

NEWSLETTER



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Alcohol Clin Exp Res. 2017;41:231A.

SOCIAL ANXIETY, HEAVY DRINKING, AND AUD SYMPTOMS AMONG YOUNG ADULTS WITH AND WITHOUT CHILDHOOD ADHD.

McKone KMP, Kennedy TM, Walther CAP, et al.

Adults with ADHD as children have increased risk for developing alcohol use disorder (AUD; Lee, Humphreys, Flory, Liu, & Glass, 2011). Concurrently, social anxiety has been identified as an important factor in the development of alcohol use problems (Morris, 2005; Schry & White, 2013). However, the extent to which those with childhood ADHD report elevated levels of social anxiety as adults is less known. Many children with ADHD experience social impairment; hence, social anxiety may play an important role in the relation between ADHD and AUD. This study examines the extent to which young adults with a history of childhood ADHD exhibit higher levels of social anxiety and problems with alcohol use in young adulthood, when heavy drinking is at its peak. Participants in the Pittsburgh ADHD Longitudinal Study (N = 537; 314 ADHD, 223 non ADHD; 89% male; 82% White) provided self-reports on current levels of social anxiety (as assessed by the Fear of Negative Evaluation Scale; Watson & Friend, 1969); frequency of alcohol use, binge drinking, and drunkenness; and demographic information (e.g., educational status, SES) at ages 21 and 22. AUD symptom scores were generated from highly structured clinical interviews at both time points. Social anxiety at age 21 was unrelated to ADHD status ($r = 0.002$, $p = 0.97$). Social anxiety at age 21 was positively correlated with AUD symptom score both concurrently at age 21 ($r = 0.14$, $p = 0.013$) and prospectively to age 22 ($r = 0.13$, $p = 0.029$). Social anxiety was unrelated with all other alcohol use outcomes, and no significant interaction between ADHD and social anxiety was detected when predicting concurrent or prospective AUD symptom score using regression analysis. These results provide additional support for a modest role of social anxiety in the development of alcohol use problems; however, the relation between ADHD and social anxiety is less clear. Future analyses will explore the associations among social anxiety, ADHD symptom persistence, and other measures of anxiety (e.g., SCID interview) in young adulthood; examine whether the persistence of ADHD leads to increased social anxiety for some; and evaluate how these relations exacerbate or alleviate risk for AUD in young adulthood

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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.

Alcohol Clin Exp Res. 2017;41:232A.

ASSOCIATION BETWEEN ADULTHOOD DEPRESSIVE SYMPTOMS AND ALCOHOL PROBLEMS BY ADHD STATUS.

Wang FL, Pedersen SL, Gnagy EM, et al.

According to the self-medication hypothesis, depressed individuals might use alcohol to decrease negative emotions, thereby negatively reinforcing alcohol consumption and leading to problematic levels of use (Zucker, 1986). However, the literature on this topic is somewhat inconsistent. Some studies show that greater depressive symptoms predict more problematic adulthood alcohol use outcomes (e.g., D'Amico et al., 2005), whereas others show that greater depressive symptoms predict less problematic drinking in adulthood (e.g., Merline et al., 2008). Thus, it might be important to consider potential moderators of this relation. The current study tested childhood ADHD status as a moderator of the relation between depressive symptoms and alcohol problems in adulthood. Those with ADHD exhibit elevated depression symptoms (Meinzer et al., 2015) and higher rates of conduct problems; the relation between depression and alcohol problems may be stronger among individuals with versus without histories of ADHD. The current study utilized data from the Pittsburgh ADHD Longitudinal Study. ADHD was comprehensively diagnosed in childhood for probands. Participants without ADHD were recruited after childhood and absence of ADHD was confirmed at time of enrollment (59.9%ADHD; 40.4% nonADHD; 81.9%Caucasian; 89.1%male). Data for the current study include participants interviewed at ages 18 and 29 where CES-D depression symptoms and alcohol problems were assessed. After controlling for demographics and age 18 alcohol problems, age 18 depressive symptoms, but not childhood ADHD or the interaction between depression and ADHD, predicted age 29 alcohol problems. After controlling for age 18 delinquency, those without childhood histories of ADHD showed greater alcohol problems and the effect of depression was marginally significant. Findings show that although depressive symptoms in early adulthood may influence later alcohol problems, co-occurring delinquency accounts for this association to a large extent. This may be one reason for the inconsistent results previously found in how depression relates to alcohol problems. Examining delinquency in conjunction with depression may be particularly relevant in understanding risk for alcohol use outcomes. Additional analyses will consider the contribution of ADHD symptom persistence as well as growth trajectories of depression and alcohol problems, taking into account the contribution of co-occurring delinquency

Alcohol Clin Exp Res. 2017;41:77A.

PROSPECTIVE SPECIFICITY OF EXPECTANCIES PREDICTING SUBSTANCE USE AMONG ADULTS WITH AND WITHOUT CHILDHOOD ADHD.

Walther CAP, Pedersen SL, Gnagy EM, et al.

Children with ADHD are at increased risk of substance use problems as adolescents and young adults compared to those without ADHD histories (Lee et al., 2011; Molina et al., 2007). Substance use expectancies are widely studied risk factors for substance use that have been found to be less associated with substance use for adolescents and adults with, than without, childhood ADHD (Harty et al., 2015; Pedersen et al., 2014). Given the differential functioning of this risk factor for individuals with ADHD, examining if expectancies also have less specificity in relation to particular substances is an important next step. In this study, we tested the specificity of associations between alcohol and marijuana expectancies in the early twenties with alcohol and marijuana use at these ages and at age 30 as a function of ADHD history. Participants were 491 young adults (281 with, 210 without childhood ADHD) interviewed at ages 21-23 and 30 in the Pittsburgh ADHD Longitudinal Study. Participants reported positive and negative expectancies about alcohol (CEOA; Fromme et al., 1993) and marijuana use (CEOA-adapted) and past year frequency of alcohol and marijuana use. Multigroup analyses inMplus revealed significant ADHD/nonADHD group differences in associations. Specifically, associations between substance use expectancies and substance use were primarily present for the nonADHD group from ages 21 to 23, and many of the associations between expectancies and substance use were specific to the substance the expectancy directly assessed (5 out of 6). Prospectively, only higher negative marijuana expectancies in the early twenties were associated with less frequent marijuana use at age 30 for participants without a history of ADHD ($\pm = -0.24$, $p < 0.05$). These findings support specificity of association between expectancies and substance use, for participants without ADHD. Expectancies were largely unrelated to concurrent or prospective substance use for those with ADHD. Given well-documented deficits in executive function and insight, implicit expectancies (cognitions

accessed via automatic rather than rational, effortful processing) may be more predictive for individuals with ADHD compared to explicit expectancies

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Am J Epidemiol. 2017;185:924-32.

SPATIAL VARIABILITY IN ADHD-RELATED BEHAVIORS AMONG CHILDREN BORN TO MOTHERS RESIDING NEAR THE NEW BEDFORD HARBOR SUPERFUND SITE.

Vieira VM, Fabian MP, Webster TF, et al.

Attention-deficit/hyperactivity disorder (ADHD) has an uncertain etiology, with potential contributions from different risk factors such as prenatal environmental exposure to organochlorines and metals, social risk factors, and genetics. The degree to which geographic variability in ADHD is independent of, or explained by, risk factors may provide etiological insight. We investigated determinants of geographic variation in ADHD-related behaviors among children living near the polychlorinated biphenyl-contaminated New Bedford Harbor (NBH) Superfund site in Massachusetts. Participants were 573 children recruited at birth (1993-1998) who were born to mothers residing near the NBH site. We assessed ADHD-related behaviors at age 8 years using Conners' Teacher Rating Scale- Revised: Long Version. Adjusted generalized additive models were used to smooth the association of pregnancy residence with ADHD-related behaviors and assess whether prenatal organochlorine or metal exposures, sociodemographic factors, or other factors explained spatial patterns. Models that adjusted for child's age and sex displayed significantly increased ADHD-related behavior among children whose mothers resided west of the NBH site during pregnancy. These spatial patterns persisted after adjusting for prenatal exposure to organochlorines and metals but were no longer significant after controlling for sociodemographic factors. The findings underscore the value of spatial analysis in identifying high-risk subpopulations and evaluating candidate risk factors

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Am J Med Genet Part B Neuropsychiatr Genet. 2017;174:381-89.

SEQUENCING OF SPORADIC ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) IDENTIFIES NOVEL AND POTENTIALLY PATHOGENIC DE NOVO VARIANTS AND EXCLUDES OVERLAP WITH GENES ASSOCIATED WITH AUTISM SPECTRUM DISORDER.

Kim DS, Burt AA, Ranchalis JE, et al.

Attention-Deficit Hyperactivity Disorder (ADHD) has high heritability; however, studies of common variation account for <5% of ADHD variance. Using data from affected participants without a family history of ADHD, we sought to identify de novo variants that could account for sporadic ADHD. Considering a total of 128 families, two analyses were conducted in parallel: first, in 11 unaffected parent/affected proband trios (or quads with the addition of an unaffected sibling) we completed exome sequencing. Six de novo missense variants at highly conserved bases were identified and validated from four of the 11 families: the brain-expressed genes TBC1D9, DAGLA, QARS, CSMD2, TRPM2, and WDR83. Separately, in 117 unrelated probands with sporadic ADHD, we sequenced a panel of 26 genes implicated in intellectual disability (ID) and autism spectrum disorder (ASD) to evaluate whether variation in ASD/ID-associated genes were also present in participants with ADHD. Only one putative deleterious variant (Gln600STOP) in CHD1L was identified; this was found in a single proband. Notably, no other nonsense, splice, frameshift, or highly conserved missense variants in the 26 gene panel were identified and validated. These data suggest that de novo variant analysis in families with independently adjudicated sporadic ADHD diagnosis can identify novel genes implicated in ADHD pathogenesis. Moreover, that only one of the 128 cases (0.8%, 11 exome, and 117 MIP sequenced participants) had putative deleterious variants within our data in 26 genes related to ID and ASD suggests significant independence in the genetic pathogenesis of ADHD as compared to ASD and ID phenotypes

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American Journal of Rhinology and Allergy. 2017;31:161-67.

ASSOCIATION OF PEDIATRIC ALLERGIC RHINITIS WITH THE RATINGS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Feng B, Jin H, Xiang H, et al.

Background: Allergic rhinitis (AR) is currently the most prevalent allergic disease in children and adolescents. Objective: Surveys conducted by population-based studies of East Asia revealed an increased prevalence of behavioral disorders in patients with AR. Thus, in this study, we explored the prevalence of attention-deficit/hyperactivity disorder (ADHD) in pediatric patients with AR.

Methods: A total of 333 children (6-12 years of age) with AR and a total of 322 age-matched controls were included in this study. An otorhinolaryngologist diagnosed all AR cases and evaluated the severity of the disease. Skin-prick test results for 18 major allergens, Paediatric Rhinoconjunctivitis Quality of Life Questionnaire (PRQLQ), Child Behavior Checklist (CBCL), and Swanson, Nolan, and Pelham version IV (SNAP-IV) scores were recorded.

Results: In total, 320 age-matched controls and 323 children with AR completed the study. With respect to the Total Nasal Symptom Score and the PRQLQ, the condition of the experimental group was more serious than that of the controls. The scores on the hyperactivity/impulsivity and inattention subscales, which evaluate ADHD symptoms, and those on the CBCL subscales were significantly higher in patients with AR than in the controls (all p values were <0.01). From the results of the Pearson correlation, we deduced that there were significant positive correlations between the AR-related data and each subscale of the CBCL and SNAP-IV in the AR group. Moreover, two basic characteristics (males and environmental exposure to tobacco smoke) present significant positive and age showed a significant negative correlations affect ADHD symptom in both the AR group and the control group. Also, in the "pure AR" group, hierarchical regression analyses were performed to determine the subtests of the PRQLQ, which are significant predictors of SNAP-IV and CBCL.

Conclusions: Apart from AR per se, the possible comorbidities of impulsivity and inattention are important when managing children with AR. It is essential to evaluate the symptoms of ADHD in children and adolescents with AR

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Anadolu Psikiyatr Derg. 2017;18:79-84.

EARLY DIAGNOSIS AND TREATMENT OF ADHD ARE IMPORTANT FOR A SECURE TRANSITION TO ADOLESCENCE.

Zahmacioglu O, Kilic EZ.

Objective: Attention-deficit hyperactivity disorder (ADHD) is one of the most common psychiatric disorders that begins in childhood. By using self-esteem and loneliness scales, our aim was to compare the adolescents who were diagnosed "early" and are currently receiving treatment with the ones with "late" diagnoses. By examining loneliness and self-esteem directly, we wish to emphasize a possibility of positive impact of early diagnosis and treatment. We hypothesized that the duration of treatment is an important factor in reducing several negative psychosocial impacts of ADHD.

Methods: The study included 62 adolescent patients with a "late" ADHD diagnosis between the ages of 12 and 14 years, and 55 adolescent patients with "early" diagnosis between the ages of 6 and 8 years who have been followed up regularly with appropriate treatment for nearly 6 years. These groups were compared with regard to self-esteem and feelings of loneliness.

Results: The UCLA Loneliness Scale scores were higher, but the Rosenberg Self-esteem Scale scores were lower in the late-diagnosed group. These results did not change with regard to ADHD subtypes and gender.

Conclusion: The late-diagnosed adolescents with ADHD feel they are alone more than the early-diagnosed adolescents, and they like themselves less compared to the early-diagnosed group

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Appl Cogn Psychol. 2017;31:302-14.

INDIVIDUAL DIFFERENCES IN TRAINING GAINS AND TRANSFER MEASURES: AN INVESTIGATION OF TRAINING CURVES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

van der Donk MLA, van VS, Hiemstra-Beernink A-C, et al.

Currently, evidence for the beneficial effects of working memory (WM) training on transfer measures in children with attention-deficit/hyperactivity disorder (ADHD) is inconsistent. Although there is accumulating evidence for the role of individual differences in training and transfer gains of cognitive training, this area has been left unexplored for children with ADHD. In the current study, an advanced latent growth curve model analysis was used to investigate the individual differences in learning curves (training gains) of WM training tasks within a new cognitive intervention *Paying Attention in Class*. It was investigated whether certain baseline variables (age, intelligence quotient, externalizing behaviour problems and presence of learning disability) predicted the learning curves and how these individual learning curves influenced near-transfer and far-transfer measures. A total of 164 children diagnosed with ADHD, between the age of 8 and 12-áyears old, followed this new *Paying Attention in Class* intervention. WM (near-transfer) and academic performance (far-transfer) measures were assessed before treatment and directly after treatment. Results showed that individual differences at the start of training were predicted by age and intelligence quotient, but the individual differences in learning curves were not predicted by any of the baseline variables. Both for the verbal and the visuospatial WM training, children with larger training gains (i.e. steeper training curves) showed larger benefits on the near untrained transfer measures. These effects were absent for the far-transfer measures. Current study shows that training WM is quite complex and has its limitations for children with ADHD. Nonetheless, it highlights that training and transfer gains are affected by many different factors and warrants the need of a more in-depth investigation of individual differences in future studies

Aust New Zealand J Psychiatry. 2017;51:703-10.

INVERSE ASSOCIATIONS BETWEEN CORD VITAMIN D AND ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS: A CHILD COHORT STUDY.

Mossin MH, Aaby JB, Dalg+Ñrd C, et al.

Objective: To examine the association between cord 25-hydroxyvitamin D₂₊₃ (25(OH)D) and attention deficit hyperactivity disorder symptoms in toddlers, using Child Behaviour Checklist for ages 1.5-5.

Method: In a population-based birth cohort, a Child Behaviour Checklist for ages 1.5-5 questionnaire was returned from parents of 1233 infants with mean age 2.7 (standard deviation 0.6) years. Adjusted associations between cord 25(OH)D and Child Behaviour Checklist-based attention deficit hyperactivity disorder problems were analysed by multiple regression.

Results The median cord 25(OH)D was 44.1 (range: 1.5-127.1) nmol/L. Mean attention deficit hyperactivity disorder problem score was 2.7 (standard deviation 2.1). In adjusted analyses, cord 25(OH)D levels >25 nmol/L and >30 nmol/L were associated with lower attention deficit hyperactivity disorder scores compared to levels 1/225 nmol/L ($p = 0.035$) and 1/230 nmol/L ($p = 0.043$), respectively. The adjusted odds of scoring above the 90th percentile on the Child Behaviour Checklist-based attention deficit hyperactivity disorder problem scale decreased by 11% per 10 nmol/L increase in cord 25(OH)D.

Conclusion: An inverse association between cord 25(OH)D and attention deficit hyperactivity disorder symptoms in toddlers was found, suggesting a protective effect of prenatal vitamin D

Behav Ther. 2017.

CHILDHOOD ADHD AND NEGATIVE SELF-STATEMENTS: IMPORTANT DIFFERENCES ASSOCIATED WITH SUBTYPE AND ANXIETY SYMPTOMS.

Castagna PJ, Calamia M, Davis TE.

The current study examined the role negative self-statements have on the comorbidity between anxious symptomatology and ADHD-combined presentation (ADHD-C) and ADHD-predominantly inattentive (ADHD-I). A total of 114 children and adolescents with ADHD (M age = 10.15; $SD = 2.30$; range = 7–16) from a clinic-

referred sample were grouped based on a semistructured diagnostic interview and consensus approach (ADHD-C, $n = 62$; ADHD-I, $n = 52$). Negative self-statements were measured using the Children's Automatic Thoughts Scale and the total score from the Multidimensional Anxiety Scale for Children was used to measure anxious symptomatology. Findings indicated youth diagnosed with ADHD-C, compared to those diagnosed with ADHD-I, had more frequent personal failure (Cohen's $d = .40$) and hostile intent negative self-statements (Cohen's $d = .47$). The association of ADHD subtype and negative self-statements was moderated by anxiety; negative self-statements of personal failure were highest in anxious ADHD-C children ($\beta = .31$). A second sample of 137 children and adolescents (M age = 10.61; $SD = 2.26$; range = 7–16) from a larger clinic-referred sample was utilized to replicate our results dimensionally. Results indicated that both hyperactivity/impulsivity ($\beta = .23$, $p < .01$) and the interaction of hyperactivity/impulsivity and anxiety ($\beta = .17$, $p < .05$) were significant predictors of negative self-statements regarding personal failure, while holding child age, child gender, oppositional symptoms, and inattention constant. In all, negative self-statements should be considered in the treatment and assessment of ADHD with particular attention paid to ADHD subtype and internalizing comorbidity

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Bipolar Disord. 2017;19:62.

THE RELATION BETWEEN BIPOLAR DISORDER OF MOTHERS AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER AMONG THEIR CHILDREN.

Ramadan M, Mekky A, Ennabawy A, et al.

Background and Aims: Some studies suggested that bipolar disorder in mothers is a risk factor for developing ADHD. Aim of the Study: Is to find the relationship between bipolar disorders in mothers and ADHD in their children.

Methods: The sample was consisted of two groups, the first group was mothers that has bipolar disorder their number were 18 mother and they come to psychiatry clinic in AL Hussein hospital to seek medical help, their ages 25 to 45 years. Their children were 50 children, their ages 4 to 18 years old. The control group was mothers who didn't have any psychiatric illness, their number was 30 mother, they came to psychiatry clinic in al Hussein hospital to complain some behavioral and academic problems with their children, their ages 25 to 45 years old and their children were 50 children. Ages of the control group of children 4 to 18 years old. Clinical psychiatric interview applied by Items of bipolar disorder of Standardized Clinical Interview for the fourth edition of the Diagnostic and Statistical Manual (DSM-IV) (SCID1). Conner's test for ADHD has been applied to confirm the diagnosis of ADHD in children. The informed consent was done.

Results: The results revealed that children of bipolar mothers have ADHD 78%, while children of non-bipolar mothers who have ADHD 40% with statistical significance. This shows the relation between bipolar disorder in mother and ADHD in their children.

Conclusions: The relation between bipolar disorder in mothers and ADHD in their children was positive

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BMJ (Online). 2017;357.

PRENATAL ANTIDEPRESSANT USE AND RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN OFFSPRING: POPULATION BASED COHORT STUDY.

Man KKC, Chan EW, Ip P, et al.

Objective To assess the potential association between prenatal use of antidepressants and the risk of attention-deficit/hyperactivity disorder (ADHD) in offspring.

Design Population based cohort study. Setting Data from the Hong Kong population based electronic medical records on the Clinical Data Analysis and Reporting System.

Participants 190 618 children born in Hong Kong public hospitals between January 2001 and December 2009 and followed-up to December 2015.

Main outcome measure Hazard ratio of maternal antidepressant use during pregnancy and ADHD in children aged 6 to 14 years, with an average follow-up time of 9.3 years (range 7.4-11.0 years).

Results Among 190 618 children, 1252 had a mother who used prenatal antidepressants. 5659 children (3.0%) were given a diagnosis of ADHD or received treatment for ADHD. The crude hazard ratio of maternal antidepressant use during pregnancy was 2.26 ($P < 0.01$) compared with non-use. After adjustment for potential confounding factors, including maternal psychiatric disorders and use of other psychiatric drugs, the adjusted hazard ratio was reduced to 1.39 (95% confidence interval 1.07 to 1.82, $P = 0.01$). Likewise, similar results were observed when comparing children of mothers who had used antidepressants before pregnancy with those who were never users (1.76, 1.36 to 2.30, $P < 0.01$). The risk of ADHD in the children of mothers with psychiatric disorders was higher compared with the children of mothers without psychiatric disorders even if the mothers had never used antidepressants (1.84, 1.54 to 2.18, $P < 0.01$). All sensitivity analyses yielded similar results. Sibling matched analysis identified no significant difference in risk of ADHD in siblings exposed to antidepressants during gestation and those not exposed during gestation (0.54, 0.17 to 1.74, $P = 0.30$).

Conclusions The findings suggest that the association between prenatal use of antidepressants and risk of ADHD in offspring can be partially explained by confounding by indication of antidepressants. If there is a causal association, the size of the effect is probably smaller than that reported previously

Brain Imaging Behav. 2017;11:846-58.

ALTERED STRUCTURAL CONNECTIVITY IN ADHD: A NETWORK BASED ANALYSIS.

Beare R, Adamson C, Bellgrove MA, et al.

Attention deficit/hyperactivity disorder (ADHD) is increasingly being viewed as a dysfunction of distributed brain networks rather than focal abnormalities. Here we investigated the structural brain network differences in children and adolescents with ADHD and healthy controls, using graph theory metrics to describe the anatomic networks and connectivity patterns, and the Network Based Statistic (NBS) to isolate the network components that differ between the two groups. Using DWI high-angular resolution diffusion imaging (HARDI), whole brain tractography was conducted on 21 ADHD-combined type boys (m 13.3-á-1-á1.9-áyrs) and 21 typically developing boys (m 14.8-á-1-á2.1-áyrs). This study presents a comprehensive structural network investigation in ADHD covering a range of commonly used methodologies, including both streamline and probabilistic tractography, tensor and constrained spherical deconvolution (CSD) models, as well as different edge weighting methods at a range of densities and t-thresholds. Using graph metrics, ADHD was associated with local neighbourhoods that were more modular and interconnected than controls, where there was a decrease in the global, long-range connections, indicating reduced communication between local, specialised networks in ADHD. ADHD presented with a sub-network of stronger connectivity encompassing bilateral frontostriatal connections as well as left occipital, temporal, and parietal regions, of which the white matter microstructure was associated with ADHD symptom severity. Probabilistic tractography using CSD and the Hagmann weighting method produced that highest stability and most robust network differences across t-thresholds. It demonstrates topological organisation disruption in distributed neural networks in ADHD, supportive of the theory of maturation delay in ADHD

Can J Psychiatry. 2017;62:393-402.

ADHD TREATMENT IN PRIMARY CARE: DEMOGRAPHIC FACTORS, MEDICATION TRENDS, AND TREATMENT PREDICTORS.

Hauck TS, Lau C, Wing LLF, et al.

Background: The aim of this study is to determine the prevalence and characteristics of youth with attention-deficit hyperactivity disorder (ADHD) in Ontario, Canada, and to determine the predictors of psychotropic medication prescriptions in youth with ADHD.

Method: This is a cross-sectional retrospective chart abstraction of more than 250 000 medical records from youth aged 1 to 24 years in a large geographical region in Ontario, Canada, linked to population-based health administrative data. A total of 10 000 charts were randomly selected and manually reviewed using predetermined criteria for ADHD and comorbidities. Prevalence, comorbidities, demographic indicators, and

health service utilization characteristics were calculated. Predictors of treatment characteristics were determined using logistic regression modelling.

Results: The prevalence of ADHD was 5.4% (7.9% males, 2.7% females). Youth with ADHD had significant psychiatric comorbidities. The majority (70.0%) of ADHD patients received prescriptions for stimulant or nonstimulant ADHD medication. Antipsychotic prescriptions were provided to 11.9% of ADHD patients versus 0.9% of patients without ADHD. Antidepressant prescriptions were provided to 19.8% versus 5.4% of patients with and without ADHD, respectively. Predictors of antidepressant prescriptions were increasing age (odds ratio [OR], 1.14; 95% confidence interval [CI], 1.07 to 1.21), psychiatric consultation (OR, 2.04; 95% CI, 1.16 to 3.58), and diagnoses of both anxiety and depression (OR, 18.4; 95% CI, 8.03 to 42.1), whereas the only predictor of antipsychotic prescriptions was psychiatric consultation (OR, 3.85; 95% CI, 2.11 to 7.02).

Conclusions: Youth with ADHD have more psychiatric comorbidities than youth without ADHD. The majority of youth with ADHD received stimulant medications, and a significant number received additional psychotropic medications, with psychiatric consultation predicting medication use

Can J Psychiatry. 2017;62:403-12.

A MULTIMODAL INTERVENTION FOR CHILDREN WITH ADHD REDUCES INEQUITY IN HEALTH AND EDUCATION OUTCOMES.

Enns JE, Randall JR, Smith M, et al.

Objective: To evaluate whether a multimodal intervention for children with attention-deficit hyperactivity disorder (ADHD) resulted in better long-term health and education outcomes and reduced inequity across the socioeconomic gradient.

Method: We analyzed administrative data held in the Manitoba Population Research Data Repository describing recipients of a combined pharmacological/behavioural intervention for ADHD. The study cohort included children aged 5 to 17 years who visited the Manitoba Adolescent Treatment Centre's ADHD intervention service at least 3 times (2007-2012). Controls were matched on age, sex, year of ADHD diagnosis, and income quintile. We compared rates of hospital and emergency department visits, medication use and adherence, contact with child welfare services, and whether children were in their age-appropriate grade. We used concentration curves to estimate differences in outcomes between children from high- and low-income families.

Results: Children who received the intervention (n = 485) had higher rates of medication use (rate ratio [RR], 1.21; 95% CI, 1.08 to 1.36) and adherence (RR, 1.42; 95% CI, 1.03 to 1.96) and were more likely to be in their age-appropriate grade (RR, 1.33; 95% CI, 1.09 to 1.63) compared with controls (n = 1884). The intervention was also associated with reduced inequity in these outcomes across income deciles. There was no difference in the rates of hospital or emergency department visits or contacts with child welfare services.

Conclusions: A multimodal ADHD intervention was associated with increased medication use and adherence and higher academic achievement. It was also related to lower inequity across the socioeconomic gradient. These results suggest that multimodal approaches may provide more equitable health and education outcomes for children with ADHD

Child Adolesc Psychiatr Clin North Am. 2017;26:523-38.

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN PRESCHOOL-AGE CHILDREN.

Tandon M, Pergjika A.

Attention deficit hyperactivity disorder is a neurodevelopmental disorder marked by age-inappropriate deficits in attention or hyperactivity/impulsivity that interfere with functioning or development. It is highly correlated with other disorders, such as oppositional defiant disorder, conduct disorder, and mood symptoms. The etiology is multifactorial, and neuroimaging findings are nonspecific. Although assessment tools exist, there is variability among them, and historically, parent-teacher agreement has not been consistent. Treatment algorithm for attention deficit hyperactivity disorder in preschoolers includes behavioral interventions first

followed by psychopharmacologic treatment when behavioral therapies fail. Other nonpharmacologic and nonbehavioral interventions are discussed including the role of exercise and nutrition Child

Adolesc Psychiatry Ment Health. 2017;11.

ONE-YEAR TRAJECTORY ANALYSIS FOR ADHD SYMPTOMS AND ITS ASSOCIATED FACTORS IN COMMUNITY-BASED CHILDREN AND ADOLESCENTS IN TAIWAN.

Tsai C-J, Chen Y-L, Lin H-Y, et al.

Background: Several longitudinal studies have shown the partial symptomatic persistence of attention-deficit hyperactivity disorder (ADHD) in clinic-based samples. However, little is known about the patterns and trajectories of ADHD symptoms in community-based populations.

Methods: To differentiate developmental trajectories of ADHD symptoms over 1 year, with a four-wave quarterly follow-up in children and adolescents in the community of Taiwan, we conducted this prospective study in 1281 students in grade 3, 5, and 8. All the students in the regular classes rather than special educational classes were eligible and recruited to the study. Inattention, hyperactivity-impulsivity, and opposition-defiance were rated by parent reports on the Chinese version of the Swanson, Nolan, and Pelham Version IV Scale (SNAP-IV). Group-based trajectory modeling and multivariable regression analyses were used to explore the individual, family and social factors associated with differential trajectories.

Results: Trajectories were classified as Low (29.9-40.6%), Intermediate (52.5-58.5%) and High (6.9-12.5%) based on the symptom severity of ADHD symptoms assessed by the SNAP-IV. The proportion of children in the high ADHD trajectory might approximately reflect the prevalence of ADHD in Taiwan. The following factors differentiated High from Low trajectories: male gender, more externalizing problems, fewer prosocial behaviors, school dysfunction, more home behavioral problems, and less perceived family support.

Conclusions: Our findings that the concurrent conditions of emotional or externalizing problems, as well as impaired school and home function at baseline, might differentiate the high ADHD symptoms trajectory from others could help developing the specific measures for managing high ADHD symptoms over time in a school setting

Child Neuropsychol. 2017;23:692-712.

VIRTUAL-REALITY-BASED ATTENTION ASSESSMENT OF ADHD: CLINICAVR: CLASSROOM-CPT VERSUS A TRADITIONAL CONTINUOUS PERFORMANCE TEST.

Neguț A, Jurma AM, David D.

Virtual-reality-based assessment may be a good alternative to classical or computerized neuropsychological assessment due to increased ecological validity. ClinicaVR: Classroom-CPT (VC) is a neuropsychological test embedded in virtual reality that is designed to assess attention deficits in children with attention deficit hyperactivity disorder (ADHD) or other conditions associated with impaired attention. The present study aimed to (1) investigate the diagnostic validity of VC in comparison to a traditional continuous performance test (CPT), (2) explore the task difficulty of VC, (3) address the effect of distractors on the performance of ADHD participants and typically-developing (TD) controls, and (4) compare the two measures on cognitive absorption. A total of 33 children diagnosed with ADHD and 42 TD children, aged between 7 and 13-áyears, participated in the study and were tested with a traditional CPT or with VC, along with several cognitive measures and an adapted version of the Cognitive Absorption Scale. A mixed multivariate analysis of covariance (MANCOVA) revealed that the children with ADHD performed worse on correct responses had more commissions and omissions errors than the TD children, as well as slower target reaction times. The results showed significant differences between performance in the virtual environment and the traditional computerized one, with longer reaction times in virtual reality. The data analysis highlighted the negative influence of auditory distractors on attention performance in the case of the children with ADHD, but not for the TD children. Finally, the two measures did not differ on the cognitive absorption perceived by the children

Child Neuropsychol. 2017;1-21.

SECONDARY ATTENTION-DEFICIT/HYPERACTIVITY DISORDER FOLLOWING PERINATAL AND CHILDHOOD STROKE: IMPACT ON COGNITIVE AND ACADEMIC OUTCOMES.

Williams TS, Roberts SD, Coppens AM, et al.

This cross-sectional retrospective clinical research study examines a large group of children followed within a pediatric stroke program and a developmental attention-deficit/hyperactivity disorder (ADHD) clinic at the Hospital for Sick Children, between May 2004 and June 2016. All children with a history of stroke who participated in a neuropsychological assessment between the ages of 4 and 18-áyears were considered for inclusion. From a sample of 275 participants with a history of stroke, 36 children (13.1%) received a diagnosis of secondary ADHD. Children with secondary ADHD were younger at the time of stroke and more likely to be identified as having a presumed perinatal stroke and persistent seizures than children without secondary ADHD diagnoses. There were no differences in pattern of lesion, size, or laterality between children who developed secondary ADHD and those who did not. Children with secondary ADHD had the lowest scores across all cognitive and academic measures compared to children with stroke-only and developmental ADHD. Findings highlight the added risk of receiving a diagnosis of secondary ADHD following pediatric stroke. Implications for future research and directed intervention are discussed

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Child Psychiatry Hum Dev. 2017 Jun;48:370-84.

NEUROPSYCHOLOGICAL FUNCTIONING AND ATTACHMENT REPRESENTATIONS IN EARLY SCHOOL AGE AS PREDICTORS OF ADHD SYMPTOMS IN LATE ADOLESCENCE.

Salari R, Bohlin G, Rydell AM, et al.

This study aimed to examine relations between parent and child attachment representations and neuropsychological functions at age 8, as well as relations between these constructs and ADHD symptoms over a 10-year period. A community-based sample of 105 children (52 boys) participated. Measures of attachment representations and a range of neuropsychological functions were collected at age 8. Parents rated emotion dysregulation and ADHD symptoms at age 8 and ADHD symptoms again at age 18. Significant, although modest, relations were found between disorganized attachment and some aspects of neuropsychological functioning in childhood. When studying outcomes in late adolescence and controlling for early ADHD symptom levels, spatial working memory and disorganized attachment remained significant in relation to both ADHD symptom domains, and one measure of inhibition remained significant for hyperactivity/impulsivity. When examining independent effects, spatial working memory and disorganized attachment were related to inattention, whereas spatial working memory and dysregulation of happiness/exuberance were related to hyperactivity/impulsivity. Our findings showing that disorganized attachment is longitudinally related to ADHD symptoms over and above the influence of both neuropsychological functioning and early ADHD symptom levels highlights the importance of including measures of attachment representations when trying to understand the development of ADHD symptoms. If replicated in more “at-risk” samples, these findings could also suggest that parent–child attachment should be taken into consideration when children are referred for assessment and treatment of ADHD

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Chin Med J. 2017;130:1513-20.

EFFECT OF AN ECOLOGICAL EXECUTIVE SKILL TRAINING PROGRAM FOR SCHOOL-AGED CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A RANDOMIZED CONTROLLED CLINICAL TRIAL.

Qian Y, Chen M, Shuai L, et al.

BACKGROUND: As medication does not normalize outcomes of children with attention deficit hyperactivity disorder (ADHD), especially in real-life functioning, nonpharmacological methods are important to target this field. This randomized controlled clinical trial was designed to evaluate the effects of a comprehensive executive skill training program for school-aged children with ADHD in a relatively large sample.

METHODS: The children (aged 6-12 years) with ADHD were randomized to the intervention or waitlist groups. A healthy control group was composed of gender- and age-matched healthy children. The

intervention group received a 12-session training program for multiple executive skills. Executive function (EF), ADHD symptoms, and social functioning in the intervention and waitlist groups were evaluated at baseline and the end of the final training session. The healthy controls (HCs) were only assessed once at baseline. Repeated measures analyses of variance were used to compare EF, ADHD symptoms, and social function between intervention and waitlist groups.

RESULTS: Thirty-eight children with ADHD in intervention group, 30 in waitlist group, and 23 healthy children in healthy control group were included in final analysis. At posttreatment, intervention group showed significantly lower Behavior Rating Inventory of Executive Function (BRIEF) total score (135.89 ± 16.80 vs. 146.09 ± 23.92 , $P = 0.04$) and monitoring score (18.05 ± 2.67 vs. 19.77 ± 3.10 , $P = 0.02$), ADHD-IV overall score (41.11 ± 7.48 vs. 47.20 ± 8.47 , $P < 0.01$), hyperactivity-impulsivity (HI) subscale score (18.92 ± 5.09 vs. 21.93 ± 4.93 , $P = 0.02$), and inattentive subscale score (22.18 ± 3.56 vs. 25.27 ± 5.06 , $P < 0.01$), compared with the waitlist group. Repeated measures analyses of variance revealed significant interactions between time and group on the BRIEF inhibition subscale ($F = 5.06$, $P = 0.03$), working memory ($F = 4.48$, $P = 0.04$), ADHD-IV overall score ($F = 21.72$, $P < 0.01$), HI subscale score ($F = 19.08$, $P < 0.01$), and inattentive subscale score ($F = 12.40$, $P < 0.01$). Multiple-way analysis of variance showed significant differences on all variables of BRIEF, ADHD-rating scale-IV, and WEISS Functional Impairment Scale-Parent form (WFIRS-P) among the intervention and waitlist groups at posttreatment and HCs at baseline.

CONCLUSIONS: This randomized controlled study on executive skill training in a relatively large sample provided some evidences that the training could improve EF deficits, reduce problematic symptoms, and potentially enhance the social functioning in school-aged children with ADHD.

CLINICAL TRIAL REGISTRATION: <http://www.clinicaltrials.gov; NCT02327585>

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Clin EEG Neurosci. 2017;48:246-50.

MEDICATION EFFECTS ON EEG BIOMARKERS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Isiten HN, Cebi M, Sutcubasi KB, et al.

EEG biomarkers have become increasingly used to aid in diagnosis of attention-deficit/hyperactivity disorder (ADHD). Despite several studies suggesting that EEG theta/beta ratio may help discriminating ADHD from other disorders, the effect of medications on theta/beta ratio is not known. Forty-three children with ADHD that were evaluated with quantitative EEG before and after methylphenidate were included in the study. Theta/beta ratio, theta and beta powers for whole brain, central, and frontal areas were calculated. Theta/beta power decreased significantly after treatment; however, this change was largely due to an increase in beta power, rather than a fall in theta power. The results suggest that beta power is sensitive to medication effects, while theta power remains as a trait biomarker unaffected by medication status. The value of EEG biomarkers for monitoring neuropsychological performance and clinical status should be explored by future studies

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Clin EEG Neurosci. 2017;48:235-42.

AN INVESTIGATION OF STIMULANT EFFECTS ON THE EEG OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Clarke AR, Barry RJ, Baker IE, et al.

Stimulant medications are the most commonly prescribed treatment for Attention-Deficit/Hyperactivity Disorder (AD/HD). These medications result in a normalization of the EEG. However, past research has found that complete normalization of the EEG is not always achieved. One reason for this may be that studies have used different medications interchangeably, or groups of subjects on different stimulants. This study investigated whether methylphenidate and dexamphetamine produce different levels of normalization of the EEG in children with AD/HD. Three groups of 20 boys participated in this study. There were 2 groups with a diagnosis of AD/HD; one group, good responders to methylphenidate, and the second, good responders to dexamphetamine. The third group was a normal control group. Baseline EEGs were recorded using an eyes-closed resting condition, and analyzed for total power and relative delta, theta, alpha, and beta. Subjects were placed on a 6-month trial of methylphenidate or dexamphetamine, after which a second EEG was

recorded. At baseline, the children with AD/HD had elevated relative theta, less relative alpha and beta compared with controls. Baseline differences were found between the two medication groups, with the dexamphetamine group having greater EEG abnormalities than the methylphenidate group. The results indicate that good responders to methylphenidate and dexamphetamine have different EEG profiles when assessed before medication, and these differences may represent different underlying central nervous system deficits. The 2 medications were found to result in substantial normalization of the EEG, with no significant differences in EEG changes occurring between the 2 medications. This indicates that the degree of pretreatment EEG abnormality was the major factor contributing to the degree of normalization of the EEG. As good responders to the 2 medications appear to have different central nervous system abnormalities, it is recommended that stimulant medications be treated independently and not used interchangeably in research and treatment of AD/HD

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Clin Pediatr. 2017;56:729-36.

ADHD: INSURANCE AND MENTAL HEALTH SERVICE USE.

Pastor PN, Simon AE, Reuben CA.

We describe mental health service use by insurance among children aged 4 to 17 with diagnosed attention-deficit/ hyperactivity disorder (ADHD). Using parent reports from 2010-2013 National Health Interview Survey, we estimate the percentage that received services for emotional and behavioral difficulties (EBD): medication, other nonmedication services, and none (neither medication nor other nonmedication services). Among children with diagnosed ADHD, 56.0% had used medication for EBD, 39.8% had contact with a mental health professional, 32.2% had contact with a general doctor about the child's EBD, and 20.4% received special education services for EBD. Medication use was more often reported for privately or publicly insured children than uninsured children ($P < .001$), and uninsured children more often received no services ($P < .001$). Publicly insured children were more likely than privately insured children to receive other nonmedication services ($P < .001$). Less than a third (28.9%) of all children received no services as compared to almost half (48.8%) of uninsured children

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CMAJ. 2017;189:E755.

INCREASED RATE OF EARLY SMOKING IN CHILDREN AND ADOLESCENTS WITH ATTENTIONDEFICIT/HYPERACTIVITY DISORDER.

Jerome L.

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Compr Psychiatry. 2017;77:60-70.

NEUROCOGNITIVE CHARACTERISTICS OF YOUTH WITH NONCOMORBID AND COMORBID FORMS OF CONDUCT DISORDER AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Glenn AL, Rimmel RJ, Ong MY, et al.

OBJECTIVE: Studies investigating neurocognitive deficits in youth with conduct disorder (CD) and attention deficit hyperactivity disorder (ADHD) are often confounded by the high rates of comorbidity between the two.

METHOD: Neurocognitive functioning was examined in three diagnostic groups (ADHD only, CD only, comorbid ADHD and CD) matched by age, sex, IQ, and medication status ($n=28-32$ per group).

RESULTS: No significant differences emerged between the diagnostic groups on measures of risk-taking or response inhibition. Children with CD performed better on a measure of spatial planning than those with comorbid ADHD and CD, and dimensional analyses in the full sample ($n=265$) revealed a small association between ADHD symptoms and poorer spatial planning.

CONCLUSION: These results suggest that deficits in spatial planning may be more pronounced in individuals with ADHD, but that the neurocognitive functioning of youth with noncomorbid and comorbid CD and ADHD are largely similar

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Dev Med Child Neurol. 2017 Jun;59:581-90.

EVENT-RELATED POTENTIAL MEASURES OF EXECUTIVE FUNCTIONING FROM PRESCHOOL TO ADOLESCENCE.

Downes M, Bathelt J, De HM.

Executive functions are a collection of cognitive abilities necessary for behavioural control and regulation, and are important for school success. Executive deficits are common across acquired and developmental disorders in childhood and beyond. This review aims to summarize how studies using event-related potential (ERP) can provide insight into mechanisms underpinning how executive functions develop in children from preschool to adolescence. We specifically focus on ERP components that are considered to be well-established markers of executive functioning, including the ability to resist distraction (inhibition, N200), hold scenes in mind (visuospatial working memory, contralateral delay activity), attend to specific stimuli (information processing, P300), follow rules (response monitoring, error-related negativity [ERN], and error-related positivity [Pe]), and adjust to feedback (outcome monitoring, feedback-related negativity). All of these components show developmental changes from preschool to adolescence, in line with behavioural and neuroimaging findings. These ERP markers also show altered developmental trajectories in the context of atypical executive functions. As an example, deficits in executive function are prominently implicated in attention-deficit-hyperactivity disorder. Therefore, this review highlights ERP studies that have investigated the above ERP components in this population. Overall, ERPs provide a useful marker for the development and dysfunction of executive skills, and provide insight into their neurophysiological basis

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Dev Cognitive Neurosci. 2017;26:84-90.

CALLOUS-UNEMOTIONAL TRAITS MODERATE EXECUTIVE FUNCTION IN CHILDREN WITH ASD AND ADHD: A PILOT EVENT-RELATED POTENTIAL STUDY.

Tye C, Bedford R, Asherson P, et al.

Attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are associated with varied executive function (EF) difficulties. Callous-unemotional (CU) traits, a proposed antecedent of adult psychopathy, are often associated with intact or enhanced EF. Here we test whether CU traits may therefore modulate EF in ASD and ADHD, in which EF is typically impaired. We collected CU traits and measured event-related potentials (ERPs) that index EF during a cued-continuous performance test (CPT-OX) in boys with ASD, ADHD, comorbid ASD-á+-áADHD and typical controls. We examined attentional orienting at cues (Cue-P3), inhibitory processing at non-targets (NoGo-P3) and conflict monitoring between target and non-target trials (Go-N2 vs. NoGo-N2). In children with ASD, higher CU traits were associated with an enhanced increase in N2 amplitude in NoGo trials compared to Go trials, which suggests relatively superior conflict monitoring and a potential cognitive strength associated with CU traits. The results emphasise the importance of considering the effects of co-occurring traits in the assessment of heterogeneity of EF profiles in neurodevelopmental disorders

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Dev Neurorehabilitation. 2017;1-10.

PREDICTIVE FACTORS OF SUCCESS IN NEUROFEEDBACK TRAINING FOR CHILDREN WITH ADHD.

Okumura Y, Kita Y, Omori M, et al.

Introduction: Neurofeedback (NF) training aims the enhancement of self-regulation over brain activities. While it is largely recognized as an effective treatment for attention deficit hyperactivity disorder (ADHD), the existence of non-learners has also been reported. The present study explored pre-training assessment indices that could predict learners prior to NF training.

Methods: Twenty-two children with ADHD participated in slow cortical potential (SCP) NF training and completed pre- and post-training assessments. Participants were classified into learners or non-learners based on their progress in the SCP regulation, and pre-training indices that differentiate the two groups were examined by decision tree analysis.

Results and Discussion: The learner rate in NF training was 45.5%. Learners were predicted by pre-training cognitive and neurophysiological measures regarding Stroop tasks, which suggested relatively intact executive function as their characteristics. Given that NF training is not universally effective for children with ADHD, further studies are necessary to establish application criteria

Environmental Pollution. 2017;229:375-85.

ASSOCIATIONS OF PHTHALATES EXPOSURE WITH ATTENTION DEFICITS HYPERACTIVITY DISORDER: A CASE-CONTROL STUDY AMONG CHINESE CHILDREN.

Hu D, Wang Y-X, Chen W-J, et al.

Researches on associations between phthalates exposure and child attention deficit hyperactivity disorder (ADHD) are inconsistent. This study aimed to evaluate the associations of urinary phthalates with ADHD, co-occurring oppositional defiant disorder (ODD), related symptoms and behavior problems among Chinese children. We enrolled 225 ADHD cases and 225 healthy controls aged 6-13 years old in Liuzhou, China. Each child provided repeated urine samples at 4 visits. Eight phthalate metabolites were measured by high-performance liquid chromatography and tandem mass spectrometry. Child ADHD symptoms and related behaviors were assessed using Swanson, Nolan, and Pelham Version IV scale and child behavior checklist. Higher urinary concentrations of mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono-(2-ethyl)-hexyl phthalate (MEHP) were dose-dependently associated with ADHD [odds ratios (ORs) ranged from 2.35 to 3.04 for the highest vs. the lowest tertile] and co-occurring ODD (ORs ranged from 3.27 to 4.44 for the highest vs. the lowest tertile) in the multivariable logistic regression models (all p for trend ≤ 0.01), which were consistent with positive trends of increased scores of inattention domain, hyperactive domain and ODD symptoms (all p for trend ≤ 0.01). Besides, the monomethyl phthalate (MMP) concentration was associated with higher scores of inattention domain and ODD symptoms (both $p < 0.05$). Additionally, the MEHHP, MEOHP and MEHP concentrations were related to child attention problems, aggressive behaviors and externalizing behaviors (all $p < 0.05$). We also observed positive associations of the MEHP concentration with depressed behaviors and internalizing behaviors (all $p < 0.05$). Our results indicate that child exposure to phthalates may contribute to ADHD, ODD and externalizing and internalizing behavior problems

Eur Arch Psychiatry Clin Neurosci. 2017;1-9.

ADHD MODULATES THE COURSE OF DELINQUENCY: A 15-YEAR FOLLOW-UP STUDY OF YOUNG INCARCERATED MEN.

Philipp-Wiegmann F, et al.

There is growing evidence of an association between ADHD and rule-breaking behaviour and that subjects with ADHD are more likely to be involved in the legal system. However, the research on ADHD as a risk factor not only for delinquency but also for recidivism is scarce and findings are controversial. Therefore, we explored the impact of ADHD on the course of delinquency in a sample of incarcerated young men. We conducted a 15-year follow-up study by investigating the criminal records of 106 former youth prisoners. Criminal recidivism was operationalized through three variables: criminal recidivism; frequency of recidivism; and time to recidivism. The incremental predictive validity of ADHD was analysed using survival analysis and controlled for confounders associated with recidivism. Offenders with ADHD ($n = 74$) reoffended 2.5 times faster and showed a higher rate of recidivism and further incarcerations compared to non-ADHD offenders ($n = 33$), even when controlling for general risk factors such as antisocial personality disorder. Median survival rate ranged between 6 and 7 months in the ADHD groups and 25 months in the non-ADHD group. Our results revealed that ADHD has an incremental predictive power on criminal recidivism, even above general risk factors. Moreover, the criminogenic influence of ADHD appeared to be crucial in terms of the interplay of

childhood ADHD, irrespectively of the persistence of the symptomatology into later life. Our findings therefore highlight the importance of early intervention and consequently prevention

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Eur Child Adolesc Psychiatry. 2017;1-19.

SYSTEMATIC REVIEW OF MEDITATION-BASED INTERVENTIONS FOR CHILDREN WITH ADHD.

Evans S, Ling M, Hill B, et al.

Meditation-based interventions such as mindfulness and yoga are commonly practiced in the general community to improve mental and physical health. Parents, teachers and healthcare providers are also increasingly using such interventions with children. This review examines the use of meditation-based interventions in the treatment of children with Attention-Deficit Hyperactivity Disorder (ADHD). Electronic databases searched included PsycINFO, Medline, CINAHL, and AMED. Inclusion criteria involved children (aged to 18 years) diagnosed with ADHD, delivery of a meditation-based intervention to children and/or parents, and publication in a peer-reviewed journal. Studies were identified and coded using standard criteria, risk of bias was assessed using Risk of Bias in Non-randomised Studies- of interventions (ROBINS-I), and effect sizes were calculated. A total of 16 studies were identified (8 that included children in treatment, and 8 that included combined parent-child treatment). Results indicated that risk of bias was high across studies. At this stage, no definitive conclusions can be offered regarding the utility of meditation-based interventions for children with ADHD and/or their parents, since the methodological quality of the studies reviewed is low. Future well designed research is needed to establish the efficacy of meditation-based interventions, including commonly used practices such as mindfulness, before recommendations can be made for children with ADHD and their families

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Eur Child Adolesc Psychiatry. 2017;1-7.

PRESCRIBING OF MEDICATION FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG YOUNG PEOPLE IN THE CLINICAL PRACTICE RESEARCH DATALINK 2005-2013: ANALYSIS OF TIME TO CESSATION.

Newlove-Delgado T, Ford TJ, Hamilton W, et al.

The aim of this study was to examine the time to cessation of ADHD medication amongst young people with ADHD aged 16 in the period 2005-2013. Previous studies of prescribing in primary care reported high rates of medication cessation amongst 16 and 17 year olds with ADHD. The examination of trends since the introduction of new NICE guidance in 2008 will support service planning and improvement of outcomes over the vulnerable transition period from child to adult services. We used primary care records from the Clinical Practice Research Datalink and identified cases prescribed ADHD medication at the time of their 16th birthday during the study period. The outcome was time to medication cessation from the age of 16. Cessation of medication was defined as occurring at the beginning of a gap of over 6 months in prescriptions. 1620 cases were included. The median time to cessation was 1.51 years (95% CI 1.42-1.67). The estimated probability of remaining on medication was 0.63 (95% CI 0.61-0.65) at age 17 (i.e., at 1 year) and 0.41 (95% CI 0.39-0.43) at age 18. Young people with ADHD remain at high risk of cessation of medication during the transition from child to adult services. Despite the restriction that only primary care prescribing data were available, the results suggest continuing disparity between expected levels of symptom persistence and continuation of medication

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Eur Child Adolesc Psychiatry. 2017;1-12.

ALTERED EEG SPECTRAL POWER DURING REST AND COGNITIVE PERFORMANCE: A COMPARISON OF PRETERM-BORN ADOLESCENTS TO ADOLESCENTS WITH ADHD.

Rommel A-S, James S-N, McLoughlin G, et al.

Preterm birth has been associated with an increased risk for ADHD-like behavioural symptoms and cognitive impairments. However, direct comparisons across ADHD and preterm-born samples on neurophysiological

measures are limited. The aim of this analysis was to test whether quantitative EEG (QEEG) measures identify differences or similarities in preterm-born adolescents, compared to term-born adolescents with and without ADHD, during resting-state and cognitive task conditions. We directly compared QEEG activity between 186 preterm-born adolescents, 69 term-born adolescents with ADHD and 135 term-born control adolescents during an eyes-open resting-state condition (EO), which previously discriminated between the adolescents with ADHD and controls, and during a cued continuous performance task (CPT-OX). Absolute delta power was the only frequency range to demonstrate a significant group-by-condition interaction. The preterm group, like the ADHD group, displayed significantly higher delta power during EO, compared to the control group. In line with these findings, parent-rated ADHD symptoms in the preterm group were significantly correlated with delta power during rest. While the preterm and control groups did not differ with regard to absolute delta power during CPT-OX, the ADHD group showed significantly higher absolute delta power compared to both groups. Our results provide evidence for overlapping excess in the absolute delta range in preterm-born adolescents and term-born adolescents with ADHD during rest. During CPT-OX, preterm-born adolescents resembled controls. Increased delta power during rest may be a potential general marker of brain trauma, pathology or neurotransmitter disturbances

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FASEB J. 2017;31.

BLOOD LEAD, IRON DEFICIENCY AND ATTENTIONAL ADHD SYMPTOMS IN URUGUAYAN FIRSTGRADERS.

Barg G, Queirolo El, Ma+lay N, et al.

The combined effect of iron deficiency and lead exposure on attentional ADHD symptoms is not well studied. We investigated the associations among blood lead level (BLL), iron deficiency (ID, serum ferritin <15 ++g/L) and inattention/cognitive problems (I/CP-measured by the Conners Teacher Rating Scale) in a cross-sectional study of first-grade children (n=257, age 6.7-!0.5 years, 55.6% boys) from Montevideo, Uruguay. Aspects of children's attention (ex., attention shifting) were measured by teacher reports on the BRIEF questionnaire. Generalized linear models (GLM) accounting for the school-based cluster design and adjusting for maternal education and employment, parental smoking, household crowding and SES, as well as child's general intelligence and attention problems were used to model the association of BLL and ID with I/CP scores. Mean of BLL was 4.19-!2.2 ++g/dL, 39% of children had ID and 25% had mild to severe inattention problems (I/CP > 60 T score). BLL and serum ferritin were not independently associated with I/CP. However, in children with ID, BLL was associated with more problematic I/CP scores (0.32-!0.14, p=0.026). This was not observed among non-ID children (0.09 -!0.08, p=0.239). General intelligence and maternal education were protective factors against I/CP (both at p<0.000). The ability to shift attention, commonly beneficial for cognitive performance, was negatively associated with I/CP in children with ID, presumably by ID's negative effect on the ability to control the attentional focus. In sum, our early findings suggest an adverse effect of the combination of ID and higher BLLs on sustained attention, a key competence for learning and socialization

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Forensische Psychiatrie, Psychologie, Kriminologie. 2017 May;11:96-102.

ATTENTION DEFICIT HYPERACTIVITY DISORDER - RISK OF DELINQUENCY IN ADOLESCENCE AND ADULTHOOD?

Just M, Kaiser A, Retz W, et al.

Attention deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder with childhood onset and a prevalence rate of 5%. The ADHD has a complex, heterogeneous etiology with a high genetic component and numerous neurobiological alterations. Furthermore, up to 75% of ADHD patients develop comorbid disorders, which make the diagnosis as well as the therapy difficult and worsens the prognosis of the course of the disorder. In a complex multifactorial interplay childhood ADHD is one potential risk factor for delinquent and antisocial behavior in adolescence and early adulthood. Pharmacotherapy of ADHD can significantly reduce this risk for delinquent behavior but is just one aspect in the therapy of ADHD, which is based on

psychoeducation and an individual combination of cognitive behavioral therapy and medication for the treatment of the core symptoms of ADHD and associated psychiatric disorders.

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Front Human Neurosci. 2017 May;11.

AGE-RELATED CHANGES IN RESTING-STATE EEG ACTIVITY IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A CROSS-SECTIONAL STUDY.

Giertuga K, Zakrzewska MZ, Bielecki M, et al.

Numerous studies indicate that attention deficit/hyperactivity disorder (ADHD) is related to some developmental trends, as its symptoms change widely over time. Nevertheless, the etiology of this phenomenon remains ambiguous. There is a disagreement whether ADHD is related to deviations in brain development or to a delay in brain maturation. The model of deviated brain development suggests that the ADHD brain matures in a fundamentally different way, and does not reach normal maturity at any developmental stage. On the contrary, the delayed brain maturation model assumes that the ADHD brain indeed matures in a different, delayed way in comparison to healthy age-matched controls, yet eventually reaches proper maturation. We investigated age-related changes in resting-state EEG activity to find evidence to support one of the alternative models. A total of 141 children and teenagers participated in the study; 67 diagnosed with ADHD and 74 healthy controls. The absolute power of delta, theta, alpha, and beta frequency bands was analyzed. We observed a significant developmental pattern of decreasing absolute EEG power in both groups. Nonetheless, ADHD was characterized by consistently lower absolute EEG power, mostly in the theta frequency band, in comparison to healthy controls. Our results are in line with the deviant brain maturation theory of ADHD, as the observed effects of age-related changes in EEG power are parallel but different in the two groups

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Indian Pediatr. 2017;54:481-88.

CONSENSUS STATEMENT OF THE INDIAN ACADEMY OF PEDIATRICS ON EVALUATION AND MANAGEMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Dalwai S, Unni J, Kalra V, et al.

Justification: Attention-Deficit/Hyperactivity Disorder (ADHD) is highly prevalent in children worldwide. Management of ADHD requires a systematic, multidisciplinary approach and therefore evidence-based, standardized national guidelines are essential.

Process: A meeting for formulation of national consensus guidelines on neurodevelopmental disorders was organized by Indian Academy of Pediatrics in Mumbai, on 18th and 19th December, 2015. The invited experts included Pediatricians, Developmental Pediatricians, Pediatric Neurologists, Psychiatrists, Remedial Educators and Clinical Psychologists. The participants framed guidelines after extensive discussions.

Objective: To provide consensus guidelines on evaluation and management of ADHD in children in India.

Recommendations: ADHD is a chronic condition and thus education of patients, families, and teachers regarding the diagnosis is an integral part of management. Involvement of patient the and the family in the management program is extremely vital. Management of ADHD centers on the achievement of target outcomes, which are chosen in collaboration with the child, parents, and school personnel. Coexisting conditions must be treated concurrently with ADHD. Modalities of management of ADHD include behavioral interventions, medications, and educational interventions. These modalities can be implemented individually or in combination

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Int J Psychophysiol. 2017 Jun;116:32-44.

GAME-BASED COMBINED COGNITIVE AND NEUROFEEDBACK TRAINING USING FOCUS POCUS REDUCES SYMPTOM SEVERITY IN CHILDREN WITH DIAGNOSED AD/HD AND SUBCLINICAL AD/HD.

Johnstone SJ, Roodenrys SJ, Johnson K, et al.

Previous studies report reductions in symptom severity after combined working memory (WM) and inhibitory control (IC) training in children with AD/HD. Based on theoretical accounts of the role of arousal/attention modulation problems in AD/HD, the current study examined the efficacy of combined WM, IC, and neurofeedback training in children with AD/HD and subclinical AD/HD. Using a randomized waitlist control design, 85 children were randomly allocated to a training or waitlist condition and completed pre- and post-training assessments of overt behavior, trained and untrained cognitive task performance, and resting and task-related EEG activity. The training group completed twenty-five sessions of training using Focus Pocus software at home over a 7 to 8-week period. Trainees improved at the trained tasks, while enjoyment and engagement declined across sessions. After training, AD/HD symptom severity was reduced in the AD/HD and subclinical groups according to parents, and in the former group only according to blinded teachers and significant-others. There were minor improvements in two of six near-transfer tasks, and evidence of far-transfer of training effects in four of five far-transfer tasks. Frontal region changes indicated normalization of atypical EEG features with reduced delta and increased alpha activity. It is concluded that technology developments provide an interesting a vehicle for delivering interventions and that, while further research is needed, combined WM, IC, and neurofeedback training can reduce AD/HD symptom severity in children with AD/HD and may also be beneficial to children with subclinical AD/HD

J Adolesc. 2017 Apr;56:52-63.

COGNITIVE AND BEHAVIOURAL PREDICTORS OF ADOLESCENTS' COMMUNICATIVE PERSPECTIVE-TAKING AND SOCIAL RELATIONSHIPS.

Nilsen ES, Bacso SA.

Given the pivotal role that social interactions play for adolescents' well-being, understanding the factors that influence communication is key. The present study examined relations between adolescents' communicative perspective-taking, executive function skills, and ADHD traits and explored the role communicative perspective-taking plays in peer relations. Data was collected from a community sample of 15 to 19-years-olds (N = 46) in Waterloo, Canada. Two communicative perspective-taking tasks required participants to infer speakers' communicative intentions. A battery of tasks assessed adolescents' working memory and inhibitory control. Elevated ADHD traits were associated with weaker working memory, inhibitory control, and communicative perspective-taking. Working memory was the strongest predictor of communicative perspective-taking. Highlighting the importance of communicative perspective-taking for social interactions, adolescents with weaker skills in this area reported worse peer relations. Findings underscore the importance of communicative perspective-taking for adolescents' social relations and have relevance for understanding the social difficulties faced by adolescents with elevated ADHD traits

JAMA. 2017 Apr;317:1553-62.

ASSOCIATIONS OF MATERNAL ANTIDEPRESSANT USE DURING THE FIRST TRIMESTER OF PREGNANCY WITH PRETERM BIRTH, SMALL FOR GESTATIONAL AGE, AUTISM SPECTRUM DISORDER, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN OFFSPRING.

Sujan AC, Rickert ME, Oberg AS, et al.

Importance: Prenatal antidepressant exposure has been associated with adverse outcomes. Previous studies, however, may not have adequately accounted for confounding.

Objective: To evaluate alternative hypotheses for associations between first-trimester antidepressant exposure and birth and neurodevelopmental problems.

Design, Setting, and Participants: This retrospective cohort study included Swedish offspring born between 1996 and 2012 and followed up through 2013 or censored by death or emigration. Analyses controlling for

pregnancy, maternal and paternal covariates, as well as sibling comparisons, timing of exposure comparisons, and paternal comparisons, were used to examine the associations.

Exposures: Maternal self-reported first-trimester antidepressant use and first-trimester antidepressant dispensations.

Main Outcomes and Measures: Preterm birth (<37 gestational weeks), small for gestational age (birth weight <2 SDs below the mean for gestational age), and first inpatient or outpatient clinical diagnosis of autism spectrum disorder and attention-deficit/hyperactivity disorder in offspring.

Results: Among 1580629 offspring (mean gestational age, 279 days; 48.6% female; 1.4% [n = 22544] with maternal first-trimester self-reported antidepressant use) born to 943776 mothers (mean age at childbirth, 30 years), 6.98% of exposed vs 4.78% of unexposed offspring were preterm, 2.54% of exposed vs 2.19% of unexposed were small for gestational age, 5.28% of exposed vs 2.14% of unexposed were diagnosed with autism spectrum disorder by age 15 years, and 12.63% of exposed vs 5.46% of unexposed were diagnosed with attention-deficit/hyperactivity disorder by age 15 years. At the population level, first-trimester exposure was associated with all outcomes compared with unexposed offspring (preterm birth odds ratio [OR], 1.47 [95% CI, 1.40-1.55]; small for gestational age OR, 1.15 [95% CI, 1.06-1.25]; autism spectrum disorder hazard ratio [HR], 2.02 [95% CI, 1.80-2.26]; attention-deficit/hyperactivity disorder HR, 2.21 [95% CI, 2.04-2.39]). However, in models that compared siblings while adjusting for pregnancy, maternal, and paternal traits, first-trimester antidepressant exposure was associated with preterm birth (OR, 1.34 [95% CI, 1.18-1.52]) but not with small for gestational age (OR, 1.01 [95% CI, 0.81-1.25]), autism spectrum disorder (HR, 0.83 [95% CI, 0.62-1.13]), or attention-deficit/hyperactivity disorder (HR, 0.99 [95% CI, 0.79-1.25]). Results from analyses assessing associations with maternal dispensations before pregnancy and with paternal first-trimester dispensations were consistent with findings from the sibling comparisons.

Conclusions and Relevance: Among offspring born in Sweden, after accounting for confounding factors, first-trimester exposure to antidepressants, compared with no exposure, was associated with a small increased risk of preterm birth but no increased risk of small for gestational age, autism spectrum disorder, or attention-deficit/hyperactivity disorder

JAMA Psychiatry. 2017 May;74:520-26.

THE WORLD HEALTH ORGANIZATION ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SELF-REPORT SCREENING SCALE FOR DSM-5.

Ustun B, Adler LA, Rudin C, et al.

Importance: Recognition that adult attention-deficit/hyperactivity disorder (ADHD) is common, seriously impairing, and usually undiagnosed has led to the development of adult ADHD screening scales for use in community, workplace, and primary care settings. However, these scales are all calibrated to DSM-IV criteria, which are narrower than the recently developed DSM-5 criteria.

Objectives: To update for DSM-5 criteria and improve the operating characteristics of the widely used World Health Organization Adult ADHD Self-Report Scale (ASRS) for screening.

Design, Setting, and Participants: Probability subsamples of participants in 2 general population surveys (2001-2003 household survey [n = 119] and 2004-2005 managed care subscriber survey [n = 218]) who completed the full 29-question self-report ASRS, with both subsamples over-sampling ASRS-screened positives, were blindly administered a semistructured research diagnostic interview for DSM-5 adult ADHD. In 2016, the Risk-Calibrated Supersparse Linear Integer Model, a novel machine-learning algorithm designed to create screening scales with optimal integer weights and limited numbers of screening questions, was applied to the pooled data to create a DSM-5 version of the ASRS screening scale. The accuracy of the new scale was then confirmed in an independent 2011-2012 clinical sample of patients seeking evaluation at the New York University Langone Medical Center Adult ADHD Program (NYU Langone) and 2015-2016 primary care controls (n = 300). Data analysis was conducted from April 4, 2016, to September 22, 2016.

Main Outcomes and Measures: The sensitivity, specificity, area under the curve (AUC), and positive predictive value (PPV) of the revised ASRS.

Results: Of the total 637 participants, 44 (37.0%) household survey respondents, 51 (23.4%) managed care respondents, and 173 (57.7%) NYU Langone respondents met DSM-5 criteria for adult ADHD in the semistructured diagnostic interview. Of the respondents who met DSM-5 criteria for adult ADHD, 123 were

male (45.9%); mean (SD) age was 33.1 (11.4) years. A 6-question screening scale was found to be optimal in distinguishing cases from noncases in the first 2 samples. Operating characteristics were excellent at the diagnostic threshold in the weighted (to the 8.2% DSM-5/Adult ADHD Clinical Diagnostic Scale population prevalence) data (sensitivity, 91.4%; specificity, 96.0%; AUC, 0.94; PPV, 67.3%). Operating characteristics were similar despite a much higher prevalence (57.7%) when the scale was applied to the NYU Langone clinical sample (sensitivity, 91.9%; specificity, 74.0%; AUC, 0.83; PPV, 82.8%).

Conclusions and Relevance: The new ADHD screening scale is short, easily scored, detects the vast majority of general population cases at a threshold that also has high specificity and PPV, and could be used as a screening tool in specialty treatment settings

J Affective Disord. 2017;221:246-53.

BORDERLINE PERSONALITY AND ATTENTION-DEFICIT HYPERACTIVITY TRAITS IN CHILDHOOD ARE ASSOCIATED WITH HYPOMANIC FEATURES IN EARLY ADULTHOOD.

Mistry S, Zammit S, Price V-E, et al.

Background There is limited understanding of the symptomatic development of bipolar disorder from childhood to early adulthood. **Aims** We assessed whether borderline personality disorder traits, ADHD, and emotional, behavioural and social difficulties during childhood were associated with hypomania assessed in young adulthood.

Method We used data from the Avon Longitudinal Study of Parents and Children (ALSPAC), to examine associations between measures of childhood psychopathology and lifetime hypomanic features assessed at age 22–23 years using the Hypomania Checklist-32 (HCL-32; n = 3372). We also conducted a factor analysis of the HCL to identify latent constructs underlying hypomania, and the extent to which childhood psychopathology was associated with these.

Results We identified two factors of the HCL corresponding to energy/mood and risk-taking/irritability. There was evidence of association between childhood borderline personality disorder traits and both hypomania factors, with evidence that the association was stronger with the risk-taking/irritability factor. All individual borderline traits, with the exception of fear of abandonment, were associated with hypomania. There was also evidence of association between most other measures of childhood psychopathology (ADHD, hyperactivity, conduct problems, peer relationship problems and reduced prosocial behaviour) and the risk-taking/irritability factor, but much less consistent evidence of association with the energy/mood factor. **Limitations** The HCL cannot diagnose bipolar disorder and may be subject to reporting bias.

Conclusions A broad range of childhood psychopathologies may represent early markers of risk for hypomania. Further studies are required to understand the mechanisms underlying these associations, and to inform earlier detection of bipolar disorder

J Autism Dev Disord. 2017 Jun;47:1595-604.

A CAUSAL AND MEDIATION ANALYSIS OF THE COMORBIDITY BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AND AUTISM SPECTRUM DISORDER (ASD).

Sokolova E, Oerlemans AM, Rommelse NN, et al.

Autism spectrum disorder (ASD) and Attention-deficit/hyperactivity disorder (ADHD) are often comorbid. The purpose of this study is to explore the relationships between ASD and ADHD symptoms by applying causal modeling. We used a large phenotypic data set of 417 children with ASD and/or ADHD, 562 affected and unaffected siblings, and 414 controls, to infer a structural equation model using a causal discovery algorithm. Three distinct pathways between ASD and ADHD were identified: (1) from impulsivity to difficulties with understanding social information, (2) from hyperactivity to stereotypic, repetitive behavior, (3) a pairwise pathway between inattention, difficulties with understanding social information, and verbal IQ. These findings

may inform future studies on understanding the pathophysiological mechanisms behind the overlap between ASD and ADHD

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J Autism Dev Disord. 2017;1-9.

THE STABILITY OF SELF-REPORTED ANXIETY IN YOUTH WITH AUTISM VERSUS ADHD OR TYPICAL DEVELOPMENT.

Schiltz H, McIntyre N, Swain-Lerro L, et al.

Children with autism spectrum disorder (ASD) are at risk for anxiety symptoms. Few anxiety measures are validated for individuals with ASD, and the nature of ASD raises questions about reliability of self-reported anxiety. This study examined longitudinal stability and change of self-reported anxiety in higher functioning youth with ASD (HFASD) compared to youth with symptoms of attention deficit hyperactivity disorder and typical development (TD) using the Multidimensional Anxiety Scale for Children (March, 2012; March et al. J Am Acad Child Adolesc Psychiatry 36(4):554-565, 1997). Diagnostic groups demonstrated comparable evidence of stability for most dimensions of anxiety. The HFASD group displayed higher anxiety than both comparison groups, especially physical symptoms. These findings have implications for identification and measurement of anxiety in ASD

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J Autism Dev Disord. 2017;1-23.

THE SCOPE AND NATURE OF READING COMPREHENSION IMPAIRMENTS IN SCHOOL-AGED CHILDREN WITH HIGHER-FUNCTIONING AUTISM SPECTRUM DISORDER.

McIntyre NS, Solari EJ, Gonzales JE, et al.

This study of 8-16-year-olds was designed to test the hypothesis that reading comprehension impairments are part of the social communication phenotype for many higher-functioning students with autism spectrum disorder (HFASD). Students with HFASD (n = 81) were compared to those with high attention-deficit/hyperactivity disorder symptomatology (ADHD; n = 39), or typical development (TD; n = 44), on a comprehensive battery of oral language, word recognition, and reading comprehension measures. Results indicated that students with HFASD performed significantly lower on the majority of the reading and language tasks as compared to TD and ADHD groups. Structural equation models suggested that greater ASD symptomatology was related to poorer reading comprehension outcomes; further analyses suggested that this relation was mediated by oral language skills

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J Child Adolesc Psychopharmacol. 2017;27:429-32.

THE POSSIBLE EFFECT OF METHYLPHENIDATE TREATMENT ON EMPATHY IN CHILDREN DIAGNOSED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, BOTH WITH AND WITHOUT COMORBID OPPOSITIONAL DEFIANT DISORDER.

Golubchik P, Weizman A.

Objective: To assess the Empathizing Quotient (EQ) of patients diagnosed with attention-deficit/hyperactivity disorder (ADHD) only or comorbid with oppositional defiant disorder (ODD) and compare the two groups' responses to methylphenidate (MPH) treatment.

Methods: Fifty-two children (8-18 years) diagnosed with ADHD, 26 of whom were also diagnosed with comorbid ODD (ADHD/ODD), were treated with MPH for 12 weeks. The level of EQ was assessed with the Children's version of the Empathizing Quotient (EQ-C) and the severity of ADHD symptoms with the ADHD Rating Scale (ADHD-RS). Assessments were done at baseline and at end point.

Results: A significant increase in EQ scores was obtained in both groups following MPH treatment (p = 0.003 for ADHD/ODD; p = 0.002 for ADHD). Significant correlation was found in the ADHD group between the changes in ADHD-RS and those in EQ, following MPH treatment (p = 0.015), but not in the ADHD/ODD group (p = 0.48).

Conclusions: A correlation exists between MPH-related improvement in ADHD symptoms and between more empathy in children with ADHD not comorbid with ODD

J Child Adolesc Psychopharmacol. 2017 Apr;27:285-88.

LITHIUM AND HEART BLOCK IN AN ADOLESCENT BOY.

Anon

Presents the case study of a 14-year-old boy, the youngest of three children, referred for medication management of bipolar I disorder and attention-deficit/hyperactivity disorder (ADHD), combined type. B. was referred for increasing agitation, manic symptoms, and violent behavior who developed AV heart block in the context of lithium treatment

J Child Adolesc Psychopharmacol. 2017;27:433-39.

EMPATHY AND FACIAL EXPRESSION RECOGNITION IN CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: EFFECTS OF STIMULANT MEDICATION ON EMPATHIC SKILLS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Gumustas F, Yilmaz I, Yulaf Y, et al.

OBJECTIVE: The aim of this study was to compare children and adolescents with attention-deficit/hyperactivity disorder (ADHD) to healthy children and adolescents in terms of state and trait empathy and emotion expression recognition skills. The goal was also to determine whether there are changes in emotion recognition and empathy measures in children with ADHD after methylphenidate (MPH) treatment.

METHODS: The research sample consisted of outpatient drug-naïve children and adolescents between the age of 8 and 14 years (n = 65) with ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. criteria, and healthy children and adolescents of the same age (n = 61). Scores of the oppositional problems (OPs) and conduct problems (CPs) were obtained to evaluate their impact on children's empathy skills with the Child Behavior Checklist. Self-reported (Bryant Index of Empathy, BEI) and parent-reported (Griffith Empathy Measurement-Parent Rating, GEM-PR) scales were used to evaluate trait empathy. The Empathy Response Task (ERT) was used to evaluate state empathy, and the Diagnostic Analysis of Nonverbal Accuracy-2 (DANVA-2) was used to evaluate facial expression recognition skills. The scales and tests were repeated after 12 weeks of MPH treatment in the ADHD group.

RESULTS: There were no significant statistical differences in trait empathy skills evaluated by parent-reported and self-reported measures, ERT, and DANVA-2 scores. In self-reported measures, the girls had higher scores than boys. From the results of the regression analysis, it was concluded that OPs were not associated with the measures. However, CPs were associated with the scores of the BEI, GEM-PR, and the match scores of the ERT. The average dosage of MPH in the group with ADHD was 0.83 ± 0.21 mg/(kg·d). While there was no change in the BEI and GEM-PR scores after 12 weeks of treatment, there was a significant increase in the ERT interpretation subscore and a significant decrease in the recognition error of anger and sadness expressions in the DANVA-2.

CONCLUSIONS: The findings of our study suggest that children with ADHD have similar levels of trait and state empathy skills and facial expressions as healthy controls and CPs negatively affect their empathy skills. MPH treatment does not change trait empathy skills, yet there are some improvements in state empathy skills

J Child Psychol Psychiatry. 2017 Jun;58:655-62.

DEFINING ADHD SYMPTOM PERSISTENCE IN ADULTHOOD: OPTIMIZING SENSITIVITY AND SPECIFICITY.

Sibley MH, Swanson JM, Arnold LE, et al.

Objective: Longitudinal studies of children diagnosed with ADHD report widely ranging ADHD persistence rates in adulthood (5–75%). This study documents how information source (parent vs. self-report), method

(rating scale vs. interview), and symptom threshold (DSM vs. norm-based) influence reported ADHD persistence rates in adulthood.

Method: Five hundred seventy-nine children were diagnosed with DSM-IV ADHD-Combined Type at baseline (ages 7.0–9.9 years) 289 classmates served as a local normative comparison group (LNCG), 476 and 241 of whom respectively were evaluated in adulthood (Mean Age = 24.7). Parent and self-reports of symptoms and impairment on rating scales and structured interviews were used to investigate ADHD persistence in adulthood.

Results: Persistence rates were higher when using parent rather than self-reports, structured interviews rather than rating scales (for self-report but not parent report), and a norm-based (NB) threshold of 4 symptoms rather than DSM criteria. Receiver-Operating Characteristics (ROC) analyses revealed that sensitivity and specificity were optimized by combining parent and self-reports on a rating scale and applying a NB threshold.

Conclusion: The interview format optimizes young adult self-reporting when parent reports are not available. However, the combination of parent and self-reports from rating scales, using an ‘or’ rule and a NB threshold optimized the balance between sensitivity and specificity. With this definition, 60% of the ADHD group demonstrated symptom persistence and 41% met both symptom and impairment criteria in adulthood

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J Child Psychol Psychiatry. 2017 Jun;58:682-90.

TELEPHONE-ASSISTED SELF-HELP FOR PARENTS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WHO HAVE RESIDUAL FUNCTIONAL IMPAIRMENT DESPITE METHYLPHENIDATE TREATMENT: A RANDOMIZED CONTROLLED TRIAL.

Dose C, Hautmann C, Buerger M, et al.

Background: Self-help parenting interventions have been shown to be effective in the management of children with attention-deficit/hyperactivity disorder (ADHD) and may be useful when there are barriers to face-to-face therapist-led parent trainings. Previous studies indicate that behavioral interventions might be a useful adjunct to medication in children with residual ADHD symptoms, and regarding comorbid oppositional symptoms and multiple domains of functional impairment. In the present study, we examined whether a telephone-assisted self-help (TASH) parenting behavioral intervention (written materials plus telephone counseling) enhanced the effects of methylphenidate treatment in children with ADHD.

Methods: In this randomized controlled trial, parents of 103 school-aged children with ADHD and residual functional impairment despite methylphenidate treatment were randomly assigned to either the enhancement group, which received the TASH intervention as adjunct to routine clinical care (including continued medication), or to the active control group, which received routine clinical care only (including continued medication). Parent-completed outcome measures at baseline and at 12 months (postassessment) included functional impairment, ADHD symptoms, oppositional defiant disorder (ODD) symptoms, parenting behavior, and parental satisfaction with the intervention (ClinicalTrials.gov: NCT01660425; URL: <https://clinicaltrials.gov/ct2/show/NCT01660425>).

Results: Intention-to-treat analyses of covariance (ANCOVAs), which controlled for baseline data, revealed significant and moderate intervention effects for ODD symptoms and negative parenting behavior at the postassessment, whereas per-protocol analyses additionally showed significant and moderate effects on functional impairment (primary outcome). Parents expressed high satisfaction with the program.

Conclusions: The TASH program enhances effects of methylphenidate treatment in families who complete the intervention. The discontinuation rate of about 30% and comparison between completing and discontinuing families suggest that the program may be more suitable for families with a higher educational level and fewer additional stresses

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J Child Psychol Psychiatry. 2017 Jun;58:640-54.

RESEARCH REVIEW: LANGUAGE PROBLEMS IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER—A SYSTEMATIC META-ANALYTIC REVIEW.

Korrel H, Mueller KL, Silk T, et al.

Background: Children with Attention-Deficit Hyperactivity Disorder (ADHD) appear to have a higher risk of language problems compared with typically developing children, although the types of language problems experienced are less clear. This review aims to establish the types of language problems experienced by children with ADHD according to systematically reviewed literature and determine the empirical evidence for language problems in children with ADHD compared with non-ADHD controls.

Methods: A standardized search protocol was used on databases: CINAHL, Medline, and PsychINFO. We identified studies with the following inclusion criteria: (a) confirmed ADHD status at the time of the study, (b) inclusion of a non-ADHD control group, (c) use of a validated language measure, and (d) age = 18. t-Tests, Pearson's r, and Hedges g effect sizes (ES) were calculated using summary statistics. Random effects meta-analyses were conducted for the language domain suitable for analysis. Publication bias was investigated using both the trim and fill and p-curve techniques.

Results: Twenty-one studies were included in the systematic review (ADHD = 1,209; Control = 1,101), within which 60 of 68 separate analyses found significant differences between the ADHD and control group on the language measures ($p < .05$). Follow-up meta-analyses found evidence for large deficits in the ADHD groups overall (10/11 studies met $p < .05$; weighted mean ES [WMES]: 1.04); expressive (10/10 met $p < .05$; WMES: 1.23); receptive (12/14 met $p < .05$; WMES: 0.97), and pragmatic language (4/4 studies met $p < .05$; WMES: 0.98) compared with controls.

Conclusions: This study demonstrates that children with ADHD have poorer performance on measures of overall, expressive, receptive, and pragmatic language compared with controls. A screening of language functioning may be a valuable addition to the assessment of ADHD

J Clin Psychopharmacol. 2017 Jun;37:374.

IS THERE AN EFFECT OF METHYLPHENIDATE ON THROMBOCYTOPENIA?

Ercan ES, Inci SB, Ipci M.

The letter presents a case report of a 13-year-old adolescent boy who was admitted to the clinic with the complaints of difficulty sustaining focus and lack of persistence. Currently, the most common medication used for attention deficit hyperactivity disorder in Turkey and worldwide is methylphenidate (MPH), which is a potent dopamine and noradrenergic reuptake inhibitor. In this case, it was reported that MPH has a possible effect on thrombocytopenia in a patient in whom MPH was initiated. Methylphenidate has several potential well known adverse effects. However, adverse hematologic effects have occurred only rarely, and a causal relationship was not conclusively established. The study showed that the prevalence of idiopathic thrombocytopenic purpura in the 11- to 14-year age group was 4.1 per 100,000 people.⁷ As a conclusion, clinicians have to be aware that there can be an association between thrombocytopenia and MPH use

J Consult Clin Psychol. 2017;85:737-50.

META-ANALYSIS OF COGNITIVE-BEHAVIORAL TREATMENTS FOR ADULT ADHD.

Knouse LE, Teller J, Brooks MA.

Objective: We conducted a meta-analysis of cognitive-behavioral treatment (CBT) studies for adult attention-deficit/hyperactivity disorder (ADHD), examining effects versus control and effects pre-to-post treatment to maximize the clinical and research utility of findings from this growing literature.

Method: Eligible studies tested adults meeting criteria for Diagnostic and Statistical Manual of Mental Disorders ADHD as determined by interview or using a standardized rating scale and measured ADHD symptoms or related impairment at baseline and posttreatment. We analyzed data from 32 studies from published and unpublished sources available through December 2015. Effect size calculations included up to 896 participants.

Results: Using a random effects model, we found that CBTs had medium-to-large effects from pre- to posttreatment (self-reported ADHD symptoms: $g = 1.00$; 95% confidence interval [CI: 0.84, 1.16]; self-reported functioning $g = .73$; 95% CI [0.46, 1.00]) and small-to-medium effects versus control ($g = .65$; 95% CI [0.44, 0.86] for symptoms, $.51$; 95% CI [0.23, 0.79] for functioning). Effect sizes were heterogeneous for most outcome measures. Studies with active control groups showed smaller effect sizes. Neither participant medication status nor treatment format moderated pre-to-post treatment effects, and longer treatments were not associated with better outcomes.

Conclusions: Current CBTs for adult ADHD show comparable effect sizes to behavioral treatments for children with ADHD, which are considered well-established treatments. Future treatment development could focus on identifying empirically supported principles of treatment-related change for adults with ADHD. We encourage researchers to report future findings in a way that is amenable to meta-analytic review

Journal of Medical Signals and Sensors. 2017;7:26-32.

AUTOMATED AND ERP-BASED DIAGNOSIS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDREN.

Jahanshahloo HR, Shamsi M, Ghasemi E, et al.

Event-related potential (ERP) is one of the most informative and dynamic methods of monitoring cognitive processes, which is widely used in clinical research to deal with a variety of psychiatric and neurological disorders such as attention-deficit/hyperactivity disorder (ADHD). In this study, there were 60 participants including 30 patients with ADHD and 30 subjects as a control group. Their ERP signals were recorded by three electrodes in two modalities. After a preprocessing step, several features such as band power, fractal dimension, autoregressive (AR) model coefficients and wavelet coefficients were extracted from recorded signals. The aim of this study is to achieve a high classification rate. The results show that the fractal dimension-wavelet combination features provided a good discriminative capability; it should be noted that this improvement was achieved by combining all sets of features and applying a feature selection algorithm, which resulted in a maximum accuracy rate of 88.77 and 95.39% in support vector machine (SVM) and v-SVM classification algorithms using a 10-fold cross-validation approach, respectively. ERP has been widely used for clinical diagnosis and cognitive processing deficits in children with ADHD. To increase the accuracy of the diagnostic process of ADHD, ERP signals were recorded to extract some specific ERP features related to this disease for classifying the two groups. The results show that the Fra-wave characterization produced the best average accuracy with an efficiency of 99.43% for v-SVM classifier, compared with 97.65% efficiency for the wavelet features and the other features

J Nerv Ment Dis. 2017.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND LIFE SATISFACTION IN A REPRESENTATIVE ADOLESCENT AND ADULT SAMPLE.

Hennig T, Koglin U, Schmidt S, et al.

Although it is well documented that attention-deficit/hyperactivity disorder (ADHD) is associated with reduced life satisfaction, the mechanisms that might explain this co-occurrence are unclear. We examined the correlation of ADHD symptoms with life satisfaction and whether this association is mediated by (lacking) social support and depressive symptoms. Self-reported ADHD symptoms, life satisfaction, social support, and depressive symptoms were assessed in a representative, predominantly adult sample from the general population (14-91 years, $N = 2517$). Attention-deficit/hyperactivity disorder symptoms correlated negatively with life satisfaction ($r = -0.41$, $p < 0.01$), even after demographic factors (gender, age, income) and common risk factors (not being in a relationship, being unemployed) were controlled for ($r = -0.39$, $p < 0.01$). Social support mediated up to 23% and depressive symptoms up to 44% in the association between ADHD symptoms and life satisfaction. Counteracting problems with social relationships and treating depressive symptoms may help to increase life satisfaction in adults with ADHD symptoms

Journal of Neurotrauma. 2016;33:2077-80.

CONCUSSION HISTORY IN ADOLESCENT ATHLETES WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Iverson GL, Atkins JE, Zafonte R, et al.

Little is known about the rate of concussions in adolescents with attention-deficit hyperactivity disorder (ADHD). We hypothesized that high school athletes with ADHD would report a greater history of concussion than students without ADHD. A total of 6529 adolescent and young adult student athletes, between the ages of 13 and 19 years (mean, 15.9; standard deviation, 1.3), completed a preseason health survey in 2010. Of those with ADHD, 26.1% reported a history of one or more concussions, compared to 17.1% of those without ADHD ($p < 0.00001$; odds ratio [OR], 1.71). Stratified by gender, 27.0% of boys with ADHD reported a history of one or more concussions, compared to 20.0% of boys without ADHD ($p < 0.004$; OR, 1.48), and 23.6% of girls with ADHD reported a history of one or more concussions, compared to 13.6% of girls without ADHD ($p < 0.003$; OR, 1.97). Of those with ADHD, 9.8% reported a history of two or more concussions, compared to 5.5% of those without ADHD ($p < 0.0003$; OR, 1.87). Stratified by gender, 10.0% of boys with ADHD reported a history of two or more concussions, compared to 6.7% of boys without ADHD ($p < 0.033$; OR, 1.54), and 9.1% of girls with ADHD reported a history of two or more concussions, compared to 3.8% of girls without ADHD ($p < 0.006$; OR, 2.51). In this large-scale, retrospective survey study, boys and girls with ADHD were significantly more likely to report a history of concussion. Additional research is needed to determine whether students with ADHD are more susceptible to injury (i.e., have a lower threshold) or have different recovery trajectories

J Pediatr Gastroenterol Nutr. 2017;64:976.

SHORT-TERM EFFECTS OF SUPPLEMENTATION WITH OMEGA-3 FATTY ACIDS IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Checa-Ros A, Seiquer I, Folgado CC, et al.

Objectives and study: Positive effects of omega-3 polyunsaturated fatty acids (-3 PUFAs) on cognition and learning might make them a helpful treatment in children with Attention Deficit/Hyperactivity Disorder (ADHD). However, the choice of the most appropriated doses and combinations of these fatty acids is still controversial. A short-term, open-label clinical trial was conducted with the following aims: 1) to investigate the influence of exogenous intake of -3 PUFAs over the general lipid profile, fatty acid categories (saturated fatty acids SFAs, monounsaturated fatty acids MFAs and polyunsaturated fatty acids PUFAs) and the values of PUFA/SFA and -6/-3 indices; 2) to report the tolerability and safety profile; and 3) analyse the short-term cognitive effects.

Methods: Children and adolescents newly diagnosed with ADHD according to the criteria established by the 5th revision of the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-5) were included. Each of them was administered a therapeutic combination of methylphenidate (MPH) and -3 fatty acids (eicosapentaenoic acid EPA 70 mg + docosahexaenoic acid DHA 250 mg). Serum fatty acid profiles were analysed by gas chromatography. As well, attention levels were measured in relation to the results obtained in a specific scale of visual attention (Magallanes Scale of Visual Attention). One-way analysis of variance (ANOVA) with Least Significant Difference (LSD) method investigated differences in fatty acid profiles before and 1 month after treatment, whereas Student t test was used to analyse differences in attention levels. Written informed consent signed by parents or tutors was required to participate in the study. All procedures were carried out in accordance with the Helsinki Declaration as revised in 1998.

Results: 38 ADHD patients were enrolled at start of intervention period (28 boys; mean age 10.42 \pm 2.41 years; range 7-15 years). In relation to serum fatty acid profile, the total sum of SFAs significantly increased after supplementation with EPA/DHA (from 32.80 \pm 0.60 to 35.38 \pm 0.36, $p < 0.0005$). In consequence, PUFA/SFA index significantly decreased ($p < 0.028$). Some values barely changed before and after treatment, as it was with MUFA and PUFA total values. However, several -6 fatty acids significantly decreased, like arachidonic acid (from 12.44 \pm 1.28 to 9.25 \pm 0.57, $p < 0.026$). EPA and DHA concentrations increased by 27% and 3% respectively ($p > 0.05$). Thereupon, total -3 fatty acid levels increased by 13% and -6/-3 index decreased (8%), although these differences were not statistically significant ($p > 0.05$) (Table 1). Results of visual attention scale showed a significant improvement of quality of attention percentile after 1

month of treatment (from 32th percentile to 51th percentile, $p < 0,026$). An overall improvement of core symptoms of ADHD was reported by parents and teachers. Medication was well-tolerated and no severe side effects appeared.

Conclusion: These findings suggest that -3 fatty acids represent a possible adjuvant therapy in children with ADHD and may enhance the effects of MPH with an adequate safety profile. Further long-term follow-up studies are required to confirm these initial findings

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Journal of Psychoactive Drugs. 2017;1-10.

CHILDHOOD MALTREATMENT, EMOTIONAL LABILITY, AND ALCOHOL PROBLEMS IN YOUNG ADULTS AT-RISK FOR ADHD: TESTING MODERATION AND MODERATED MODERATION.

Bunford N, Wymbs BT, Dawson AE, et al.

Childhood maltreatment and alcohol problems are common among young adults with attention-deficit hyperactivity disorder (ADHD). However, little is known about the degree to which maltreatment and alcohol problems are associated; potential pertinent mediating or moderating mechanisms, such as emotional lability; and whether this association varies by sex. We examined, in a sample of adults at risk for ADHD ($N=122$, 37% male), the association between childhood maltreatment and alcohol problems, whether emotional lability mediated or moderated this association, and whether either role of emotional lability differed between men and women. Emotional lability moderated the association between emotional neglect and alcohol problems; maltreatment increased risk for alcohol problems for those scoring high to very high on emotional lability, but not for those with very low-moderate levels. The association between emotional abuse and alcohol problems depended both on emotional lability and sex; emotional abuse decreased the risk for alcohol problems among men very low/low on emotional lability, but not for men who were moderate to very high on emotional lability, or for women. These findings have implications for the way in which targeting maltreatment and emotional lability may be incorporated into prevention and intervention programs to prevent alcohol problems among men and women at risk for ADHD

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J Psychopathol Behav Assess. 2017;1-11.

SLEEP AND PRETEEN DELINQUENCY: IS THE ASSOCIATION ROBUST TO ADHD SYMPTOMATOLOGY AND ADHD DIAGNOSIS?

Jackson DB, Vaughn MG.

Both qualitative and quantitative aspects of sleep have been linked to multiple dimensions of well-being. An emerging body of research has also revealed that poor sleep during adolescence can increase the likelihood of delinquent involvement. The contribution of early sleep difficulties to later delinquency, however, is often overlooked. Furthermore, the role that ADHD symptomatology and/or diagnosis might play in this association has not been adequately addressed, despite findings suggesting that both sleep disturbances and delinquent involvement are more common among children with ADHD symptomatology or an ADHD diagnosis. The current study examines the associations between sleep behaviors and preteen delinquency, and the extent to which ADHD symptomatology and/or diagnosis might inform these associations. Data from the Fragile Families and Child Wellbeing Study (FFCWS) were employed to explore these associations and logistic regression techniques were utilized to analyze the data. The findings reveal that both sleep problems and sleep duration are associated with the odds of ADHD symptomatology, an ADHD diagnosis, and preteen delinquency. Even so, the results also suggest that persistent sleep problems are not significantly associated with the odds of preteen delinquency once ADHD symptomatology and diagnosis are taken into account. The influence of sleep duration on preteen delinquency, however, is robust to the association between ADHD measures and preteen delinquency. Poor sleep, therefore, appears to be an important modifiable risk factor for preteen delinquency. Even so, future investigations into the link between sleep and delinquency should account for developmental risks and/or disorders that commonly co-occur with sleep problems

J Am Acad Child Adolesc Psychiatry. 2017 Jun;56:460-61.

THE NEED FOR PRACTICE TRANSFORMATION IN CHILDREN'S MENTAL HEALTH CARE.

Sarvet B.

Comments on an article by J. N. Epstein et al. (see record [rid]2017-23132-012[rid]). Epstein et al. highlight the importance of the organization and process of care for effective treatment of attention deficit/ hyperactivity disorder (ADHD) in the primary care setting. The study by Epstein et al. showed that processes of care, such as timeliness of first contact with the parent after initial prescription and the frequency of teacher-reported symptom measures received, powerfully influenced the clinical effectiveness of ADHD treatment delivered in the pediatric primary care setting. Although the study by Epstein et al. was exclusively focused on care of ADHD in the pediatric setting, it is quite plausible that similar effects would be realized in mental health specialty care

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Korean J Pediatr. 2017;60:189-95.

EFFECTS OF LAMOTRIGINE ON ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN PEDIATRIC EPILEPSY PATIENTS.

Han S-A, Yang EJ, Song M-K, et al.

Purpose: The purpose of this study was to investigate the effects of lamotrigine for the treatment of attention-deficit hyperactivity disorder (ADHD) symptoms in children with epilepsy.

Methods: Pediatric patients newly diagnosed with epilepsy (n=90 [61 boys and 29 girls]; mean age, 9.1±3.4 years) were enrolled. All patients were evaluated with the Korean ADHD rating scale (K-ARS)-IV before treatment with lamotrigine and after doses had been administered. The mean interval of ADHD testing was approximately 12.3 months. The initial dosage of lamotrigine was 1 mg/kg/day (maximum 25 mg/day for the first 2 weeks), and increased by 1 mg/kg every 2 weeks until titrated up to 7 mg/kg/day (or maximum 200 mg/day).

Results: The mean ADHD test score of the 90 subjects was 17.0±1.8 at baseline. It was slightly reduced to 15.6±1.7 after lamotrigine monotherapy (P >0.01). Prior to treatment, a total of 31 patients (34.4%) met the diagnostic criteria for ADHD according to Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision. Of these 31 patients, 27 (87.1%) had significantly improved ADHD scores with lamotrigine monotherapy (28.0±1.6 reduced to 18.1±2.6, P<0.001). Among these 27 patients, 25 (92.6%) showed normalized electroencephalogram (EEG) and 26 (96.3%) achieved total freedom from seizures within 12 months of the initiation of lamotrigine monotherapy.

Conclusion: The results from our study show that lamotrigine had a positive effect in pediatric epilepsy patients by reducing ADHD symptoms, preventing seizures, and normalizing EEG. However, further research is required to determine whether lamotrigine is efficacious against ADHD symptoms independent of its effects on epileptic seizures

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Milli Nevrologiya Jurnalı. 2016;43-46.

COMORBID DISORDERS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN.

Saidkhodjaeva SN.

In the article on the basis of a survey of 86 children the problem of comorbidity with attention deficit hyperactivity disorder, which are found in 69.8% of patients and lead to additional complications of intra-family, school and social adaptation. The structure is characterized by the presence of comorbid disorders, oppositional defiant behavior disorders (43.0%) and various forms of anxiety disorders (39.5%). At 9.3% of children with the disease have met tics, 17.4% - nocturnal enuresis and 5.8 - faecal incontinence

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Molecular Autism. 2017;8.

THE EU-AIMS LONGITUDINAL EUROPEAN AUTISM PROJECT (LEAP): CLINICAL CHARACTERISATION.

Charman T, Loth E, Tillmann J, et al.

Background: The EU-AIMS Longitudinal European Autism Project (LEAP) is to date the largest multi-centre, multi-disciplinary observational study on biomarkers for autism spectrum disorder (ASD). The current paper describes the clinical characteristics of the LEAP cohort and examines age, sex and IQ differences in ASD core symptoms and common co-occurring psychiatric symptoms. A companion paper describes the overall design and experimental protocol and outlines the strategy to identify stratification biomarkers.

Methods: From six research centres in four European countries, we recruited 437 children and adults with ASD and 300 controls between the ages of 6 and 30 years with IQs varying between 50 and 148. We conducted in-depth clinical characterisation including a wide range of observational, interview and questionnaire measures of the ASD phenotype, as well as co-occurring psychiatric symptoms.

Results: The cohort showed heterogeneity in ASD symptom presentation, with only minimal to moderate site differences on core clinical and cognitive measures. On both parent-report interview and questionnaire measures, ASD symptom severity was lower in adults compared to children and adolescents. The precise pattern of differences varied across measures, but there was some evidence of both lower social symptoms and lower repetitive behaviour severity in adults. Males had higher ASD symptom scores than females on clinician-rated and parent interview diagnostic measures but not on parent-reported dimensional measures of ASD symptoms. In contrast, self-reported ASD symptom severity was higher in adults compared to adolescents, and in adult females compared to males. Higher scores on ASD symptom measures were moderately associated with lower IQ. Both inattentive and hyperactive/impulsive ADHD symptoms were lower in adults than in children and adolescents, and males with ASD had higher levels of inattentive and hyperactive/impulsive ADHD symptoms than females.

Conclusions: The established phenotypic heterogeneity in ASD is well captured in the LEAP cohort. Variation both in core ASD symptom severity and in commonly co-occurring psychiatric symptoms were systematically associated with sex, age and IQ. The pattern of ASD symptom differences with age and sex also varied by whether these were clinician ratings or parent- or self-reported which has important implications for establishing stratification biomarkers and for their potential use as outcome measures in clinical trials

Mov Disord. 2017;32:761.

TIC SEVERITY AND TREATMENT IN CHILDREN: THE EFFECT OF COMORBID ATTENTION DEFICIT HYPERACTIVITY DISORDER AND OBSESSIVE COMPULSIVE BEHAVIOURS.

Pringsheim T.

Objective: This study sought to understand how the presence, severity and treatment of Attention Deficit Hyperactivity Disorder (ADHD) and Obsessive Compulsive Disorder (OCD) influence tic severity and the need for treatment of tics.

Background: While both ADHD and OCD comorbidity in individuals with Tourette Syndrome (TS) have major impacts on psychosocial quality of life, there is comparatively little data on how the presence of ADHD and OCD influence tic severity and the need for treatment.

Methods: Participants in the study were children seen at a single specialty clinic. Differences in the Yale Global Tic Severity Scale (YGTSS) score by treatment status, sex, ADHD diagnosis and treatment, presence of Obsessive Compulsive Behaviours (OCBs), OCD diagnosis and treatment were analyzed. Correlations between YGTSS total tic scores and age, ADHD and OCD severity were examined. Associations between treatment for tics and ADHD diagnosis, medical treatment for ADHD, presence of OCBs, OCD diagnosis and treatment of OCD were studied.

Results: There were 114 children in the sample, with a mean age of 10.25 years. A diagnosis of comorbid ADHD was present in 39%; OCBs in 35%; and OCD in 7%. The mean total tic severity score on the YGTSS was 17.10 points. There was no difference in YGTSS scores between children diagnosed with versus without ADHD. YGTSS scores were significantly higher in children with OCBs by 4.13 points (95% CI 0.78-7.47, $p=0.008$). Evaluation of Spearman correlations revealed a borderline positive correlation between the YGTSS total tic score and the Conners' Parent Report Hyperactivity T-score (Spearman's rho 0.227,

p=0.016). Analysis of covariance examining the relationship between YGTSS total tic score and all covariates revealed a significant relationship only with age and treatment for tics. Children with a comorbid ADHD diagnosis were more likely to be treated for their tics, with an odds ratio of 3.51 (95% CI 1.37-8.95).

Conclusions: This study demonstrates that tic severity in children is most strongly associated with age, and the presence of obsessive compulsive behaviours. The treatment of tics early in the course of the disorder is most strongly associated with ADHD, and as tic severity does not appear to be greater in these children, may relate to the greater overall psychosocial impairment in children with this comorbidity

Neuroethics. 2017;1-12.

PERSONAL AUTONOMY AND AUTHENTICITY: ADOLESCENTS' DISCRETIONARY USE OF METHYLPHENIDATE.

Fleishmann A, Kaliski A.

Minors with attention-deficit-hyperactivity disorders are liable to use pharmacological treatment against their will and may find their authentic "I" modified. Thus, their use is widely criticized. In this study, the effect of ADHD drugs on adolescents' personal experience is examined. The goal is to understand how psychological changes that young people experience when they take these medications interrelate with their attitude toward being medicated. Methylphenidate is the most common pharmacological treatment for ADHD. We look into the change that Israeli adolescents undergo when they use it; their experience in controlling the change, and their assessment of the meaning of the change for their lives. Thirty-eight adolescents participated in semi-structured interviews. The findings, analyzed using grounded theory, show that methylphenidate affects the participants' demeanor, mood, and even preferences. The participants, aware of these effects, apply discretion in taking methylphenidate and thus influence their traits and their willingness to engage in various activities. When needing to prepare for a matriculation exam, for example, they take methylphenidate; when they need to be creative or sociable, they avoid it and enjoy what they consider the advantages of ADHD, such as creativity and spontaneity. As discretionary users, they shape their life stories in a way that makes them more meaningful and diverse, better tailored to their social surroundings, and more useful in maintaining personal autonomy in the course of pharmacological treatment of ADHD

Neurology and Therapy. 2017;6:115-30.

TREATMENT PATTERNS AMONG CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH OR WITHOUT PSYCHIATRIC OR NEUROLOGIC COMORBIDITIES IN SWEDEN: A RETROSPECTIVE COHORT STUDY.

Sikirica V, Gustafsson PA, Makin C.

INTRODUCTION: Attention-deficit/hyperactivity disorder (ADHD) is a common psychiatric disorder in children/adolescents and occurs frequently with psychiatric/neurologic comorbidities. The objective of this study was to assess the impact of psychiatric/neurologic comorbidities on pharmacotherapy patterns among patients with ADHD in Sweden.

METHODS: A retrospective cohort analysis was conducted using medical records from a regional database in Sweden. Patients aged 6-17 years, with ≥ 1 prescription for ADHD medication between July 1, 2007 and June 30, 2009, and continuously active in the database for ≥ 12 months before and after their prescription index date were selected. Patients were categorized as ADHD alone (ADHD-only) or with comorbidities (ADHD-comorbid). Between-group differences were analyzed before and after adjusting for potentially confounding variables.

RESULTS: Data on 1794 patients (1083 ADHD-only; 711 ADHD-comorbid) were analyzed. Among newly treated patients, 21.7% augmented their index therapy (ADHD-only, 20.5%; ADHD-comorbid, 24.4%; $p = 0.23$). After adjustment, ADHD-only patients were less likely ($p = 0.002$) to augment versus ADHD-comorbid patients [odds ratio = 0.44, 95% confidence interval (CI) 0.27, 0.73]. ADHD-comorbid patients received more prescriptions versus ADHD-only patients (mean 13.1 vs 10.0; $p < 0.001$), and had more outpatient visits (mean 11.9 vs. 8.1; $p < 0.001$) and hospitalizations (10.7% vs. 6.0%; $p < 0.001$). After adjustment, ADHD-

only patients had fewer outpatient visits ($p < 0.001$) and referrals ($p < 0.001$) versus ADHD-comorbid patients (visits: $\beta = -0.21$, 95% CI -0.28, -0.13; referrals: $\beta = -0.25$, 95% CI -0.33, -0.18).

CONCLUSION: Patients with ADHD with comorbidities had more hospitalizations, physician visits, and medication prescriptions during 12 months' follow-up than did those with ADHD alone. ADHD therapy augmentation was prevalent among children/adolescents with ADHD, even among those without psychiatric/neurologic comorbidities

Neuropsychiatr Dis Treat. 2017;13:1541-49.

INTELLIGENCE PROFILES OF CHINESE SCHOOL-AGED BOYS WITH HIGH-FUNCTIONING ASD AND ADHD.

Li G, Jiang W, Du Y, et al.

Purpose: This study aimed to explore the intelligence profiles of Chinese school-aged boys with high-functioning autism spectrum disorder (HFASD) and attention-deficit/hyperactivity disorder (ADHD). Additionally, differences in intelligence quotient (IQ) between the HFASD group and the ADHD group were examined.

Patients and methods: Thirty-two boys with HFASD, 58 boys with ADHD, and 39 typically developing (TD) boys aged 6–16 years participated in this study. The ADHD group was divided into subgroups: ADHD-I (predominantly inattentive) and ADHD-C (combined type). (The ADHD-H [hyperactive] group was excluded because of small sample size). The Wechsler Intelligence Scale for Children-IV Chinese version was administered to every participant, and the FSIQ (Full-Scale IQ) score was used as the measure of IQ.

Results: Both boys with HFASD and ADHD (ADHD-I and ADHD-C) showed impairments in Processing Speed Index and FSIQ, as compared to the TD group. Lower Verbal Comprehension Index scores were found in the ASD and ADHD-I groups. Interestingly, Working Memory Index was only impaired in children with ADHD. Additionally, equivalent Perceptual Reasoning Index (PRI) scores were found among the HFASD, ADHD, and TD groups.

Conclusion: Results indicated that both children with ADHD and HFASD have difficulty in processing speed, which may be explained by these children having neurodevelopmental disorders. These results also indicated that working memory appears to only be impacted by having ADHD. Children with ASD are known to have language difficulties while children with ADHD typically display working memory deficits; thus, these findings were expected

Neuropsychiatr Dis Treat. 2017;13:1559-67.

RISK FACTORS FOR THE EXISTENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS IN CHILDREN WITH AUTISM SPECTRUM DISORDERS.

Lamanna AL, Craig F, Matera E, et al.

Over the years, several authors have reported symptoms of attention deficit hyperactivity disorder (ADHD) in patients with autism spectrum disorders (ASD); however, studies on the risk factors of ADHD symptoms in children with ASD are lacking. The aim of this cross-sectional study was to identify the risk factors for the development of ADHD symptoms in children with ASD. The sample consisted of 67 children with ASD who were assessed with Conner's Parent Rating Scale-Revised (CPRS-R), and with a semi-structured detailed interview administered to parents, to collect a series of clinical data such as coexisting somatic and neuropsychiatric problems and familial and pre/peri/postpartum risk factors. We found that 55% of ASD children exceeded the cut-off of CPRS-R Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), total scale. The univariate analyses showed that children's age ($P=0.048$), motor delay ($P=0.039$), enuresis ($P=0.014$), allergies ($P=0.01$), comorbid oppositional defiant disorder ($P=0.026$) and intellectual disabilities comorbidities ($P=0.034$) were associated to the CPRS-R DSM-IV total score. Some familial predictors such as neuropsychiatric family history of intellectual disabilities ($P=0.003$) and psychosis ($P=0.039$) were related to the CPRS-R DSM-IV total score. In particular, a model including allergies ($P=0.000$) and family history of psychosis ($P=0.03$) explained 25% (corrected $R^2=0.25$) of the variance of

the DSM-IV ADHD score. In conclusion, we identified some risk factors associated with the development of ADHD symptoms in ASD children that need to be studied further

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Neuropsychologia. 2017;102:45-51.

FRONTAL ALPHA ASYMMETRY PREDICTS INHIBITORY PROCESSING IN YOUTH WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Ellis AJ, Kinzel C, Salgari GC, et al.

Introduction Atypical asymmetry in brain activity has been implicated in the behavioral and attentional dysregulation observed in ADHD. Specifically, asymmetry in neural activity in the right versus left frontal regions has been linked to ADHD, as well as to symptoms often associated with ADHD such as heightened approach behaviors, impulsivity and difficulties with inhibition. Clarifying the role of frontal asymmetry in ADHD-like traits, such as disinhibition, may provide information on the neurophysiological processes underlying these behaviors.

Method ADHD youth (ADHD: n = 25) and healthy, typically developing controls (TD: n = 25) underwent an electroencephalography (EEG) recording while completing a go/no-go task a commonly used test measuring behavioral inhibition. In addition, advanced signal processing for source localization estimated the location of signal generators underlying frontal alpha asymmetry (FA) during correct and incorrect trials.

Results This is the first study in ADHD to demonstrate that the dorsal-lateral prefrontal cortex (DLPFC) may be responsible for generating frontal alpha. During failed inhibition trials, ADHD youth displayed greater FA than TD youth. In addition, within the ADHD group, frontal asymmetry during later processing stages (i.e., 400–800 ms after stimulus) predicted a higher number of commission errors throughout the task.

Conclusions These results suggest that frontal alpha asymmetry may be a specific biomarker of cognitive disinhibition among youth with ADHD

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NeuroReport. 2017.

EXCESSIVE HEMODYNAMIC ACTIVITY IN THE SUPERIOR FRONTAL CORTEX DURING THE FLANKER TASK IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Suzuki K, Okumura Y, Kita Y, et al.

Near-infrared spectroscopy studies in children with attention deficit hyperactivity disorder (ADHD) have shown excessive prefrontal activity responsible for coping with interference. However, it is possible that the previous results were influenced by verbal, reading, and memory developments. The flanker task is an interference task that does not require a verbal response, reading, or memorization. We examined activity in the superior frontal cortex (SFC) during the flanker task in 12 children with ADHD and 14 children with typical development using near-infrared spectroscopy. SFC activity was significantly greater in children with ADHD than in those with typical development. The results showed excessive interference coping activity in children with ADHD irrespective of verbal, reading, and memory development. Moreover, SFC activity was positively correlated with the inattention subscale score of the ADHD rating scale. We suggest that children with ADHD need greater SFC activation to cope with interference, and the inefficient mechanism is demanding and hard to sustain, which causes inattention symptoms of children with ADHD

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Nord J Psychiatry. 2017 May;71:270-76.

PREDICTIVE VALIDITY OF THE K-SADS-PL 2009 VERSION IN SCHOOL-AGED AND ADOLESCENT OUTPATIENTS.

Jarbin H, Andersson M, Rastam M, et al.

BACKGROUND: The schedule for affective disorders and schizophrenia for school-age children (K-SADS) is one of the most commonly used standardized diagnostic interviews in child and adolescent psychiatry. Validity studies are scarce, and limited to concurrent validity with other measures and clinical diagnoses.

AIMS: To evaluate the K-SADS interview in an outpatient child and adolescent psychiatry (CAP) setting with a Longitudinal Expert All Data (LEAD) procedure. **METHODS:** CAP residents performed a K-SADS-PL interview with the revised 2009 version containing the new PDD section on 239 clinically referred outpatients of 6-17 years old and their parent(s). A consensus LEAD diagnosis by two senior clinicians 1.2 (SD = 0.6) years later was based on clinical records including the K-SADS and subsequent information from further assessments, information from teachers and other informants, outcome of treatment, and at least three visits after the K-SADS.

RESULTS: Predictive validity for K-SADS vs LEAD diagnoses were good-to-excellent for broader categories of anxiety disorders ($\kappa = 0.94$), depressive ($\kappa = 0.91$), behavioural ($\kappa = 0.91$) and tic ($\kappa = 0.81$) disorders, good for ADHD ($\kappa = 0.80$), and good-to-moderate for autism spectrum disorders ($\kappa = 0.62$). Bipolar, psychotic, and eating disorders were too few to be analysed.

CONCLUSION: The K-SADS diagnoses elicited from an interview with the child and one from parents on one occasion have an excellent validity for most major child psychiatric disorders. ADHD can be reliably diagnosed at one visit, but clinicians need to stay alert for possible undiagnosed ADHD. Diagnosing autism with K-SADS-PL 2009 version at one visit is not advisable

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Nord J Psychiatry. 2017;1-9.

A DOUBLE-BLIND RANDOMIZED PILOT TRIAL COMPARING COMPUTERIZED COGNITIVE EXERCISES TO TETRIS IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Bikic A, Christensen T+, Leckman JF, et al.

Background: The purpose of this trial was to examine the feasibility and efficacy of computerized cognitive exercises from Scientific Brain Training (SBT), compared to the computer game Tetris as an active placebo, in a pilot study of adolescents with attention-deficit/hyperactivity disorder (ADHD).

Method: Eighteen adolescents with ADHD were randomized to treatment or control intervention for 7 weeks. Outcome measures were cognitive test, symptom, and motivation questionnaires.

Results: SBT and Tetris were feasible as home-based interventions, and participants' compliance was high, but participants perceived both interventions as not very interesting or helpful. There were no significant group differences on cognitive and ADHD-symptom measures after intervention. Pre–post intra-group measurement showed that the SBT had a significant beneficial effect on sustained attention, while the active placebo had significant beneficial effects on working memory, both with large effect sizes.

Conclusion: Although no significant differences were found between groups on any measure, there were significant intra-group changes for each group

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Noropsikiyatrs. 2017;54:149-54.

AFFECTIVE TEMPERAMENTS IN PARENTS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Yazici E, et al.

Introduction: The objective of this study was to investigate affective temperaments of parents of children with ADHD and the relationship between ADHD and affective temperaments.

Methods: The children diagnosed with ADHD were evaluated with a structured interview and the Turgay DSM-IV-Based Child and Adolescent Disruptive Behavioral Disorders Screening and Rating Scale (T-DSM-IV-S) was filled by parents. Then parents were evaluated by a structured clinical interview for DSM-IV (SCID-I), and those with no diagnosis of psychiatric disorder (in the past and at the time of the study) were included to the study. The Turkish version of the Temperament Evaluation of Memphis, Pisa, Paris and San Diego Auto-questionnaire was used to evaluate affective temperaments of parents. A control group of parents who has no children with ADHD was applied the same evaluation protocol.

Results: The study was conducted with 123 parents (66 mothers, 57 fathers) of 66 children with ADHD and 119 control parents (65 mothers, 54 fathers) of 71 children without ADHD. Affective temperament scores of parents of children with ADHD were significantly higher than those of the control group. When the scores of mothers and fathers were compared separately, mothers had higher scores in all temperaments except

hyperthymic temperament, and fathers had higher scores in all temperaments except anxious temperament in the ADHD group. Additionally, the T-DSM-IV-S attention deficit and hyperactivity/impulsivity scores of children were moderately correlated with most of the affective temperaments scores of their parents.

Conclusion: There is a relationship between ADHD and affective temperaments. Further studies are needed to understand the etiology, strength, and nature of this relationship

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Pediatrics. 2017 Mar;139.

POVERTY AND TRENDS IN THREE COMMON CHRONIC DISORDERS.

Pulcini CD, Zima BT, Kelleher KJ, et al.

OBJECTIVES: For asthma, attention-deficit/hyperactivity disorder (ADHD), and autism spectrum disorder (ASD), the objectives were to (1) describe the percent increases in prevalence and comorbidity and how these vary by poverty status, and (2) examine the extent to which poverty status is a predictor of higher than average comorbid conditions.

METHODS: Secondary analyses of the National Survey of Children's Health for years 2003, 2007, and 2011-2012 were conducted to identify trends in parent reported lifetime prevalence and comorbidity among children with asthma, ADHD, and ASD and examine variation by sociodemographic characteristics, poverty status, and insurance coverage. Using 2011-2012 data, multivariable regression was used to examine whether poverty status predicted higher than average comorbid conditions after adjusting for other sociodemographic characteristics.

RESULTS: Parent-reported lifetime prevalence of asthma and ADHD rose 18% and 44%, respectively, whereas the lifetime prevalence of ASD rose almost 400% (from 0.5% to 2%). For asthma, the rise was most prominent among the poor at 25.8%. For ADHD, the percent change by poverty status was similar (<100% federal poverty level [FPL]: 43.20%, 100% to 199% FPL: 52.38%, 200% to 399% FPL: 43.67%), although rise in ASD was associated with being nonpoor (200% to 399% FPL: 43.6%, \geq 400% FPL: 36.0%). Publicly insured children with asthma, ADHD, and ASD also had significantly higher odds (1.9x, 1.6x, 3.0x, respectively) of having higher than average comorbidities.

CONCLUSIONS: Poverty status differentially influenced parent-reported lifetime prevalence and comorbidities of these target disorders. Future research is needed to examine parent and system-level characteristics that may further explain poverty's variable impact

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Pediatrics. 2017 Feb;139.

THE MEDITERRANEAN DIET AND ADHD IN CHILDREN AND ADOLESCENTS.

Rios-Hernandez A, Alda JA, Farran-Codina A, et al.

OBJECTIVES: Although attention-deficit/hyperactivity disorder (ADHD) has been related to nutrient deficiencies and "unhealthy" diets, to date there are no studies that examined the relationship between the Mediterranean diet and ADHD. We hypothesized that a low adherence to a Mediterranean diet would be positively associated with an increase in ADHD diagnosis.

METHODS: A total of 120 children and adolescents (60 with newly diagnosed ADHD and 60 controls) were studied in a sex- and age-matched case-control study. ADHD diagnosis was made according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Energy, dietary intake, adherence to a Mediterranean diet, and familial background were measured. Logistic regression was used to determine associations between the adherence to a Mediterranean diet and ADHD.

RESULTS: Lower adherence to a Mediterranean diet was associated with ADHD diagnosis (odds ratio: 7.07; 95% confidence interval: 2.65-18.84; relative risk: 2.80; 95% confidence interval: 1.54-5.25). Both remained significant after adjusting for potential confounders. Lower frequency of consuming fruit, vegetables, pasta, and rice and higher frequency of skipping breakfast and eating at fast-food restaurants were associated with ADHD diagnosis ($P < .05$). High consumption of sugar, candy, cola beverages, and noncola soft drinks ($P < .01$) and low consumption of fatty fish ($P < .05$) were also associated with a higher prevalence of ADHD diagnosis

CONCLUSIONS: Although these cross-sectional associations do not establish causality, they raise the question of whether low adherence to a Mediterranean diet might play a role in ADHD development. Our data support the notion that not only "specific nutrients" but also the "whole diet" should be considered in ADHD

Pediatrics. 2017;139.

RACIAL AND ETHNIC DIFFERENCES IN ADHD TREATMENT QUALITY AMONG MEDICAID-ENROLLED YOUTH.

Cummings JR, Ji X, Allen L, et al.

Objectives: We estimated racial/ethnic differences in attention-deficit/hyperactivity disorder (ADHD) care quality and treatment continuity among Medicaid-enrolled children.

Methods: Using Medicaid data from 9 states (2008 to 2011), we identified 172 322 youth (age 6 to 12) initiating ADHD medication. Outcome measures included: (1) adequate follow-up care in the (a) initiation and (b) continuation and maintenance (C&M) treatment phases; (2) combined treatment with medication and psychotherapy (versus medication alone); (3) medication discontinuation; and (4) treatment disengagement (ie, discontinued medication and received no psychotherapy). Logistic regressions controlled for confounding measures.

Results: Among those initiating medication, three-fifths received adequate follow-up care in the initiation and C&M phases, and under two-fifths received combined treatment. Compared with whites, African American youth were less likely to receive adequate follow-up in either phase ($P < .05$), whereas Hispanic youth were more likely to receive adequate follow-up in the C&M phase ($P < .001$). African American and Hispanic youth were more likely than whites to receive combined treatment ($P < .05$). Over three-fifths discontinued medication, and over four-tenths disengaged from treatment. Compared with whites, African American and Hispanic children were 22.4% and 16.7% points more likely to discontinue medication, and 13.1% and 9.4% points more likely to disengage from treatment, respectively ($P < .001$).

Conclusions: Care quality for Medicaid-enrolled youth initiating ADHD medication is poor, and racial/ethnic differences in these measures are mixed. The most important disparities occur in the higher rates of medication discontinuation among minorities, which translate into higher rates of treatment disengagement because most youth discontinuing medication receive no psychotherapy

Pediatrics. 2017 Mar;139.

PSYCHIATRIC DISORDERS IN ADOLESCENTS WITH SINGLE VENTRICLE CONGENITAL HEART DISEASE.

DeMaso DR, Calderon J, Taylor GA, et al.

BACKGROUND AND OBJECTIVES: Mental health outcomes for survivors of critical congenital heart disease (CHD) remain under-investigated. We sought to examine psychiatric disorders and psychosocial functioning in adolescents with single ventricle CHD and to explore whether patient-related risk factors predict dysfunction.

METHODS: This cohort study recruited 156 adolescents with single ventricle CHD who underwent the Fontan procedure and 111 healthy referents. Participants underwent comprehensive psychiatric evaluation including a clinician-rated psychiatric interview and parent- and self-report ratings of anxiety, disruptive behavior, including attention-deficit/hyperactivity disorder (ADHD), and depressive symptoms. Risk factors for dysfunction included IQ, medical characteristics, and concurrent brain abnormalities.

RESULTS: Adolescents with single ventricle CHD had higher rates of lifetime psychiatric diagnosis compared with referents (CHD: 65%, referent: 22%; $P < .001$). Specifically, they had higher rates of lifetime anxiety disorder and ADHD ($P < .001$ each). The CHD group scored lower on the primary psychosocial functioning measure, the Children's Global Assessment Scale, than referents (CHD median [interquartile range]: 62 [54-66], referent: 85 [73-90]; $P < .001$). The CHD group scored worse on measures of anxiety, disruptive behavior, and depressive symptoms. Genetic comorbidity did not impact most psychiatric outcomes. Risk factors for anxiety disorder, ADHD, and lower psychosocial functioning included lower birth weight, longer duration of deep hypothermic circulatory arrest, lower intellectual functioning, and male gender.

CONCLUSIONS: Adolescents with single ventricle CHD display a high risk of psychiatric morbidity, particularly anxiety disorders and ADHD. Early identification of psychiatric symptoms is critical to the management of patients with CHD

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PLoS ONE. 2017;12.

REVISITING THE CO-EXISTENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND CHRONIC TIC DISORDER IN CHILDHOOD - THE CASE OF COLOUR DISCRIMINATION, SUSTAINED ATTENTION AND INTERFERENCE CONTROL.

Uebel-Von SH, Albrecht B, Rothenberger A, et al.

Objective: Attention Deficit / Hyperactivity Disorder (ADHD) and Chronic Tic Disorder (CTD) are two common and frequently co-existing disorders, probably following an additive model. But this is not yet clear for the basic sensory function of colour processing sensitive to dopaminergic functioning in the retina and higher cognitive functions like attention and interference control. The latter two reflect important aspects for psychoeducation and behavioural treatment approaches.

Methods: Colour discrimination using the Farnsworth-Munsell 100-hue Test, sustained attention during the Frankfurt Attention Inventory (FAIR), and interference liability during Colour- and Counting-Stroop-Tests were assessed to further clarify the cognitive profile of the co-existence of ADHD and CTD. Altogether 69 children were classified into four groups: ADHD (N = 14), CTD (N = 20), ADHD+CTD (N = 20) and healthy Controls (N = 15) and compared in cognitive functioning in a 2x2-factorial statistical model.

Results: Difficulties with colour discrimination were associated with both ADHD and CTD factors following an additive model, but in ADHD these difficulties tended to be more pronounced on the blue-yellow axis. Attention problems were characteristic for ADHD but not CTD. Interference load was significant in both Colour- and Counting-Stroop-Tests and unrelated to colour discrimination. Compared to Controls, interference load in the Colour-Stroop was higher in pure ADHD and in pure CTD, but not in ADHD+CTD, following a sub-additive model. In contrast, interference load in the Counting-Stroop did not reveal ADHD or CTD effects.

Conclusion: The co-existence of ADHD and CTD is characterized by additive as well as sub-additive performance impairments, suggesting that their co-existence may show simple additive characteristics of both disorders or a more complex interaction, depending on demand. The equivocal findings on interference control may indicate limited validity of the Stroop-Paradigm for clinical assessments

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PLoS ONE. 2017;12.

GASTROINTESTINAL ADVERSE EVENTS DURING METHYLPHENIDATE TREATMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW WITH META-ANALYSIS AND TRIAL SEQUENTIAL ANALYSIS OF RANDOMISED CLINICAL TRIALS.

Holmskov M, et al.

Objectives: To study in more depth the relationship between type, dose, or duration of methylphenidate offered to children and adolescents with attention deficit hyperactivity disorder and their risks of gastrointestinal adverse events based on our Cochrane systematic review.

Methods and findings: We use data from our review including 185 randomised clinical trials. Randomised parallelgroup trials and cross-over trials reporting gastrointestinal adverse events associated with methylphenidate were included. Data were extracted and quality assessed according to Cochrane guidelines. Data were summarised as risk ratios (RR) with 95% confidence intervals (CI) using the inverse variance method. Bias risks were assessed according to domains. Trial Sequential Analysis (TSA) was used to control random errors. Eighteen parallel group trials and 43 cross-over trials reported gastrointestinal adverse events. All trials were at high risk of bias. In parallel group trials, methylphenidate decreased appetite (RR 3.66, 95% CI 2.56 to 5.23) and weight (RR 3.89, 95% CI 1.43 to 10.59). In cross-over trials, methylphenidate increased abdominal pain (RR 1.61, 95% CI 1.27 to 2.04). We found no significant differences in the risk according to type, dose, or duration of administration. The required information size was achieved in three out of four outcomes.

Conclusion: Methylphenidate increases the risks of decreased appetite, weight loss, and abdominal pain in children and adolescents with attention deficit hyperactivity disorder. No differences in the risks of gastrointestinal adverse events according to type, dose, or duration of administration were found

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PLoS ONE. 2017;12.

MATERNAL PRENATAL ANXIETY AND CHILD COMT GENOTYPE PREDICT WORKING MEMORY AND SYMPTOMS OF ADHD.

O'Donnell KJ, Glover V, Lahti J, et al.

Maternal prenatal anxiety is an important risk factor for altered child neurodevelopment but there is uncertainty concerning the biological mechanisms involved and sources of individual differences in children's responses. We sought to determine the role of functional genetic variation in COMT, which encodes catechol-O-methyltransferase, in the association between maternal prenatal anxiety and child symptoms of ADHD and working memory. We used the prospectively-designed ALSPAC cohort (n = 6,969) for our primary data analyses followed by replication analyses in the PREDO cohort (n = 425). Maternal prenatal anxiety was based on self-report measures; child symptoms of ADHD were collected from 4-15 years of age; working memory was assessed from in-person testing at age 8 years; and genetic variation in COMT at rs4680 was determined in both mothers and children. The association between maternal prenatal anxiety and child attention/hyperactivity symptoms and working memory was moderated by the child's rs4680 genotype, with stronger effects obtained for the val/val (G:G) genotype relative to val/met (A:G) (all p<0.01) and met/met (A:A) groups (all p<0.05). Similar findings were observed in the PREDO cohort where maternal prenatal anxiety interacted with child rs4680 to predict symptoms of ADHD at 3.5 years of age. The findings, from two cohorts, show a robust gene-environment interaction, which may contribute to inter-individual differences in the effects of maternal prenatal anxiety on developmental outcomes from childhood to mid-adolescence

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Psicologia Clinica dello Sviluppo. 2017 Apr;21:121-41.

LE ABILITÀ DI TIME PROCESSING NEI BISOGNI EDUCATIVI SPECIALI. = TIME PROCESSING SKILLS IN SPECIAL EDUCATIONAL NEEDS.

Di Nuovo S, Belluardo G, Belluardo D, et al.

We have hypothesized, on the basis of neuropsychological findings and of previous studies, that temporal processing is an important component not only in Attention Deficit Hyperactivity Disorders (ADHD), but also in various forms of Special Educational Needs such as Specific Learning Disorders (SLD), Borderline Intellectual Functioning (BIF). Two studies have been carried out on the specific abilities of processing temporal stimuli. The first study compared 60 children with Special Educational Needs, with 60 children from the same classes, with typical development and learning. The second study compared three groups of children, all with Special Educational Needs: 27 ADHD, 27 SLD, 16 BIF. The results showed significant difficulties in time management in students with Special Educational Needs, with a worst performance in BIF compared to SLD, also with respect to ADHD in the discrimination of intervals

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Psicologia: Reflexão e Crítica. 2017 May;30.

GROUP COGNITIVE BEHAVIORAL THERAPY FOR CHILDREN AND ADOLESCENTS WITH ADHD.

Coelho LF, Barbosa DLF, Rizzutti S, et al.

The present study analyzed the use of group CBT protocol to treat ADHD by comparing two types of treatment, unimodal (medication only) and multimodal (medication combined with CBT), in terms of their effects on cognitive and behavioral domains, social skills, and type of treatment effect by ADHD subtype. Participants were 60 children with ADHD, subtypes inattentive and combined, aged 7 to 14, 48 boys. Combined treatment included 20 CBT sessions while all children were given Ritalin LA® 20 mg. Cognitive and behavioral outcome measures showed no differences between treatment groups. On social skills,

multimodal showed more improvement in frequency indicators on empathy, assertiveness, and self-control subscales and in the difficulty on assertiveness and self-control subscales. Using a group CBT protocol for multimodal ADHD treatment may improve patient adherence and ADHD peripheral symptoms

Psych J. 2017 Mar;6:83-97.

ADAPTING AN ATTENTION-DEFICIT HYPERACTIVITY DISORDER PARENT TRAINING INTERVENTION TO DIFFERENT CULTURAL CONTEXTS: THE EXPERIENCE OF IMPLEMENTING THE NEW FOREST PARENTING PROGRAMME IN CHINA, DENMARK, HONG KONG, JAPAN, AND THE UNITED KINGDOM.

Thompson MJ, Au A, Laver-Bradbury C, et al.

The New Forest Parenting Programme (NFPP) is a parenting program developed for parents who have a child with attention-deficit hyperactivity disorder (ADHD). It is a manualized program that is delivered in a parent's home over 8 weeks, or in a group format, or through a self-help manual. Three randomized controlled trials have been carried out in the United Kingdom. The NFPP group has adapted the program according to feedback from parents and therapists, and for use with different populations, both within the United Kingdom and internationally. The first international trial took place in New York, United States. Trials in Denmark, Hong Kong, and Japan followed. More recently, a trial of the self-help manual has been carried out in mainland China. This paper will outline the adaptations that were needed in order to be able to deliver the program in different countries with their own expectations of parenting, culture, and language. Training had to be differently focused; manuals and handouts had to be revised, translated and back-translated; and supervision had to be delivered at a distance to maintain the fidelity of the program. The international group will outline their experience of running trials in their own countries with the NFPP in a face-to-face format (Denmark), a group format (Hong Kong and Japan), and a self-help format (mainland China)

Psychiatry Res. 2017;256:96-101.

NEUROLOGICAL SOFT SIGNS, BUT NOT THEORY OF MIND AND EMOTION RECOGNITION DEFICIT DISTINGUISHED CHILDREN WITH ADHD FROM HEALTHY CONTROL.

Pitzianti M, Grelloni C, Casarelli L, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is associated with social cognition impairment, executive dysfunction and motor abnormalities, consisting in the persistence of neurological soft signs (NSS). Theory of mind (ToM) and emotion recognition (ER) deficit of children with ADHD have been interpreted as a consequence of their executive dysfunction, particularly inhibitory control deficit. To our knowledge, there are not studies that evaluate the possible correlation between the ToM and ER deficit and NSS in the population with ADHD, while this association has been studied in other psychiatric disorders, such as schizophrenia. Therefore, the aim of this study was to evaluate ToM and ER and NSS in a sample of 23 drug-naïve children with ADHD and a sample of 20 healthy children and the possible correlation between social cognition dysfunction and NSS in ADHD. Our findings suggest that ToM and ER dysfunction is not a constant feature in the population with ADHD, while NSS confirmed as a markers of atypical neurodevelopment and predictors of the severity of functional impairment in children with ADHD

Psychiatry Res. 2017;256:298-304.

LOCUS-SPECIFIC DNA METHYLATION CHANGES AND PHENOTYPIC VARIABILITY IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Sengupta SM, Smith AK, Grizenko N, et al.

Maternal smoking during pregnancy is the most commonly cited risk factor for ADHD. While the causal relation between this factor and ADHD is debated, several lines of evidence suggest that it modulates the severity of ADHD, particularly through higher association with conduct disorder (CD). We hypothesized that maternal smoking during pregnancy may be associated with differential methylation in selected genes in

children with ADHD. DNA extracted from peripheral blood was used to examine methylation between 25 children exposed, and 22 children not exposed to maternal smoking during pregnancy. Three genes (AHRR, CYP1A1, GFI1) were selected based on previous results observed in the general population. Regression analysis was conducted between methylation levels in these candidate genes and: (a) total number of ADHD and CD symptoms; (b) birth weight. Significant differences in methylation were observed in each of the candidate genes between children exposed and not exposed to maternal smoking during pregnancy. Methylation at the selected sites showed significant association with specific phenotypes. Significant correlations were observed between methylation within AHRR and number of CD symptoms; GFI1 and number of ADHD symptoms and GFI1 and birth weight. These initial results may have important clinical implications if confirmed in a larger independent sample

Psychopharmacology. 2017;1-15.

DISCONTINUATION OF PHARMACOLOGICAL TREATMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: META-ANALYSIS OF 63 STUDIES ENROLLING 11,788 PATIENTS.

Riera M, Castells X, Tobias A, et al.

Background: The risk-benefit balance of pharmacological treatment for children and adolescents with ADHD and the factors that moderate this relationship are unclear.

Methods: A systematic review and meta-analysis of randomised, placebo-controlled clinical trials (RPCCTs) investigating the efficacy of pharmacological treatment in children or adolescents with ADHD was carried out. Meta-analysis of treatment discontinuation, clinician-, parent- and teacher-rated efficacy and adverse events was performed. The effect of covariates was studied.

Results: Sixty-three studies were included. Ten drugs were investigated, with atomoxetine and methylphenidate the most frequently studied. RPCCTs had mostly a short duration (7.9 weeks). All-cause treatment discontinuation was lower with pharmacological treatment than placebo (OR = 0.68). Pharmacological treatment was more efficacious than placebo independently of the rater (clinician, standardised mean difference (SMD) 0.74; parent, SMD = 0.63; or teacher, SMD = 0.75). Evidence of publication bias was found for clinician-rated efficacy, especially in industry-sponsored RPCCT. Psychostimulants showed a higher efficacy and were associated with a better outcome on treatment discontinuation than non-stimulant drugs. Efficacy was smaller in RPCCTs for which a psychiatric comorbid disorder was an inclusion criterion, was larger in studies with a commercial sponsorship and showed a negative association with treatment length.

Conclusions: In the short term, pharmacological treatment provides moderate high symptom relief, is safe and shows lower treatment discontinuation than placebo, suggesting a suitable risk-benefit balance, particularly with psychostimulants. The efficacy is lower in patients with a comorbid psychiatric disorder and should be assessed periodically, as it appears to reduce over time. Publication bias of clinician-rated efficacy in studies with a commercial sponsor is suggested

Res Dev Disabil. 2017;66:34-43.

EVALUATING RELATIONSHIPS AMONG CLINICAL WORKING MEMORY ASSESSMENT AND INATTENTIVE AND HYPERACTIVE/IMPULSIVE BEHAVIORS IN A COMMUNITY SAMPLE OF CHILDREN.

Colbert AM, Bo J.

Objective This study examined relationships between inattentive and hyperactive/impulsive behaviors and working memory (WM) functioning, and the utility of WM in categorical diagnosis of ADHD versus considering ADHD symptoms on a continuum.

Method The study included 50 male children (6–12 years). Inattentive and hyperactive/impulsive behaviors were measured by the Conners-3P parent report, and WM was assessed by the WISC-IV WM subtests and Working Memory Index (WMI).

Results WISC-IV Arithmetic and Digit Span Backward were most consistently related to inattentive behaviors, and no WM measure was consistently related to ADHD hyperactive/impulsive behaviors.

Arithmetic and Digit Span Backward also accounted for significant variance in inattentive behaviors and ADHD inattention symptoms, respectively. Neither the WMI nor the Arithmetic subtest correctly classified individuals diagnosed with ADHD.

Conclusion Measurement of inattentive behaviors on a continuum best characterized relationships between symptoms of ADHD and WM functioning; WM functioning did not have utility in categorical understanding of ADHD

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Rev Chil Pediatr. 2017;88:292-98.

COMPLEMENTARY/ALTERNATIVE MEDICINE IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND MOOD DISORDERS.

Pérez Carmona MP.

The Complementary/Alternative Medicine (CAM) have been increasingly used by patients such as children and adolescents. The Ministry of Health in Chile (MINSAL) has recognized and regulated some CAM, although there is still unknown their effectiveness and safety of these.

Objective: Review the available evidence regarding the use of CAM in adolescents with the attention deficit hyperactivity syndrome (ADHD) and mood disorders.

Methodology: A review of the related literature about this topic on PubMed, focus on the last 10 years and using as a keywords Complementary/Alternative Medicine/Therapies, Attention deficit disorder with hyperactivity, Mood disorders, and Children/Adolescents. The revision was also complemented with other sources of information.

Results: Globally there has been a progressive increase in publications in relation to the CAM. However, not all studies follow a good methodology and the majority of the studies in adolescents show inconclusive results. The ADHD studies have shown benefits when using omega 3 fatty acids. Regarding other CAM and ADHD, the evidence does not show any favorable results beyond placebo. Though some of these studies have methodological mistakes or lack of enough studies, making it impossible to have conclusive. In mood disorders, there are several promising therapies, such as: physical exercise, light therapy, St. John's Wort and some kinds of meditation like Mindfulness. In Chile, there are still no studies in this age group, which makes important the development of a line of research in this area

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Revista Ecuatoriana de Neurologia. 2016;25:61-69.

NEUROPSYCHOLOGICAL TREATMENT OF ADHD IN PRESCHOOL: TRAINING OF EXECUTIVE FUNCTION.

Ramos-Galarza C, Bolaños M, Paredes L, et al.

Preschoolers who have symptoms of impulsivity, hyperactivity and attention deficit manifest alterations in the executive functions: inhibitory control, working memory, monitoring and self-directed speech. It is essential in the preschool classroom to identify children who have difficulty regulating their behavior. The importance of this early detection is the possibility of avoiding a picture of ADHD with greater complexity in the child's future. Training of executive function in children who could present these symptoms has been described as a highly effective strategy. Researches affirm that training of executive function would decrease the likelihood that a child will have ADHD at school age if he had received early attention from preschool. From the clinical experience it has witnessed the evolution of cases of children identified preschool with symptoms of ADHD, and then do a training executive functions for periods of one to two years better, and even at the beginning of schooling have a less severe psychopathology, unlike children who have not received this early intervention. In this paper I will describe the clinical picture of ADHD in initial preschool, the relationship between this disorder and executive function and some strategies in the training of executive functions

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Scand J Public Health. 2017 Jun;45:343-49.

ADHD TREATMENT AND DIAGNOSIS IN RELATION TO CHILDREN'S BIRTH MONTH: NATIONWIDE COHORT STUDY FROM NORWAY.

Karlstad O, Furu K, Stoltenberg C, et al.

BACKGROUND: Studies from several countries have reported that children youngest in grade are at higher risk of attention-deficit/hyperactivity disorder (ADHD) diagnosis and treatment. Norwegian children start school the year they turn six, making children born in December youngest in their grade. We used data on medication, specialist healthcare diagnoses, and primary healthcare diagnoses from national registers to investigate associations between birth month and ADHD.

METHODS: All children born in Norway between 1998 and 2006 (N=509,827) were followed from age six until 31 December 2014. We estimated hazard ratios for ADHD medication and diagnoses by birth month in Cox proportional-hazards models. We compared risk among siblings to control for potentially confounding socioeconomic factors, and assessed risk of receiving ADHD medication by birth month while attending different grades in cross-sectional time-series analyses.

RESULTS: At end of follow-up, 5.3% of boys born in October-December had received ADHD medication, compared with 3.7% of boys born in January-March. Corresponding numbers for girls were 2.2% and 1.3%, respectively. The adjusted hazard ratio for ADHD medication for children born in October-December (reference: January-March) was 1.4 (95% confidence interval: 1.4-1.5) for boys and 1.8 (1.7-2.0) for girls. Analyses with diagnoses as outcome showed consistent results, and analyses restricted to siblings within the study population also supported the findings. Analysis by grade revealed an increased risk for children born late in the year from grade 3 onwards, with most marked differences in higher grades.

CONCLUSIONS: Children youngest in grade had the highest risk of receiving ADHD treatment. Differences were most marked among older children

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School Ment Health. 2017 Jun;9:143-56.

EVALUATING THE FACTOR VALIDITY OF THE CHILDREN'S ORGANIZATIONAL SKILLS SCALE IN YOUTH WITH ADHD.

Molitor SJ, Langberg JM, Evans SW, et al.

Children and adolescents with ADHD often have difficulties with organization, time management, and planning skills, and these skills are a common target of intervention. A limited array of tools for measuring these abilities in youth is available, and one of the most prominent measures is the Children's Organizational Skills Scale (COSS). Although the COSS fills an important need, a replication of the COSS factor structure outside of initial measure development has not been conducted in any population. Given that the COSS is frequently used in ADHD research, the current study evaluated the factor structure of the parent-rated COSS in a sample (N = 619) of adolescents with ADHD. Results indicated that the original factor structure could be replicated, although the use of item parcels appeared to affect model fit statistics. An alternative bi-factor model was also tested that did not require the use of parcels, with results suggesting similar model fit in comparison with the original factor structure. Exploratory validity tests indicated that the domain-general factor of the bi-factor model appears related to broad executive functioning abilities

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Soc Psychiatry Psychiatr Epidemiol. 2017 Apr;52:423-33.

FAMILY STRUCTURE AND CHILDHOOD MENTAL DISORDERS: NEW FINDINGS FROM AUSTRALIA.

Perales F, Johnson SE, Baxter J, et al.

PURPOSE: Many children now live in non-traditional families-including one-parent, blended, and step families. While a substantial body of international evidence indicates that these children display poorer cognitive and socio-emotional outcomes than children living in traditional families, research on childhood mental disorders is scarce. This report provides new evidence of the relationships between family structure and childhood mental disorders in an under-researched context, Australia.

METHODS: We use recent, nationally representative data on children aged 4-17 from Young Minds Matter, the second Australian Child and Adolescent Survey of Mental Health and Well-being (N = 6310). Mental

disorders were assessed using the Diagnostic Interview Schedule for Children-Version IV and included social phobia, separation anxiety disorder, generalised anxiety disorder, obsessive-compulsive disorder, major depressive disorder, attention-deficit/hyperactivity disorder, and conduct disorder.

RESULTS: Compared to children living in original families, children in one-parent, blended, and step families experienced a higher prevalence of mental disorders. Amongst children whose parents separated, the time since separation was not statistically significantly related to the prevalence of mental disorders.

CONCLUSIONS: Although we are unable to assess causality, our findings highlight the strength of the association between family structure and child and adolescent mental health. They also stress the need for programs to support children, parents, and families in non-traditional family types to reduce mental health inequalities in childhood and later life

Topics in Spinal Cord Injury Rehabilitation. 2016;22:253-59.

ADHD AND ATTENTION PROBLEMS IN CHILDREN WITH AND WITHOUT SPINA BIFIDA.

Wasserman RM, Stoner AM, Stern A, et al.

Objectives: To identify differences in the diagnosis and treatment of attention deficit/hyperactivity disorder (ADHD) between typically developing children and children with spina bifida.

Method: Sixty-eight children with spina bifida and 68 demographically matched, typically developing children participated in a larger, longitudinal study. Rates of maternal, paternal, and teacher reports of attention problems, as well as rates of maternal reports of ADHD diagnosis, diagnosing provider, pharmaceutical treatment, mental health treatment, and academic accommodations were obtained at 5 time points over a period of 8 years and were compared across groups.

Results: Children with spina bifida were more likely to have an ADHD diagnosis and attention problems. Attention problems and ADHD diagnoses were first reported at earlier time points for children with spina bifida than typically developing children. Among children with ADHD or attention problems, children with spina bifida were more likely to be treated with medication, but they were just as likely to use mental health services and receive resource services at school.

Conclusions: Children with spina bifida were diagnosed with ADHD and identified as having attention problems more frequently and at an earlier age. This finding could be due to earlier symptom development, greater parental awareness, or more contact with providers. Among those with ADHD or attention problems, stimulant medication was more likely to be prescribed to children with spina bifida, despite research that suggests it may not be as beneficial for them. Further research on the effectiveness of ADHD pharmacological treatment for children with spina bifida is recommended

Transl Psychiatry. 2017;7.

PREDICTING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SEVERITY FROM PSYCHOSOCIAL STRESS AND STRESS-RESPONSE GENES: A RANDOM FOREST REGRESSION APPROACH.

Van Der Meer D, Hoekstra PJ, Van DM, et al.

Identifying genetic variants contributing to attention-deficit/hyperactivity disorder (ADHD) is complicated by the involvement of numerous common genetic variants with small effects, interacting with each other as well as with environmental factors, such as stress exposure. Random forest regression is well suited to explore this complexity, as it allows for the analysis of many predictors simultaneously, taking into account any higher-order interactions among them. Using random forest regression, we predicted ADHD severity, measured by Conners' Parent Rating Scales, from 686 adolescents and young adults (of which 281 were diagnosed with ADHD). The analysis included 17 374 single-nucleotide polymorphisms (SNPs) across 29 genes previously linked to hypothalamic-pituitary-adrenal (HPA) axis activity, together with information on exposure to 24 individual long-term difficulties or stressful life events. The model explained 12.5% of variance in ADHD severity. The most important SNP, which also showed the strongest interaction with stress exposure, was located in a region regulating the expression of telomerase reverse transcriptase (TERT). Other high-ranking SNPs were found in or near NPSR1, ESR1, GABRA6, PER3, NR3C2 and DRD4. Chronic

stressors were more influential than single, severe, life events. Top hits were partly shared with conduct problems. We conclude that random forest regression may be used to investigate how multiple genetic and environmental factors jointly contribute to ADHD. It is able to implicate novel SNPs of interest, interacting with stress exposure, and may explain inconsistent findings in ADHD genetics. This exploratory approach may be best combined with more hypothesis-driven research; top predictors and their interactions with one another should be replicated in independent samples

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Turkish Journal of Biochemistry. 2017;42:187-93.

ELEVATED SERUM UBIQUITIN-PROTEASOME PATHWAY RELATED MOLECULE LEVELS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Cetin I, Bulut H, et al.

Introduction: We aimed to determine the serum levels of transactive response of DNA-binding protein 43 (TDP-43) and ubiquitin C-terminal hydrolase-L1 (UCH-L1), which are ubiquitin-proteasome pathway related molecules and have not been investigated so far, in children with attention-deficit/hyperactivity disorder (ADHD).

Methods: The study group was composed of thirty children aged between 6 and 10. They were diagnosed with ADHD according to DSM-IV criteria. They were the subjects who applied to Dicle University, Faculty of Medicine, and Department of Child Psychiatry in Diyarbakir, Turkey. Children with ADHD were assessed via Turgay DSM-IV Based Child and Adolescent Behavior Disorders Screening and Rating Scale and Stroop test. Serum TDP-43 and UCH-L1 levels were analysed with enzyme-linked immunosorbent assay.

Results: The TDP-43 and UCH-L1 serum levels of children with ADHD were found to be statistically significantly higher than those of controls. On the other hand, we found that serum levels of TDP-43 correlated with interference effect and hyperactivity-impulsivity in children with ADHD.

Conclusion: Imbalances in serum UCH-L1 and TDP-43 levels, and the correlation of TDP-43 levels with clinical parameters in children with ADHD may suggest that ubiquitin-proteasome pathway alterations are associated with ADHD. Deterioration of this pathway may cause intracellular TDP-43 aggregation

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Risk factors for the existence of attention deficit hyperactivity disorder symptoms in children with autism spectrum disorders

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Abstract: Over the years, several authors have reported symptoms of attention deficit hyperactivity disorder (ADHD) in patients with autism spectrum disorders (ASD); however, studies on the risk factors of ADHD symptoms in children with ASD are lacking. The aim of this cross-sectional study was to identify the risk factors for the development of ADHD symptoms in children with ASD. The sample consisted of 67 children with ASD who were assessed with Conner's Parent Rating Scale-Revised (CPRS-R), and with a semi-structured detailed interview administered to parents, to collect a series of clinical data such as coexisting somatic and neuropsychiatric problems and familial and pre/peri/postpartum risk factors. We found that 55% of ASD children exceeded the cut-off of CPRS-R *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (DSM-IV), total scale. The univariate analyses showed that children's age ($P=0.048$), motor delay ($P=0.039$), enuresis ($P=0.014$), allergies ($P<0.01$), comorbid oppositional defiant disorder ($P=0.026$) and intellectual disabilities comorbidities ($P=0.034$) were associated to the CPRS-R DSM-IV total score. Some familial predictors such as neuropsychiatric family history of intellectual disabilities ($P=0.003$) and psychosis ($P=0.039$) were related to the CPRS-R DSM-IV total score. In particular, a model including allergies ($P=0.000$) and family history of psychosis ($P=0.03$) explained 25% (corrected $R^2=0.25$) of the variance of the DSM-IV ADHD score. In conclusion, we identified some risk factors associated with the development of ADHD symptoms in ASD children that need to be studied further.

Keywords: neurodevelopmental disorders, autism spectrum disorders, ASD, attention deficit hyperactivity disorder, ADHD, risk factors

Introduction

ADHD and ASD are neurodevelopmental disorders. According to the *Diagnostic and Statistical Manual of Mental Disorders 5*,¹ ADHD is characterized by inattention and hyperactivity/impulsivity, while ASD is characterized by deficit in social interaction skills and in social communication as well as repetitive and restricted behavior and interests.

Epidemiological studies report that around 30%–80% of children with ASD meet the criteria for ADHD and that around 20%–50% of children with ADHD meet the criteria for ASD.^{2–5}

There is evidence of an overlap between ASD and ADHD, including clinical, neuroanatomic and genetic research. Studies that have assessed some clinical features, such as executive control and aggression, in samples of children with ASD and ADHD, indicated a shared behavioral alteration in the two disorders.^{6–8}

Lundström et al⁹ showed that there is a correlation between autistic traits and traits of other disorders, and that the correlation between them is largely mediated by

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genetic factors. In a review study, Taurines et al¹⁰ suggest that comorbidity between ASD and ADHD is caused by overlapping genetic or nongenetic biological risk factors.

Furthermore, several studies have described, in children with ADHD, disturbed social functioning,^{11–13} subclinical ASD symptoms,^{6,14} including emotion-processing difficulties,^{15–17} and autistic traits.^{18–20} In a study which compared gray matter volumes in patients with ASD and ADHD, Brieber et al²¹ found gray matter reductions in the left medial temporal lobe and higher gray matter volumes in the left inferior parietal cortex, in both disorders. Behavioral genetic studies, as well as research about familial aggregation^{5,22,23} and twin studies,^{5,24,25} show that ASD symptoms are hereditary within ADHD families, as indicated by elevated levels of ASD symptoms in affected and unaffected siblings of ADHD probands. The genetic correlation between ADHD and ASD suggests that a substantial part of the genetic influences on ADHD and ASD symptoms can be shared by the two disorders. Molecular genetic research about candidate genes,^{26–33} overlapping linkage studies,^{34–37} and genome-wide association studies³⁸ suggest genetic risk loci, single-nucleotide polymorphisms and rare mutations are shared in individuals with ASD and ADHD. Given the high prevalence of comorbidity between ADHD and ASD, we hypothesize that both disorders may share common risk factors. In a study about risk factors of ASD symptoms in children with ADHD, including genetic factors and pregnancy and perinatal factors, it was found that perinatal risk factors interacting with catechol O-methyltransferase and the serotonin transporter gene predict ASD symptoms in children with ADHD.¹³

Some authors have identified language delay, motor coordination deficits, ODD, CD, maternal autistic traits, hyperactive symptoms and several psychosocial environmental risk factors as predictors of autistic symptoms in children with ADHD.^{39–41} On the other hand, we found no studies in the literature about predictors of ADHD symptoms in children with ASD. For this reason, it is important to examine risk factors for the development of ADHD symptoms in ASD because co-occurring psychiatric symptoms may negatively affect individual's social and academic functioning. There is some evidence that when ADHD is comorbid with ASD, the risk for increased severity of psychosocial problems and maladaptive behaviors increases.⁴² Considering the several evidences about the overlap between ASD and ADHD, we hypothesized that the specific associated and risk factors for ADHD may be the same factors that increase the ADHD symptoms in children with ASD. In the current study, we considered child somatic or neuropsychiatric problems as

possible factors associated with ADHD symptoms, while familial and pregnancy factors as possible predictors/risk factors of ADHD symptoms. Therefore, the aim of this cross-sectional study was to identify associated and risk factors for the development of ADHD symptoms in population cohort of children with ASD.

Methods

The participants were recruited during hospitalization and outpatient visits, in the period between January 2011 and November 2013. The administration of the assessment tools and the semi-structured interview were undertaken by child and adolescent psychiatrists and psychologists who had undergone intensive training in the administration of these procedures. The study was approved by the local ethical committee “Azienda Ospedaliero-Universitaria Consorziata Policlinico di Bari” (DNr: 2012/592); all the parents who were interviewed provided written consent.

Participants

All patients were enrolled at the Child Neuropsychiatry Unit of the University Hospital of Bari (Puglia, Italy). Puglia is a vast region in Southern Italy, where the rates of children with ASD or ADHD are consistent with epidemiological Italian data. Exclusion criteria included severe intellectual disabilities (IQ <35), Rett syndrome, a known genetic syndrome or any other severe medical condition (ie, an history of serious head injury, encephalitis or tumors) and non-Italian-speaking parents.

Clinical diagnosis of the ASD group

ASD was diagnosed according to the DSM-IV-TR criteria, supported by the ADOS-G, the ADI-R and the SCQ. The ADOS-G is a session of semi-structured observation that consists of various activities that allow the examiner to observe the social and communicative behaviors for the diagnosis of ASD.⁴³ The ADI-R is a wide-ranging structured interview addressed to parents, in order to produce a full range of information on child development and the presence of autistic symptoms.⁴⁴ The SCQ was developed as a companion tool to the ADI-R and shows good psychometric properties.⁴⁵

Intelligence testing was performed on each subject enrolled in the study by standardized intelligence test, in relation to age and presence/absence of verbal language, and included the Wechsler Intelligence Scale for Children (WISC-III),⁴⁶ the Wechsler Preschool and Primary Scale of Intelligence (WPPSI)⁴⁷ and the revised Leiter International Performances Scales (LEITER-R).⁴⁸

Assessment

Demographic and clinical data were collected about gender, age, IQ, head circumference and BMI. The assessment included the administration of clinical standardized scales including the CPRS-R long version, including 80 items, validated for the Italian population.⁴⁹ Furthermore, a semi-structured detailed interview was administered to parents or mothers of the ASD children to collect a series of clinical data. The CPRS-R and retrospective semi-structured interview were administered when ASD diagnosis was confirmed during hospitalization and outpatient visits. The CPRS-R is a parent-report measure that assesses children's problem behaviors, particularly symptoms of ADHD and related disorders (including oppositional defiant disorder and CD). The CPRS-R is frequently used in several studies. The area assessed by CPRS-R includes conduct problems, hyperactivity, inattention, aggression, anxiety, somatic complaints, fears, obsessive compulsive behavior and school adjustment problems. Each item is to be rated by the parent on a four-part scale of "not at all", "just a little", "pretty much" or "very much" with scores of 0, 1, 2 and 3 for these respective responses.

The retrospective semi-structured interview was developed ad hoc for the current study to collect a series of data, to assess risk factors associated with ADHD symptoms grouped into (1) coexisting somatic or neuropsychiatric problems, (2) familial predictors and (3) pregnancy and birth factors.

- (1) Current somatic or neuropsychiatric problems included neuropsychiatric comorbidity, neurodevelopmental delay (motor or speech delay and history of enuresis), minor neurological signs (ie, clumsiness), abnormalities in EEG measured at the same time of the clinical evaluation of the patient, allergies and/or immunological diseases and obesity (BMI above the 95th percentile). Neuropsychiatric comorbidities were diagnosed by clinical evaluation according to DSM-IV-TR criteria.
- (2) Familial predictors included a family history of neuropsychiatric disorders, parent's age at birth of the child and psychosocial risk factors. All parents were asked whether there are family members with a diagnosis of neuropsychiatric disorders. Neuropsychiatric family history comprehended neurological history (epilepsy, migraine, cerebral palsy) and psychiatric history (intellectual disabilities, specific learning disorders, ADHD, ASD, anxiety disorders, mood disorders, psychosis, tic disorders, substance abuse) and psychosocial risk factors (absence of a parent, quarrels, parental separation/divorce, excessive severity, excessive worries, special predilections, deaths

in the family, hospitalizations, institutional education outside the family, migration, frequent removals, frequent changes of school classes, discrimination and adverse school circumstances, severe financial difficulties, belonging to a group of disadvantage, very inadequate home, not fluent in the local language).

- (3) Pre/peri- and postpartum risk factors included both risk factors for a high-risk pregnancy and risk factors implicated in ADHD.

Parturition risk factors comprised abortions, threatened miscarriage, maternal smoking, infections, preeclampsia, medications during pregnancy, placental abruption, gestational diabetes and intrauterine growth retardation. Peripartum risk factors included premature birth, low birth weight (newborn weighed 2,500 g or less), difficult delivery, respiratory distress and perinatal cyanosis. Postpartum risk factors included early infections, respiratory distress and cardiac rhythm disturbances in the neonatal period.

Statistical analysis

All demographic and clinical variables were subjected to statistical analysis. Regression analyses or analysis of variance with the Conner's DSM-IV ADHD score (examined dimensionally) as dependent variable was conducted to explore the univariate association with the following independent variables (examined categorically): (1) coexisting somatic or neuropsychiatric problems (neuropsychiatric comorbidities, neurodevelopmental delay, minor neurological signs and EEG abnormalities), (2) familial predictors (family history of neuropsychiatric disorders, parent's age at birth of the child and psychosocial risk factors) and (3) pregnancy and birth factors (pre/peri- and postpartum risk factors). Putting together the results obtained, the independent variables that showed a *P*-value of <0.05 in univariate analyses were included as predictors or associated factors in the multiple linear regression analysis, while the risk factors that did not show an association in the multiple regression analysis ($P \leq 0.05$) were excluded by backward selection from the model. The R^2 value was calculated in order to evaluate the goodness of fit about the model and included risk factors (observed versus estimated). Statistical significance was considered for *P*-values <0.05. We used the Statistical Package for Social Science 20 software.

Results

Out of 84 patients, four were excluded from the study because they failed to meet the inclusion criteria or were unwilling to participate. In addition, 13 children were excluded from the study

because the cognitive assessment was not performed due to low cooperation. The final sample consisted of 67 children with ASD (57 males and 10 females; mean age 91.9 ± 52.2 months).

The mean IQ score of the ASD sample was 79.4 ± 23.8 ; in particular, normal intellectual function ($IQ > 84$) was found in 42 (63%) children, borderline intellectual level ($71 < IQ < 84$) in eight (12%) children, mild intellectual disability ($50-55 < IQ < 70$) in nine (13%) children and moderate intellectual disability ($35-40 < IQ < 50-55$) in eight (12%) children. According to DSM-IV-TR criteria, autistic disorder was diagnosed in 10 (15%) children, Asperger syndrome in eight (12%) children and pervasive developmental disorder not otherwise specified in 49 (73%) children. We found that 55% of ASD patients met the cut-offs for ADHD diagnosis at CPRS-R DSM-IV total subscale (mean score: 65.4 ± 14), 50% at CPRS-R DSM-IV-Inattentive (mean score: 64.4 ± 13.9) and 43% at CPRS-R DSM-IV-Hyperactive-Impulsive (mean score: 60.8 ± 14).

Factors associated with ADHD symptoms in ASD sample

(1) Frequencies and univariate analyses of coexisting somatic or neuropsychiatric problems are reported in Table 1.

Table 1 Univariate correlation of coexisting somatic or neuropsychiatric problems with CPRS-R DSM-IV ADHD scores in children with ASD

Coexisting somatic or neuropsychiatric problems	N (%)	Mean	P-value
Gender (male)	57 (85%)	0.124	0.174
Age (mean \pm SD)	88.12 ± 44.1	0.207	0.048*
IQ (mean \pm SD)	66.9 ± 37.1	-59	0.33
Macrocephaly	7 (10%)	-0.141	0.144
Obesity (BMI >95th percentile)	19 (28%)	-0.141	0.195
Motor delay	19 (28%)	0.231	0.039*
Speech delay	59 (88%)	-0.177	0.189
Enuresis	22 (32%)	0.285	0.014*
Minor neurological signs	37 (52%)	0.053	0.353
EEG abnormalities	12 (18%)	0.064	0.315
Allergies	20 (30%)	0.474	0.0001*
Neuropsychiatric comorbidities			
Tic disorders	7 (10%)	-0.015	0.454
ODD	1 (1.5%)	0.255	0.026*
Intellectual disabilities	15 (22%)	0.24	0.034*
Anxiety disorders	1 (1.5%)	0.162	0.11
Sleep disorders	1 (1.5%)	-0.075	0.287
Mood disorders	1 (1.5%)	0.145	0.136

Note: * $P < 0.05$.

Abbreviations: CPRS-R, Conner's Parent Rating Scale-Revised; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; IQ, intelligent quotient; BMI, body mass index; EEG, electroencephalogram; ODD, comorbid oppositional defiant disorder; SD, standard deviation.

The results showed that children's age ($P=0.048$), motor delay ($P=0.039$), enuresis ($P=0.014$), allergies ($P < 0.001$), ODD ($P=0.026$) and intellectual disabilities comorbidities ($P=0.034$) were associated to the Conner's DSM-IV total score.

- (2) Frequencies and univariate analyses of familial predictors are reported in Table 2. The results showed that neuropsychiatric family history of intellectual disabilities ($P=0.003$) and psychosis ($P=0.039$) was related to the CPRS-R DSM-IV total score.
- (3) Frequencies and univariate analyses of the pregnancy and birth factors are reported in Table 3.

We have not found a significant association between specific risk factors and CPRS-R DSM-IV total score.

The associated factors were included in a multiple linear regression model with the CPRS-R DSM-IV total scores as dependent variable. Children's age, motor delay, enuresis, ODD and intellectual disabilities comorbidities and neuropsychiatric family history of intellectual disabilities were excluded by backward selection from the model. The final model included family history of allergies ($F=3.84$, $P=0.001$) and family history of psychosis ($F=2.22$, $P=0.03$). In ASD

Table 2 Univariate correlation of familial predictors with CPRS-R DSM-IV ADHD scores in children with ASD

Familial predictors	N (%)	Mean	P-value
Neurological familiarity			
Migraine	9 (13%)	202	0.062
Epilepsy	17 (25%)	-0.06	0.327
Cerebral palsy	4 (6%)	-0.171	0.097
Psychiatric familiarity			
Intellectual disabilities	12 (18%)	0.355	0.003*
Specific learning disorders	3 (4%)	-0.088	0.253
Tic disorders	6 (9%)	0.083	0.266
Psychosis	12 (18%)	0.231	0.039*
Anxiety disorders	12 (18%)	0.165	0.106
Depression	12 (18%)	0.075	0.285
Substance abuse	1 (1.5%)	0.162	0.11
Autism spectrum disorders	3 (4.5%)	0.022	0.434
ADHD	2 (3%)	0.189	0.076
Mother's age (mean \pm SD)	38.5 ± 5.9	-0.106	0.213
Father's age (mean \pm SD)	41.8 ± 6.6	-0.104	0.216
Psychosocial risk factors ^a	16 (30%)	-0.031	0.408

Notes: * $P < 0.05$. ^aAbnormal intrafamilial relationship patterns and dysfunctional parenting (absence of a parent, quarrels, parental separation/divorce, excessive severity, excessive worries, special predilections), deaths in the family, hospitalizations, psychiatric disorder or disability in parent or sibling, institutional education outside the family, migration, frequent removals, frequent changes of school classes, discrimination and adverse school circumstances (ie, bullying), severe financial difficulties, belonging to a group of disadvantage, very inadequate home and not fluent in the local language.

Abbreviations: CPRS-R, Conner's Parent Rating Scale-Revised; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; SD, standard deviation.

Table 3 Univariate correlation of pregnancy risk factors with CPRS-R DSM-IV ADHD scores in children with ASD

Pregnancy risk factors	N (%)	F value, r_p	P-value
Recurrent abortions	9 (13%)	-0.072	0.293
Threatened miscarriage	10 (15%)	0.078	0.28
Maternal smoking	8 (11.9%)	0.173	0.095
Infections	1 (1.5%)	0.164	0.95
Preeclampsia	3 (4.5%)	0.191	0.073
Medications during pregnancy	4 (6%)	-0.127	0.17
Placental abruption	1 (1.5%)	0.12	0.183
Gestational diabetes	2 (3%)	-0.082	0.267
Intrauterine growth retardation	1 (1.5%)	0.179	0.087
Peripartum risk factors			0.489
Premature birth	8 (12%)	0.189	0.18
Low birth weight	10 (15%)	0.202	0.062
Difficult delivery	7 (10%)	0.231	0.342
Perinatal cyanosis	3 (4.5%)	0.056	0.336
Postpartum risk factors			
Early infections	4 (6%)	0.016	0.452
Respiratory distress	1 (1.5%)	-0.004	0.488
Neonatal cardiac rhythm disturbances	2 (3%)	0.08	0.272

Note: No statistically significant difference was found.

Abbreviations: CPRS-R, Conner's Parent Rating Scale-Revised; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder.

group, corrected $R^2=0.25$ indicated that family history of allergies ($\beta=0.39$; CI 6.31–21.03) and family history of psychosis ($\beta=0.22$; CI 2.01–23.6) explained 25% of the variance of the Conner's DSM-IV total score. The multiple linear regression model with the total CPRS-R DSM-IV score as dependent variable is shown in Table 4.

Discussion

Over the years, several authors have reported symptoms of inattention/hyperactivity in patients with ASD.^{50,51} More

Table 4 Factors associated with increased DSM-IV ADHD scores in children with ASD

Factors associated	t	β	CI _{95%} for β	P-value
Age	1.66	0.23	-0.16 to 0.16	0.1
Motor delay	1.57	0.17	-13.8 to 1.66	0.12
Intellectual disabilities	0.72	0.14	-12.8 to 13.66	0.91
Enuresis	1.77	0.3	-0.7 to 11.4	0.83
ODD	0.29	1.62	-9.04 to 12.64	0.76
NPF for intellectual disabilities	0.19	1.53	-2.5 to 18.4	0.13
Allergies	3.84	0.39	6.31–21.03	0.001*
NPF for psychosis	2.22	0.22	2.01–23.6	0.03*

Notes: Model with two predictors (allergies and NPF for psychosis): $R^2=0.28$ (corrected $R^2=0.25$). * $P<0.05$.

Abbreviations: DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition; ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; ODD, comorbid oppositional defiant disorder; NPF, neuropsychiatric familiarity.

recently, Gjevick et al⁵² detected a prevalence of 31% of ADHD in children with ASD assessed through the administration of Kiddie-SADS-PL to parents; Sikora et al⁵³ found that 41% of children received T scores >70 in only 1 subscale (either the Attention Problems scale or DSM-Oriented Attention Deficit Hyperactivity Problem scale) and 19% had elevated T scores in both subscales of the Child Behavior Checklist. Kaat et al⁵⁴ showed that the ADHD was the most common impairing condition in children with ASD as reported by parent (67%) and teacher (71%) DSM-IV rating scales. The results of the current study are in line with those of previous studies. We found that 55% of ASD patients reported ADHD symptoms at CPRS-R DSM-IV total subscale, 61% at Swanson, Nolan and Pelham Questionnaire IV Inattention and 49% at Hyperactivity/Impulsivity subscales.

Although the risk factors of autistic symptoms in children with ADHD have been investigated in some studies,^{23,41} studies about factors associated with ADHD symptoms in children with ASD are lacking. For this reason, in the current study, we probed the impact of coexisting somatic or neuropsychiatric problems, familiar predictors and pregnancy factors on ADHD symptoms in children with ASD. At first, we conducted our analyses distinguishing between coexisting somatic or neuropsychiatric problems, familiar predictors and pregnancy factors.

Regarding somatic or neuropsychiatric problems, we observed that motor delay, enuresis, allergies, ODD and intellectual disabilities comorbidities were associated with increased ADHD symptoms in children with ASD.

These results are in line with those of previous studies which showed that developmental delays in motor function could be related to ADHD symptoms.^{55,56} Other research found that the prevalence of enuresis is higher in children with ADHD than non-ADHD controls.^{57–59} In the same vein, previous studies have identified allergic diseases as possible factors associated with ADHD.^{60–65} One possible explanation for the association between allergic diseases and ADHD is that some consequences of allergic pediatric diseases such as behavioral abnormalities and sleep disorders sometimes are so severe that they lead to easy fatigue daytime, sleepiness, inattention and impulsivity. Another hypothesis suggests the interaction between neurodevelopmental abnormalities and dysregulation of the immune system. In particular, proinflammatory cytokines, activated B-lymphocytes and NK cells, due to an abnormal stimulation of the immune system (as in autoimmune diseases, allergic diathesis), would lead to a neuronal glia response interfering with the development of different areas of the central nervous system including the

prefrontal cortex.^{64,65} In a study that assessed the relationship between allergic manifestations in early life and the occurrence of newly diagnosed ASD and ADHD throughout childhood, an increased risk of ASD and ADHD was found to be associated with atopic disorders in infancy; this finding suggests that a disordered immunologic response may exert effects on neurodevelopment and have implications for research into etiology and treatment strategies.⁶⁶

In addition, some studies detected that ADHD and ASD were significantly positively associated with ODD-like problems in both genders,^{67–69} and other studies showed that children with intellectual disabilities are at least three times more likely to develop a mental disorder compared with typically developing children, with ADHD constituting the most frequent comorbid diagnosis.^{70–72}

Taken together, these findings suggest that specific somatic or neuropsychiatric problems for ADHD could increase the ADHD symptoms in children with ASD. Concerning familial predictors, we identified neuropsychiatric family history of intellectual disabilities and psychosis as predictors of ADHD symptoms in children with ASD. The family history of intellectual disabilities in ADHD children has received less attention in prior research, and no study has addressed the occurrence of intellectual disabilities in relatives of ADHD probands. On the contrary, our results are in accord with previous studies that showed an increased risk of schizophrenia in relatives of ADHD probands.^{73,74} Studies about familial aggregation patterns indicate that these disorders share genetic factors which is consistent with prior twin study results for ADHD⁷⁵ and schizophrenia,⁷⁶ suggesting substantial heritability. This result is also interesting because ASD and ADHD have been reported to share familiarity with schizophrenia and bipolar disorder.^{77,78} One possible interpretation of the association between neuropsychiatric family history and ADHD symptoms in ASD children is that the mechanisms underlying intergenerational transmission could be complex and may involve a heritable common genetic and environmental liability.

Regarding pregnancy risk factors, a large and growing body of literature has demonstrated that pre–peri–postnatal complications (threatened miscarriage, preeclampsia, prenatal exposure to nicotine, low birth weight, low Apgar score, prematurity, postnatal exposure to lead) increase the risk of ADHD.^{79–84} However, we did not find a significant correlation with specific risk factors (maternal smoking, abortions, threatened miscarriage, infections, preeclampsia, medications during pregnancy, placental abruption, gestational diabetes, intrauterine growth retardation). Further research

with a larger sample needs to examine more closely the links between ADHD and specific risk factors. In addition, we did not find a significant association between peri- and postnatal risk factors and ADHD as showed by previous research.

Moreover, the final model was created with the variables that showed an association with the increase of ADHD symptoms in children with ADHD. The final model including allergies and family history of psychosis explained 25% (corrected $R^2=0.25$) of the variance of the CPRS-R DSM-IV ADHD score. These shared factors could explain the high presence of ADHD symptoms in children with ASD. In addition, the co-presence of these factors may be used for future research investigating the impact of these factors combined together on the development of ADHD symptoms in children with ASD. However, certainly, there are other environmental factors (such as exposure to electromagnetic fields, chronic poisoning by heavy metals, aflatoxins, pesticides content in some food and other more) and also genetic factors that we have not assessed in our study, which might be related to ADHD symptoms in ASD. A research comparing individuals with both diagnoses to individuals with a single diagnosis suggests that co-occurring symptoms are associated with greater impairment than a single diagnosis;⁸⁵ in fact, the co-occurring conditions may be less responsive to standard treatments for either disorder. Children with ASD and additional ADHD symptoms showed more strongly expressed autistic symptoms than participants with ASD and no additional ADHD symptoms.^{86,87} The present study highlights the importance of studying the relationship between the development of ADHD symptoms among children with ASD, particularly with regard to their development, as this knowledge may help to identify and treat children at a young age to minimize some of the longer-term deficits associated with the disorders. Further studies are needed to confirm this finding and explore the role of specific risk factors in the development of ADHD symptoms among individuals with ASD.

This study should be considered in the light of its limitations. One limitation of the study is the sample size that may limit the power to detect significant risk factors, especially when using regression analysis. Therefore, these results need to be interpreted with caution. Another source of uncertainty is that these familial factors were measured by interview of the parents and not by clinical diagnoses or withdrawal of data from registers. Additionally, major biases with retrospective survey studies can impact the recall of former exposure to risk variables. Among the biases which can negatively impact the veracity of retrospective surveys

are selection bias and misclassification or information bias as a result of the retrospective aspect. Another limitation of the study is the inability to compare the males and females due to the heterogeneous distribution of the sample.

Despite these limitations, the findings of the current study represent a starting point for future research that needs to investigate the differences in rates of ADHD and associated factors between males and females with ASD, and the association between co-occurring ASD and subtype of ADHD. However, more research with larger samples and more accurate measurements of family factors needs to be undertaken before the association between risk factors and ADHD symptoms in ASD children is more clearly understood.

Conclusion

In our study, we identified some coexisting somatic or neuropsychiatric problems, familial predictors and pregnancy risk factors associated with the development of ADHD symptoms in ASD children. These factors included children's age, motor delay, enuresis, allergies, ODD and intellectual disabilities comorbidities, neuropsychiatric family history of intellectual disabilities and psychosis. Since factors associated with ADHD symptoms in children with ASD have not been investigated by other authors, further studies are needed about this topic.

Abbreviations

ADHD, attention deficit hyperactivity disorder; ADI-R, Autism Diagnostic Interview-Revised; ADOS-G, Autism Diagnostic Observation Schedule-Generic; ASD, autism spectrum disorders; BMI, body mass index; CD, conduct disorder; CPRS-R, Conner's Parent Rating Scale-Revised; DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition; EEG, electroencephalogram; IQ, intelligent quotient; ODD, comorbid oppositional defiant disorder; SCQ, Social Communication Questionnaire.

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Author contributions

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflict of interest in this work.

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Neurological soft signs, but not theory of mind and emotion recognition deficit distinguished children with ADHD from healthy control

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Abstract

Attention Deficit Hyperactivity Disorder (ADHD) is associated with social cognition impairment, executive dysfunction and motor abnormalities, consisting in the persistence of neurological soft signs (NSS). Theory of mind (ToM) and emotion recognition (ER) deficit of children with ADHD have been interpreted as a consequence of their executive dysfunction, particularly inhibitory control deficit. To our knowledge, there are not studies that evaluate the possible correlation between the ToM and ER deficit and NSS in the population with ADHD, while this association has been studied in other psychiatric disorders, such as schizophrenia. Therefore, the aim of this study was to evaluate ToM and ER and NSS in a sample of 23 drug-naïve children with ADHD and a sample of 20 healthy children and the possible correlation between social cognition dysfunction and NSS in ADHD. Our findings suggest that ToM and ER dysfunction is not a constant feature in the population with ADHD, while NSS confirmed as a markers of atypical neurodevelopment and predictors of the severity of functional impairment in children with ADHD.

Keyword: ADHD, ToM, Emotion Recognition and NSS

1. Introduction

Attention Deficit/Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder diagnosed on the basis of pervasive behavioural symptoms of hyperactivity, impulsivity and inattention, beginning in childhood (APA, 2013). Its prevalence is estimated to be 5.9-7.1% in childhood and adolescence and 5% in adults (Willcutt, 2012). ADHD is associated with an impairment in executive functions (EFs) and recent neuropsychological theories emphasize the role of executive dysfunction in the disorder (Castellanos et al., 2006; Willcutt et al., 2005). EFs can be defined as a set of general-purpose control mechanisms, often linked to the prefrontal cortex, that regulate the dynamics of human cognition and action (Miyake and Friedman, 2012). EFs generally include inhibitory control, encompassing behavioural inhibition and interference control (selective

attention and cognitive inhibition), working memory (WM) and cognitive flexibility (Diamond, 2013). These EFs promote the development of higher order of EFs, such as reasoning, problem solving and planning (Diamond, 2013). Children with ADHD show deficits in inhibition (response inhibition and interference control), WM (short-term storage and active manipulation of information) and cognitive flexibility (adaptation to changed demands) (Diamond, 2013). In addition to executive dysfunction, children with ADHD show a compromised functioning in the social domain (Barkley, 2003) and they appear to display inadequate social behaviour (Nijmeijer et al., 2008) and to have impaired social cognition (Uekermann et al., 2010). Social cognition has multiple domains, including emotion recognition (ER), theory of mind (ToM), social knowledge, attributional style and social perception (Green et al., 2008). The most studied domains of social cognition are the ER and ToM. ER is the ability to recognize the six basic emotions based on facial expressions and vocal expression. ToM can be briefly defined as the ability to understand other people's minds and, more specifically, to perceive emotion, attribute false beliefs and understand the implied meaning of the situations (Green et al., 2008). This ability allows us to understand and attribute mental states to both oneself and other people (Baron-Choen et al., 1985). Several studies show that children with ADHD experience deficit in emotion perception and/or processing (Sinzig et al., 2008; Pelc et al., 2006), empathy (Marton et al., 2009; Dick et al., 2001), ToM (Gonzalez-Gadea et al., 2013; Ibàñez et al., 2011) and pragmatics (Staikova et al., 2013; Geurts and Embrechts, 2008; Bignell and Cain, 2007). Regarding typical development children, scientific evidence show that ToM is correlated with performances on EFs tasks (Perner and Lang, 1999), particularly for inhibitory control, even when chronological and mental age are controlled for (Flynn, 2007; Flynn et al., 2004; Carlson et al., 2002; Carlson and Moses, 2001). Similarly, ToM deficits of children with ADHD have been interpreted as a consequence of their executive dysfunction, particularly inhibitory control deficit (Mary et al., 2015; Sabbagh et al., 2006; Ozonoff and McEvoy, 1994). Motor ability of children with ADHD is often significantly poorer than it should be based on their age and level of intellectual functioning. Indeed, besides the core symptoms, they experience motor impairment and neurological soft signs (NSS) (Pasini and D'Agati, 2009; D'Agati et al., 2010; Pasini et al., 2012). NSS are subtle motor, sensory and integrative abnormalities that cannot be related to impairment of a specific brain region and result in considerable sociopsychological dysfunction (Shafer et al., 1983). Approximately 84% of children with ADHD shows NSS, that are equally present in both the inattentive-hyperactive and impulsive-hyperactive types of ADHD. Their presence (in particular a greater dysrhythmia and a greater number of OM) correlates with a higher severity of the disorder (Patankar et al., 2012) and is indirectly involved in the sociopsychological dysfunction associated with increased severity of ADHD core symptoms. The

most common NSS are perceptual-sensory signs, poor motor coordination, poor right-left orientation, poor balance and overflow movements (Marcus et al., 1985). Therefore, NSS seem to be linked to three main neurological domains: integrative sensory function, motor coordination and motor sequencing (Buchanan et al., 1989). Integrative sensory dysfunction (possibly resulting from a parietal dysfunction) is reflected in higher rates of bilateral extinction, impaired audio-visual integration, agraphesthesia and astereognosis. Deficits in motor coordination have been reported through tests of general coordination, finger-thumb opposition, balance and gait. Finally, poor performance in complex motor tasks (possibly resulting from a dysfunction of the frontal-basal ganglial circuitry) has been reported in tests that involve repetitive alternating hand positions (Buchanan et al., 1989; Griffiths et al., 1998). Although NSS are commonly observed in children with typical development and reflect the immaturity of the central nervous system, their persistence into later childhood and adolescence suggests motor dysfunction and could be a “marker” of atypical neurodevelopment (Larson et al., 2007). In ADHD population NSS are mainly represented by overflow movements (OM) and dysrhythmia. OM are defined as co-movements of body parts not specifically needed to efficiently complete a motor task (Larson et al., 2007). Dysrhythmia is defined as an improper timing and/or rhythm of movement otherwise normal (Cole et al., 2008). OM, impaired timing of motor responses and poor motor coordination seem to be the most prominent motor abnormalities in children with ADHD (Pasini and D’Agati, 2009; D’Agati et al., 2010; Pasini, et al., 2012). Recently, an exploratory study by Romeo et al. (2014) investigated the possible correlation between NSS and ToM in patients with Schizophrenia. The authors found that impaired sequencing of complex motor acts was the only neurological abnormality correlated with ToM deficits. Sensory integration, motor coordination and the Neurological Evaluation Scale (NES) others subscales had no association with patients’ ability to pass first or second order false belief tasks (Romeo et al., 2014). In the present study we evaluated ToM and ER by Development Neuropsychological Assessment-II (NEPSY-II) (Korkman et al., 2011) and NSS by the Physical and Neurological Assessment of Subtle Signs (PANESS) (Denckla, 1985) in patients with ADHD compared with typically developing children. Our assessment has also included measures of planning and cognitive flexibility. We hypothesized that children with ADHD have worse performance on ToM, ER, planning and cognitive flexibility tasks and a greater number of NSS when compared with healthy children. Moreover, we tested the hypothesis that NSS are correlated with ToM deficits in ADHD group.

2. Materials and methods

2.1 Participants

The study included 43 subjects divided into a clinical group and a control group: 23 patients with ADHD (14 boys, 9 girls) and 20 healthy controls (11 boys, 9 girls) aged 7-15 years with an $IQ \geq 85$. The subjects of the clinical group were consecutive referrals of the Unit of Child Neurology and Psychiatry of “Tor Vergata” University of Rome, Italy. In accordance with the DSM-5 criteria (APA, 2013), the diagnosis of ADHD was based on clinical assessment, observations of children and interviews with parents and children, which were carried out by an experienced child psychiatrist. Both the long version of the Conners’ Parents Rating Scale-Revised (CPRS-R) (Nobile et al., 2007a) and the Conners’ Teachers Rating Scale-Revised (CTRS-R) (Nobile et al., 2007b) were used to make the diagnosis of ADHD. 13 patients met the criteria for ADHD predominantly inattentive type and 10 for combined type. The interview with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997) was used to exclude other psychiatric co-morbidities in the ADHD group. The healthy children were recruited in schools and selected from a pool of subjects who participated voluntarily in the study. None of them had a history of neurological or psychiatric disease or learning disability. Both the long version of the Conners’ Parents Rating Scale-Revised (CPRS-R) (Nobile et al., 2007a) and the Conners’ Teachers Rating Scale-Revised (CTRS-R) (Nobile et al., 2007b) were used to exclude the diagnosis of ADHD in all healthy participants. The interview with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997) was used to exclude other psychiatric disorders in the control group. All subjects included in the study had a normal IQ as measured with the Wechsler Intelligence Scale for Children-IV (WISC-IV) (Wechsler, 1991). At the time of the study, no participants were taking medication known to affect the central nervous system. Prior to the testing, every parent or legal guardian of the subjects included gave written informed consent.

2.2 Assessment of ToM and ER

Development Neuropsychological Assessment-II (NEPSY-II) (Korkman et al., 2011) is a flexible test battery, that can be completed by individuals aged 3-16 years. It assesses six neuropsychological domains: attention and executive functions, memory and learning, sensorimotor functions, social perception and visuospatial processing. All subjects enrolled in this study have completed the two tests included in the social perception domain: theory of mind (ToM) and emotions recognition (ER). ToM test evaluates the capacity to understand mental functions, such as emotions, imagination, beliefs, intentions, deceptions and pretending. Moreover, it evaluates the ability to understand how emotions are linked to social situations. ToM test includes verbal tasks (A) and contextual items (B). In ToM tasks A, children are shown pictures or read various scenarios

and is asked questions that require knowledge of another individual's point of view. In ToM tasks B, children are shown a series of pictures describing certain social situations and have to select the photograph representing the emotion appropriate for the social settings. ER test evaluates the ability to identify facial expressions. This test requires children to match from photographs of children's faces the two images expressing the same emotions (happy, sad, anger, fear, disgust and neutral) among three or more alternatives.

2.3 Assessment of neurological soft signs

For the assessment of NSS, the *Physical and Neurological Assessment of Subtle Signs* (PANESS) (Denckla, 1985) was applied. These evaluations were performed by a child neurologist who underwent training for the reliable application of the PANESS. The examiner was blind to the child's diagnostic status at the time of assessment and during scoring. The PANESS has been found to have adequate test-retest reliability (Holden et al., 1982), inter-rater reliability, internal consistency (Vitiello et al., 1989) and sensitivity to age-related changes (Larson et al., 2007) in more current and diverse cohorts. The PANESS measures salient components of motor function, including lateral preference, gaits, balance, motor persistence, coordination, overflow, dysrhythmia and timed movements. Three primary outcome variables were obtained: 1) *total overflow movements* included the total number of abnormal movements for age observed during stressed gaits (i.e. walking on heels, toes or sides of feet), tandem gaits (walking in tandem forward and backward, touching heels to toes) and during timed movements; 2) *total dysrhythmia* included total number of timed the motor examination trials in which the children failed to maintain a steady rhythm throughout the task; 3) *total speed of timed activities* of hands/feet included three repetitive movements and three sequenced movements which were performed bilaterally: toe tapping, alternating heel-toe tapping, repetitive hand patting, hand pronation/supination, repetitive finger tapping and finger sequencing.

2.4 Assessment of planning and cognitive flexibility

Tower of London (ToL) to evaluate planning ability (Shallice, 1982; Krikorian et al., 1994). The task material includes three wooden pegs of different lengths mounted on a strip of wood and three colored balls (red, yellow and blue). These balls are manipulated on the pegs to reproduce a picture. The same initial position is set for the practice problem and each of the 12 problems of graded difficulty. The demand for planning is changed by presenting problems whose solution requires a different number of minimum moves. For each problem, scores ranged from zero (the problem was not solved after the third attempt) to three (the problem was solved at the first attempt).

Performance is evaluated with two scores: the sum of the total scores and the total time spent to complete the 12 different patterns.

Animal sorting test of NEPSY-II to evaluate cognitive flexibility (Korkman et al., 2011). This test requires the child to sort eight cards into two groups of four cards, each using various self-initiated sorting criteria.

2.5 Statistical analysis

For the statistical analysis, an alpha level of 0.05 was applied. All statistical analyses were carried out using the Statistical Package for Social Sciences SPSS software (version 17.0, Inc., Chicago, IL, USA). The Mann-Whitney-U test is used to compare differences between the clinical and control groups in regard to the variables collected for each subject enrolled for this study. Effect sizes for differences between paired observations were computed. Cohen's d was used to calculate the effect size. Cohen's d is defined as the difference between two means divided by a standard deviation of the data. Following Cohen's (1988) guidelines for interpreting effect sizes, small effects ($d \geq 0.20$), medium effects ($d \geq 0.50$) and large effects ($d \geq 0.8$) were distinguished (Bezeau and Graves, 2001). The Kendall's rank correlation coefficient or Kendall's τ is used to find a correlation among multiple independent variables examined. The Kendall's τ is a non-parametric measure of the statistical dependence among various variables and it is indicative of the strength and direction of the association among various variables measured on at least an ordinal scale.

3. Results

3.1 Comparisons between ADHD and control groups

In our study patients with ADHD (23 subjects, 14 boys and 9 girls) and healthy controls (20 subjects, 11 boys and 9 girls) did not differ in terms of age ($Z=-1.848$; $p=0.06$) and IQ ($Z=-0.512$; $p=0.61$). We found significant differences between the ADHD group and the control group with regard to the following ratings: Conners' Parents Rating Scale-Oppositional ($Z=-2.863$; $p=0.01$), Conners' Parents Rating Scale-Inattention ($Z=-5.609$; $p=0.01$), Conners' Parents Rating Scale-Hyperactivity ($Z=-3.780$; $p=0.01$) and Conners' Parents Rating Scale-ADHD-Index ($Z=-5.606$; $p=0.01$). There are no significant differences between the ADHD group and the control group with regard to the performance to ToM tasks ($Z=-0.099$; $p=0.92$) as well as with regard to ER tasks ($Z=-0.957$; $p=0.34$). We found significant differences between the ADHD group and the control group with regard to total overflow movements ($Z=-5.247$; $p=0.01$), total dysrhythmia ($Z=-2.073$; $p=0.03$) and total speed of timed activities ($Z=-2.618$; $p=0.01$). Significant differences between patients with ADHD and healthy controls were observed with regard to ToL Total Score ($Z=-3.296$; $p=0.01$), but not with regard to ToL Total Time ($Z=-1.620$; $p=0.10$). Compared to healthy controls, children with

ADHD showed a worse performance on cognitive flexibility task ($Z=-2.162$; $p=0.03$). (See **Table 1**).

[Table 1]

3.2 Correlations analysis between score on ToM/ER tasks and NSS within the clinical group

The correlation analysis according to Kendall showed no significant correlations ToM and OM ($\tau=-0.004$; $p=0.49$), ToM and Total Dysrhythmia ($\tau=-1.154$; $p=0.17$), ToM and Total Speed of Timed Activities ($\tau=-1.154$; $p=0.17$), as well as among ER and OM ($\tau=-0.216$; $p=0.09$), ER and Total Dysrhythmia ($\tau=-0.071$; $p=0.33$) and ER and Total Speed of Timed Activities ($\tau=-0.226$; $p=0.07$). In Table 2 results of correlation analysis according to Kendall for ADHD group are summarized (See **Table 2**).

[Table 2]

4. Discussion

In the present study we evaluated the social perception in a sample of 23 drug-naïve children with ADHD compared with a sample of 20 healthy children. Using ToM test of NEPSY-II (Korkman et al., 2011), we compared the ability to decode/interpret the intentions and beliefs of others of the ADHD group with that of the control group. Moreover, using ER test of NEPSY-II (Korkman et al., 2011), we compared the ability to identify facial expressions of the clinical group with that of the control group. Our hypothesis that children with ADHD have worse performance on ToM and emotions recognition tasks compared with healthy children has not been confirmed. In fact, the comparison analysis revealed no statistically significant differences between children with ADHD and healthy children with regard to ToM and ER ability. Our findings suggest that it is not possible to conclude with certainty that children with ADHD exhibit ToM and ER deficits. This is in line with the investigations of ToM and emotions recognition features in population with ADHD that have led to conflicting findings. Contradicting the hypothesis of a deficit in ToM functions in ADHD, several studies have found similar performances in various ToM tasks in children with ADHD in comparison with typically developing children (Yang et al., 2009; Perner et al., 2002; Charman et al., 2001) and better performance when compared to children with autism spectrum disorder (ASD) (Yang et al., 2009). Despite, many children with ASD may experience ADHD-like symptoms and the two disorders are often comorbid (Goldstein and Schwebach, 2004), in the classification systems DSM-IV and ICD-10 an exclusionary criterion is held for the two disorders

(APA 2005; WHO 1993). On the contrary, according with diagnostic criteria of the DSM-5 it is possible to make the diagnosis of the two disorders in comorbidity (APA, 2013). However, the social deficits are especially evident in ASD, while the core symptoms of ADHD are deficits in the area of attention functioning (Adrien et al., 1993). Several studies showed that in children with ADHD ToM impairment become evident in tasks of “advanced” ToM with high inhibitory control. On the contrary children with ADHD are unimpaired on first and second order ToM tasks with low inhibitory control (Sodian and Hulsken, 2005; Charman et al., 2001). Recently Mary and colleagues showed that children with ADHD performed more poorly than typically developing children in attentional, EFs and ToM tasks. Moreover, when controlled for inhibition and attentional variables, ToM performance in children with ADHD was actually similar to typically developing children. Contrarily, controlling for ToM scores did not normalize performance for inhibition and attentional tasks in children with ADHD. Therefore, this unidirectional relationships suggests that deficits in EFs and attentional domains are responsible for ToM deficits in children with ADHD (Mary et al., 2015). A recent meta-analysis showed that in children with ADHD ER deficits are not extended to all emotions: the most severe deficits were evident in recognition of anger and fear (Bora and Pantelis, 2016). Investigating the developmental course of social cognition in ADHD, some studies showed that there is a significant improvement of social cognition abilities in adolescence and adulthood (Brizio et al., 2015; Choudhury et al., 2006). Emerging evidence suggests that ADHD may be also associated with deficits ToM and ER abilities, but this association is inconstant. When the socioemotional difficulties is present, they may have long-term repercussions on the futures of children with ADHD in that poor social relationships are strong predictors and mediators of negative adult outcomes (Daly et al., 2007). Several studies showed that ER mostly involves occipitotemporal brain systems, while ToM in its cognitive features (inferences on others’ beliefs and intentions) and affective features (inferences on others’ emotions and feelings) involves the dorsomedial prefrontal cortex, as well as dorsal anterior cingulate cortex, dorsal striatum, ventromedial and orbitofrontal cortices (Abu-Akel and Shamay-Tsoory, 2011; Kalbe et al., 2010; Shamay-Tsoory et al. 2009). ToM is dependent on integrity of the dopaminergic system (Abu-Akel and Shamay-Tsoory, 2011; Lackner et al., 2010) and stimulants, (e.g. methylphenidate-MPH) used in treatment of ADHD, target their action mainly on catecholaminergic system in the prefrontal cortex and striatum (Abu-Akel and Shamay-Tsoory, 2011; Stahl, 2010). This explains the improvement of social perception deficits in subjects with ADHD treated with MPH (Maoz et al., 2013; Swanson et al., 2011; Williams et al., 2008). The present study confirms our hypothesis that children with ADHD have worse performance on planning and cognitive flexibility tasks compared with healthy children. In fact, the comparison analysis revealed statistically significant differences

between children with ADHD and healthy children with regard to scores of ToL and animal sorting test used to evaluate planning and cognitive flexibility skills respectively. Our findings are in line with scientific evidence demonstrating the involvement of cortical networks responsible for EFs in the pathophysiology of ADHD (Kingdon et al., 2016; Emond et al., 2009). In a recent tractography study Chiang and colleagues showed that ADHD core symptoms and EFs deficits are significantly correlated with integrity of the frontostriatal tracts in left orbitofrontal and ventrolateral regions (Chiang et al., 2016). The same authors found poorer performance in various domains of executive functioning, including planning and cognitive flexibility, in subjects with ADHD (Chiang et al., 2016). Executive dysfunction was associated with lower generalized fractional anisotropy in the left frontostriatal tract, left superior longitudinal fasciculus, left arcuate fasciculus and right cingulum bundle (Chiang et al., 2016). In a previous study Chiang and colleagues investigated the correlation between ADHD core symptoms and planning. The authors demonstrated that inattention, hyperactivity and impulsivity were significantly associated with planning deficit and only inattention independently predicted planning in a model that included all three ADHD symptoms and subtypes (Chiang et al., 2013). As starting hypothesis, in the present study ADHD group showed a greater number of NSS compared to control group. In fact, according to the comparison analysis children with ADHD presented a greater number of OM, a greater dysrhythmia and a greater slowness in execution of timed movements when compared to healthy children. These results confirm our recent studies of motor impairment in ADHD (Pitzianti et al., 2016a; Pitzianti et al., 2016b) and are consistent with findings of previous investigations, that emphasize the presence of motor dysfunction in children with ADHD. Increased OM (Mostofsky et al., 2003; Uslu et al., 2007), impaired timing of motor responses (Rubia et al., 1999), deficits in motor coordination (Watemberg et al., 2007) and deficit in fine motor abilities (Pitcher et al., 2003) were frequently observed in children with ADHD. Moreover, Meyer and Sagvolden found that children with ADHD performed worse on measure of manual dexterity, motor coordination, movement speed, accuracy and stability of movement in comparison to healthy children (Meyer and Sagvolden, 2006). OM likely reflects dysfunction within motor and premotor circuits that are important for the preparation and execution of motor responses (Cincotta et al., 2002). A functional neuroimaging study showed a smaller extent of activation in the contralateral primary motor cortex in patients with ADHD during performing a simple motor task. It may represent insufficient recruitment of neuronal activity necessary to mobilize transcallosal interhemispheric inhibition (Mostofsky et al., 2006). Dysfunctions in motor and premotor circuits, responsible for increased prevalence rate of OM in patients with ADHD, may be due to abnormalities in white matter tracts, including the corpus callosum, important for the effective transfer of transcallosal inhibition (Pasini

and D'Agati, 2009; D'Agati et al., 2010). Dysrhythmia may reflect cerebellar dysfunction (Schmahmann, 2004) and slowness of timed activities may be due to functional deficits in frontal-striatal networks, cerebellum and basal ganglia structures (Pasini and D'Agati, 2009). It is interesting to note that NSS provides valuable information about brain maturation in a variety of neurodevelopmental conditions, including early onset psychosis (EOP) (Mayoral et al., 2008), early onset bipolar disorder (Dickstein et al., 2005), specific language impairment (Henry et al., 2011), ASD (Halayem et al., 2010; Mayoral et al., 2010) and ADHD (Mostofsky et al., 2003; Uslu et al., 2007). The persistence of NSS into later childhood and adolescence may be considered as a "biomarker" of atypical brain development (Larson et al., 2007) and in young adults is often associated with a number of neuropsychiatric disorders, such as psychosis, obsessive-compulsive disorder and also in conditions of atypical development, like ASD, learning disability and ADHD (Mandelbaum et al., 2006; Shafer et al., 1986). However, longitudinal studies showed that patients with EOP presented more NSS than controls both at baseline and at 2-year follow-up, but the number of NSS was significantly reduced over the follow-up period (Mayoral et al., 2008; Mayoral et al., 2012). This decrease in patients with psychosis is influenced by changes in symptomatology. In fact, several studies showed that NSS decrease in parallel with remission of psychopathological symptoms. This effect is more pronounced in patients with a remitting compared to a non-remitting, chronic course and is significantly correlated with length of the follow-up period, but not with age (Bachmann et al., 2014). In ADHD population a marked improvement or a complete resolution of the NSS was observed after treatment with methylphenidate (MPH), the most frequently stimulant drug prescribed in the treatment of children with ADHD (Lerer and Lerer, 1976). Therefore, we suggest that evaluation of NSS is useful to monitor the effectiveness of pharmacological treatment with MPH in children with ADHD. Despite the lack of a statistically significant difference between clinical group and the control group with regard to ToM and ER, anyway we conducted the correlation analysis to assess whether there is a relationship between scores on ToM and ER test and NSS. The Kendall's correlation analysis did not reveal any correlation between performance on measures of ToM and ER and NSS in children with ADHD.

5. Conclusions

The first strength of our study is the inclusion of a well-defined group of drug-naive children with ADHD, who were carefully screened for other comorbid psychiatric conditions. The second strength of this study is the inclusion of subjects with normal IQ. Indeed, lower IQ and psychiatric comorbidities (e.g. ASD, oppositional defiant disorder and conduct disorder) appear to be related to an increase of ToM and emotion recognition deficits and increased NSS in children with ADHD.

The main limitation of our study is the small sample size, constraining the interpretation of the presented findings. Based on the data discussed above, we suggest that ToM and ER dysfunction is not a constant feature in the population with ADHD, while NSS confirmed as a markers of atypical neurodevelopment and predictors of the severity of functional impairment in children with ADHD. Future studies will need to confirm this result on larger samples of subjects with ADHD.

Conflict of Interest Statement

The author(s) declare that they have no competing interests.

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List of Tables

Table 1. Results of Mann-Whitney-U Test

	ADHD group (14 boys and 9 girls)	Control group (11 boys and 9 girls)	ADHD group vs Control group		
	Mean±SD	Mean±SD	Z	p	d
Age	10.39±2.35	9.10±1.92	-1.848	0.06	0.60
IQ	104.61±13.31	106.00±12.19	-0.512	0.61	-0.11
CPRS-Oppositional	64.35±15.61	51.25±9.74	-2.863	0.01*	1.01
CPRS-Inattention	77.78±9.35	50.30±6.05	-5.609	0.01*	3.49
CPRS-Hyperactivity	66.00±14.81	51.35±5.67	-3.780	0.01*	1.30
CPRS-Index	80.52±11.04	50.70±7.25	-5.606	0.01*	3.19
Theory of Mind (ToM)	21.00±2.11	20.70±2.30	-0.099	0.92	0.13
Emotions Recognition (ER)	26.87±3.63	27.90±2.00	-0.957	0.33	-0.35
Overflow Movements (OM)	13.87±6.69	3.65±2.30	-5.247	0.01*	2.04
Total Dysrhythmia	5.65±2.04	4.10±2.40	-2.073	0.04*	0.69
Total Speed of Timed Activities	181.09±52.63	222.50±52.29	-2.618	0.01*	-0.79
ToL-Score	28.30±2.63	31.05±1.96	-3.296	0.01*	-1.18
ToL-Time	296.74±110.66	317.40±88.75	-1.620	0.10	-0.20
Cognitive flexibility	4.00±2.15	5.30±2.23	-2.162	0.03*	-0.59

Level of significance (*) $p \leq 0.05$

Table 2. Results of correlation analysis according to Kendall for ADHD group

	Theory of Mind (ToM)		Emotions Recognition (ER)	
	τ	p	τ	p
Overflow Movements (OM)	-0.004	0.49	-0.216	0.09
Total Dysrhythmia	-1.154	0.17	-0.071	0.33
Total Speed of Timed Activities	-0.173	0.135	-0.226	0.07

Level of significance (*) $p \leq 0.05$

Highlights

The aims of this paper are:

- 1) to increase knowledge about social cognition impairment and neurological soft signs in children with ADHD;
- 2) to increase knowledge about possible correlation between theory of mind deficit and neurological soft signs in children with ADHD.

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