome; *, adjusted for gender and age; CI, Confidence Interval; SOT, Sensory Organization Test; EO, Eyes Open; EC, Eyes Closed; SV, Sway-referenced Vision; EOSS, Eyes Open Sway-referenced Support; ECSS, Eyes Closed Sway-referenced Support; SVSS, Sway-referenced Vision Sway-referenced Support.

Further, there were differences approaching the significance in the median APAV for the SOT1-EO ($p = 0.065$) and SOT2-EC conditions ($p = 0.086$) between ASD and ADHD children/adolescents. Moreover, there were statistically significant differences for the SOT2-EC ($p = 0.007$) and SOT5-ECSS ($p = 0.041$) conditions between ASD children/adolescents and TS children/adolescents. Finally, there was a difference approaching significance in the median APAV for the SOT5-ECSS condition between ADHD and TS children/adolescents ($p = 0.061$).

3.2.4. Lateral Average Velocity

Medians adjusted for gender and age for the four groups (ASD, ADHD, TS, and healthy controls) are reported in Table 5. A graphical representation of such data is also presented in Supplementary Figure S4. After Bonferroni correction for multiple comparisons, the median Lateral Average Velocity (LAV) for the SOT1-EO ($p = 0.019$) and SOT2-EC ($p = 0.036$) conditions was significantly higher in ASD children/adolescents as compared to healthy controls.

Table 5. Performance in the Lateral Average Velocity (LAV) parameter among NDD conditions and controls.

Conditions	ASD	ADHD	TS	Controls
		Adjusted Median * (95% CI)		
SOT1-EO	4 (4–5)	3 (3–4)	3 (3–4)	3 (2–3)
SOT2-EC	6 (5–6)	5 (5–6)	4 (3–5)	4 (3–5)
SOT3-SV	5 (4–6)	5 (4–6)	4 (3–4)	4 (3–4)
SOT4-EOSS	5 (5–6)	5 (5–6)	5 (5–6)	5 (4–6)
SOT5-ECSS	10 (8–11)	10 (8–11)	8 (7–10)	9 (7–10)
SOT6-SVSS	10 (8–12)	9 (8–11)	8 (6–9)	7 (6–9)

LAV, Lateral Average Velocity; NDD, Neurodevelopmental Disorder; ASD, Autism Spectrum Disorder; ADHD, Attention Deficit Hyperactivity Disorder; TS, Tourette Syndrome; *, adjusted for gender and age; CI, Confidence Interval; SOT, Sensory Organization Test; EO, Eyes Open; EC, Eyes Closed; SV, Sway-referenced Vision; EOSS, Eyes Open Sway-referenced Support; ECSS, Eyes Closed Sway-referenced Support; SVSS, Sway-referenced Vision Sway-referenced Support.

Further, the median LAV for the SOT2-EC condition was significantly higher in ASD children/adolescents as compared to TS children/adolescents ($p = 0.013$) as well as in ADHD children/adolescents as compared to TS children/adolescents ($p = 0.042$).

4. Discussion

To the best of our knowledge, this is the first case-control study to examine whether children/adolescents with neurodevelopmental disorders (NDDs) and healthy controls

differ in terms of postural control, also examining whether NDD children/adolescents present with a different degree of impairment depending on the specific neurodevelopmental condition, in line with the neurodevelopmental gradient hypothesis. Results indicate that, as for any other impairment observed in atypical neurodevelopment [20], postural instability severity could be seen as lying on a neurodevelopmental gradient continuum, with decreasing severity from Autism Spectrum Disorder (ASD) to late-onset NDD. More specifically, four patterns of postural balance were observed in this study. First, ASD children/adolescents performed worse than healthy controls in a number of sensory conditions across all parameters. Second, Attention Deficit Hyperactive Disorder (ADHD) children/adolescents performed worse than healthy controls only for the most complex sensory condition (SOT6-SVSS) in the area parameter, when their vision and somatosensory functions were both compromised. Third, differences between Tourette syndrome (TS) children/adolescents and healthy controls in the performance across all parameters and conditions investigated failed to reach statistical significance. Fourth, differences were also observed between clinical groups. Specifically, ASD children/adolescents performed worse than TS children/adolescents in a number of conditions across all parameters, especially when sensory systems were not operationally accurate. To a much lesser extent, when receiving inaccurate sensory orientation cues, ADHD children/adolescents also tended to perform or performed worse than TS children/adolescents. Finally, ASD children/adolescents tended to perform worse than ADHD children/adolescents during the baseline condition (SOT1-EO) and when the visual input was absent (SOT2-EC) for the Anterior–Posterior Average Velocity (APAV) parameter. Therefore, in terms of postural control, ASD resulted in the most severely impaired neurodevelopmental condition, followed by ADHD and TS.

To date, while neuromotor symptoms are recognized as a core feature of most neurodevelopmental conditions, from those with childhood onset (e.g., stereotypic movements in ASD) to disorders with early adulthood onset (e.g., catatonia in psychosis) [3], normative motor development throughout a child's early life is not clearly defined [53]. As a consequence, it is still not completely clear when to consider motor difficulties of pathological relevance rather than part of the child's physiological brain maturation [53,54]. Moreover, at a research level, focusing on predefined motor characteristics of atypical neurodevelopment (e.g., stereotypic movements for ASD, hyperactivity for ADHD, tics for TS) [29] has offered limited support to our ability to differentiate pathognomonic from non-specific or benign motor phenomena [55]. Most research evidence agrees that motor difficulties in childhood do not necessarily imply a neuropsychiatric disorder, especially if not corroborated by additional evidence of brain lesions or abnormalities [30]. However, if such motor difficulties do persist in late childhood, they may require clinical attention as a potential sentinel of an underlying maturational delay, with implications for the child's ability to integrate sensorimotor stimuli to perform complex motor acts, including maintaining postural balance [31,32].

A further level of complexity affecting our ability to completely understand neuromotor functioning in the context of neuropsychiatric conditions is reflected in the debate whether poor sensorimotor integration would be specific to psychosis symptom formation, as historically assumed, or independent of such diagnosis [56,57]. More recent research evidence of psychomotor dysfunction in major psychiatric conditions including depression [58,59], anxiety [60], and schizophrenia [61,62], seems to support the hypothesis that such dysfunction might reflect a generalized deficit of neural integration, which is not related to a single condition. However, psychomotor dysfunction would present with specific characteristics to each condition, possibly depending on the severity, timing, and predominant pattern of brain aberrances and resulting neuropsychological manifestations.

The conceptualization of NDDs in a neurodevelopmental continuum results from evidence for pleiotropy between ASD, ADHD, and TS, which refers to shared neurobiological risk explaining correlations among NDDs [63,64]. Findings from the present study are in line with such conceptual framework and seem to point toward a trans-diagnostic role

of poor sensorimotor integration in atypical neurodevelopment, rather than lying on the discrete etiological pathway to a specific neurodevelopmental condition. Further, in line with the neurodevelopmental gradient hypothesis [20], poor postural control may be a useful biomarker for patient stratification across diagnostic boundaries in neurodevelopment, where the higher the sensorimotor severity, the greater the neurodevelopmental impairment.

Converging research evidence indicates that individuals with NDD present with both functional and structural brain abnormalities [65–70]. Interestingly, more limited evidence suggests both shared [71] and disorder-specific [72] structural brain alterations that vary over time and differently depending on the specific neurodevelopmental condition [73]. Distinct functional abnormalities have also been described, being more pronounced in ASD compared to other NDDs [74]. Further, differential alterations in functional connectivity between primary and supplementary motor cortex, and regions involved in brain motor circuitry such as putamen, thalamus, and cerebellum, have been suggested depending on the severity of the clinical presentation of atypical neurodevelopment [75]. Such evidence raises the question of a possible resulting impairment in the process of sensorimotor integration, that is the brain process allowing, by complex neural operations, the connection of the sensory and motor domains [76]. Deficiencies in sensorimotor integration would then present as difficulties in effectively utilizing sensory feedback to correct movements, resulting in the coordination difficulties and sensory reactivity abnormalities phenotypically observed among individuals with an NDD [77]. Altogether, the findings suggest a combination of shared and age-specific patterns of brain abnormalities reflecting overlapping and unique symptom presentations occupying a gradient of neurodevelopmental impairment.

While results seem to suggest that the impairment in sensorimotor integration can be graded according to the severity of the neurodevelopmental impairment putatively attributed to each NDD, with ASD being the most severe condition, we must beware of the risk of oversimplifying the diagnostic conundrum. Future studies will need to improve our understanding of the mechanisms underlying the co-occurrence of symptomatic manifestations such as deficits in sensorimotor integration among individuals with neurodevelopmental conditions. Such knowledge acquisition will help disentangle whether deficits in sensorimotor integration among NDDs reflect distinct dysfunctions or could imply different degrees of impairment on a common underlying neurodevelopmental continuum. Moreover, whether the degree of impairment in sensorimotor integration can make clear predictions about the outcome of NDDs, in line with the neurodevelopmental gradient hypothesis, is currently unclear. In addition, while motor impairments are described in both ASD and ADHD, evidence for specificity of motor impairment within different NDDs remains unclear. For instance, some studies indicate specific ASD-associated impairments in tasks requiring rapid integration of visual feedback, suggesting that individuals with ASD are less likely to rely on visual feedback when learning a novel movement pattern, instead showing a bias towards reliance on proprioceptive feedback [78,79]. In contrast, neither individuals with ADHD nor TS would present with such atypical bias in sensory-motor integration. Further, poor performance on manual dexterity tasks would be more strongly related to ADHD group membership, possibly as a consequence of ADHD-associated inefficient response selection negatively impacting motor control [80].

Results presented here need be seen in the light of some strengths and limitations. On the one hand, strengths include the implementation of rigorous inclusion criteria for each diagnostic group, as well as the investigation of postural control by instrumental assessment. As a consequence, the study design allows excluding that the observed postural instability would be due to the copresence of other physical of neuropsychiatric conditions or a poorly reliable postural assessment. On the other, the main limitations of the current research are that the sample size and gender imbalance did not allow to fully investigate the contribution of age and gender in the manifestation of NDD-related postural instability, though controlling for the confounding effects of such variables. Moreover, the study design did not contemplate a longitudinal evaluation of the phenomenon, thus requiring prospective studies to assess the evolution of postural control over time. Finally, future

studies will need to explore the impact of sensorimotor difficulties on the development and maintenance of NDD core symptom severity as well as specific predominant subtype (e.g., ASD severity level, ADHD inattentive/hyperactive–impulsive presentation, TS motor/vocal tic presentation).

5. Conclusions

In conclusion, while requiring replication in larger samples, evidence from this study indicates that poor postural control may be a useful biomarker for risk assessment in individuals suspected of having an atypical neurodevelopment. Moreover, such impairment seems to answer to the neurodevelopmental gradient hypothesis, with autism spectrum disorder children/adolescents presenting with the most severe postural instability, followed by children/adolescents with attention deficit hyperactive disorder and Tourette syndrome. Altogether, findings from this study add to the growing evidence stressing the importance of orienting public-health decisions in the direction of improving atypical neurodevelopment detection by also including the evaluation of sensorimotor skills. In the presence of such difficulties, interventions aimed at enhancing motor abilities should be supported along with preexisting therapies targeting psychological, behavioral, and cognitive difficulties.

Supplementary Materials: The following are available online at https://www.mdpi.com/1660-4601/18/4/1693/s1, Table S1: Performance among NDD children/adolescents as a whole group and controls; Table S2: Performance in the Area parameter among NDD and controls; Table S3: Performance in the Perimeter parameter among NDD and controls; Table S4: Performance in the APAV parameter among NDD and controls; Table S5: Performance in the LAV parameter among NDD and controls; Figure S1: The figure shows performance in the Area parameter among neurodevelopmental disorders and controls and bars show medians adjusted for gender and age; Figure S2. The figure shows performance in the Perimeter parameter among neurodevelopmental disorders and controls and bars show medians adjusted for gender and age; Figure S3. The figure shows performance in the Anterior-Posterior Average Velocity parameter among neurodevelopmental disorders and controls and bars show medians adjusted for gender and age; Figure S4. The figure shows performance in the Lateral Average Velocity parameter among neurodevelopmental disorders and controls and bars show medians adjusted for gender and age.

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