NEWSLETTER

INDICE:

BIBLIOGRAFIA ADHD LUGLIO 2020

Acad Pediatr. 2020.
ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN 2- TO 5-YEAR-OLDS: A PRIMARY CARE NETWORK EXPERIENCE.
Bannett Y, Feldman HM, Gardner RM, et al.
Objective: To assess 1) rates of primary care provider (PCP) diagnosis of attention-deficit/hyperactivity disorder (ADHD) in young children, 2) documented PCP adherence to ADHD clinical practice guidelines, and 3) patient factors influencing PCP variation in diagnosis and management.
Methods: Retrospective cohort study of electronic health records from all office visits of children aged 2 to 5 years, seen ΓëÑ2 times between 2015 and 2019, in 10 practices of a community-based primary health care network. Outcomes included ADHD diagnosis (symptom or disorder), and adherence to guidelines in 1) comorbidity documentation at or after ADHD diagnosis, 2) ADHD medication choice, and 3) follow-up of medicated patients. Logistic regressions assessed associations between outcomes and patient characteristics.
Results: Of 29,408 eligible children, 195 (0.7%) had ADHD diagnoses. Of those, 56% had solely symptom-level diagnoses (eg, hyperactivity); 54% had documented comorbidities. ADHD medications were prescribed only to 4- to 5-year olds (40 of 195 [21%]); 85% received stimulants as first-line medication; 48% had follow-up visits within 2 months. Likelihood of ADHD diagnosis was higher for children with public or military insurance (odds ratio [OR] 1.94; 95% confidence interval [CI] 1.40-2.66; OR 3.17; 95% CI 1.93-4.96). Likelihood of comorbidity documentation was lower for older ADHD patients (OR 0.48; 95% CI 0.32-0.71) and higher for those with military insurance (OR 3.11; 95% CI 1.13-9.58).
Conclusion: PCPs in this network frequently used symptom-level ADHD diagnoses in 2- to 5-year olds; ADHD diagnosis rates were below estimated population prevalence, with evidence for sociodemographic disparities. PCP comorbidity documentation and choice of stimulant medications were consistent with guidelines. Rates of timely follow-up were low

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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.

Acad Pediatr. 2020.

MEDICATION USE IN YOUTH WITH AUTISM AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Rast JE, Anderson KA, Roux AM, et al.

Objective: Children with autism spectrum disorder (ASD) may benefit from medication to treat a diverse array of behaviors and health conditions common in this population including co-occurring conditions associated with ASD, such as attention-deficit/hyperactivity disorder (ADHD) and anxiety. However, prescribing guidelines are lacking and research providing national estimates of medication use in youth with ASD is scant. We examined a nationally representative sample of children and youth ages 6 to 17 with a current diagnosis of ASD to estimate the prevalence and correlates of psychotropic medication.

Methods: This study used data from the 2016 and 2017 National Survey of Children's Health. We estimated unadjusted prevalence rates and used multivariable logistic regression to estimate the odds of medication use in children and youth across 3 groups: those with ASD-only, those with ASD and ADHD, and those with ADHD-only.

Results: Two thirds of children ages 6 to 11 and three quarters of youth ages 12 to 17 with ASD and ADHD were taking medication, similar to children (73%) and youth with ADHD-only (70%) and more than children (13%) and youth with ASD-only (22%). There were no correlates of medication use that were consistent across group and medication type. Youth with ASD and ADHD were more likely to be taking medication for emotion, concentration, or behavior than youth with ADHD-only, and nearly half took ASD-specific medication.

Conclusions: This study adds to the literature on medication use in children and youth with ASD, presenting recent, nationally representative estimates of high prevalence of psychotropic drug use among children with ASD and ADHD

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Acta Clin Croat. 2019 Dec;58:662-71.

DO ORTHOPTIC EXERCISES HAVE ANY INFLUENCE ON CHILDREN AND ADOLESCENTS DIAGNOSED WITH CONVERGENCE INSUFFICIENCY AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER?

Dawidowsky B, Cerovski B, et al.

The aim was to determine whether improvement of near point of convergence (NPC) and binocular vision after orthoptic exercises had any impact on children and adolescents diagnosed with attention deficit/hyperactivity disorder (ADHD) and convergence insufficiency (CI). In this clinical trial, 50 children and adolescents aged 6 to 18 years diagnosed with ADHD and CI received orthoptic therapy that included home-based exercises (pencil push-ups and stereograms) and office-based therapy on synoptophore. Binocular vision and NPC were measured before, during and after therapy. Study subjects showed significant improvement ($p<0.05$) in NPC and binocular vision after orthoptic exercises. We found statistically significant correlation between stereovision improvement (Lang I) and near point of convergence, suggesting that improvement of binocular function is possible in children with ADHD and CI. Our results showed that NPC enhancement improved stereovision in patients with ADHD. Since progress of binocular function has positive effect on near work and diminishes visual symptoms in children and adolescents with ADHD and CI, it might be reasonable to suppose that orthoptic therapy helps these children improve concentration as well. Further studies are needed to determine whether it might have positive impact on attention

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Acta Paediatr Int J Paediatr. 2020.

NEONATAL JAUNDICE, ATTENTION DEFICIT HYPERACTIVITY DISORDER AND FAMILIAL EFFECTS: A SWEDISH REGISTER STUDY WITH SIBLING ANALYSIS.

Le R, I, Wang C, Almqvist C, et al.

Aim: Neonatal jaundice is associated with higher risk of attention deficit hyperactivity disorder (ADHD), but it is unclear if the association is influenced by genetic and other familial factors. In this large population-based study, we investigated the association between neonatal jaundice and ADHD while adjusting for familial factors.

Methods: We linked several Swedish registers to identify all singleton births without congenital malformations between 1992 and 2000 (n-á=-á814-á420, including 384-á290 full siblings) and followed them up until 2009. We calculated hazard ratios (HRs) for the association between neonatal jaundice and ADHD, adjusting for pregnancy, delivery and neonatal characteristics including prematurity, and parental age and education. We repeated the analyses among siblings to adjust for shared familial factors.
Results: At a population level, children treated for neonatal jaundice had an increased risk of ADHD (adjusted HR (aHR): 1.13, 95% CI: 1.05-1.22). In the sibling comparisons, there was no clear association between neonatal jaundice and ADHD (aHR: 1.03, 95% CI: 0.82-1.29).
Conclusion: We found no evidence of an independent association between neonatal jaundice and ADHD within siblings in this large population-based study, suggesting that the association is probably influenced by shared familial factors, such as parental genetic and/or lifestyle effects

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Alcohol Clin Exp Res. 2020;44:131A.

ALCOHOL USE BY ADOLESCENTS PRESCRIBED STIMULANTS FOR ADHD INCREASES RISK OF DIVERSION.

Molina BSG, Lindstrom RA, Pedersen SL, et al .

Purpose: Misuse of stimulant medications prescribed for ADHD commonly occurs among college students and also occurs in adolescence (SAMHSA, 2017). Diversion (sharing, selling, and trading) by individuals with prescriptions is the most commonmeans by whichmisuse is supplied (e.g., Compton et al., 2018). Although research (mostly cross-sectional) describes individuals who misuse, there is very limited data on diversion behavior (Chen et al., 2014) and none that address emerging diversion risk factors in adolescence. Our working model of stimulant diversion risk postulates intrapersonal, attitudinal/behavioral, and social/normative factors that may explain emerging diversion risk in adolescence and the extent to which diversion occurs in the context of typical health behavior risk (here, increased alcohol, tobacco, marijuana, and delinquency).
Method: As part of a larger randomized clinical trial on the prevention of stimulant diversion by pediatric primary care patients stimulant-treated for ADHD, 357 13-18 year olds completed surveys four times, ~6 months apart (>90%retention across T1-T4). Three hypothesized diversion risk factors (see Results) at T4 were each regressed on frequency of alcohol, tobacco, and marijuana use at T3, delinquency at T3, demographic variables (T3 age, household education, gender-74%male; and race-80%White/non-Hispanic/Latinx).
Resuts: Above and beyond age and T3 diversion risk, alcohol but not tobacco or marijuana frequency prospectively predicted adolescents' self-reported experience of being approached to divert theirmedication, B = 1.02, p < 0.000. Delinquency predicted being approached, B = 0.16, p < 0.05, as well as intolerance of stimulant misuse and diversion, B = -¦0.03, p < 0.05 - a variable we adapted from the well-known attitudinal intolerance of deviancemeasure (Jessor et al., 1989). Intolerance of misuse/diversion and diversion approaches were correlated (e.g., r = -¦0.22, p = 0.001 at T4). Disclosure of treatment to others was not predicted by any variables.
Conclusions: Alcohol, but not tobacco or marijuana, use appear to index emerging risk of being approached to sell, share, or trade prescribed stimulant medication in adolescence. Given the social nature of adolescent alcohol use, teens prescribed stimulants for ADHD who drink alcohol may be inadvertently elevating their risk of being approached to divert their medication. Future research will benefit from testing whether parental and provider attitudes and behaviors (e.g., proactive discussions about peer approaches) reduces this risk

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Alcohol Clin Exp Res. 2020;44:94A.

DAILY FLUCTUATION IN IMPULSIVITY: A CORRELATE OF ALCOHOL USE AND PROBLEMS IN ADOLESCENTS WITH ADHD.

Kennedy TM, Molina BSG, Pedersen SL.

Purpose: ADHD is a risk factor for problematic alcohol use across the lifespan (Lee et al., 2011). Research demonstrates that trait levels of impulsivity are positively associated with alcohol use and related outcomes (Dick et al., 2010), and that heightened trait impulsivity mediates the relation between ADHD and alcohol use

and problems (Pedersen et al., 2016; Rooney et al., 2015). Research has also shown that fluctuation in state impulsivity may further differentiate risk for alcohol outcomes for adults with a history of ADHD (Pedersen et al., 2019). This study extends this research to adolescence, when alcohol use is beginning. We hypothesized that among adolescents with ADHD, alcohol use and problems would be associated withmore variable impulsivity across a 17- day ecological momentary assessment (EMA) period. We also explored variability in inattention and hyperactivity domains.

Method: As part of a larger study, 94 adolescents aged 13-18 (Mage = 14.7; 67% boys; 76% White) prescribed medication for ADHD by their pediatricians completed questionnaires of demographics, any alcohol use in the past 6-months, and past 6-month likelihood of experiencing any alcohol problem (yes/no). Parents rated teen global ADHD symptoms on the Disruptive Behavior Disorders scale. Participants then completed 17 consecutive days of EMA in which they rated their ADHD symptoms (impulsivity, hyperactivity, inattention) four times daily. Average EMA completion across the 17 days was 80%.

Results: ADHD symptom variability (indexed by person-level SD) was significantly greater than zero for all three domains (Ms = 0.25-¦0.30, SD = 0.181-¦0.184, ts(93)13.5-16.0, ps < 0.001). Adjusting for age, race, gender, EMA completion rate, and parent-rated global ADHD symptoms, linear regressions showed that adolescents with any alcohol use experienced greater variability in impulsivity across EMA (b = 0.26, p < 0.05). Those who reported any alcohol problems similarly experienced greater variability in impulsivity (b = 0.23, p < 0.05). Additionally, alcohol use (not problems) was positively associated with variability in hyperactivity symptoms (b = 0.26, p < 0.05). Alcohol variables were unrelated to inattention symptomvariability.

Conclusions: Fluctuation in impulsivity and hyperactivity may index adolescents with ADHD at heightened risk for alcohol use and problems, whichmay be due to dysregulated behavior. Malleable momentary precursors that affect symptom expression (e.g., social context) should be identified as targets for in-the-moment interventions to reduce risk for alcohol outcomes

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Alcohol Clin Exp Res. 2020;44:129A.

THE NATURE OF ALCOHOL PROBLEMS DIFFERS FOR YOUNG ADULTSWITH AND WITHOUT CHILDHOOD ADHD.

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

Aims: Individuals with a history of ADHD may be more likely to experience alcohol problems at equivalent or lower levels of use compared to drinkers without ADHD (Wang et al., under review). However, it remains unknown whether those with ADHD show heightened risk for different kinds of alcohol problems when compared to those without ADHD. For example, ADHD-related impulsivity and social deficits may further worsen while drinking and lead to heightened alcohol-related impaired control and social consequences, respectively, relative to those without ADHD. However, given the lack of differences in alcohol consumption, tolerance/withdrawal could be equivalent for ADHD and non-ADHD individuals. We hypothesized that adults with versus without childhood ADHD would show more severe patterns of alcohol-related role impairments, interpersonal consequences, and impaired control, but equivalent (or less severe) physiological symptoms.

Methods: Participants were from the Pittsburgh ADHD Longitudinal Study (N = 565, ADHD = 60.3%; male = 89.1%, White = 81.9%, Black = 10.8%). Using YAAPST-measured lifetime alcohol problems (age 29; Hurlburt & Sher, 1992), four separate latent class analyses (LCAs) uncovered unique groups in these domains: (1) school/work role impairments; (2) interpersonal consequences; (3) control/cut down attempts; (4) physiological symptoms. Probability of groupmembership was regressed on childhood ADHD accounting for sex, race/ethnicity, and heavy drinking.

Resuts: Three classes representing high, moderate, and low severity fit best for role impairment, interpersonal, and impaired control LCAs. For interpersonal (b=0.16, p < 0.001) and role impairments (b=0.11, p = 0.009), high-severity groups were predominated by ADHD and elevated in all symptoms compared to moderate- and low-groups. For control attempts, the high-severity group was predominated by ADHD (b=0.17, p < 0.001) and similar to the moderate-severity group on all control attempts except treatment-seeking. Five classes fit best for physiological symptoms. Group 1 showed virtually no symptoms, and each subsequent group added a new symptom: (2) hangover/ sick; (3) passed/blacked out; (4) tolerance (predominated by non-ADHD; b=-0.14, p < 0.001); (5) withdrawal.

Conclusions: Our findings are the first to demonstrate important differences across alcohol problems for people with, compared to without, a history of ADHD. ADHD-related social deficits and impulsivity may exacerbate drinking-related consequences for this at-risk population. Future research examining social skills and impulsivity while sober and intoxicated is needed to further identify important treatment targets in this at-risk population

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Allergy Eur J Allergy Clin Immunol. 2020.

ADHD IN SCHOOL-AGE CHILDREN IS RELATED TO INFANT EXPOSURE TO SYSTEMIC H1-ANTIHISTAMINES.

Fuhrmann S, Tesch F, Romanos M, et al.

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American Journal of Neuroradiology. 2020;41:758-65.

METHYLPHENIDATE EFFECTS ON CORTICAL THICKNESS IN CHILDREN AND ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED CLINICAL TRIAL.

Walhovd KB, Amlien I, Schrantee A, et al.

BACKGROUND AND PURPOSE: Although methylphenidate is frequently used to treat children with attention-deficit/hyperactivity disorder, it is currently unknown how methylphenidate affects brain development. In a randomized controlled trial, we investigated whether the cortical effects of methylphenidate are modulated by age.

MATERIALS AND METHODS: Between June 1, 2011, and June 15, 2015, we conducted a randomized, double-blind, placebo-controlled trial (Effects of Psychotropic Drugs on Developing Brain-Methylphenidate) in 99 males with attention-deficit/hyperactivity disorder (according to Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, criteria) from referral centers in the greater Amsterdam area in the Netherlands. The trial was registered on March 24, 2011 (identifier NL34509.000.10) and subsequently at the Netherlands National Trial Register (identifier NTR3103). Participants (first enrolled October 13, 2011) were 10–12 years or 23–40 years of age and randomized to treatment with either methylphenidate or a placebo for 16 weeks. Our main outcome was a change in cortical thickness in predefined ROIs as measured by MR imaging pre- and posttreatment.

RESULTS: We observed a time × medication × age interaction ($F[1,88.825] = 4.316$, $P < .05$) for the right medial cortex ROI, where methylphenidate treatment yielded less cortical thinning in children, but not in adults or the placebo groups.

CONCLUSIONS: Our finding that the effects of methylphenidate on right medial cortical thickness differ between children and adults infers that the drug affects gray matter development in this brain region. This warrants replication in larger groups with longer follow-up to determine whether this effect can also be observed in other cortical brain regions and whether it may have long-term consequences

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Anadolu Psikiyatr Derg. 2020;21:423-28.

EXECUTIVE FUNCTIONS IN PRESCHOOL CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Kacamak Ogut D., et al.

Objective: Attention deficit hyperactivity disorder (ADHD) affects development and functionality of children in almost all fields including learning, behavior, family and peer relationships, physical safety and emotional progress. Except for this data, it is stated that preschool children with ADHD can differ from typically developing children in terms of their executive functions. In this study it is aimed to evaluate executive functions of preschool (36-71 months) ADHD cases by comparing these outcomes with control cases.

Methods: In our study 47 ADHD and 47 healthy control cases are included. ADHD group is made up of cases who refer to Ege University Faculty of Medicine Child and Adolescent Psychiatry 0-6 Age Outpatient Clinic. DSM-IV criteria used for diagnostic assessment of ADHD. Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P) administered by parents of cases.

Results: In comparison of ADHD and healthy control group we have found difference in all BRIEF-P scales. The biggest effect size values were observed in inhibition, working memory, inhibitory self-control and emergent metacognition.
Conclusion: As result of our study it was detected that preschool ADHD cases differ from healthy controls with regard to executive functions. It is important to support executive functions and take care of enhancing appropriate therapeutic strategies as from preschool years in children with ADHD, and also to prevent from long term problems like social, academic and self-regulation areas that can occur in this children

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Anadolu Psikiyatr Derg. 2020 Jun;21:319-26.

LOW HO-1 AND HIGH KEAP1 SERUM LEVELS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: THE FIRST CLINICAL STUDY.

Ayaydin H, Koyuncu i, et al.

Decrease plasma total antioxidant status (TAS)57 7 serum glutathione peroxidase (GSH-Px),8 paraoxonase-1(PON-1), arylesterase (ARE),6 and glutathione S-transferase (GST) activities9 and 8-hydroxy-2'-deoxyguanosine (8-OHdG) (a marker of DNA oxidative stress)10 level in children with ADHD than in control subjects have been reported. ADHD patients exhibited higher serum nitric oxide synthase (NOS), xanthine oxidase (XO) and adenosine deaminase (ADA) (a marker of cellular immunity) activities,9 and nitric oxide (NO) and malondialdehyde (MDA) (an indicator of lipid peroxidation) levels,8 plasma total oxidant status (TOS)6 and oxidative stress index (OSI).6'7'11 In the light of these studies, there appears to be an imbalance between the oxidant and antioxidant systems in children with ADHD. The activity of the antioxidant enzyme heme oxygenase-1 (HO-1) mediates the catabolism of toxic heme to carbon monoxide (CO), free ferrous iron (Fe++), biliverdin and bilirubin.12'13 The products that form following this activity then contribute to protection against oxidative damage, apoptosis regulation, inflammation regulation and angiogenesis.14'15 Nuclear factor erythroid 2 related factor 2 (NRF2) is a cytoprotective transcription factor that regulates cytoprotective genes such as HO-1.14 NRF2 is normally present in the form of an inactive complex with kelch-like ECH-associated protein 1 (KEAP1). Severe, many symptoms in excess of those required to make the diagnosis, or several symptoms that are particularly severe, are present, or the symptoms result in marked impairment in social or occupational functioning.18 Patient group exclusion criteria; insufficient intellectual capacity to understand the questions, use of any drugs within the previous two weeks (including antioxidant medication), presence during evaluation of any comorbid mental disorder (except for oppositional defiant disorder and conduct disorder) or physical, neurological, genetic, or other medical diseases (autism spectrum disorder, fragile-X syndrome, tuberous sclerosis, phenylketonuria, Lesch-Nyhan syndrome, fetal alcohol syndrome, history of head trauma, cardiovascular disease, autoimmune disease, infection, renal and hepatic diseases, malignancy, obesity, history of atopic eczema and/or allergy) and a history of maternal substance use during pregnancy

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Anadolu Psikiyatr Derg. 2020;21:557-60.

SUCCESSFUL MANAGEMENT OF METHYLPHENIDATE RELATED THROMBOCYTOPENIA DURING ADHD TREATMENT: A CASE REPORT.

Kaan H, Karaya-ƒmurlu A.

Methylphenidate is an effective and well tolerated agent frequently used in the treatment of attention deficit hyperactivity disorder. Thrombocytopenia is defined as a blood platelet count less than 150,000/mm3, and is an important hematological side-effect capable of causing mild symptoms or severe complications such as intracranial hemorrhage. Thrombocytopenia may develop in association with various causes, including drug use. There have been very few case reports of thrombocytopenia developing during methylphenidate use, and to the best of our knowledge there have been no reports concerning the management of this side-effect. This report describes the development of thrombocytopenia likely related to methylphenidate therapy

in an adolescent with attention deficit hyperactivity disorder and successful management with a safety switch to atomoxetine

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Anadolu Psikiyatr Derg. 2020 Aug;21:423-28.

Executive functions in preschool children with attention deficit hyperactivity disorder

Ögüt DK, Özbaran NB, Köse S, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) affects development and functionality of children in almost all fields including learning, behavior, family and peer relationships, physical safety and emotional progress. Except for this data, it is stated that preschool children with ADHD can differ from typically developing children in terms of their executive functions. In this study it is aimed to evaluate executive functions of preschool (36-71 months) ADHD cases by comparing these outcomes with controlcases.

Methods: In our study 47 ADHD and 47 healthy control cases are included. ADHD group is made up of cases who refer to Ege University Faculty of Medicine Child and Adolescent Psychiatry 0-6 Age Outpatient Clinic. DSM-IV criteria used for diagnostic assessment of ADHD. Behavior Rating Inventory of Executive Function-Preschool Version (BRIEF-P) administered by parents of cases.

Results: In comparison of ADHD and healthy control group we have found difference in all BRIEF-P scales. The biggest effect size values were observed in inhibition, working memory, inhibitory self-control and emergent metacognition.

Conclusion: As result of our study it was detected that preschool ADHD cases differ from healthy

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Anadolu Psikiyatr Derg. 2020 Aug;21:435-42.

PRENATAL ANDROGENS AND AUTISTIC, ATTENTION DEFICIT HYPERACTIVITY DISORDER, AND DISRUPTIVE BEHAVIOR DISORDERS TRAITS.

Günes H, Tanidir C, Doktur H, et al.

INTRODUCTION Autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) are both neurodevelopmental conditions.1 ASD is characterized by deficits in social communication and interactions, stereotypic behaviors, and restricted interests. Attention-deficit/hyperactivity disorder (ADHD) is defined by developmentally inappropriate levels of inattention, hyperactivity, and/or impulsivity, with onset before the age of 12 years.1 ASD and ADHD frequently co-occur, and a substantial body of research has shown that many similarities are present in genetic factors, brain characteristics, and cognitive profiles of these disorders.2'3 ASD and ADHD both are more prevalent in males than females. Males are approximately four times more likely than females to receive a diagnosis of ASD4 and males are more likely than females to receive a diagnosis of ADHD, with ratios varying from 2:1 to 9:1.5 Oppositional defiant disorder/ODD and conduct disorder/CD are childhood and adolescent onset disruptive behavior disorders/DBDs, characterized by symptoms including angry/irritable mood, argumentative/defiant behavior and vindictiveness in ODD and violating the basic rights of others or major age-appropriate societal norms or rules, aggression to people or animals, destruction of property, deceitfulness or theft in CD.1 ODD and CD frequently co-occur with ADHD6 and similar to that in ASD and ADHD, ODD and CD are also more prevalent in males with ratios found 1.59:1 for ODD7 and varying between 2.4:1 and 3:1 for CD.8'9 Prenatal androgen exposure has been proposed to account for the male predominance in ASD.10 In accordance with this, elevated prenatal testosterone levels have shown to be associated with autistic traits in children between 18-24 months11 and 6-10 years;12 but recent research has reported contradictory findings.13-16 To date, more research has been conducted regarding hormone exposures in the prenatal environment for ASD compared to ADHD.17 However, there are studies showing a link between ADHD or DBDs and lower second and fourth digits (2D:4D) ratio.18-20 Being lower in males than in females, the 2D:4D ratio is a sexually dimorphic trait;18-20 and evidence suggests that sex differences in 2D:4D is associated with prenatal testosterone exposure.18'19 Furthermore, in their recent study utilizing maternal polycystic ovary syndrome (PCOS) as a model for prenatal androgen exposure in the offspring, Kosidou et al.17 reported an increased risk of ADHD in children of women with

PCOS. The most common form of CAH is caused by mutations in the CYP21A2 gene encoding 21-hydroxylase, which interferes with cortisol production and increases androgen production beginning prenatally.21 Classic forms of CAH result in exposure to excess androgen levels in utero; therefore, CAH has been suggested as a model to elucidate the organizational effects of prenatal androgen exposure since direct manipulation of the prenatal hormones to investigate its effects on human behavior is unethical.22 Although they are diagnosed and treated early due to genital virilization at birth,23 studies in females with CAH have shown masculinization in various aspects of behavior such as childhood play preferences, physical aggression, empathy, sexual orientation and gender identity.22 Conversely, males with CAH generally do not differ from the normal population regarding sex-linked behavior;22 and the evidence does not support that they are exposed to heightened levels of androgens prenatally.24'25 Research on ASD, ADHD and DBD symptomatology in children and adolescents with CAH is sparse and had produced inconsistent findings.14'26-28 The aim of this cross-sectional study is to investigate the prevalence of ASD, ADHD, and DBD traits in children and adolescents with CAH

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Autism Res. 2020.

ASSOCIATIONS BETWEEN THEORY OF MIND AND CONDUCT PROBLEMS IN AUTISTIC AND NONAUTISTIC YOUTH.

Carter L, V, Chandler S, White P, et al.

Many autistic young people exhibit co-occurring behavior difficulties, characterized by conduct problems and oppositional behavior. However, the causes of these co-occurring difficulties are not well understood. Impairments in theory of mind (ToM) are often reported in autistic individuals and have been linked to conduct problems in nonautistic individuals. Whether an association between ToM ability and conduct problems exists in autistic populations, whether this association is similar between individuals who are autistic versus nonautistic, and whether these associations are specific to conduct problems (as opposed to other domains of psychopathology) remains unclear. ToM ability was assessed using the FrithΓÇôHapp+® Triangles task in a pooled sample of autistic (N = 128; mean age 14.78 years) and nonautistic youth (N = 50; mean age 15.48 years), along with parent-rated psychiatric symptoms of conduct problems, hyperactivity/inattention and emotional problems. Analyses tested ToM ability between autistic versus nonautistic participants, and compared associations between ToM performance and conduct problems between the two groups. Where no significant group differences in associations were found, the pooled association between ToM and conduct problems was estimated in the combined sample. Results showed no evidence of moderation in associations by diagnostic status, and an association between poorer ToM ability and higher levels of conduct problems, hyperactivity/inattention and emotional problems across the total sample. However, these associations became nonsignificant when adjusting for verbal IQ. Results provide support for theoretical models of co-occurring psychopathology in autistic populations, and suggest targets for intervention for conduct problems in autistic youth. Lay Summary: Many young people with autism spectrum disorder show co-occurring behavior problems, but the causes of these are not well understood. This paper found an association between difficulties recognizing what others think and intend (so-called ΓÇ£theory of mindΓÇØ) in a simple animated task, and emotional and behavioral problems in autistic and nonautistic young people. However, a substantial part of this association was explained by individual differences in verbal ability. These findings may have implications for intervention efforts to improve young people's mental health

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Behav Genet. 2020;50:247-62.

EXAMINING THE ROLE OF GENETIC RISK AND LONGITUDINAL TRANSMISSION PROCESSES UNDERLYING MATERNAL PARENTING AND PSYCHOPATHOLOGY AND CHILDRENΓÇÖS ADHD SYMPTOMS AND AGGRESSION: UTILIZING THE ADVANTAGES OF A PROSPECTIVE ADOPTION DESIGN.

Sellers R, Harold GT, Thapar A, et al.

Although genetic factors may contribute to initial liability for ADHD onset, there is growing evidence of the potential importance of the rearing environment on the developmental course of ADHD symptomatology. However, associations between family-level variables (maternal hostility, maternal depressive symptoms)

and child behaviors (developmental course of ADHD and aggression) may be explained by genes that are shared by biologically related parents and children. Furthermore, ADHD symptoms and aggression commonly co-occur: it is important to consider both simultaneously to have a better understanding of processes underlying the developmental course of ADHD and aggression. To addresses these issues, we employed a longitudinal genetically sensitive parentΓÇôoffspring adoption design. Analyses were conducted using Cohort I (n = 340) of the Early Growth and Development Study with cross-validation analyses conducted with Cohort II (n = 178). Adoptive mother hostility, but not depression, was associated with later child ADHD symptoms and aggression. Mothers and their adopted children were genetically unrelated, removing passive rGE as a possible explanation. Early child impulsivity/activation was associated with later ADHD symptoms and aggression. Child impulsivity/activation was also associated with maternal hostility, with some evidence for evocative gene-environment correlation processes on adoptive mother depressive symptoms. This study provides novel insights into family-based environmental influences on child ADHD and aggression symptoms, independent of shared parental genetic factors, implications of which are further explicated in the discussion

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Behav Genet. 2020;50:203-12.

PSYCHIATRIC POLYGENIC RISK SCORES AS PREDICTOR FOR ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER IN A CLINICAL CHILD AND ADOLESCENT SAMPLE.

Jansen AG, Dieleman GC, Jansen PR, et al.

Neurodevelopmental disorders such as attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are highly heritable and influenced by many single nucleotide polymorphisms (SNPs). SNPs can be used to calculate individual polygenic risk scores (PRS) for a disorder. We aim to explore the association between the PRS for ADHD, ASD and for Schizophrenia (SCZ), and ADHD and ASD diagnoses in a clinical child and adolescent population. Based on the most recent genome wide association studies of ADHD, ASD and SCZ, PRS of each disorder were calculated for individuals of a clinical child and adolescent target sample (N = 688) and for adult controls (N = 943). We tested with logistic regression analyses for an association with (1) a single diagnosis of ADHD (N = 280), (2) a single diagnosis of ASD (N = 295), and (3) combining the two diagnoses, thus subjects with either ASD, ADHD or both (N = 688). Our results showed a significant association of the ADHD PRS with ADHD status (OR 1.6, P = 1.39 +ù 10ΓêÆ07) and with the combined ADHD/ASD status (OR 1.36, P = 1.211 +ù 10ΓêÆ05), but not with ASD status (OR 1.14, P = 1). No associations for the ASD and SCZ PRS were observed. In sum, the PRS of ADHD is significantly associated with the combined ADHD/ASD status. Yet, this association is primarily driven by ADHD status, suggesting disorder specific genetic effects of the ADHD PRS

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Behav Genet. 2020;50:273-88.

THE (BROAD-SENSE) GENETIC CORRELATIONS AMONG FOUR MEASURES OF INATTENTION AND HYPERACTIVITY IN 12 YEAR OLDS.

Dolan CV, De Zeeuw EL, Zayats T, et al.

We estimated the genetic covariance matrix among four inattention (INATT) and four hyperactivity (HYP) measures in the classical twin design. Data on INATT and HYP symptom counts were obtained in mono- and dizygotic twin pairs (N = 1593) with an average age of 12.2-áyears (sd =.51). We analyzed maternal ratings of INATT and HYP based on the ConnersΓÇÖ Parent Rating Scale (CPRS), the Strengths and Weaknesses of ADHD-symptoms and Normal-behavior (SWAN), and teacher ratings based on the Conners' Teacher rating scale (CTRS) and the ASEBA Teacher Rating Form (TRF). Broad-sense heritabilities, corrected for the main effects of sex and for random teacher rater effects, were large (ranging from.658 to.912). The results reveal pervasive and strong broad-sense genetic effects on INATT and HYP phenotypes with the phenotypic covariance among the phenotypes-álargely due to correlated genetic effects.-áSpecifically between 79.9 and 99.9% of the phenotypic covariance among the HYP measures, and between 81.0 and 93.5% of the INATT measures are attributable to broad-sense genetic effects. Overall, the present

results, pertaining to the broad-sense heritabilities and shared genetic effects, support the current genome-wide association meta-analytic approach to identifying pleiotropic genetic variants

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BJGP Open. 2020;4.

THE DIAGNOSIS AND MANAGEMENT OF ADHD (ATTENTION DEFICIT HYPERACTIVITY DISORDER) IN CHILDREN AND YOUNG PEOPLE: A COMMENTARY ON CURRENT PRACTICE AND FUTURE RECOMMENDATIONS.

Bowling Z, Nettleton A.

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BJOG Int J Obstet Gynaecol. 2020.

ASSOCIATION OF MATERNAL ATTENTION DEFICIT HYPERACTIVITY DISORDER AND PRETERM BIRTH: A COHORT STUDY.

Hesselman S, Wikman A, Skoglund C, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) affects 3–7% of women of childbearing age. Whether ADHD is associated with an increased risk of preterm birth is unclear.

Design National register-based cohort study.

Setting Sweden.

Population Nulliparous women giving birth to singleton infants 2007–2014 (n = 377 381).

Methods Women were considered to have ADHD if they had been dispensed at least one prescription for ADHD medication, i.e. a central nervous system stimulant or non-stimulant drugs for ADHD, prior to, during or after pregnancy (2005–2014). Women with ADHD were compared with women without ADHD in regard to prevalence, severity and mode of onset of preterm birth. Logistic regression models were used, estimating adjusted odds ratios (aOR) with 95% confidence intervals (CI). Adjustments were made for maternal age and country of birth (model 1), and in addition for body mass index (BMI), education, alcohol or substance use disorders, and pre-gestational medical and psychiatric co-morbidity (model 2).

Main outcome measures Preterm birth (<37 weeks).

Results During the study period, 6327 (1.7%) women gave birth and had ADHD according to our definition. These women had a higher rate of preterm birth compared with women without ADHD (7.3 versus 5.8%, aOR model 2: 1.17; 95% CI 1.05–1.30). ADHD was particularly associated with very (<32 weeks) preterm births, and associations were seen with both spontaneous and medically indicated onsets.

Conclusions Women with ADHD (i.e. who had been dispensed ADHD medication at any time in 2005–2014) had an increased risk of preterm birth.

Tweetable abstract Women with ADHD have a higher risk of preterm birth but most of it is due to modifiable risk factors

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BJPsych Open. 2020 Jul;6.

MAPPING UK MENTAL HEALTH SERVICES FOR ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: NATIONAL SURVEY WITH COMPARISON OF REPORTING BETWEEN THREE STAKEHOLDER GROUPS.

Price A, Janssens A, Newlove-Delgado T, et al.

Background UK clinical guidelines recommend treatment of attention-deficit hyperactivity disorder (ADHD) in adults by suitably qualified clinical teams. However, young people with ADHD attempting the transition from children's to adults' services experience considerable difficulties in accessing care.

Aims To map the mental health services in the UK for adults who have ADHD and compare the reports of key stakeholders (people with ADHD and their carers, health workers, service commissioners).

Method A survey about the existence and extent of service provision for adults with ADHD was distributed online and via national organisations (e.g. Royal College of Psychiatrists, the ADHD Foundation). Freedom of information requests were sent to commissioners. Descriptive analysis was used to compare reports from the different stakeholders.

Results A total of 294 unique services were identified by 2686 respondents. Of these, 44 (15%) were dedicated adult ADHD services and 99 (34%) were generic adult mental health services. Only 12 dedicated services (27%) provided the full range of treatments recommended by the National Institute for Health and Care Excellence. Only half of the dedicated services (55%) and a minority of other services (7%) were reported by all stakeholder groups (P < 0.001, Fisher's exact test).
Conclusions There is geographical variation in the provision of NHS services for adults with ADHD across the UK, as well as limited availability of treatments in the available services. Differences between stakeholder reports raise questions about equitable access. With increasing numbers of young people with ADHD graduating from children's services, developing evidence-based accessible models of care for adults with ADHD remains an urgent policy and commissioning priority

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BMC Neurol. 2020;20.

MIGRAINE, ATTENTION DEFICIT HYPERACTIVITY DISORDER AND SCREEN TIME IN CHILDREN ATTENDING A SRI LANKAN TERTIARY CARE FACILITY: ARE THEY ASSOCIATED?

Attygalle UR, Hewawitharana G, Wijesinghe CJ.

Background: Headache and Attention Deficit Hyperactivity Disorder (ADHD) are two relatively common, neuropsychiatric conditions seen in children. Recent studies have shown an association between these two disorders, which are otherwise distinct conditions. This study aims to assess the association between migraine and ADHD, as well as the association between screen-time and these two conditions, among children attending a Sri Lankan tertiary care facility. Possible associations will have important implications in the clinical management of these conditions.
Methods: This was a comparative cross-sectional study of 226 children aged 5-14 years, attending clinics at a tertiary care hospital in Galle, Sri Lanka. Of them, 141 had a diagnosis of migraine and 85 did not have migraine. The presence or absence of ADHD and the use of screen-time among the two groups was analysed. Chi-square test and Mann-Whitney U test was used to assess the associations between these variables.
Results: Approximately 5% of the children with migraine had clinically diagnosed ADHD, compared to 3.5% of those without migraine (p = 0.862). The median SNAP-IV scores (inter-quartile range) of the children with migraine and without migraine were 0.60 (0.27-1.00) and 0.44 (0.16-0.80) respectively (p = 0.014). There was no significant difference in screen-time hours per day between children with and without clinically diagnosed ADHD. However, a significant difference in median screen-time (hours per day) was observed between children with and without migraine (2.0 h and 1.0 h respectively; p = 0.012).
Conclusions: Our findings suggest that children with migraine are more likely to show features of hyperactivity/impulsivity and inattentiveness than those without migraine. While no association was found between clinically diagnosed ADHD and screen-time, migraine was associated with longer daily screen use. Screening for ADHD in children diagnosed with migraine may be of benefit. Further studies are required to understand the possible benefits of reducing screen-time in children with migraine

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BMC Psychiatry. 2020;20.

EXAMINING THE AUTISTIC TRAITS IN CHILDREN AND ADOLESCENTS DIAGNOSED WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND THEIR PARENTS.

Okyar E, Gàker I.

Background: Attention-Deficit Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD) are two of the most frequently-observed neurodevelopmental disorders. Autistic traits are detected frequently in children who have ADHD. This study aimed to examine autism symptoms in children diagnosed with ADHD and their parents; and also, to investigate parental risk factors that increase autistic traits in children. Besides the risk factors related to pregnancy, birth and developmental history were examined.
Methods: Two groups were created consisting of 66 children diagnosed with ADHD and 33 children not diagnosed with ADHD and their parents. Autism symptoms were screened with the Autism Behavior

Checklist (ABC) in children, and Autism Spectrum Quotient (AQ) in parents. Also, Adult ADD/ADHD DSM-IV Based Diagnostic Screening and Rating Scale and Wender Utah Rating Scale (WURS) were used to determine ADHD symptoms in parents.
Results: It was determined that there were more autism symptoms in children who were diagnosed with ADHD than in the control group without ADHD. There were more autistic symptoms in boys and the presence of Oppositional Defiant Disorder (ODD). Although there were more ADHD symptoms in the parents of children diagnosed with ADHD, it was determined that they did not differ from parents in the control group in terms of autism symptoms. It was also determined that maternal and paternal ADHD symptoms were predictive for autism symptoms in children. It was also shown that maternal smoking during pregnancy is associated with more autistic traits.
Conclusion: ASD and ADHD show high levels of comorbidity. The etiology remains unclear. Both ADHD and ASD show strong hereditary transition. We found that maternal and paternal ADHD symptoms predict autism symptoms in children with ADHD. However, more studies are needed to reveal the etiology

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Brain Sciences. 2020;10:1-20.

THE EFFECTS OF THE EARLY START DENVER MODEL FOR CHILDREN WITH AUTISM SPECTRUM DISORDER: A META-ANALYSIS.

Fuller EA, Oliver K, Vejnoska SF, et al.

This meta-analysis examined the effects of the Early Start Denver Model (ESDM) for young children with autism on developmental outcome measures. The 12 included studies reported results from 640 children with autism across 44 unique effect sizes. The aggregated effect size, calculated using a robust variance estimation meta-analysis, was 0.357 (p = 0.024), which is a moderate effect size with a statistically significant overall weighted averaged that favored participants who received the ESDM compared to children in control groups, with moderate heterogeneity across studies. This result was largely driven by improvements in cognition (g = 0.412) and language (g = 0.408). There were no significant effects observed for measures of autism symptomology, adaptive behavior, social communication, or restrictive and repetitive behaviors

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Brain Stimul. 2020 Jul;13:1153-55.

TRANSCRANIAL DIRECT CURRENT STIMULATION FOR COMPULSIVITY IN ADOLESCENT FRATERNAL TWINS WITH NEURODEVELOPMENTAL DISORDERS.

Francis SM, Beard KL, Tseng A, et al.

The current article aims to design a symptom specific, biobehavioral treatment strategy for youth experiencing compulsivity. Participants were diagnosed with autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), and anxiety. Both twins had parent-reported compulsive symptoms, and one had obsessive-compulsive disorder (OCD) as a comorbid diagnosis (P1). In the present pilot study, we applied this approach to evaluate the design of a multi-modal intervention pairing tDCS with computerized cognitive training. A decrease in compulsivity symptoms was found in P1 (active tDCS) as compared to P2 (sham) on two distinct parent-report measures that capture heterogeneous expressions of compulsive symptomatology. Study limitations included: no observed change on the clinician-rated compulsivity measure and differing baseline scores between participants. Future symptom-specific approaches will need to include measures that test impact on presumably distinct symptoms directly. Furthermore, investigations into how this intervention may differentially impact specific categories of RRBs is warranted, as we observed in the different subscales of the RBS-R and OCI. (PsycInfo Database Record (c) 2020 APA, all rights reserved)

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British Journal of Educational Psychology. 2020 Jun;90:193-209.

ADHD AND EMOTIONAL ENGAGEMENT WITH SCHOOL IN THE PRIMARY YEARS: INVESTIGATING THE ROLE OF STUDENT-TEACHER RELATIONSHIPS.

Rushton S, Giallo R, Efron D.

Background Attention deficit hyperactivity disorder (ADHD) is consistently associated with poor school-level outcomes. Although school engagement is recognized as a protective factor associated with increased academic achievement, school retention/completion, and student well-being in the general population, little research has focused on school engagement in children with ADHD.

Aims To explore a model of the relationships between ADHD symptoms at age 7, student–teacher closeness and conflict at age 10, and emotional engagement with school at age 10 and 12.

Sample Participants were 498 grade one children (mean age = 7.3), recruited from 43 socio-economically diverse government primary schools in Melbourne. Follow-up occurred at 36 months (mean age = 10.5) and 54 months (mean age = 12.0).

Methods Data were drawn from a controlled community-based longitudinal study examining the long-term effects of ADHD on children's behaviour, learning, and day-to-day living. Data were collected via direct assessment and child, parent, and teacher surveys.

Results Path analysis revealed a significant, negative relationship between ADHD symptoms and emotional engagement with school, which was partially mediated by student–teacher conflict. This remained significant after controlling for differences in ADHD status (ADHD, high-risk, or control group), ADHD medication use, and socio-economic status.

Conclusions These findings highlight the negative impact of ADHD symptoms on children's emotional engagement with school. Given the role of student–teacher conflict in mediating this relationship, interventions aiming to reduce conflict in the student–teacher relationship may promote school engagement for students with ADHD, with potential to improve longer-term outcomes

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Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz. 2020 Jul;63:910-15.

ADHD IN THE TRANSITION TO ADULTHOOD: PREVALENCE, SYMPTOMS, RISKS, AND CARE.

Philipsen A, Dàpfner M.

Attention-deficit/hyperactivity disorder (ADHD) is aÂ common neurodevelopmental disorder. In contrast to earlier assumptions, ADHD at least partially persists into adulthood in 50-80% of the patients.This narrative review article highlights the risks, treatment options, and care requirements associated with the transition to adulthood. Available epidemiological and routine care data and guidelines are reviewed and screened for indications and recommendations to improve the health-care of adolescents with ADHD.Epidemiological and routine care data point to aÂ care gap for adolescents with ADHD in the sensitive phase of transition from adolescence to adulthood. Specific transition concepts should be expanded and their effectiveness scientifically investigated

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Child's Nerv Syst. 2020.

CLINICAL CHARACTERIZATION OF CHILDREN AND ADOLESCENTS WITH NF1 MICRODELETIONS.

Kehrer-Sawatzki H, Kluwe L, Salamon J, et al.

Purpose: An estimated 5-11% of patients with neurofibromatosis type 1 (NF1) harbour NF1 microdeletions encompassing the NF1 gene and its flanking regions. The purpose of this study was to evaluate the clinical phenotype in children and adolescents with NF1 microdeletions.

Methods: We retrospectively analysed 30 children and adolescents with NF1 microdeletions pertaining to externally visible neurofibromas. The internal tumour load was determined by volumetry of whole-body magnetic resonance imaging (MRI) in 20 children and adolescents with NF1 microdeletions. Furthermore, the prevalence of global developmental delay, autism spectrum disorder and attention deficit hyperactivity disorder (ADHD) were evaluated.

Results: Children and adolescents with NF1 microdeletions had significantly more often cutaneous, subcutaneous and externally visible plexiform neurofibromas than age-matched patients with intragenic NF1 mutations. Internal neurofibromas were detected in all 20 children and adolescents with NF1 microdeletions analysed by whole-body MRI. By contrast, only 17 (61%) of 28 age-matched NF1 patients without microdeletions had internal tumours. The total internal tumour load was significantly higher in NF1 microdeletion patients than in NF1 patients without microdeletions. Global developmental delay was observed in 28 (93%) of 30 children with NF1 microdeletions investigated. The mean full-scale intelligence quotient in our patient group was 77.7 which is significantly lower than that of patients with intragenic NF1 mutations. ADHD was diagnosed in 15 (88%) of 17 children and adolescents with NF1 microdeletion. Furthermore, 17 (71%) of the 24 patients investigated had T-scores 60 up to 75, indicative of mild to moderate autistic symptoms, which are consequently significantly more frequent in patients with NF1 microdeletions than in the general NF1 population. Also, the mean total T-score was significantly higher in patients with NF1 microdeletions than in the general NF1 population.
Conclusion: Our findings indicate that already at a very young age, NF1 microdeletions patients frequently exhibit a severe disease manifestation which requires specialized long-term clinical care

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Child Adolesc Ment Health. 2020.

CONTEXT-DEPENDENT IRRITABILITY IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER: CORRELATES AND STABILITY OF FAMILY-RESTRICTED VERSUS CROSS-SITUATIONAL TEMPER OUTBURSTS .

Courbet O, Slama H, Purper-Ouakil D, et al.

Background: Impairing irritability is highly prevalent in children with attention deficit/hyperactivity disorder (ADHD), although manifestations of irritability are not necessarily present in all settings (home, school, with peers). At the moment, little is known about the relative prevalence, stability, and etiologies of contextual versus cross-situational manifestations of irritability in ADHD. In this study, levels of dysfunctional parenting practices and sleep problems were compared in irritable versus nonirritable children with ADHD, in cases of family-restricted versus cross-situational irritability, and examined as predictors of irritability levels over a one-year interval. Stability of irritability manifestations over time was investigated, and prevalence of cross-situational disruptive mood dysregulation disorder (DMDD) versus 'family-restricted' DMDD was compared.
Method: One hundred and seventy children with ADHD (age 6–11) were examined. Parents completed a semi-structured interview and questionnaire to assess irritability, and parent-report questionnaires were used to evaluate parenting practices and sleep problems. Questionnaires were completed for a second time after a one-year interval.
Results: Parenting practices were more dysfunctional in the irritable group compared to the nonirritable group, while sleep problems did not differ between these two groups. Levels of parenting practices and sleep problems did not predict later irritability after correction for multiple comparison nor did they differ between the family-restricted and cross-situational irritable groups. Finally, family-restricted irritability was as prevalent and as stable over time as cross-situational irritability and family-restricted DMDD as prevalent as cross-situational DMDD.
Conclusions: Factors associated with contextual versus cross-situational manifestations of irritability in ADHD remain elusive. More subtle measures of parenting practices should be considered, including psychological control or accommodation, and other constructs such as social inhibition. Despite not being captured by current nosography, severe forms of family-restricted irritability may be as prevalent as severe forms of cross-situational irritability

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Child Dev. 2020 Jul;91:e853-e865.

ATTENTION DEFICIT HYPERACTIVITY DISORDERÂ€• SYMPTOMS, SOCIAL MEDIA USE INTENSITY, AND SOCIAL MEDIA USE PROBLEMS IN ADOLESCENTS: INVESTIGATING DIRECTIONALITY.

Boer M, Stevens G, Finkenauer C, et al.

Cross-sectional research shows that adolescents' social media use (SMU) and attention deficit hyperactivity disorder (ADHD)-symptoms are related, but it is unclear whether this relation is explained by SMU intensity or by addiction-like SMU problems. Also, due to the lack of longitudinal studies, the direction of this relation remains unknown. This study aims to disentangle which type of SMU is related to ADHD-symptoms, and in which direction, using a three-wave longitudinal study among Dutch adolescents aged 11–15 years (n = 543). Findings suggest a unidirectional relation: SMU problems increased ADHD-symptoms over time, SMU intensity did not. This implies that problematic use, rather than the intensity of use harmfully affects adolescents' ADHD-symptoms

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Child Neuropsychol. 2020;1-20.

ADHD AND HYPERACTIVITY: THE INFLUENCE OF COGNITIVE PROCESSING DEMANDS ON GROSS MOTOR ACTIVITY LEVEL IN CHILDREN.

Dekkers TJ, Rapport MD, Calub CA, et al.

Excessive gross motor activity is a prominent feature of children with ADHD, and accruing evidence indicates that their gross motor activity is significantly higher in situations associated with high relative to low working memory processing demands. It remains unknown, however, whether children's gross motor activity rises to an absolute level or accelerates incrementally as a function of increasingly more difficult cognitive processing demands imposed on the limited capacity working memory (WM) system–a question of both theoretical and applied significance. The present investigation examined the activity level of 8- to 12-year-old children with ADHD (n = 36) and Typically Developing (TD) children (n = 24) during multiple experimental conditions: a control condition with no storage and negligible WM processing demands; a short-term memory (STM) storage condition; and a sequence of WM conditions that required both STM and incrementally more difficult higher-order cognitive processing. Relative to the control condition, all children, regardless of diagnostic status, exhibited higher levels of gross motor activity while engaged in WM tasks that required STM alone and STM combined with upper level cognitive processing demands, and children with ADHD were motorically more active under all WM conditions relative to TD children. The increase in activity as a consequence of cognitive demand was similar for all experimental conditions. Findings suggest that upregulation of physical movement rises and remains relatively stable to promote arousal related mechanisms when engaged in cognitive activities involving WM for all children, and to a greater extent for children with ADHD

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Clin EEG Neurosci. 2020.

FRONTAL BETA ACTIVITY IN THE META-INTENTION OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Liao Y-C, Guo N-W, Su B-Y, et al.

Children with attention deficit hyperactivity disorder (ADHD) have high theta and low beta activity in the frontal lobe. The higher the theta/beta ratio, the lower the level of central nervous system (CNS) cortical arousal. However, there is seldom evidence between electroencephalograms (EEGs) and the patientΓÇÖs intentionality to regulate the cortical activity of executive attention tasks. We investigated whether children with ADHD intended to improve their performance in executive attention tasks and whether that increased their brain activity. Fifty-one children with ADHD (ADHD) and 51 typical developing (TD) children were investigated using focused attention (FA) and search attention (SA) tasks and a simultaneous EEG. The children were then regrouped as faster (ADHD-F, TD-F) and slower (ADHD-S, TD-S) depending on reaction time (RT). Quantitative EEGs of frontal lobe theta and beta activity at frontal F3, F4, and Fz were used. Twenty-eight (54.9%) ADHD children were regrouped as ADHD-S and 14 (27.5%) as TD-S. The ADHD-S group, however, had poorer FA and SA performance than the other 3 groups did: fewer correct answers,

more frequent impulsive and missing errors, and higher RT variations. There were no significant differences in theta activity, but the TD-S group had higher beta activity than the ADHD-S group did. We conclude that the ADHD-F and ADHD-S groups had different attention processes. beta activity did not increase in the ADHD-S group, and their executive attention performance in the FA and SA tests was poor. It seems ADHD-S had poor meta-intention function. The frontal beta activity might be a feasible training target of neurofeedback in ADHD-S patients

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Clin Neuropharmacol. 2020;43:50-51.

A Severe Adverse Effect of Atomoxetine: Hypertensive Crisis.

Guldiken G, Karayagmurlu A.

Atomoxetine, a selective norepinephrine (noradrenaline) reuptake inhibitor, is an effective medication in attention-deficit hyperactivity disorder with a generally well-tolerated adverse effect profile. However, unusual side effects may occur during treatment. Here we report a case of hypertensive crisis in an 8-year-old male patient with autism spectrum disorder and attention-deficit hyperactivity disorder receiving atomoxetine treatment. We plan to discuss the clinical picture of the subject and importance of close monitoring during atomoxetine treatment

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Clin Neuropharmacol. 2020;43:46-47.

Atomoxetine Induced Skin Picking: A Case Report.

Kasar N, Yurteri N.

"Skin picking disorder,"also known as "dermatillomania"or "psychogenic excoriation,"is classified in the "Obsessive Compulsive and Related Disorders"category in Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition and characterized by repetitive skin picking behaviors resulting in skin lesions. Atomoxetine (ATX) is a selective norepinephrine (noradrenaline) reuptake inhibitor commonly used in the management of attention-deficit/hyperactivity disorder. Atomoxetine is considered to increase levels of noradrenaline and dopamine by inhibiting norepinephrine transporters. In this case report, we present an 8-year-old male attention-deficit/hyperactivity disorder patient with skin picking behavior due to ATX treatment. We discussed possible explanations of skin picking behavior with ATX in the light of the current literature. To our knowledge, this is the first report of skin picking due to ATX in literature, and further studies are needed to investigate the frequency and mechanisms of skin picking with ATX

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Clin Neurophysiol. 2020;131:2236-49.

Error and post-error processing in children with attention-deficit/hyperactivity disorder: An electrical neuroimaging study.

Janssen TWP, van AN, Oosterlaan J.

Objective: Inaccurate and inconsistent response styles in attention-deficit/hyperactivity disorder (ADHD) have been observed in a wide variety of cognitive tasks, in line with regulatory deficit models of ADHD. Event-related potential (ERP) studies of error processing have provided evidence for these models, but are limited in specificity. We aimed to improve the isolation, localization and identification of error (self-monitoring and adaptive control) and post-error (implementation of cognitive control) processing in ADHD.

Methods: ERPs were obtained for 46 ADHD and 51 typically developing (TD) children using the stop-signal task. Response-locked error (Ne and Pe) and stimulus-locked post-error (N2) components were compared between groups. Ne/Pe were corrected for preceding stimulus overlap and group differences were localized.

Results: Ne was intact, while Pe amplitude was markedly reduced in children with ADHD (p2 = 0.14). Pe differences were localized in the dorsal posterior/midcingulate (BA31/24) cortex. While the TD group showed increased N2 amplitude in post-error trials (+Àp2 = 0.24), localized in the left ventrolateral prefrontal cortex (VLPFC) and angular gyrus, the ADHD group did not.

Conclusions: Self-regulation deficits in ADHD are associated with later stages of error processing and subsequent implementation of cognitive control. Significance: We contribute to the literature by further specifying error processing deficits in ADHD

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Clin Neurophysiol. 2020;131:2115-30.

CORTICAL SOURCE ANALYSIS OF RESTING STATE EEG DATA IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Ahmadi M, Kazemi K, Kuc K, et al.

Objective: This study investigated age-dependent and subtype-related alterations in electroencephalography (EEG) power spectra and current source densities (CSD) in children with attention deficit and hyperactivity disorder (ADHD).

Methods: We performed spectral and cortical source (exact low-resolution electromagnetic tomography, eLORETA) analyses using resting state EEG recordings from 40 children (8-16 years) with combined and inattentive subtypes of ADHD and 41 age-matched healthy controls (HC). Group differences in EEG spectra and CSD were investigated at each scalp location, voxel and cortical region in delta, theta, alpha and beta bands. We also explored associations between topographic changes in EEG power and CSD and age.

Results: Compared to healthy controls, combined ADHD subtype was characterized with significantly increased diffuse theta/beta power ratios (TBR) with a widespread decrease in beta CSD. Inattentive ADHD subtype presented increased TBR in all brain regions except in posterior areas with a global increase in theta source power. In both ADHD and HC, older age groups showed significantly lower delta source power and TBR and higher alpha and beta source power than younger age groups. Compared to HC, ADHD was characterized with increases in theta fronto-central and temporal source power with increasing age.

Conclusions: Our results confirm that TBR can be used as a neurophysiological biomarker to differentiate ADHD from healthy children at both the source and sensor levels.

Significance: Our findings emphasize the importance of performing the source imaging analysis in order to better characterize age-related changes in resting-state EEG activity in ADHD and controls

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Clin Pediatr. 2020;59:787-800.

EFFECTS OF COLLABORATIVE CARE FOR COMORBID ATTENTION DEFICIT HYPERACTIVITY DISORDER AMONG CHILDREN WITH BEHAVIOR PROBLEMS IN PEDIATRIC PRIMARY CARE.

Kolko DJ, Hart JA, Campo J, et al.

This study evaluates the impact of a 6-month care management intervention for 206 children diagnosed with comorbid attention deficit hyperactivity disorder (ADHD) from a sample of 321 five- to 12-year-old children recruited for treatment of behavior problems in 8 pediatric primary care offices. Practices were cluster-randomized to Doctor Office Collaboration Care (DOCC) or Enhanced Usual Care (EUC). Chart reviews documented higher rates of service delivery, prescription of medication for ADHD, and titration in DOCC (vs EUC). Based on complex conditional models, DOCC showed greater acute improvement in individualized ADHD treatment goals and follow-up improvements in quality of life and ADHD and oppositional defiant disorder goals. Medication use had a significant effect on acute and follow-up ADHD symptom reduction and quality of life. Medication continuity was associated with some long-term gains. A collaborative care intervention for behavior problems that incorporated treatment guidelines for ADHD in primary care was more effective than psychoeducation and facilitated referral to community treatment

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Clin Psychopharmacol Neurosci. 2020;18:261-69.

ASSOCIATIONS BETWEEN EXPOSURE TO BISPHENOL A AND BEHAVIORAL AND COGNITIVE FUNCTION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A CASE-CONTROL STUDY.

Yoo S-J, Joo H, Kim D, et al.

Objective: Bisphenol A (BPA) is a widely produced synthetic chemical used to manufacture polycarbonate plastics and epoxy resins. We aimed to investigate the association between exposure to BPA and behavioral and cognitive function in children with attention-deficit/hyperactivity disorder (ADHD) and healthy controls.

Methods: The study included 444 children aged from 6 to 10 years. The ADHD and control groups included 195 and 249 children, respectively. BPA levels were assessed via urinalysis, while behavior was assessed using the Korean version of the ADHD Rating Scale (K-ARS) and the Behavior Assessment System for Children (BASC-2). Cognitive function was assessed using the Continuous Performance Test (i.e., ADHD Diagnostic System [ADS]). Participants were categorized into tertile groups based on urinary BPA concentration.

Results: Scores on the K-ARS and the hyperactivity, aggression, anxiety, and depression subscales of the BASC-2 were significantly different among tertile groups for urinary BPA levels. Scores on visual omission error, commission error, response time variability, and auditory commission error of the ADS were significantly different among three BPA groups. Subgroup analysis revealed that these differences of behavior and cognition among three BPA groups were observed in only boys and normal controls.

Conclusion: Exposure to BPA was associated with unfavorable behavioral and cognitive outcomes. Our study extends the findings of previous studies regarding the association between BPA exposure and behavior/cognitive function by including children with ADHD. Further studies are required to determine the mechanisms underlying sex- and group-based differences in these associations

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Clin Toxicol. 2020.

SUSTAINED STIMULATION? CHARACTERISTICS OF MODIFIED RELEASE AND IMMEDIATE RELEASE STIMULANT EXPOSURES REPORTED TO THE NATIONAL POISON DATA SYSTEM.

Darracq MA, Thornton SL.

Objective: We sought to examine ADHD modified release (MR) and immediate release (IR) stimulant ingestion exposures reported to the National Poison Data System (NPDS) to characterize the nature of the exposures and the outcomes associated with them.

Methods: The NPDS was queried for all single-substance exposures to MR and IR ADHD preparations between January 1, 2007 and December 31, 2017. MR and IR preparations were identified by a generic code of amphetamine and related compounds or methylphenidate and specific product name containing XR, CD, ER, LA, and SR.

Results: A total of 15,796 MR ingestions and 23,418 IR ingestions were identified and followed to known outcome. The majority of ingestions occurred in male patients and in own residence. More serious outcomes (moderate, major, or death) were more common in adult IR and MR ingestions as compared to pediatric; rates of serious outcome increased with age amongst pediatric ingestions. Unintentional ingestions were more common in both MR and IR pediatric cases while intentional ingestions occurred more frequently in adult cases. Symptoms consistent with a hyperadrenergic state were experienced in adult and pediatric patients for both MR and IR ingestions. Supportive care including benzodiazepine administration was more common in IR than MR ingestions. Decontamination with whole bowel irrigation was infrequent.

Conclusion: Rates of more serious outcome were similar between IR and MR ADHD stimulant ingestions. More serious outcomes were associated with advancing age and intentional ingestions. Similar rates of agitation, tachycardia, and hypertension were experienced by pediatric IR and MR ingestions while more common in adult IR as compared to MR ingestions. Rates of decontamination with whole bowel irrigation were overall low

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CMAJ. 2020;192:527-35.

PRENATAL ANTIBIOTIC EXPOSURE AND RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A POPULATION-BASED COHORT STUDY.

Hamad AF, Alessi-Severini S, Mahmud S, et al.

BACKGROUND: Abnormal microbiota composition induced by prenatal exposure to antibiotics has been proposed as a potential contributor to the development of attention-deficit/hyperactivity disorder (ADHD). We examined the association between prenatal antibiotic exposure and risk of ADHD.

METHODS: We conducted a populationbased retrospective cohort study of children born in Manitoba, Canada, between 1998 and 2017 and their mothers. We defined exposure as the mother having filled 1 or more antibiotic prescriptions during pregnancy. The outcome was diagnosis of ADHD in the offspring, as identified in administrative databases. We estimated hazard ratios (HRs) using Cox proportional hazards regression in the overall cohort, in a separate cohort matched on high-dimensional propensity scores and in a sibling cohort.

RESULTS: In the overall cohort, consisting of 187 605 children, prenatal antibiotic dispensation was associated with increased risk of ADHD (HR 1.22, 95% confidence interval [CI] 1.18-1.26). Similar results were observed in the matched cohort of 129 674 children (HR 1.20, 95% CI 1.15-1.24) but not in the sibling cohort (HR 1.06, 95% CI 0.99-1.13). Two negative-control analyses indicated a positive association with ADHD despite the lack of a reasonable biological mechanism, which suggested that the observed association between prenatal antibiotic dispensation and risk of ADHD was likely due to confounding

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CNS Drugs. 2020 Jul;34:731-47.

ASSOCIATIONS OF PRESCRIBED ADHD MEDICATION IN PREGNANCY WITH PREGNANCYÂ€'RELATED AND OFFSPRING OUTCOMES: A SYSTEMATIC REVIEW.

Li L, Sujan AC, Butwicka A, et al.

Background Increasing numbers of reproductive-aged women are using attention-deficit/hyperactivity disorder (ADHD) medications. Findings from studies exploring the safety of these medications during pregnancy are mixed, and it is unclear whether associations reflect causal effects or could be partially or fully explained by other factors that differ between exposed and unexposed offspring.

Objectives The aim of this systematic review was to evaluate the adverse pregnancy-related and offspring outcomes associated with exposure to prescribed ADHD medication during pregnancy with a focus on how studies to date have handled the influence of confounding.

Methods We searched PubMed, Embase, PsycINFO, and Web of Science up to 1 July 2019 without any restrictions on language or date of publication. We included all observational studies (e.g., cohort studies, case-control studies, case-crossover studies, cross-sectional studies, and registry-based studies) with pregnant women of any age or from any setting who were prescribed ADHD medications and evaluated any outcome, including both short- and long-term maternal and offspring outcomes. Two independent authors then used the Newcastle-Ottawa Scale to rate the quality of the included studies.

Results Eight cohort studies that estimated adverse pregnancy-related and offspring outcomes associated with exposure to ADHD medication during pregnancy were included in the qualitative review. The included studies had substantial methodological differences in data sources, type of medications examined, definitions of studied pregnancy-related and offspring outcomes, types of control groups, and confounding adjustment. There was no convincing evidence for teratogenic effects according to the relative risk of pregnancy-related and offspring outcomes, and the observed differences in absolute risks were overall small in magnitude. Adjustment for confounding was inadequate in most studies, and none of the included studies adjusted for ADHD severity in the mothers.

Conclusion The current evidence does not suggest that the use of ADHD medication during pregnancy results in significant adverse consequences for mother or offspring. However, the data are too limited to make an unequivocal recommendation. Therefore, physicians should consider whether the advantages of using ADHD medication outweigh the potential risks for the developing fetus according to each woman's specific circumstances. Future research should attempt to triangulate research findings based on a combination of different designs that differ in their underlying strengths and limitations and should investigate

specific confounding factors, the potential impact of timing of exposure, and potential long-term outcomes in the offspring

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Compr Psychiatry. 2020 Aug;101:7.

CLINICAL CORRELATES OF SOCIOECONOMIC STATUS IN ADOLESCENT BIPOLAR DISORDER.

Lu W, Dimick MK, Fiksenbaum LM, et al.

Background: Lower socioeconomic status (SES) is associated with symptomatic severity, comorbidity, and functional impairment in adults with bipolar disorder (BD). Little is known about clinical correlates of SES in adolescents with BD.

Methods: Participants included 195 adolescents, 13–20 years old, with BD type I, II or not otherwise specified (NOS). Diagnoses were determined by standardized semi-structured interviews. Based on the Hollingshead scale, participants were divided into “low” (SES 1–3) and the “high” (SES 4–5) SES groups. Demographic and clinical correlates of SES were evaluated in univariate analyses; significant variables were evaluated in a logistic regression model.

Results: Compared to participants in the high SES group (n = 150), participants in the low SES group (n = 45) were significantly younger, less likely to be of Caucasian race and living with natural parents. In the logistic regression model, controlling for age and race, the low SES group had higher risk of police contact or arrest (OR = 2.41, 95% CI:1.14–5.11, p = 0.022), less treatment with stimulants (OR = 0.20 95% CI: 0.06–0.67, p = 0.009), and more post-traumatic stress disorder (PTSD) (OR = 4.08, 95% CI:1.33–12.46, p = 0.014) compared to the high SES group. In sensitivity analyses that further controlled for intact family, the finding of higher rates of police contact or arrest was no longer significant.

Limitations: Cross-sectional design; higher-skewed SES sample.

Conclusions: Lower SES in adolescent BD is associated with higher legal risk, increased PTSD, and under-treatment of attention-deficit/hyperactivity disorder (ADHD). Future studies are needed to evaluate the inter-relationships of these correlates, using prospective designs that can evaluate the direction of these associations. Further studies incorporating neurobiological markers are also needed to explore mechanisms underlying SES-related differences in BD

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eNeurologicalSci. 2020;20.

A PEDIATRIC NEUROBEHAVIORAL TREATMENT CHALLENGE.

Whitley LE, Chepke C.

Tourette’s syndrome (TS) currently has very limited FDA approved treatment options, despite the fact that TS and other pediatric tic disorders are not uncommon and can cause significant emotional and physical distress for patients and their families. For providers who regularly see these conditions in practice this inadequacy is highly frustrating on the treatment side as there are such limited options to offer to these families, and the outcome to hope for is not highly optimistic. The outcome of this case presentation is an example of how health care providers can use clinical knowledge in combination with evidence-based practice to advocate for their patients and find new solutions that could be, and in this case were, life changing. It promotes providers to advocate for their patients and expand their knowledge. The final medication treatment utilized in this case is currently off label, however the method of finding and obtaining the treatment explained in the case additionally reveal to readers how to cautiously but judiciously make off label treatment decisions that can be important to practice and patient outcomes. In the course of this case the off-label medication use decision was backed by scientific literature and ongoing FDA studies as well as consulting with a collaborating psychiatrist. The subject matter and method of reasoning within this case also promote psychiatric providers use of evidence-based practice and implementation of science into active practice

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Environ Res. 2020;188.

RESIDENTIAL PYRETHROID INSECTICIDE USE, URINARY 3-PHENOXYBENZOIC ACID LEVELS, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-LIKE SYMPTOMS IN PRESCHOOL-AGE CHILDREN: THE ENVIRONMENT AND DEVELOPMENT OF CHILDREN STUDY.

Lee W-S, Lim Y-H, Kim B-N, et al.

Previous animal studies have reported that pyrethroids can cause dopamine system abnormalities and attention-deficit/hyperactivity disorder (ADHD) phenotypes. However, epidemiological studies investigating the associations between pyrethroid exposure and ADHD are limited. We aimed to investigate the association between pyrethroid exposure and ADHD-like symptoms among preschool-age children. We used data from 385 children at 4 years of age participating in the Environment and Development of Children (EDC) study. We evaluated pyrethroid exposure through questionnaires and urinary 3-phenoxybenzoic acid (3-PBA) concentrations. We assessed ADHD-like symptoms using the Korean ADHD rating scale (K-ARS). We conducted negative binomial regressions to evaluate the associations between pyrethroid exposure and ADHD-like symptoms. Residential use of insecticide adhesive (+¦ = 0.42, 95% CI: 0.11, 0.74) and insecticide spray (+¦ = 0.33, 95% CI: 0.08, 0.59) was associated with an increase in log-transformed creatinine-adjusted urinary 3-PBA concentrations. Residential insecticide adhesive use was associated with a 51.6% increase in K-ARS scores (95% confidence interval [CI]: 6.3, 116.1) among boys, when compared with non-users. When compared with creatinine-adjusted 3-PBA levels <0.50 ++g/g creatinine, creatinine-adjusted 3-PBA levels 3.80 ++g/g creatinine were associated with a 58% increase in K-ARS scores (95% CI: 0.1, 150.5) among boys. We found associations of residential pyrethroid insecticide use and urinary 3-PBA concentrations with K-ARS scores among preschool-age boys. Since the present study explored cross-sectional associations in preschool-age children, the possibility of reverse causality cannot be dismissed. Further studies implementing a cohort study design are warranted

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Epidemiol Psychiatr Sci. 2020.

METHYLPHENIDATE AND THE RISK OF BURN INJURY AMONG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Chen VCH, Yang Y-H, Yu KT, et al.

Aims Attention-deficit/hyperactivity disorder (ADHD) is associated with a higher risk of burn injury than in the normal population. Nevertheless, the influence of methylphenidate (MPH) on the risk of burn injury remains unclear. This retrospective cohort study analysed the effect of MPH on the risk of burn injury in children with ADHD.

Method Data were from Taiwan's National Health Insurance Research Database (NHIRD). The sample comprised individuals younger than 18 years with a diagnosis of ADHD (n = 90 634) in Taiwan's NHIRD between January 1996 and December 2013. We examined the cumulative effect of MPH on burn injury risk using Cox proportional hazards models. We conducted a sensitivity analysis for immortal time bias using a time-dependent Cox model and within-patient comparisons using the self-controlled case series model.

Results Children with ADHD taking MPH had a reduced risk of burn injury, with a cumulative duration of treatment dose-related effect, compared with those not taking MPH. Compared with children with ADHD not taking MPH, the adjusted hazard ratio for burn injury was 0.70 in children taking MPH for <90 days (95% confidence interval (CI) 0.64-0.77) and 0.43 in children taking MPH for 90 days (95% CI 0.40-0.47), with a 50.8% preventable fraction. The negative association of MPH was replicated in age-stratified analysis using time-dependent Cox regression and self-controlled case series models.

Conclusion This study showed that MPH treatment was associated with a lower risk of burn injury in a cumulative duration of treatment dose-related effect manner

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Epilepsia. 2020.

SELF-INJURIOUS AND SUICIDAL BEHAVIOR IN YOUNG ADULTS, TEENS, AND CHILDREN WITH EPILEPSY: A POPULATION-BASED STUDY.

Wirrell EC, Bieber ED, Vanderwiel A, et al.

Objective: Whereas studies in adult epilepsy patients have shown higher rates of suicidal ideation and attempt, such studies in children are limited. Using the Rochester Epidemiology Project database, we compared the risk of self-injurious behavior and suicidal ideation in a population-based cohort of childhood epilepsy to controls.

Methods: We studied 339 cases with epilepsy and 678 age- and sex-matched controls followed to a median age of 24.7 and 23.4-áyears, and identified 98 subjects with self-injurious behavior or suicidal ideation (43 with epilepsy and 55 controls). All behaviors were categorized using the Columbia Suicide Severity Rating Scale.

Results: Those with epilepsy had a significantly higher rate of any self-injurious behavior and suicidal ideation (hazard ratio [HR] = 1.56, 95% confidence interval [CI] = 1.04-2.35) and tended to have an increased risk of suicidal ideation and attempt (HR = 1.48, 95% CI = 0.93-2.37). The prevalence of preceding mood and substance abuse disorders was similarly high in both cases and controls with self-injurious behavior or suicidal ideation; however, preceding attention-deficit/hyperactivity disorder was more than twice as common in the epilepsy cases. Among cases with epilepsy, we did not identify any specific epilepsy-related variable that was significantly correlated with risk of self-injurious behavior or suicidal ideation.

Significance: Children, teens, and young adults with a history of childhood epilepsy are at greater risk of self-injurious behavior, highlighting the need for careful screening of mental health concerns as part of routine epilepsy care

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Epilepsy Behav. 2020;111.

CLINICAL AND ELECTROENCEPHALOGRAPHIC FEATURES OF BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES COMORBIDITY WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN SOUTHWEST CHINA.

Huang C, Hu W, Tan G, et al.

Purpose: This study was conducted to analyze the clinical and electroencephalographic (EEG) features of attention-deficit hyperactivity disorder (ADHD) in children with benign partial epilepsy with centrotemporal spikes (BECTS) in Southwest China, to address the question of what the risk factors are for patients with BECTS who suffer from ADHD.

Methods: Overall 118 right-handed children with BECTS were included from two medical centers. Of them, 29 patients were with diagnosed ADHD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) at baseline, and the remaining were considered as typical BECTS. Clinical and EEG characteristics were collected at baseline and follow-up endpoint of one year. All the patients completed an eight-hour video-electroencephalogram (VEEG) without sedation at those two time points using a digital system with international 10-20 array electrode placement. At the follow-up endpoint, we also evaluated the intelligence level of all patients using the Wechsler Intelligence Scale for Children-IV (WISC-IV). Multivariate logistical regression model was performed to assess the risk factors of ADHD in BECTS patients.

Results: Compared with typical BECTS, patients with BECTS-ADHD had an earlier age of onset, a longer disease course and tended to have lower intelligence quotient (IQ) scores. Their epileptiform discharges were more likely to diffuse to one or both hemispheres, and a higher percentage of patients with BECTS-ADHD patients needed multitherapy to control seizures. Multivariate analysis showed that age of onset, disease course, intelligence score, number of antiepileptic drugs (AEDs), and bilateral or diffusing discharges were independently associated with the occurrence of ADHD in patients with BECTS ($p < .05$). Additionally, we found that delayed diagnosis (37.3%) and nonadherence to treatment (16.1%) were the main reasons of a long disease course.

Conclusion: Benign partial epilepsy with centrotemporal spikes with ADHD has the characteristics of early age of onset, long course of disease and low intelligence score. In addition, the epileptiform discharges of BECTS-ADHD were prone to be bilateral or diffuse, and polypharmacological treatment is also common in this group

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Eur Addict Res. 2020.

SCREENED ATTENTION DEFICIT/HYPERACTIVITY DISORDER AS A PREDICTOR OF SUBSTANCE USE INITIATION AND ESCALATION IN EARLY ADULTHOOD AND THE ROLE OF SELF-REPORTED CONDUCT DISORDER AND SENSATION SEEKING: A 5-YEAR LONGITUDINAL STUDY WITH YOUNG ADULT SWISS MEN.

Moggi F, Schorno D, Soravia LM, et al.

Background: Attention deficit/hyperactivity disorder (ADHD), conduct disorder (CD), and sensation seeking (SS) have been consistently related to a higher risk of substance use (SU) and substance use disorder (SUD).

Objectives: To investigate the relationship between ADHD and prevalence rates in males at age 20 and age 25, the initiation of SU and SUD after age 20, and the escalation of SU from age 20 to age 25, and to explore the role of CD and SS in the relation of ADHD with SU and SUD initiation and escalation.

Method: Data were obtained as part of the Cohort Study on Substance Use Risk Factors (C-SURF), which focused on young Swiss men aged 20 years at baseline and 25 years at follow-up.

Results: Participants who screened positive for ADHD at baseline exhibited a higher rate of SU and SUD than participants who screened negative. The presence of ADHD symptoms at age 20 predicted initiation of all SU between age 20 and age 25, except for alcohol and smoking. After controlling for self-reported CD and SS, ADHD still predicted this late initiation of use of hallucinogens, meth-/amphetamines, and ecstasy/MDMA; non-medical use of ADHD medication and sedatives, and alcohol use disorder (AUD). No escalation of weekly drinking and smoking or annual cannabis use was observed from age 20 to age 25.

Conclusion: Screened-positive ADHD is an independent predictor of late SU and AUD, along with self-reported CD and SS. From a public health perspective, identifying ADHD is not only important in childhood and adolescence but also in early adulthood to guide specific interventions to lower risks of drug use initiation and the development of AUD in early adulthood

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Eur Addict Res. 2020.

THE INTERNATIONAL COLLABORATION ON ADHD AND SUBSTANCE ABUSE (ICASA): MISSION, RESULTS, AND FUTURE ACTIVITIES.

van de Glind G, Brynte C, Skutle A, et al.

Background: The International Collaboration on ADHD and Substance Abuse (ICASA) is a network of 28 centers from 16 countries initiated to investigate the link between attention deficit-hyperactivity disorder (ADHD) and substance use disorder (SUD). In this article, we present the mission, the results of finished studies, and the current and future research projects of ICASA.

Methods: During the past 10 years, 3 cross-sectional studies were conducted: two International ADHD in Substance use disorders Prevalence (IASP-1 and IASP-2) studies, directed at the screening, diagnosis, and the prevalence of adult ADHD in treatment-seeking patients with SUD, and the Continuous performance test for ADHD in SUD Patients (CASP) study, testing a novel continuous performance test in SUD patients with and without adult ADHD. Recently, the prospective International Naturalistic Cohort Study of ADHD and Substance Use Disorders (INCAS) was initiated, directed at treatment provision and treatment outcome in SUD patients with adult ADHD.

Results: The IASP studies have shown that approximately 1 in 6 adult treatment-seeking SUD patients also have ADHD. In addition, those SUD patients with adult ADHD compared to SUD patients without ADHD report more childhood trauma exposure, slower infant development, greater problems controlling their temperament, and lower educational attainment. Comorbid patients also reported more risk-taking behavior, and a higher rate of other psychiatric disorders compared to SUD patients without ADHD. Screening,

diagnosis, and treatment of this patient group are possible even before abstinence has been achieved. The results of the CASP study are reported separately in this special issue.
Conclusions: The ICASA research to date has demonstrated a high prevalence of comorbid ADHD and SUD, associated with elevated rates of additional comorbidities and risk factors for adverse outcomes. More research is needed to find the best way to treat these patients, which is the main topic of the ongoing INCAS study

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Eur Child Adolesc Psychiatry. 2020.
ISOLATED EPILEPTIFORM ACTIVITY IN CHILDREN AND ADOLESCENTS: PREVALENCE, RELEVANCE, AND IMPLICATIONS FOR TREATMENT.
Swatzyna RJ, Arns M, Tarnow JD, et al.
In the field of psychiatry diagnoses are primarily based on the report of symptoms from either the patient, parents, or both, and a psychiatristΓÇÖs observations. A psychiatric diagnosis is currently the most widely used basis for medication selection and the brain is seldom investigated directly as a source of those symptoms. This study addresses the request from the National Institute of Mental Health (NIMH) Research Domain Criteria Project (RDoC) for scientific research into neurological abnormalities that can be linked to psychiatric symptoms for the purpose of predicting medication response. One such neurological abnormality that has been the focus of many studies over the last three decades is isolated epileptiform discharges (IEDs) in children and adolescents without seizures. We conducted a systematic review of the literature to determine prevalence rates of IEDs within diagnostic categories. We then compared the prevalence of IEDs in the selected literature to our IRB-approved data archive. Our study found a consistent high prevalence of IEDs specifically for ADHD (majority > 25%) and ASD (majority > 59%), and consistent low prevalence rates were found for Depression (3%). If children and adolescents have failed multiple medication attempts, and more than one-third of them have IEDs, then an EEG would be justified within the RDoC paradigm

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Eur Child Adolesc Psychiatry. 2020.
PREDICTORS OF COMMUNITY VERSUS SPECIALTY MENTAL HEALTH SERVICE USE: A PROSPECTIVE COHORT STUDY.
Brattfjell ML, Jozefiak T, Wichstr+©m L.
Child and adolescent mental health specialized services (CAMHS) are supposed to serve those who are most seriously disturbed and impaired. However, little is known about how children receiving treatment at different levels of care differ. The present study seeks to determine whether having a psychiatric disorder and resulting impairment measured in early childhood increases the odds of receiving help in CAMHS versus from community services during middle childhood or whether other factors (e.g., parenting stress, family functioning) also influence service utilization. A screen-stratified sample (n = 995 of the 2003ΓÇô2004 birth cohorts) in Trondheim, Norway was assessed biennially from age 4ΓÇô12 with semi-structured diagnostic interviews and recording of service use, family functioning, parental perceived need, and parenting stress. Behavioral disorders more strongly predicted CAMHS than community service use, whereas impairment predicted community service use. However, impairment increased the odds of receiving services in CAMHS if the parents perceived a need for help. Parental perceived need for help also increased the odds of CAMHS use independent of diagnosis and impairment. Having an emotional disorder, attention deficit/hyperactivity disorder (ADHD), parenting stress, previous service use, or family functioning did not predict service use at either level. Whereas children with behavioral disorders received help from CAMHS, children with emotional disorders did not receive services at either level. ADHD did not predict service use, indicating that young children with ADHD without comorbid disorders are not sufficiently detected. Efforts to detect, refer and treat emotional disorders and ADHD at the appropriate level should be increased

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Eur Child Adolesc Psychiatry. 2020.

EFFICACY AND ACCEPTABILITY OF A SECOND DOSE OF ECOLOGICAL EXECUTIVE SKILLS TRAINING FOR CHILDREN WITH ADHD: A RANDOMIZED CONTROLLED STUDY AND FOLLOW-UP.

Qian Y, Fan Z, Gao B, et al.

To explore the efficacy and acceptability of a second dose of the 12-session ecological executive skills training (EEST) 1-áyear after the initial training in children with ADHD. A total of 97 children (aged 6ΓÇô12) with ADHD who finished the first dose for about 1-áyear were recruited in the current study. 70 children who agreed to participate the second dose were randomized to the second dose or waitlist group. Both groups were followed up 1-áyear after the second dose. Executive function, core symptoms were assessed at the time of pre-intervention first dose, pre-intervention second dose, post-intervention second dose and follow-up 1-áyear after second dose (phase 0ΓÇô3). For the immediate efficacy, the improvements in the second dose group were greater than the waitlist group on planning by Stockings of Cambridge and delay aversion by Cambridge gambling task (P = 0.02ΓÇô0.04, +À2 = 0.07Γ Çô0.08). The parent rating of symptoms assessed by ADHD-RS-IV of the second dose group were also greater than the waitlist group rated by self-report. For long term efficacy, Linear mixed model indicated that there was significant time effect for both groups between phase 3 and phase 1, phase 1 and phase 0 on Behavior Rating Scales of Executive Function and ADHD-RS-IV (F = 2.849ΓÇô21.560, P = 0.001ΓÇô0.048). The compliance rate was 94.3% for the second dose group and 49% for waitlist group. A second dose of EEST program might bring further efficacy of EF and core symptoms for children with ADHD and it was well accepted

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Eur Child Adolesc Psychiatry. 2020.

VIDEO GAMES FOR THE ASSESSMENT AND TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW.

Penuelas-Calvo I, Jiang-Lin LK, Girela-Serrano B, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent and serious disorder among children. Video games have shown potential for aiding in child healthcare. Video games could contribute to the assessment and management of ADHD, but there are no previous reviews on this topic. Here, we systematically review the evidence about video game-based assessment tools and interventions for children diagnosed with ADHD. This review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. The review protocol was registered in PROSPERO database. We searched four databases-PubMed, PsycInfo, Embase and clinicaltrials.gov-to identify original studies exploring either video game-based interventions or video game-based assessment tools in children with ADHD. After initial screening, full text revision and study selection, 22 articles were finally included in the review. Most studies used PC as platform, with a minority using a video console, pad, or 3D device. Video game-based assessment tools were generally effective in discriminating ADHD cases from controls, and in discriminating between ADHD subtypes. Video game-based therapeutic interventions were well accepted and generally effective in improving cognitive areas and decreasing ADHD symptoms. Gamification and cognitive training could be the main mechanisms underlying the usefulness and effectiveness of video game-based assessment tools and interventions. Software optimization and greater collaboration between developers and healthcare professionals are some of the priorities for future research in this area

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Eur Child Adolesc Psychiatry. 2020.

PEDIATRIC USE OF PRESCRIBED MELATONIN IN SWEDEN 2006ΓÇô2017: A REGISTER BASED STUDY.

Kimland EE, Bardage C, Collin J, et al.

Sleep disturbances are common in the pediatric population and should primarily be treated non-pharmacologically. Most medicines for sleep disturbances are not approved for pediatric use and data on long-term safety is scarce. In Sweden, melatonin is classified as a prescription medicine. The aim of the present study was to characterize the prevalence and incidence of dispensed melatonin prescriptions, long-term treatment, concomitant dispensation of psychotropic medication, and psychiatric comorbidity, in children

and adolescents aged 0ΓÇô17-áyears living in Sweden during 2006 ΓÇô2017. Data was retrieved by linking the national population-based registers, the Swedish Prescribed Drug register and the National Patient register. In 2017, nearly 2% of the pediatric population 0Γ Çô17-áyears was dispensed at least one prescription of melatonin, which was more than a 15-fold increase for girls and a 20-fold increase for boys, when compared to 2006. Among the children in the age group 5Γ Çô9 who initiated a melatonin treatment in 2009, 15% of girls and 17% of boys were found to be continuously prescribed melatonin 8-áyears later. Nearly 80% of all children with dispensed melatonin had concomitant dispensations of psychotropic medications. The most common combination was melatonin together with centrally acting sympathomimetic medicines (23% of girls and 43% of boys). About half of the children (47% of girls and 50% of boys) had at least one registered diagnosis of mental or behavioral disorders. The most common diagnosis was attention deficit hyperactive disorder, across all age groups and genders. The continuous increase of use of melatonin in children, often concomitant with other psychotropic medications, together with a high proportion of younger children with prescriptions of melatonin on a long-term basis, suggests the need for further structured follow up studies, in particular of long-term use

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Eur Child Adolesc Psychiatry. 2020.

USING THE FIVE TO FIFTEEN-COLLATERAL INFORMANT QUESTIONNAIRE FOR RETROSPECTIVE ASSESSMENT OF CHILDHOOD SYMPTOMS IN-ADULTS WITH AND WITHOUT AUTISM OR ADHD.

Hirvikoski T, Lajic S, Jokinen J, et al.

Due to lack of previous studies, we aimed at evaluating the use of the Five to Fifteen (FTF) questionnaire in adults with neurodevelopmental disorders (NDD) and in controls without NDD. The NDD group consisted of adults with autism spectrum disorder ASD (n = 183) or attention-deficit/hyperactivity disorder (ADHD) (n = 174) without intellectual disability, recruited from a tertiary outpatient clinic. A web survey was used to collect data from general population adult control group without NDD (n = 738). The participants were retrospectively rated by their parents regarding childhood symptoms, using five to fifteen-collateral informant questionnaire (FTF-CIQ). Adults with NDD had higher FTF-CIQ domain and subdomain scores than controls, and displayed similar test profiles as children with corresponding diagnosis in previous studies. Based on the FTF-CIQ domain scores, 84.2% of the study participants (93% of the controls; 64% of the adults with NDD) were correctly classified in a logistic regression analysis. Likewise, Receiver Operating Characteristic (ROC) curve analysis on FTF-CIQ total sum score indicated that a cut-off value of 20.50 correctly classified 90% of the controls and 67% of the clinical cases, whilst a cut-off value of 30.50 correctly classified 84% of the controls and 77% of the clinical cases. The factor analysis revealed three underlying components: learning difficulties, cognitive and executive functions; social skills and emotional/behavioural symptoms; as well as motor and perceptual skills. Whilst not designed as a diagnostic instrument, the FTF-CIQ may be useful for providing information on childhood symptoms and associated difficulties in individuals assessed for NDD as adults

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Eur Child Adolesc Psychiatry. 2020.

THE IMPORTANCE OF PARENTAL KNOWLEDGE IN THE ASSOCIATION BETWEEN ADHD SYMPTOMATOLOGY AND RELATED DOMAINS OF IMPAIRMENT.

Dekkers TJ, Huizenga HM, Bult J, et al.

Parents of children with ADHD experience several difficulties while raising their children and report lower levels of knowledge about their childrenΓÇÖs life and behaviors. A recent study found that low levels of parental knowledge mediated the association between ADHD symptoms and risk-taking behavior (RTB) in adolescents. The current study aimed to investigate this previous finding further by replicating it, by taking peer influence into account as additional social factor of importance and by extending it and also investigate the role of parental knowledge in the association between ADHD symptoms and homework problems. Three studies were performed: study 1 (N=234) replicated previous work on parental knowledge mediating the association between ADHD symptoms and RTB, study 2 (pre-registered, N=313) added peer influence, and study 3 (pre-registered, N=315) assessed whether-áparental knowledge mediated the association between

ADHD symptoms and homework behavior. Parental knowledge consistently mediated the association between ADHD symptoms on one hand and RTB and homework problems on the other, and also predicted stronger resistance to peer influence. Because parental knowledge was repeatedly linked to ADHD-related problems, it seems promising to include parental knowledge in treatment of ADHD-related problems in adolescents, by improving the parent-child relationship. Future studies should test more directly how improvement of the parent-child relationship can be used to optimize parental knowledge, which in its turn reduces ADHD-related problems

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Eur Child Adolesc Psychiatry. 2020.

MOVEMENT DISORDERS AND USE OF RISPERIDONE AND METHYLPHENIDATE: A REVIEW OF CASE REPORTS AND AN ANALYSIS OF THE WHO DATABASE IN PHARMACOVIGILANCE.

Stampfli D, Weiler S, Burden AM.

For patients with attention deficit hyperactivity disorder and comorbid conduct-dissocial disorder, a combination therapy of the psychostimulant methylphenidate and the antipsychotic risperidone may be prescribed. Case reports describe the occurrence of movement disorders under this combination therapy, but clinical trials had limited power to detect these events. This study aimed (1) to summarise published case reports and (2) to analyse pharmacovigilance data consisting of adverse drug event reports to elucidate these reactions. PubMed, Embase, and APA PsycInfo were used to retrieve case reports. For the pharmacovigilance data, aggregated information on individual case safety reports (ICSRs) within the database of suspected adverse drug events by the WHO were analysed. ICSRs were assessed for disproportionality in reporting. Thirteen published case reports (62% male) on movement disorders were identified, with ages between 5 and 15-áyears. Seven reports (54%) described incidents when risperidone was tapered down or switched to methylphenidate. From the WHO, we identified 25,556 ICSRs (16,118 for methylphenidate, 8,614 for risperidone, and 824 for both). Of these, 953 (5.9%), 1356 (15.7%), and 159 (19.3%) ICSRs reported movement disorders in association with methylphenidate, risperidone or both, respectively. The analyses on disproportionality showed an increased number of ICSRs with movement disorders when the two drugs were coded in combination. The potential of movement disorders as adverse effects might be amplified when methylphenidate and risperidone are used in combination. The results from the literature underline the necessity of caution and patient monitoring when risperidone dosing is modified during methylphenidate therapy

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Eur Neuropsychopharmacol. 2020.

CLINICAL AND COGNITIVE CORRELATES OF CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN FIRST-EPISODE PSYCHOSIS: A CONTROLLED STUDY.

Sanchez-Gistau V., Manzanares N, Cabezas A, et al.

The relationship between childhood attention-deficit/hyperactivity disorder (c-ADHD) and psychosis has been understudied. Cognitive dysfunction is a core feature of both disorders, but no previous study has investigated whether first-episode psychosis (FEP) with c-ADHD (FEP-ADHD+) presents a different cognitive profile than FEP without c-ADHD (FEP-ADHD−). One hundred and thirty-three FEP outpatients were screened for c-ADHD through a diagnostic interview and underwent a comprehensive clinical and cognitive assessment with the MATRICS Consensus Cognitive Battery (MCCB). Cognitive differences among FEP groups, and a group of 65 healthy controls (HCs) were analysed by multivariate analysis of covariance. Nearly 25% of FEP fulfilled criteria for c-ADHD. Both FEP groups performed worse than HCs in speed processing, executive function and social cognition, but only the FEP-ADHD+group was significantly more impaired than the HC group in attention ($F = 4.35$; $p = 0.04$). Only the Trail Making Test A (TMT-A) ($F = 6.99$; $p = 0.01$) within the domain of processing speed and the Neuropsychological Assessment Battery (NAB) ($F = 6.46$; $p = 0.01$) within the domain of executive function reliably differentiated the two clinical groups. The FEP groups did not differ in the severity of psychopathology, but the FEP-ADHD+reported fewer years of education than the FEP-ADHD− and were more likely to use tobacco and cannabis and to require higher

doses of antipsychotics to achieve a clinical response. In conclusion, we found a gradient of severity in cognitive performance between groups, with FEP-ADHD+ having the greatest cognitive impairment. Our results suggest that FEP-ADHD+ represents a subgroup with a worse prognosis than FEP-ADHD−

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Evidence-Based Practice in Child and Adolescent Mental Health. 2020.

DEVELOPMENT AND REFINEMENT OF THE RELAX INTERVENTION, AN INTERVENTION TARGETING EMOTION DYSREGULATION AND INTERPERSONAL CONFLICT IN ADOLESCENTS WITH ADHD: RESULTS FROM A PILOT STUDY.

Breaux R, Langberg JM.

The purpose of this study was to refine and conduct a pilot evaluation of the RELAX (Regulating Emotions Like An eXpert) intervention for families of adolescents with ADHD. RELAX was refined based on 12 community cliniciansΓÇÖ feedback. RELAX was then implemented with 18 adolescents with ADHD and their caregivers (14 mothers, 3 fathers, 1 grandmother). Outcomes included parent and adolescent ratings of adolescent emotion dysregulation and family conflict; parent self-report of emotion dysregulation; coded parent emotion socialization behaviors during a conflict discussion; and weekly parent and clinician ratings of family conflict, emotion regulation, and communication. All outcomes were collected pre- and post-RELAX. Adolescents made large improvements on parent and adolescent ratings of emotion dysregulation (d =-á1.10 and 1.23, respectively) and family conflict (d =-á1.12 and 1.77, respectively). Parents made large increases in use of supportive reactions during the conflict discussion (d =-á1.04) and in self-reported emotion dysregulation (d =-á0.82). Large effects were found for parent and clinician weekly ratings (ds =-á1.82ΓÇô3.15). Results suggest that the RELAX intervention is a promising intervention targeting emotion dysregulation and family conflict among families of adolescents with ADHD, and warrants further evaluation of intervention effectiveness

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Exp Ther Med. 2020;20:714-26.

MAST CELLΓÇÆMEDIATED NEUROINFLAMMATION MAY HAVE A ROLE IN ATTENTION DEFICIT HYPERACTIVITY DISORDER (REVIEW).

Song Y, Lu M, Yuan H, et al.

Attention deficit hyperactivity disorder (ADHD) is a common neurodevelopmental and behavioral disorder with a serious negative impact on the quality of life from childhood until adulthood, which may cause academic failure, family disharmony and even social unrest. The pathogenesis of ADHD has remained to be fully elucidated, leading to difficulties in the treatment of this disease. Genetic and environmental factors contribute to the risk of ADHD development. Certain studies indicated that ADHD has high comorbidity with allergic and autoimmune diseases, with various patients with ADHD having a high inflammatory status. Increasing evidence indicated that mast cells (MCs) are involved in the pathogenesis of brain inflammation and neuropsychiatric disorders. MCs may cause or aggravate neuroinflammation via the selective release of inflammatory factors, interaction with glial cells and neurons, activation of the hypothalamicΓÇæpituitary adrenal axis or disruption of the bloodΓÇæbrain barrier integrity. In the present review, the notion that MC activation may be involved in the occurrence and development of ADHD through a number of ways is discussed based on previously published studies. The association between MCs and ADHD appears to lack sufficient evidence at present and this hypothesis is considered to be worthy of further study, providing a novel perspective for the treatment of ADHD

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Expert Review of Clinical Pharmacology. 2020.

AN UPDATE ON THE CLINICAL PHARMACOLOGY OF METHYLPHENIDATE: THERAPEUTIC EFFICACY, ABUSE POTENTIAL AND FUTURE CONSIDERATIONS.

Shellenberg TP, Stoops WW, Lile JA, et al.

Introduction: Methylphenidate remains a first-line medication for treating ADHD in children and adults. However, its behavioral pharmacological similarities to methamphetamine and cocaine have historically created concern for its potential as a drug of abuse. In September 2019, the FDA published a docket requesting comments for the development of abuse deterrent formulations for CNS stimulants, emphasizing the abuse of methylphenidate as a public health concern. Areas covered: We conducted a narrative review of research on the clinical pharmacology, therapeutic efficacy, and abuse potential of methylphenidate.

Expert opinion: Several studies indicate that methylphenidate has at least some abuse potential. Methylphenidate, amphetamine, methamphetamine, and cocaine overlap in their subjective, reinforcing, and discriminative stimulus effects. Regardless, methylphenidate remains an efficacious treatment for ADHD in children and adults when properly adhered to, especially when paired with non-pharmacological treatments. The development of abuse deterrent formulations of methylphenidate is warranted

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Front Behav Neurosci. 2020;14.

INCREASED TEMPORAL LOBE BETA ACTIVITY IN BOYS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER BY LORETA ANALYSIS.

Chiang C-T, Ouyang C-S, Yang R-C, et al.

Aim: Attention-deficit hyperactivity disorder (ADHD) is a common childhood neuropsychiatric disorder that affects 6.1 million US children. The mechanism of ADHD is currently unclear. Differences in ADHD presentations between boys and girls are well-established. In the present study, we used quantitative electroencephalography (EEG) to investigate the brain area and EEG bands of boys with ADHD.

Methods: This study enrolled 40 boys with ADHD and 40 age-matched controls without ADHD. Low-resolution electromagnetic tomography (LORETA) and instantaneous frequency were used to analyze EEG data to reveal the mechanisms underlying ADHD in boys.

Results: We found that the instantaneous frequencies in the T3 and T4 EEG channels in boys with ADHD were significantly higher than those in the controls. The beta band showed significant difference in current density between the ADHD and control groups. In the entire brain area, the bilateral inferior and middle temporal gyrus exhibited the most significant difference between the ADHD and control groups in the EEG beta band. Connectivity analysis revealed an increase in connectivity between the left middle frontal gyrus and fusiform gyrus of the temporal lobe in boys with ADHD.

Conclusions: LORETA is a promising tool for analyzing EEG signals and can be used to investigate the mechanism of ADHD. Our results reveal that the inferior temporal gyrus, middle temporal gyrus, and fusiform gyrus of the temporal lobe are potentially involved in the pathogenesis of ADHD in boys. In comparison with other imaging methods, such as magnetic resonance imaging, EEG is easy to perform, fast, and low cost. Our study presents a new approach for investigating the pathogenesis of ADHD in boys

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Frontiers in Genetics. 2020;11.

CATECHOL-O-METHYLTRANSFERASE VAL158MET GENOTYPE AND EARLY-LIFE FAMILY ADVERSITY INTERACTIVELY AFFECT ATTENTION-DEFICIT HYPERACTIVITY SYMPTOMS ACROSS CHILDHOOD.

Abraham E, Scott MA, Blair C.

Attention-deficit hyperactivity disorder (ADHD) is among the most commonly diagnosed psychiatric disorders of childhood. The dopaminergic system has been shown to have substantial effects on its etiology, with both functional Catechol-O-methyltransferase (COMT) Val158Met genotype and early-life environmental adversity involved in the risk of inattention and hyperactivity/impulsivity symptoms. In this prospective longitudinal study, we examined for the first time the impact of proximal and distal early-life family adversity and COMT Val158Met polymorphism gene ΓÇô both the direct and the interactive effects, on childrenΓÇÖs

ADHD symptoms across childhood. Data came from the Family Life Project, a prospective longitudinal study of 1,292 children and families in high poverty from birth to 11 years. In infancy, data regarding socioeconomic (SES)-risk-factors, observed-caregiving behaviors, and DNA genotyping were collected. In early and middle childhood teachers rated the occurrence and severity of the childΓÇÖs ADHD symptoms. Multilevel growth curve models revealed independent effects of COMT, early-life SES-risk and negative caregiving on ADHD symptoms in early and middle childhood. Significant gene-environment interactions were found, indicating that overall, carriers of at least one COMT158Met allele were more sensitive to early-life adversity, showing higher inattention and hyperactivity/impulsivity symptoms severity in childhood when exposed to high SES-risk factors in infancy, compared to Val-Val carriers. Findings provide new insights into the complex etiology of ADHD and underline the need for further investigation of the neuronal mechanisms underlying gene-environment interactions. Findings might have implications for prevention and intervention strategies with a focus on early-life family relationships in genetically at-risk children

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Frontiers in Neurology. 2020;11.

EVENT-RELATED POTENTIALS IN ADHD ASSOCIATED WITH TUBEROUS SCLEROSIS COMPLEX: A POSSIBLE BIOMARKER OF SYMPTOMS SEVERITY?

Moavero R, Marciano S, Pro S, et al.

Background and Aim: Tuberous sclerosis complex (TSC) is associated with a high rate of attention deficit-hyperactivity disorder (ADHD), usually with more severe symptoms than in idiopathic cases. Event-related potentials have been used in idiopathic ADHD, and they have been proposed as a possible biomarker of symptoms severity. Aim of this study was to investigate event-related potential (ERP) characteristics in patients with ADHD secondary to TSC, compared to patients with drug-naive idiopathic ADHD and healthy controls (HCs), to investigate whether (1) distinct clinical features can be due to different pathophysiological mechanisms, and (2) ERPs may reliably predict ADHD symptoms severity in TSC.

Materials and Methods: We enrolled 13 patients with idiopathic ADHD (iADHD), 6 patients with ADHD associated with TSC (tscADHD), and 14 age-matched HCs (7ΓÇô17 years). All of them underwent ERP recording, with mismatch negativity (MMN) preceding the P300 recording. All patients underwent neurocognitive evaluations.

Results: Mismatch negativity latency was shorter in iADHD (P = 0.04) and tscADHD (P = 0.06) than in HC, with no difference between patients' groups. Mismatch negativity amplitude was significantly higher in patients (both iADHD and tscADHD) than in HC. The P300 amplitude was significantly lower in iADHD patients than in both tscADHD patients (P = 0.03) and HCs (P < 0.001). No difference was found between tscADHD patients and HCs (P = 0.2).

Conclusion: While patients with iADHD present lower P300 amplitude than HC, in tscADHD patients P300 amplitude was not different from that in HC, suggesting that in TSC P300 amplitude does not really reflect symptom severity

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Front Syst Neurosci. 2020 Jun;14:10.

LATERAL PREFRONTAL THETA OSCILLATIONS REFLECT PROACTIVE COGNITIVE CONTROL IMPAIRMENT IN MALES WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Zamorano F, Kausel L, Albornoz C, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is a common neuropsychiatric disorder in which children present prefrontal cortex (PFC) related functions deficit. Proactive cognitive control is a process that anticipates the requirement of cognitive control and crucially depends on the maturity of the PFC. Since this process is important to ADHD symptomatology, we here test the hypothesis that children with ADHD have proactive cognitive control impairments and that these impairments are reflected in the PFC oscillatory activity. We recorded EEG signals from 29 male children with ADHD and 25 typically developing (TD) male

children while they performed a Go-Nogo task, where the likelihood of a Nogo stimulus increased while a sequence of consecutive Go stimuli elapsed. TD children showed proactive cognitive control by increasing their reaction time (RT) concerning the number of preceding Go stimuli, whereas children with ADHD did not. This adaptation was related to modulations in both P3a potential and lateral prefrontal theta oscillation for TD children. Children with ADHD as a group did not demonstrate either P3a or theta modulation. But, individual variation in theta activity was correlated with the ADHD symptomatology. The results depict a neurobiological mechanism of proactive cognitive control impairments in children with ADHD

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Gazi Medical Journal. 2020;31:345-48.

EARLY CARDIOVASCULAR EVALUATION AFTER METHYLPHENIDATE IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Cilsal E, Yurtcu E, Elatas A.

Objective: Rare cardiovascular side effects may be observed in patients after treatment with methylphenidate for Attention Deficiency and Hyperactivity Disorder (ADHD). In this study, we aimed to evaluate the cardiac effects of methylphenidate before and after treatment in our center in children with ADHD.

Method: This study included 253 ADHD patients who underwent methylphenidate treatment and involved a retrospective comparison of their demographic data, heart rate, systolic, diastolic blood pressure, corrected QT (QTc) interval with electrocardiography and echocardiographic examinations from before and two weeks after treatment.

Results: The median age of the patients was 11.8 3.3 years, palpitations were observed in 18 (7%) patients, and blood pressure elevation was observed in 5 (1.9%) patients after methylphenidate treatment. Sinus tachycardia was observed in all patients with palpitation symptoms, and echocardiography revealed an atrial septal defect in four patients, valvular pulmonary stenosis in two patients, ventricular septal defect and patent ductus arteriosus in one patient. No significant difference in heart rate, systolic and diastolic blood pressure values were identified after treatment. Although the QTc intervals recorded after treatment were significantly longer, these values did not exceed pathological levels.

Conclusion: The findings of evaluations of children with ADHD after methylphenidate treatment vary according to the characteristics of the patients. Patients with structural heart disease or with arterial hypertension should be monitored more carefully before the use of methylphenidate in the diagnosis of ADHD. Our findings suggests that both blood pressure measurement and electrocardiographic assessment appear to be useful and appropriate in the detection of side effects after methylphenidate treatment

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Gazi Medical Journal. 2020;31:410-15.

BEHAVIORAL DISORDERS IN CHILDREN: AN EXAMPLE OF PRIMARY HEALTH CARE.

Dikmen AU, Kocak C, Ertek IE, et al.

Background-Aim: In this study; it is aimed to evaluate the destructive behavioral disorders in children between the age of 6-18 years old who applied to various family health centers in Ankara.

Method: The study was conducted as a cross-sectional study including 674 children and 337 parents who applied to family health centers in 4 different districts in Ankara. It is organized according to STROBE criteria.

Results: 54.4% of the children were boys and 45.6% were girls. In children, attention deficit-hyperactivity disorder was found to be 9.9%, oppositional defiant disorder was 9.9% and behaviour disorder was 3.0%. Compared to married couples, attention deficit hyperactivity disorder was significantly more prevalent in children of divorced parents. Behaviour disorder was found to be significantly higher in families with low income. Diagnosis of attention deficit-hyperactivity was higher in boys than girls. Children with chronic illnesses and history of major accident ,poisoning or severe febrile disease had a significantly higher incidence of oppositional defiant disorder than healthy children and children who do not have any history.

Conclusion: Primary health care institutions have a strategic position in recognizing childhood mental/ behavioral disorders, it is important to increase the number of studies related to the subject in terms of protecting the social mental health

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Indian Journal of Forensic Medicine and Toxicology. 2020;14:1500-03.

KNOWLEDGE OF PARENTS TOWARD CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER IN BAGHDAD CITY.

Alwan IH.

Attention deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in child and teenage psychiatry. ADHD children are at risk for a school organization constrains a multimodal treatment database1. This study surveys parentΓÇÖs knowledge and attitudes towards attention deficit hyperactivity disorder. The study aimed to assess the level of the knowledge and perspective for Parents who have children with Attention Deficit Hyperactive Disorder. A non-probability, purposive sample of 75 child and 75 parents (40 mothers and 35 fathers), who had children with ADHD between the ages of (4 and 12) were selected. A descriptive study was conducted at the Child Psychiatric Unit at Ibn Rushed Psychiatric Teaching Hospital and Central Child Hospital Teaching in Baghdad City, from September8st to October 30th, 2017. A questionnaire format used for data collection and constructed by the researcher to achieve the objectives of the study. Reliability of questionnaires was estimated through a pilot study which was carried out for the period from December 10th 2017 to December 30th 2017. Data were analyzed through the application of descriptive statistical analysis and the application of inferential statistic. The results of the study indicate that the ADHD parents are no significant association between father knowledge and ΓÇÿ socio-demographic except income,child age, gender and received medication which was correlated significantly at p-value 0.01 respectively. The researcher recommended that future researches should be directed toward teaching parents and teacher to increase their knowledge about the ADHD and provide many strategies to help them to reduce parents burden and coping

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Indian Journal of Forensic Medicine and Toxicology. 2020;14:883-88.

THE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) MORE LIKELY CREATES TO IRRITABLE BOWEL SYNDROME.

Hamza AAK.

The research aimed study the children with attention-deficit/hyperactivity disorder (ADHD) more likely Creates to irritable bowel syndrome at Ibn-Rushd Psychiatric Teaching Hospital in Baghdad city, find out the relationship between demographic characteristic, irritable bowel syndrome and Attention-Deficit/ Hyperactivity disorder patients. A purposive (non-probability), the sample included (100) patients, from (3-11) years old. A descriptive study carried out from December 10th 2018 to the February 25th 2019, from family Attention-Deficit/Hyperactivity Disorder outpatients of Ibn-Rushd Psychiatric Teaching Hospital in Baghdad city. A questionnaire was constructed for the purpose of the study, which was a consisted of (2) part. The 1st part included the demographic characteristics and the 2nd part included the items related with irritable bowel syndrome. Data were analyzed through descriptive statistical approach (frequency and percentage) and inferential statistical approach (correlation coefficient). Scores, Perpson, lycart scale analysis that include, t-test, and stepwise multiple regression. The result of the study confirmed that the mean of score for the age of sample was (7.1) year, most of them male urban, low score for socio-economic status, strong positive to irritable bowel syndrome

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Int J Environ Res Public Health. 2020;17.

ADOLESCENT–PARENT AGREEMENT ON CALLOUS UNEMOTIONAL TRAITS IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Chen Y-L, Hsiao RC, Chou W-J, et al.

This study examined the levels of agreement between the reports of 207 adolescents with attention-deficit/hyperactivity disorder (ADHD) and their parents regarding the adolescents callous-unemotional (CU) traits and investigated the factors influencing adolescent-parent agreement. Adolescent-parent agreement about CU traits in three dimensions according to the Chinese version of the Inventory of Callous and Unemotional Traits was examined. The influence of demographic characteristics, comorbid conduct disorder (CD), oppositional defiant disorder (ODD), and ADHD symptoms on adolescent-parent agreement was also examined. The results indicated that adolescentΓÇôparent agreement on the CU trait of uncaringness was moderate, whereas agreement on the CU traits of callousness and unemotionality was poor. Adolescent-parent agreement on the three dimensions of CU traits varied depending on the adolescents sex and comorbid CD and ODD symptoms as well as parental age. Therefore, multiple sources of information are required when assessing the severity of CU traits in adolescents with ADHD. The factors influencing the levels of the agreement should also be considered

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Int J Environ Res Public Health. 2020;17:1-27.

ACUTE PHYSICAL ACTIVITY, EXECUTIVE FUNCTION, AND ATTENTION PERFORMANCE IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND TYPICALLY DEVELOPING CHILDREN: AN EXPERIMENTAL STUDY.

Miklos M., Kom+íromy D, et al.

A growing number of studies support the theory that physical activity can effectively foster the cognitive function of children with attention-deficit hyperactivity disorder (ADHD). The present study examines the effect of acute moderate physical activity on the executive functions and attention performance of (1) typically developing children (without psychological, psychiatric or neurological diagnosis and/or associated treatment stated in their medical history); (2) treatment-na+»ve ADHD children; and (3) medicated children with ADHD. In the current study, a total sample of 150 (50 non-medicated, 50 medicated, and 50 typically developing) children between the ages of 6 and 12 took part in the experiment. The Mini International Neuropsychiatric Interview for Children and Adolescents (MINI Kid) was used to measure ADHD and the child version of the Test of Attentional Performance (KiTAP) was applied to evaluate the children's attentional and executive function performance before and after two types of intervention. In order to compare the effects of physical activity and control intervention, half of the children from each group (25 participants) took part in a 20-min long, moderately intense physical activity session on the 60ΓÇô80% of their maximum heart rate, while watching a cartoon video. In the control condition, the other half of the children (25 participants) from each group watched the same cartoon video for 20 min while seated. Physical activity (compared to the just video watching control condition) had a significantly positive influence on 2 out of 15 measured parameters (median reaction time in the alertness task and error rates in the divided attention task) for the medicated group and on 2 out of the 15 measured variables (number of total errors and errors when distractor was presented, both in the distractibility task) regarding the treatment-na+»ve group. Future studies should focus on finding the optimal type, intensity, and duration of physical activity that could be a potential complementary intervention in treating deficits regarding ADHD in children

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International Journal of Methods in Psychiatric Research (Online). 2020 Jun;29.

OBJECTIVE MEASUREMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS OUTSIDE THE CLINIC USING THE QBCHECK: RELIABILITY AND VALIDITY.

Ulberstad F, et al.

Objective measurements of ADHD symptom levels can be a highly valuable complement to ratings. However, sometimes it is not feasible to bring patients into the clinic/lab for assessment. The aim of the present study was therefore to evaluate the psychometric properties of the QbCheck, an online computerized test that

measures errors and reaction time as well as activity during testing using the computer's built-in web camera. Study I (*n* = 27 adolescents/adults) investigated test–retest reliability and concurrent validity of the QbCheck. Study II included 142 adolescents/adults (69 with ADHD/73 controls) and investigated convergent and diagnostic validity, as well as usability, of the QbCheck. In Study I, the QbCheck showed high test–retest reliability and high concurrent validity. In Study II, high convergent validity was observed when studying associations between the QbCheck performed in the home and the QbTest performed at the clinic. In addition, the QbCheck discriminated well between patients with ADHD and controls, with a sensitivity of 82.6 and a specificity of 79.5. The QbCheck appears to be a valuable test with good psychometric properties and will thereby enable assessment of ADHD symptom levels in adolescents and adults outside the clinic in the home setting

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Int J Pediatr Adolesc Med. 2020.

THE RISK OF EATING DISORDERS AMONG CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: RESULTS OF A MATCHED COHORT STUDY.

Jahrami H, AlAnsari AM, Janahi AI, et al.

Background and Objectives: There are some studies on the association between attention deficit and hyperactivity disorder (ADHD) and the risk of eating disorders (ED). Only few have examined the risk of ED among children and adolescents with ADHD. Previous research which included subjects with ADHD with other comorbidities used inadequate controls and did not focus on the type of ADHD or the role of pharmacological treatment.

Methods: This matched cohort study was conducted in the Child/Adolescents Psychiatry Unit (CAPU), Bahrain. Using the CAPU diagnostic frameworks, 70 subjects with ADHD were recruited and matched with their corresponding age- and sex- healthy controls at 1:2 ratio (70 cases:140 controls). The participants were children or adolescents aged between 8 and 19 years old. A brief interview was used to collect socio-demographic information and anthropometrics. The risk of ED was estimated using the eating attitude test 26 (EAT-2). Data were analyzed using cohort analysis.

Results: A total of 31.43% of the subjects with ADHD were screened using EAT-26 and found to be at risk for ED, compared to 12.14% of the controls (OR 3.31, 95% CI 1.62-6.78). The prevalence of ED among female cases with ADHD was slightly higher than males (33.33% and 30.77%, respectively). Body weight or body mass index was a statistically significant explanatory factor for the risk of ED.

Conclusions: The present study shows that children and adolescents with ADHD have a three-fold increased risk of ED compared to healthy controls. This research raised the recommendation that children and adolescents with ADHD should be screened for disordered eating patterns

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International Ophthalmology. 2020.

OCULAR FINDINGS IN PATIENTS WITH ATTENTION DEFICIT AND HYPERACTIVITY.

Ulucan Atas PB, Ceylan OM, D+Ânmez YE, et al.

Aim: To evaluate ocular findings, contrast sensitivity, color perception, and macular and retinal nerve fiber layer (RNFL) thickness in patients with attention-deficit/hyperactivity disorder (ADHD).

Materials and methods: This prospective study included a group of 37 patients aged 6-16 years diagnosed with combined ADHD and a healthy control group of 37 children. The participants underwent an ophthalmological examination. Color-ávision-átesting-áwas administered-áusing-áthe-áIshihara-áplates test. Contrast sensitivity test was performed using the Functional Acuity Contrast Test. Macular thickness and RNFL thickness were measured by spectral-domain optical coherence tomography.

Results: No significant difference was found between the patient and control groups with regard to ocular findings, color vision, and convergence insufficiency ($p > 0.05$). Contrast sensitivity level was significantly lower at four out of five spatial frequencies (1.5, 3, 12, and 18-ácpd) in the patient group compared to the control group. The RNFL thickness in nasal quadrant and macular thickness was significantly higher in the healthy control group compared to the ADHD group.

Conclusion: Contrast sensitivity levels and the nasal quadrant RNFL thickness were significantly lower in the patient group compared to the control group. Based on the findings of the study, we suggest that the level of contrast in the tools used by ADHD patients in daily life settings should be enhanced

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Iran J Pediatr. 2020;30:1-6.

RISK OF ATTENTION DEFICIT HYPER ACTIVITY DISORDER AFTER EARLY EXPOSURE TO GENERAL ANESTHESIA; A CASE CONTROL STUDY.

Sedighnejad A, Soltanipour S, Saberi A, et al.

Background: Over the past decade, following the discovery that developing brain of immature animals was affected by anesthetic agents, the safety of general anesthesia (GA) in early life has been questioned. Objectives: We investigated the association between anesthesia exposure in children and ADHD development.

Methods: This case-control study was conducted at pediatric psychology clinic of our institution and a pediatric neurology private clinic during 2019. Firstly the responsible resident of anesthesiology separated new ADHD cases. Then a questionnaire was filled out through an almost 10 minute's telephone interview. Finally, frequency distribution of GA was compared between ADHD cases and controls.

Results: Finally, the data from 210 children were analyzed. Among 105 ADHD cases, 19% had a history of a procedure requiring GA while it was 3.8% in control group. Comparing the two groups a significant difference was observed regarding the age of receiving GA (P = 0.004), gender (P < 0.001), the history of receiving GA (P = 0.001) and the number of anesthesia exposures (P = 0.001). According to logistic regression analysis, male gender (P = 0.001) OR 3.11 (95CI = 1.63-5.93) and age (P = 0.003) OR 0.92 (95CI = 0.87-0.97) were significant predictors of early exposure to GA and ADHD development.

Conclusions: It was revealed that early exposure to GA might be a risk factor for later developing ADHD. Boys might be more sensitive to the long term adverse effects of anesthetic agents than girls. Further prospective well-planned studies are needed to confirm these findings

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Iran J Psychiatry. 2020;15:105-11.

ROAD CRASHES IN ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND RISKY DRIVING BEHAVIOR.

Sadeghi H, Shabani Y, Pakniyat A, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is one of the most common problems in adolescents. Risky behaviors in patients with ADHD are due to impaired impulse control resulting from problems with inhibition of proponent responses, controlling interference, and stopping ongoing responses after feedback on errors. The present study investigated the relationship between ADHD and risky driving behavior and the likelihood of car accident in Arak, Iran, in 2015-16.

Method: This case-control study was conducted in the Emergency Department of Vali-Asr hospital in Arak (Iran) on drivers who met the inclusion criteria. The data gathering tools included the Demographic Questionnaire, Manchester Driving Behavior Questionnaire (MDBQ), and Wender Utah Rating Scale (WURS). Statistical analyses were performed using SPSS version 20 software.

Results: The mean of ADHD (-¦SD) was higher among cases (81.64 [26.78]) than in controls (64 [24.28], P = 0.000). The mean of risky driving behaviors (-¦SD) was higher among cases (66.41[26.78]) than in controls (36.79 [25.42]). There was a significant relationship between ADHD, risky behavior, lapse errors, slips, deliberate violation, and unintentional violation and car accident (P = 0.000).

Conclusion: This study showed that ADHD increases the risk of road crashes and motor vehicle injuries. These drivers tend to drive at unauthorized speed, have less control over the vehicle, drive more carelessly, and are more likely to have an accident

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J Child Psychol Psychiatry. 2020 Jul;61:757-59.

EDITORIAL PERSPECTIVE: PERILS AND PROMISE FOR CHILD AND ADOLESCENT SLEEP AND ASSOCIATED PSYCHOPATHOLOGY DURING THE COVID-19 PANDEMIC.

Becker SP, Gregory AM.

It is anticipated that the novel coronavirus disease 2019 (COVID-19) pandemic and associated societal response will have wide-ranging impacts on youth development and mental health. Sleep is crucial for child and adolescent health and well-being, and the potential for sleep problems to emerge or worsen during and following the pandemic is high. This may be particularly true for children and adolescents who are at heightened risk for the onset of sleep and mental health disturbances and for those whom developmental changes impacting sleep are rapidly occurring. Youth with preexisting psychopathologies (including anxiety and depression) and neurodevelopmental conditions (including attention-deficit/hyperactivity disorder and autism spectrum disorder) could be especially vulnerable to disturbed sleep during this period of change and uncertainty. It is thus imperative that sleep considerations be part of research and clinical initiatives aimed at understanding and mitigating the impact of the COVID-19 pandemic in children and adolescents. This article considers ways in which the pandemic may impact sleep, including research and clinical implications

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J Adolesc. 2020;83:31-41.

FUTURE PREFERENCES AND PROSPECTION OF FUTURE OF OUTCOMES: INDEPENDENT YET SPECIFIC ASSOCIATIONS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Kostyrka-Allchorne K, Cooper NR, Wass SV, et al.

Introduction: Symptoms of attention-deficit hyperactivity disorder (ADHD) and conduct problems have been associated with heightened temporal discounting of reward value resulting in a preference for immediate over delayed outcomes. We examined the cross-sectional relationship between future preference (including intertemporal choice) and prospection (the ability to bring to mind and imagine the experience of future personally-relevant events and outcomes) in adolescents with a range of ADHD symptoms and aggressive behaviour.

Methods: A combination of behavioural tasks and self-reports measured intertemporal decision making, individual differences in preference for future outcomes and experience of prospection in a convenience sample of English adolescents aged 11ΓÇô17 (n = 64, 43.8% males). Parents rated symptoms of ADHD and aggression.

Results & Conclusions: Factor analysis identified two factors: Future Preference and Prospection. Significant negative bivariate correlations were found between ADHD and the scores of both factors and between aggression and Future Preference. A path model confirmed the independent significant association of ADHD with both factors but not with aggression. There was no evidence that Prospection was associated with Future Preference or that it reduced the associations between ADHD symptoms and Future Preference. These results provide further evidence that ADHD is associated with a tendency to prefer immediate over future outcomes. The same association with aggression seemed to be driven by the overlap with ADHD symptoms. We provide some of the first evidence that individuals with high ADHD symptoms have difficulty in prospecting about future episodes. However, this is unrelated to their preference for future outcomes

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J Adolesc Health. 2020.

ADVERSE CHILDHOOD EXPERIENCES AND MENTAL HEALTH CONDITIONS AMONG ADOLESCENTS.

Bomysoad RN, Francis LA.

Purpose: Adverse childhood experiences (ACEs) have been linked with poor physical and mental health. This study examined adult respondents' (e.g. parental) reports from the 2016-17 National Survey of Children's Health, a nationally representative study of health outcomes and social contexts of U.S. households with noninstitutionalized children.

Methods: Logistic regression was used to examine associations between ACEs and reports of current depression, anxiety, conduct/behavioral problems, attention-deficit/hyperactivity disorder, and substance use disorder among youth (n = 29,617; 49% female) aged 12-17 years.
Results: ACEs were associated with an increased likelihood of all current mental health diagnoses, particularly for youth exposed to four or more ACEs.
Conclusion: Although data relied on cross-sectional adult reports, results provide evidence of a graded association between ACEs exposure and adolescents' mental health conditions; associations with substance use disorder were particularly marked. Early childhood, multilevel, trauma-informed interventions are needed to prevent negative youth outcomes associated with ACEs

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J Affective Disord. 2020 Jul;272:104-09.

PARENTING STRESS AND FAMILY RESILIENCE AFFECT THE ASSOCIATION OF ADVERSE CHILDHOOD EXPERIENCES WITH CHILDREN'S MENTAL HEALTH AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Uddin J, Alharbi N, Uddin H, et al.

Introduction: Exposure to adverse childhood experience (ACE) has harmful consequences for children's health and well-being. However, it is less clear how different social processes may amplify or mitigate the effects of ACE on children's mental health. We examined how parenting stress mediates and family resilience moderates the associations of ACE with children's mental health and attention-deficit/hyperactivity disorder (ADHD) outcomes.
Methods: This secondary data analysis included 44,684 children aged 6-17 years from the 2016-17 National Survey of Children's Health (NSCH). Logistic regression with survey weights was used to account for the complex survey design and obtain odds ratios (OR) and 95% CI adjusted for sociodemographics.
Results: Overall, 7.3% of children had any mental health condition and 10.4% had ADHD. A higher ACE score (per 1-unit increase) was associated with a higher prevalence of any mental health condition (OR = 1.33, 95% CI: 1.27-1.40) and ADHD (OR = 1.21; 95% CI: 1.15-1.27) after adjustment for sociodemographics. Parenting stress mediated 57% of the total effect of ACE on any mental health condition and 60% of the total effect of ACE on ADHD diagnosis. The effect of ACE on mental health and ADHD outcomes was stronger among children with low levels of family resilience and connection index (FRCI) than among those with higher levels of FRCI.
Conclusions: Parenting stress may be a potential mechanism through which ACE impacts a child's mental health and behavioral outcomes. Family resilience can lessen the impact of ACE on children's mental health and behavioral disorders

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J Altern Complement Med. 2020;26:473-81.

THE EFFECTS OF A TRADITIONAL CHINESE MEDICATION ON CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Liang ZW, Ong SH, Xie YH, et al.

Objective: This feasibility study examined the effects of a particular Traditional Chinese Medicine (TCM) herbal formula on attention-deficit/hyperactivity disorder (ADHD) and related problem behaviors.
Design: A total of 79 participants aging 6-12 years consumed a granulated TCM herbal formula twice daily over a period of 3 months and underwent assessments at months 0, 3, and 6. Changes in ADHD symptoms and related behaviors were measured using the ADHD rating scale-IV (ADHD-RS-IV), child behavior checklist (CBCL), children's global sssessment scale (CGAS), as well as the clinical global impressions-severity (CGI-S) and improvement (CGI-I) scales.
Results: Repeated measures mixed model analyses revealed significant differences in scores across time on all ADHD-RS-IV and CBCL subscales as well as on the CGAS, CGI-S, and CGI-I scales. Pairwise comparisons between months 0 and 3 as well as months 0 and 6 indicated significant improvements in scores. Scores also did not differ significantly between months 3 and 6. The results may suggest that this particular TCM formula possesses potential therapeutic qualities in the treatment of ADHD. Furthermore,

changes in ADHD symptoms generally appear to be stable 3 months after discontinuation. However, these findings could also be attributed to placebo effects as well as reporting biases.
Conclusion: This particular TCM formula may prove to be a useful adjunctive treatment for children with ADHD, and randomized controlled trials need to be conducted to evaluate its efficacy

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J Altern Complement Med. 2020;26:515-20.
COMPARISON OF AURICULAR THERAPY WITH SHAM IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED CONTROLLED TRIAL.
Binesh M, Daghighi M-R, Shirazi E, et al.
Objectives: Several studies have shown the clinical effects of auricular therapy for some neuropsychological disorders. The aim of this study is to compare the effectiveness of auricular therapy with the sham procedure in attention deficit hyperactivity disorder (ADHD).
Design: Randomized sham-controlled trial. Settings/Location: Welfare Centers of Tehran (Iran). Subjects: Fifty children with ADHD (6-14 years old).
Interventions: Patients were randomly assigned into two groups to receive either auricular therapy (Group A) or a sham procedure (Group B) once a week for 6 weeks.
Outcome measures: The Children Symptom Inventory (CSI-4) and the parent's version of the Conners Comprehensive Behavior Rating Scale were used to assess the severity of symptoms of attention deficit (AD) and hyperactivity (HA). Outcome evaluation data was obtained at the first and seventh weeks after the interventions. Data were analyzed by SPSS software using Friedman and Mann-Whitney U tests.
Results: There were 23 patients in group A and 21 patients in group B who completed the study. Based on the CSI-4 assessment, AD scores decreased from the mean (±standard deviation) of 18.39 (±5.44) to 15.39 (±5.89), p = 0.006 in group A, whereas the mean AD scores for group B only changed from 15.0 (±6.4) to 14.9 (±5.94), p = 0.55 in group B. In addition, the mean of the HA scores decreased from 18.0 (±6.73) to 13.3 (±6.75), p = 0.001 in group A, whereas the change in HA scores in group B only diminished and from 11.85 (±6.44) to 11.45 (±5.44), p = 0.74. The CSI-4 assessments and the scores on the Conners questionnaire significantly decreased after the first week of intervention (p = 0.04) in group A, but not in group B. No side effects were observed.
Conclusion: Subjects who received auricular therapy in acupuncture points achieved a statistically significant greater reduction in AD and HA symptoms when compared with subjects who received sham acupuncture points

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J Child Adolesc Psychopharmacol. 2020 Jun;30:326-34.
THE DIAGNOSTIC INFANT PRESCHOOL ASSESSMENT-LIKERT VERSION: PREPARATION, CONCURRENT CONSTRUCT VALIDATION, AND TEST-RETEST RELIABILITY.
Scheeringa MS.
Objective: The Diagnostic Infant and Preschool Assessment was revised to include Likert ratings (DIPA-L) to give a broader range of severity ratings that may have greater utility for clinical and research purposes. In addition, the instrument was updated for Diagnostic and Statistical Manual of Mental Disorders, 5th ed. (DSM-5), and two types of Likert ratings-frequency versus problem intensity-were explored for posttraumatic stress disorder (PTSD) symptoms. Concurrent construct validation and test-retest reliability were examined for the five most common disorders seen in very young children in outpatient clinics: PTSD, attention-deficit/hyperactivity disorder, oppositional defiant disorder, separation anxiety disorder, and generalized anxiety disorder (GAD). A sixth disorder, disruptive mood dysregulation disorder (DMDD), which was created in DSM-5, was tested for the first time. Functional impairment was also examined.
Methods: The caregivers of 58 two- through six-year-old children (57 mothers and 1 father) were recruited from an outpatient clinic. They were interviewed at Time 1, and 52 were reinterviewed at Time 2 by research assistants (children's age M 4.7 years, standard deviation 1.2).

Results: Few differences were found between the ratings of frequency versus problem intensity for PTSD symptoms. Tests of concurrent criterion validation were acceptable for all disorders when compared against disorder-specific questionnaires; the range of Pearson correlation coefficients was 0.56-0.94. A trend for attenuation of diagnoses from Time 1 to Time 2 was evident, but not statistically significant. Test-retest reliabilities were strong when examined with continuous Likert scores, except for GAD (the range of intraclass correlation coefficients values was 0.29-0.91, but were less consistent for categorical disorder-level status [the range of Cohen's was 0.35-0.79]). The range of internal consistencies was 0.78-0.95, excluding DMDD, which could not be calculated.
Conclusions: The updated and revised DIPA-L demonstrated many acceptable features of a valid and reliable instrument for the assessment of very young children. While the findings are tentative given the small sample size, the DIPA-L is the only diagnostic instrument for young children with a replication, tested in clinic populations, updated for DSM-5, with psychometrics for functional impairment, and has Likert ratings

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J Child Adolesc Psychopharmacol. 2020 Jul;30:348-54.
THE ASSOCIATION WITH QUANTITATIVE RESPONSE TO ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MEDICATION OF THE PREVIOUSLY IDENTIFIED NEURODEVELOPMENTAL NETWORK GENES.
Zhong Y, Yang B, Su Y, et al.
Objective: A recent pharmacoimaging study suggested that methylphenidate (MPH) and atomoxetine (ATX) might have common mechanisms for the treatment of attention-deficit/hyperactivity disorder (ADHD). Previous pharmacogenetic studies have by and large only involved genes in neurotransmitter systems, which accounted for very small variances. Therefore, this study aimed to investigate whether the neurodevelopmental genes identified in a prior ADHD etiology Genome-Wide Association Study (GWAS) could predict patients' responses to MPH and ATX, given the aforementioned mechanisms of action.
Methods: For our sample of 241 patients with ADHD, we assessed the change in the ADHD rating scale (ADHD-RS) total symptom scores from baseline to the end of the 12th week of treatment with either MPH or ATX. We performed association analyses at the genetic single-marker, gene-based, set-based, and GWAS-based polygenic levels.
Results: In our analyses, neither single nucleotide polymorphism (SNP) nor gene-level analyses yielded significant markers associated with the change in the ADHD-RS score after multiple comparison correction. The polygenic risk score model, which was based on SNPs associated with ADHD etiology at a threshold of $p \leq 0.0001$ in a recent Han Chinese GWAS, predicted symptomatic improvement with ADHD medication ($p = 0.018$, $R^2 = 0.023$).
Conclusion: Our results provide new evidence for a small influence of neurodevelopmental genes on the efficacy of medications for ADHD

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J Child Adolesc Psychopharmacol. 2020 Jul;30:366-75.
FREQUENCY AND CORRELATES OF ACUTE DYSTONIC REACTIONS AFTER ANTIPSYCHOTIC INITIATION IN 441 CHILDREN AND ADOLESCENTS.
Selma TH, Ceylan MF, Kandemir GÃ, et al.
Objective: To determine the incidence of acute dystonic reactions (ADRs) and risk factors for ADRs in children and adolescents treated with antipsychotics.
Methods: This was a retrospective chart review-based cohort study of consecutive patients who attended a university hospital's child and adolescent psychiatry department between 2015 and 2017 and who were treated with antipsychotics and had at least two follow-up visits.
Results: Thirty of 441 patients (6.8%) 4–19 years of age who were treated with antipsychotics for conduct disorders (21.5%), attention-deficit/hyperactivity disorder (13.2%) and, irritability and aggression that accompanied intellectual disability (12.9%) and followed for 99.5 ± 223.3 (median: 34) days developed ADRs. ADRs developed in 11/391 patients (2.8%) treated with one antipsychotic and 19/50 patients (38.0%) treated with two antipsychotics ($p < 0.001$). In patients treated with one antipsychotic that developed ADRs, the time

to ADRs was 4.0 ± 4.0 days after antipsychotic initiation and 2.7 ± 2.4 days after an increase in the antipsychotic dose. The time to ADRs in those treated with two antipsychotics was 3.0 ± 2.3 days after the addition of the second antipsychotic and 1.6 ± 0.8 days after a dose increase in the second antipsychotic. The incidence of ADRs during antipsychotic monotherapy was 10.5% with first-generation antipsychotics (FGAs) and 2.2% with second-generation antipsychotics (SGAs; p = 0.037). The antipsychotic was changed due to ADRs in 12/30 (40.0%) of ADR cases. Independent factors associated with ADRs were antipsychotic polypharmacy (p < 0.0001), inpatient treatment (p = 0.013), FGA use (p = 0.015), and diagnoses of schizophrenia (p = 0.039) or bipolar disorder (p < 0.0001).
Conclusion: SGAs and low-potency FGA monotherapy in children and adolescents were associated with a relatively low ADR risk, whereas high- and mid-potency FGAs were associated with a high risk. Independent predictors of ADRs were antipsychotic polypharmacy, inpatient treatment, FGAs, and schizophrenia or bipolar disorder diagnoses, which may be related to more aggressive antipsychotic dosing

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J Child Adolesc Psychopharmacol. 2020 Jun;30:285-92.
PRIMARY CARE MANAGEMENT OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER APPEARS MORE ASSERTIVE FOLLOWING BRIEF PSYCHIATRIC INTERVENTION COMPARED WITH SINGLE SESSION CONSULTATION.
Rockhill CM, Carlisle LL, Qu P, et al.
Objectives: We examined primary care providers' (PCPs') management of attention-deficit/hyperactivity disorder (ADHD) during and following families' participation in two arms of the Children's ADHD Telemental Health Treatment Study. We hypothesized that more intensive treatment during the trial would show an "after-effect" with more assertive PCPs' management during short term follow-up.
Methods: We conducted a pragmatic follow-up of PCPs' management of children with ADHD who had been randomized to two service delivery models. In the Direct Service Model, psychiatrists provided six sessions over 22 weeks of pharmacotherapy followed by behavior training. In the Consultation Model, psychiatrists provided a single-session consultation and made treatment recommendations to PCPs who implemented these recommendations at their discretion for 22 weeks. At the end of the trial, referring PCPs for both service delivery models resumed ADHD treatment for 10 weeks. We performed intent-to-treat analysis using all 223 original participants. We applied linear regression models on continuous outcomes, Poisson regression models on count outcomes, and logistic regression models to binary outcomes. Missing data were addressed through imputations.
Results: Participants in the Direct Service Model had more ADHD visits than those in the Consultation Model across the full 32 weeks (mean = 7.05 visits vs. 3.36 visits; adjusted rate ratio = 2.1 [1.85–2.38]; p < 0.0001). During follow-up, participants in the DSM were more likely to be taking ADHD-related medications (82% vs. 61%; adjusted odds ratio = 2.44 [1.24–4.81], p = 0.01). At 32 weeks, participants in the Direct Service Model had higher stimulant dosages (adjusted difference = 5.64 [0.12–11.15] mg; p = 0.046).
Conclusion: These results from a pragmatic follow-up of a randomized trial suggest an "after-effect" for brief intensive treatment in the Direct Service Model on the short term follow-up management of ADHD in primary care

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J Child Fam Stud. 2020 Aug;29:2186-200.
A MINDFULNESS-BASED PROGRAM AMONG ADOLESCENT BOYS WITH BEHAVIOR DISORDERS: A QUASI-EXPERIMENTAL STUDY.
Roux B, Philippot P.
Several studies have shown that mindfulness-based programs (MBPs) may bring promising benefits for youth. However, little is known about its efficacy in specific clinical populations and even less about the psychological processes that underlie the changes. This study investigates the efficacy of a MBP among a population of adolescent boys with behavior disorders and explores the mediating role of impulsivity in the observed changes. Participants included 48 adolescents presenting conduct disorders and mild cognitive impairments, living in a residential service for youth in Belgium. Two groups of 24 adolescents aged 12 to 19

years have been constituted. Only the experimental group followed a MBP. The program was divided into two parts: the first 6 sessions were devoted to group dynamic and introduction to emotional skills whereas the second part focused on mindfulness exercises. The level of depression and impulsivity as well as the symptomatology of attention deficit hyperactivity disorder were assessed before, during and after the program for both groups. Results showed that both groups decreased their depressive symptomatology but only the MBP group decreased in impulsivity and externalizing symptomatology. No mediating effects of the facets of impulsivity on the outcomes were found. MBPs may bring psychological benefits for adolescents who suffer from behavior disorders but further research on the efficacy of MBPs among this population is needed.HighlightsMindfulness-based interventions are well-accepted among adolescents with behavior disorders.Mindfulness-based interventions may be useful to treat externalizing symptomatology in behavior disorders.The effects of mindfulness training on externalizing symptomatology may be mediated by changes in impulsivity

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J Clin Child Adolesc Psychol. 2020 Jul;49:476-92.

PARENT-TEEN GROUP VERSUS DYADIC TREATMENT FOR ADOLESCENT ADHD: WHAT WORKS FOR WHOM?

Sibley MH, Rodriguez L, Coxe S, et al.

The goal of this study was to evaluate the comparative efficacy of 2 clinic-based psychosocial treatment modalities for adolescent attention deficit/hyperactivity disorder (ADHD) and identify characteristics that facilitate patient-modality matching. Culturally diverse adolescents with ADHD (N =Â 123) were randomized to 1 of 2 versions of a parent-teen psychosocial treatment for ADHD (Supporting Teens Autonomy Daily [STAND]): (a) group parent and adolescent skills training or (b) dyadic skills training blended with motivational interviewing. Participants were assessed at baseline, posttreatment, and 6-month follow-up on ADHD symptom severity and functional treatment targets. Differences in therapy process and cost were documented. Modality differences in outcome were examined using linear mixed and general linear models. Each modality successfully engaged the proposed therapy processes. Dyadic and group STAND produced equivalent overall outcomes. However, the dyadic modality demonstrated superior efficacy when parents had elevated ADHD or depression symptoms or high conflict with the teen. Families with lower parent education level and higher parental depression showed lower overall attendance; married parents were more likely to attend dyadic STAND (vs. group). Naturalistic stimulant medication did not influence treatment outcome. At less than one third of the cost of dyadic treatment, group models may be an economical option for treating parents and adolescents with ADHD. Screening adolescents with ADHD for parental psychopathology and parent-teen conflict may allow clinics to match higher risk patients to more personalized approaches that can enhance efficacy

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J Clin Child Adolesc Psychol. 2020 Jul;49:493-508.

A TRANSDIAGNOSTIC EXAMINATION OF SELF-REGULATION: COMPARISONS ACROSS PRESCHOOLERS WITH ASD, ADHD, AND TYPICALLY DEVELOPING CHILDREN.

Rosmary R, Graziano PA.

The purpose of the current study was to identify profiles of self-regulation across executive functioning (EF) and emotion regulation (ER) and examine profiles's impact on treatment outcomes. Participants included 100 preschoolers (MageÂ =Â 4.73, 75% Male, 79% Hispanic) including 37 with autism spectrum disorder and attention-deficit/hyperactivity disorder (ASD+ADHD), 32 with ADHD-only, and 31 typically developing children. Parents and teachers reported on childrenâ' EF, ER, ASD, and ADHD symptoms. Children were administered an EF battery and observed for ER during a frustration task. Children participated in an intensive behavioral summer treatment program (STP-PreK) aimed at improving school readiness across behavioral, academic, and self-regulation domains. Latent profile analyses produced 4 profiles: (a) Low ER and EF Deficits, (b) High ER Deficits, (c) High EF Deficits, and (d) Moderate ER and EF Deficits. ASD and ADHD symptoms predicted lower membership probability within the Low ER and EF Deficits Profile and higher membership probability within the Moderate ER and EF Deficits Profile. However, only ASD symptoms

predicted membership within the High EF Deficits Profile. Only ADHD symptoms predicted membership within the High ER Deficits Profile. Even after accounting for diagnostic symptoms, profile membership was predictive of treatment response across behavioral and academic domains. Children in the High EF Deficits Profile experienced the largest gains. Results highlight the specificity of self-regulation deficits within and across diagnoses. Self-regulation profiles demonstrated clinical utility in predicting treatment response above traditional symptom based classifications, providing evidence for the use of transdiagnostic approaches

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J Consult Clin Psychol. 2020 Aug;88:738-56.

A RANDOMIZED CONTROLLED TRIAL OF CENTRAL EXECUTIVE TRAINING (CET) VERSUS INHIBITORY CONTROL TRAINING (ICT) FOR ADHD.

Kofler MJ, Wells EL, Singh LJ, et al.

Objective: Executive function deficits are well-established in ADHD. Unfortunately, replicated evidence indicates that executive function training for ADHD has been largely unsuccessful. We hypothesized that this may reflect insufficient targeting, such that extant protocols do not sufficiently and specifically target the neurocognitive systems associated with phenotypic ADHD behaviors/impairments.

Method: Children with ADHD ages 8–12 (M = 10.41, SD = 1.46; 12 girls; 74% Caucasian/Non-Hispanic) were randomized with allocation concealment to either central executive training (CET; n = 25) or newly developed inhibitory control training (ICT; n = 29). Detailed data analytic plans were preregistered.

Results: Both treatments were feasible/acceptable based on training duration, child-reported ease of use, and parent-reported high satisfaction. CET was superior to ICT for improving its primary intervention targets: phonological and visuospatial working memory (d = 0.70–0.84). CET was also superior to ICT for improving go/no-go (d = 0.84) but not stop-signal inhibition. Mechanisms of change analyses indicated that CET-related working memory improvements produced significant reductions in the primary clinical endpoints (objectively assessed hyperactivity) during working memory and inhibition testing (indirect effects: β ≥ −.11; 95% CIs exclude 0.0). CET was also superior to ICT on 3 of 4 secondary clinical endpoints (blinded teacher-rated ADHD symptoms; d = 0.46–0.70 vs. 0.16–0.42) and 2 of 4 feasibility/acceptability clinical endpoints (parent-reported ADHD symptoms; d = 0.96–1.42 vs. 0.45–0.65). CET-related gains were maintained at 2–4 month follow-up; ICT-related gains were maintained for attention problems but not hyperactivity/impulsivity per parent report.

Conclusions: Results support the use of CET for treating executive function deficits and targeting ADHD behavioral symptoms in children with ADHD. Findings for ICT were mixed at best and indicate the need for continued development/study

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Journal of Investigative Dermatology. 2020;140:S62.

466 THE RELATIONSHIP BETWEEN ATOPIC DERMATITIS AND CHILDHOOD SYMPTOMS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A LONGITUDINAL COHORT STUDY .

Lee Y, Tomaszewski N, Langan S, et al.

The rise in atopic dermatitis (AD) has been paralleled by rising prevalence of attention deficit/hyperactivity disorder (ADHD) in the past few decades, especially in developed and Western countries. Previous research shows a possible association between AD and ADHD, but data have been mixed, likely due to poorly defined phenotypes and heterogeneity in measuring AD and ADHD. Furthermore, most studies have been limited by cross-sectional designs. To test our hypothesis that active and more severe early childhood AD is associated with clinician-diagnosed ADHD at age 7, and hyperactive symptoms as measured by the Strengths and Difficulties Questionnaire (SDQ) at ages 7, 10, 13, and 16 years, we analyzed data from the Avon Longitudinal Study of Parents and Children (ALSPAC), a large population-based birth cohort from the UK. Using logistic regression models, we found that AD (defined as at least two reports of flexural dermatitis from a standardized and validated questionnaire) was not associated with clinician-diagnosed ADHD at age 7 based on the Development and Wellbeing Assessment (Odds Ratio 1.07, 95% CI 0.64-1.78, adjusted for potential confounders including maternal stress during pregnancy, maternal age at delivery, maternal

smoking during pregnancy, socioeconomic status, and maternal smoking). We found a trend toward higher effect estimates in younger ages, though this was not statistically significant, and we found no evidence of an interaction with parental-reported sleep quantity. Additionally, we did not find any significant cross-sectional associations between active AD and symptoms of hyperactivity based on the SDQ at four subsequent assessments between ages 7 and 16. Our results do not provide evidence to support an association between AD and ADHD in a large cohort of children followed from birth. Our research challenges the current paradigm that AD is strongly associated with ADHD

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Journal of Medical Internet Research. 2020;22.

EFFICACY OF A VIRTUAL REALITY BIOFEEDBACK GAME (DEEP) TO REDUCE ANXIETY AND DISRUPTIVE CLASSROOM BEHAVIOR: SINGLE-CASE STUDY.

Bossenbroek R, Wols A, Weerdmeester J, et al.

Background: Many adolescents in special education are affected by anxiety in addition to their behavioral problems. Anxiety leads to substantial long-term problems and may underlie disruptive behaviors in the classroom as a result of the individual's inability to tolerate anxiety-provoking situations. Thus, interventions in special needs schools that help adolescents cope with anxiety and, in turn, diminish disruptive classroom behaviors are needed.

Objective: This study aimed to evaluate the effect of a virtual reality biofeedback game, DEEP, on daily levels of state-anxiety and disruptive classroom behavior in a clinical sample. In addition, the study also aimed to examine the duration of the calm or relaxed state after playing DEEP.

Methods: A total of 8 adolescents attending a special secondary school for students with behavioral and psychiatric problems participated in a single-case experimental ABAB study. Over a 4-week period, participants completed 6 DEEP sessions. In addition, momentary assessments (ie, 3 times a day) of self-reported state-anxiety and teacher-reported classroom behavior were collected throughout all A and B phases.

Results: From analyzing the individual profiles, it was found that 6 participants showed reductions in anxiety, and 5 participants showed reductions in disruptive classroom behaviors after the introduction of DEEP. On a group level, results showed a small but significant reduction of anxiety (d=-0.29) and a small, nonsignificant reduction of disruptive classroom behavior (d=-0.16) on days when participants played DEEP. Moreover, it was found that the calm or relaxed state of participants after playing DEEP lasted for about 2 hours on average.

Conclusions: This study demonstrates the potential of the game, DEEP, as an intervention for anxiety and disruptive classroom behavior in a special school setting. Future research is needed to fully optimize and personalize DEEP as an intervention for the heterogeneous special school population

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Journal of Mental Health Counseling. 2020 Jul;42:234-50.

COUNSELING ADULTS WITH SENSORY PROCESSING DISORDER: AN EXPLORATORY STUDY.

Goodman-Scott E, Burgess M, Polychronopoulos G.

Sensory processing disorder (SPD) is a neurological disorder impacting up to 20% of the global population. The majority of SPD research has been conducted outside the counseling profession and typically examines the presentation of SPD in youth. Therefore, counselors often have limited awareness of this disorder. The purpose of the present study was to conduct an exploratory qualitative thematic analysis (N = 89) examining the primary concerns of adult counseling clients with SPD, as reported by their counselors. Results include 12 themes that were organized into three categories: biological, psychological, and social. Thus, the results reflected the biopsychosocial model, originally outlined by G. L. Engel, as it pertains to SPD. Researchers provided implications for mental health counselors' practice and suggestions for future research

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J Mol Neurosci. 2020.

CDH13 AND LPHN3 GENE POLYMORPHISMS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: THEIR RELATION TO CLINICAL CHARACTERISTICS.

Ozaslan A., et al.

Genetic factors play a major role in the etiopathogenesis of attention-deficit/hyperactivity disorder (ADHD). In this study, we aimed to investigate the relationship between the CDH13 (rs6565113, rs11150556) and LPHN3 (rs6551665, rs6858066, rs1947274, rs2345039) gene polymorphisms and ADHD. We also sought to examine possible relationships between these polymorphisms and the clinical course and treatment response in ADHD. A total of 120 patients (79% boys), aged 6 to 18-áyears, newly diagnosed (medication-na+»ve) with ADHD according to the DSM-5 and a group of 126 controls (74% girls) were enrolled in the study. We examined the association between the aforementioned polymorphisms and ADHD. Univariate and multivariate logistic regression analysis were used to evaluate factors influencing the treatment response of ADHD. A significant difference was found between ADHD and control groups in terms of genotype distribution of the LPHN3 rs6551665 and rs1947274 polymorphisms. The results also showed that having the GG genotype of rs6551665 and CC genotype of rs1947274 of the LPHN3 gene was associated with risk for ADHD, and this relationship was more prominent in male participants. In the multivariate logistic regression model established with variables shown to have a significant relationship with treatment response, the presence of the GG genotype of the LPHN3 rs6551665 polymorphism and high severity of ADHD assessed by CGI-S were associated with poor response to treatment. This study is the first study to investigate the relationship between ADHD and these polymorphisms among Turkish adolescents. Our results imply that the LPHN3 rs6551665 and rs1947274 polymorphisms have a significant effect on ADHD in a Turkish population, and support previous observations that the presence of the GG genotype of the LPHN3 rs6551665 polymorphism may be associated with poor response to treatment in ADHD

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J Nerv Ment Dis. 2020 Jul;208:549.

DEFENSE STYLE OF CHILDREN AND ADOLESCENTS: DIFFERENCES AND ABILITY TO DISCRIMINATE AMONG CLINICAL CATEGORIES.

Wolmer L, Erez C, Toren P.

This study assessed the defense style of children referred to an outpatient clinic and examined what this style contributes to discriminating among various disorder categories, beyond internalizing and externalizing symptoms. A sample of 433 children and adolescents were grouped into four disorder categories: disruptive, depressive, anxiety, and attention deficit hyperactivity disorder. Their parents completed the Comprehensive Assessment of Defense Style (CADS: mature, self-oriented, and other-oriented) and the Child Behavior Checklist (CBCL: internalizing and externalizing symptoms). The disorder categories differed in the use of other-oriented defenses (e.g., acting-out, projection), whereas the CADS helped in properly discriminating most diagnostic categories beyond the CBCL. Information provided by the children themselves was missing, as was a subsample of nonclinical participants; these sources could strengthen the conclusions of the study. Assessing children's defense style together with their symptoms may result in better statistical discrimination among diagnostic categories

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J Neural Transm. 2020.

EVIDENCE SUPPORTING THE ROLE OF TELOMERASE, MMP-9, AND SIRT1 IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Uzun CA, Mercan IC, Bakir S, et al.

Growing evidence suggests that telomeres, telomerase, matrix metalloproteinase-9 (MMP-9), and SIRT1 (sirtuin1) are involved in the pathophysiology of neuropsychiatric and neurodevelopmental disorders. However, whether these molecules are contributors to attention-deficit/hyperactivity disorder (ADHD) has been little explored and poorly understood. This study aimed to determine the potential role of telomerase, MMP-9, and SIRT1 in children with ADHD. The study was performed on 46 children with ADHD aged

between 8 and 14 and 43 healthy children matching in age and gender. Children were evaluated by Kiddie-Sads-Present and Lifetime Version, ConnersΓÇÖ Parent Rating Scale-Revised Short Form (CPRS-RS) and Stroop test. Serum telomerase, MMP-9, and SIRT1 levels were measured by a quantitative sandwich enzyme-linked immunosorbent assay. MMP-9 and telomerase levels were significantly higher and SIRT1 levels were significantly lower in patients with ADHD than those of controls. All three molecules were significantly associated with both the severity of ADHD symptoms and cognitive functions. This is the first attempt to indicate that the important role of telomerase, MMP-9, and SIRT1 in ADHD, and the association of all these molecules with the severity of ADHD and cognitive functions, but future studies are required to verify these results

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Journal of Pediatric Pharmacology and Therapeutics. 2020;25:228-34.

TIME TO STABLE DOSE OF PSYCHOSTIMULANTS IN PEDIATRIC PATIENTS WITH ADHD.

Pasadyn SR, Giuliano K, Labianca D, et al.

OBJECTIVES The prevalence of attention-deficit/hyperactivity disorder (ADHD) is increasing and psychostimulants are the pharmacological standard of care. Patients benefit most when there is efficient titration to a stable dose of medication as defined by maintaining that same dose for 6 months. The aims of this study were to describe time to stable dose in a cohort of children with ADHD and examine the impact of demographic factors.

METHODS A list of pediatric patients with a diagnosis of ADHD in the electronic health record was generated, and a retrospective chart review of stimulant use was conducted on 500 patients randomly selected from 2010 to 2015 who met inclusion criteria. Time to stable dosing and its association with demographic characteristics were assessed.

RESULTS Patients were predominantly male (72%), white (81%), and privately insured (67%). Fifty-five percent of patients achieved a stable dose of medication on first attempt; therefore, the median time to stable dosing for the cohort was 0 days with the interquartile range being 0 to 133.8 days. There was significant increase in time to stable dose for patients younger than 10 years compared with those ΓëÑ10 years of age (p = 0.01). Time to stable dose was not significantly associated with race (p = 0.13), sex (p = 0.72), type of insurance (p = 0.56), or formulation being immediate or extended release (p = 0.56).

CONCLUSIONS Many patients had long titration periods when trying to reach a stable dose. Given that medication switching can be challenging for patients and families, more frequent contact with providers during titration may be necessary. ABBREVIATIONS ADD, attention deficit disorder; ADHD, attention-deficit/hyperactivity disorder; EHR, electronic health record; FDA, US Food and Drug Administration; ICD, International Classification of Diseases; IQR, interquartile range

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J Psychopathol Behav Assess. 2020.

INTERNAL AND EXTERNAL VALIDITY OF SELF-REPORT AND PARENT-REPORT MEASURES OF SLUGGISH COGNITIVE TEMPO IN SOUTH KOREAN ADOLESCENTS.

Jung S-H, Lee SY, Burns GL, et al.

This study evaluated the internal and external validity of self-report and parent-report measures of sluggish cognitive tempo (SCT) in South Korean adolescents. Adolescents (N-á= 469, ages 13ΓÇô17-áyears; 50.2% boys) completed self-report measures of SCT and attention-deficit/hyperactivity disorder inattention (ADHD-IN) in addition to measures of internalizing and externalizing psychopathology, social problems, and grades. Parents rated adolescents on SCT, ADHD-IN, internalizing and externalizing psychopathology, and social problems. Using adolescent self-report, 11 of 15 SCT symptoms showed convergent and discriminant validity with ADHD-IN. Using parent-report, all 15 SCT symptoms showed convergent and discriminant validity with ADHD-IN. For within source analyses, SCT showed unique and stronger associations than ADHD-IN with internalizing psychopathology whereas ADHD-IN showed unique and stronger associations than SCT with externalizing psychopathology. SCT and ADHD-IN showed similar unique associations with social problems, whereas ADHD-IN was more strongly related than SCT to grades. Across source analyses also supported

the differential unique associations of SCT and ADHD-IN with internalizing and externalizing psychopathologies. This study provides initial evidence for the internal and external validity of SCT with South Korean adolescents, extending support for the transcultural validity of SCT to the important developmental period of adolescence

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Journal of Psychosocial Nursing & Mental Health Services. 2020 Jul;58:34-41.

EFFECT OF PSYCHOEDUCATION ON STRESS IN PARENTS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED CONTROLLED STUDY.

Gümüs F, Ergün G, Dikeç G.

The current experimental pre-/posttest study sought to determine the effect of psychoeducation on the stress levels of parents of children with attention-deficit/hyperactivity disorder (ADHD). A total of 172 parents participated and were randomly assigned to experimental (n = 86) and control (n = 86) groups. There was no significant difference between mean pretest scores of parents in the experimental and control groups on the Caregiver Stress Scale ($p > 0.005$); however, significant differences were found between pre- and posttest scores in the experimental group after psychoeducation and at 6-month follow up ($p < 0.001$). There were also significant differences between pre- and posttest scores and pretest scores and 6-month follow-up scores in the experimental group ($p < 0.05$). In the light of the findings, psychiatric nurses can use psychoeducation programs to support families of children with ADHD to reduce their stress levels. [Journal of Psychosocial Nursing and Mental Health Services, 58(7), 34â€“41.]

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J Am Acad Child Adolesc Psychiatry. 2020;59:933-43.

INDIVIDUAL PARTICIPANT DATA META-ANALYSIS: IMPACT OF CONDUCT PROBLEM SEVERITY, COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND EMOTIONAL PROBLEMS, AND MATERNAL DEPRESSION ON PARENTING PROGRAM EFFECTS.

Leijten P, Scott S, Landau S, et al.

Objective: There is concern whether established parenting programs for children's conduct problems meet the needs of families with severe and complex mental health problems. For example, many children with conduct problems show comorbid attention-deficit/hyperactivity disorder (ADHD) or emotional problems, or have parents who are depressed, but families with such complex mental health problems typically seen in real life are often underrepresented in evaluation trials. We tested whether children with more severe conduct problems, and those with more complex mental health problems, benefit less from the Incredible Years parenting program, using individual participant data meta-analysis of randomized trials in Europe.

Method: In 1,696 families from 13 children aged (child age 2-11 years; 37% girls; 58% low income; 30% ethnic minority; 98% mothers), we used moderator analysis within a multilevel model to test whether initial conduct problem severity, comorbid ADHD or emotional problems, and maternal depression would diminish intervention effects for children's conduct problems.

Results: The Incredible Years program reduced children's conduct problems overall (Cohen's d = ΓêÆ0.35), but more so in children with more severe conduct problems. There was no evidence that children's comorbid ADHD and emotional problems changed the intervention benefits. Children of mothers with more depressive symptoms benefited more.

Conclusion: Children with more severe conduct problems derive greater, rather than lesser, benefits from a high-quality group parenting program, and comorbid ADHD and emotional problems do not reduce effects; maternal depression, rather than being linked to less child change, was associated with greater reductions in children's conduct problems

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J Am Acad Child Adolesc Psychiatry. 2020;59:931-32.

EDITORIAL: RELATIVE IMMATURITY OR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A DIAGNOSTIC DILEMMA?

Cuffe SP.

Attention-deficit/hyperactivity disorder (ADHD) is among the most common disorders of childhood1 and causes significant morbidity throughout the life span.2 Appropriate diagnosis and treatment of ADHD are thus critically important. The diagnosis of ADHD, however, is not straightforward. Clinicians must rely on parent and teacher reports of the child's behavior in comparison to other children the same age.3 Although various tests or procedures may be helpful in the diagnosis of ADHD, none of them obviates the need to rely on parent and teacher reports. Making matters more complicated, the agreement between parent and teacher reports of a child's ADHD-like behavior is low.4

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J Am Acad Child Adolesc Psychiatry. 2020;59:920-22.

EDITORIAL: A SPOONFUL OF INJURY PREVENTION MAKES THE ADHD MEDICINE GO DOWN.

Rockhill CM.

Unintentional injuries are the leading cause of disability and mortality in youths across the United States1 and globally.2 Attention-deficit/hyperactivity disorder (ADHD) has been associated with an increased rate of unintentional injuries in multiple countries, as reviewed in a recent meta-analysis of studies in youths.3 The study by Ghirardi et al.4 in this issue of the Journal adds to this literature by examining this issue within stratifications of injury and of characteristics of youths with ADHD.4 The authors accessed a very large sample (nearly 2 million youths) drawn from the Truven Health MarketScan Commercial Claims and Encounters databases. They identified all youths in the databases with a diagnosis of ADHD or receiving an ADHD medication prescription from January 1, 2005, to December 31, 2014, who presented to an emergency department with unintentional injuries. To determine the differential rate of unintentional injuries, they used a case-control methodology to compare youths with a diagnosis of ADHD or an ADHD medication with a control group of youths without an ADHD diagnosis or treatment matched on a variety of characteristics. Results of the population comparison not only supported the overall association, but also demonstrated an increased rate of unintentional injuries for both boys and girls and that youths with ADHD had higher rates of traumatic brain injury compared with matched control youths without ADHD.4

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J Am Acad Child Adolesc Psychiatry. 2020;59:964-77.

TRANSLATING DISCOVERIES IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER GENOMICS TO AN OUTPATIENT CHILD AND ADOLESCENT PSYCHIATRIC COHORT.

Vuijk PJ, Martin J, Braaten EB, et al.

Objective: Genomic discoveries should be investigated in generalizable child psychiatric samples in order to justify and inform studies that will evaluate their use for specific clinical purposes. In youth consecutively referred for neuropsychiatric evaluation, we examined 1) the convergent and discriminant validity of attention-deficit/hyperactivity disorder (ADHD) polygenic risk scores (PRSs) in relation to DSM-based ADHD phenotypes; 2) the association of ADHD PRSs with phenotypes beyond ADHD that share its liability and have implications for outcome; and 3) the extent to which youth with high ADHD PRSs manifest a distinctive clinical profile.

Method: Participants were 433 youth, ages 7ΓÇô18 years, from the Longitudinal Study of Genetic Influences on Cognition. We used logistic/linear regression and mixed effects models to examine associations with ADHD-related polygenic variation from the largest ADHD genome-wide association study to date. We replicated key findings in 5,140 adult patients from a local health system biobank.

Results: Among referred youth, ADHD PRSs were associated with ADHD diagnoses, cross-diagnostic ADHD symptoms and academic impairment (odds ratios Γê+1.4; R2 values Γê+2%ΓÇô3%), as well as cross-diagnostic variation in aggression and working memory. In adults, ADHD PRSs were associated with ADHD and phenotypes beyond the condition that have public health implications. Finally, youth with a high ADHD polygenic burden showed a more severe clinical profile than youth with a low burden (+¦ coefficients Γê+.2).

Conclusion: Among child and adolescent outpatients, ADHD polygenic risk was associated with ADHD and related phenotypes as well as clinical severity. These results extend the scientific foundation for studies of ADHD polygenic risk in the clinical setting and highlight directions for further research

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Journal of the Chinese Medical Association. 2020;83:411-16.

INCREASED PROBLEMATIC SMARTPHONE USE AMONG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN THE COMMUNITY: THE UTILITY OF CHINESE VERSION OF SMARTPHONE ADDICTION PRONENESS SCALE.

Huang Y-C, Hu S-C, Shyu L-Y, et al.

Background: Problematic smartphone use is more prevalent in children than before. This study aimed to evaluate the reliability and validity of the Chinese version of the Smartphone Addiction Proneness Scale (SAPS).

Methods: We recruited 319 students aged 9 to 12 years including 70 attention-deficit/ hyperactivity disorder subjects at a university hospital and 249 controls from elementary school. Finally, 164 males and 138 females were collected for data analysis with mean age of 10.99 ± 0.88 years. Item analysis, exploratory factor analysis, internal consistency test, and t test were performed to verify the reliability and validity of the SAPS-Chinese version. Correlations were examined for relation between the score in the SAPS-Chinese version and the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition diagnostic criteria.

Results: Factor analysis showed two factors: problematic use–associated behaviors and impaired daily functions. Item analysis for every item in the SAPS-Chinese version showed significant differences in t values ($p < 0.001$) and high correlation in all items ($r = 0.37$-0.79). The Kaiser-Meyer-Olkin (KMO) was equal to 0.94 and Bartlett's test of Sphericity was significant ($p < 0.001$). Cronbach's α for the SAPS-Chinese version was 0.93. It revealed high reliability and validity.

Conclusion: The SAPS-Chinese version is reliable, valid, and suitable for clinical and research uses with satisfactory properties. Applying the modified SAPS-Chinese version offers early detection of problematic smartphone use

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J Trace Elem Med Biol. 2020;62.

LOWER STRONTIUM IN TWO DIFFERENT BODY MATRICES IN NEURODEVELOPMENTAL DISORDERS: A PRELIMINARY REPORT.

Yalcin S.S., et al.

Background: Environmental factors, including elemental homeostasis, have not been studied sufficiently in neurodevelopmental disorders (NDD). This study aims to compare the status of 13 elements in blood and deciduous teeth dentine of children having an autism spectrum disorder or attention deficit hyperactivity disorder with typically developing controls.

Methods: Elements including calcium, phosphorus, magnesium, iron, zinc, copper, chromium, manganese, mercury, lead, cadmium, molybdenum, and strontium in both deciduous teeth and blood were analyzed by inductively coupled plasma mass spectrometry.

Results: Strontium levels in both blood and teeth samples were found to be significantly lower in the NDD group. Additionally, blood cadmium and mercury levels, and copper/zinc ratio were higher in the NDD group.

Conclusions: Our results warrant further investigation in a large series of NDD examining symptom levels and genetic variations associated with elemental homeostasis

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Korean J Pediatr. 2020;63:219-25.

LONG-TERM COGNITIVE, EXECUTIVE, AND BEHAVIORAL OUTCOMES OF MODERATE AND LATE PRETERM AT SCHOOL AGE.

Jin JH, Yoon SW, Son J, et al.

Background: There is increasing concern that moderate preterm (32–33 weeks' gestation) and late preterm (34–36 weeks' gestation) birth may be associated with minor neurodevelopmental problems affecting poor school performance.

Purpose: We explored the cognitive function, cognitive visual function, executive function, and behavioral problems at school age in moderate to late preterm infants.

Methods: Children aged 7–10 years who were born at 32+0 to 36+6 weeks of gestation and admitted to the neonatal intensive care unit from August 2006 to July 2011 at the National Health Insurance Service Ilsan Hospital were included. We excluded children with severe neurologic impairments, congenital malformations, or chromosomal abnormalities. Neuropsychological assessments consisted of 5 neuropsychological tests and 3 questionnaires.

Results: A total of 37 children (mean age, 9.1±1.2 years) participated. The mean gestational age at birth was 34.6±7.5 weeks, while the mean birth weight was 2,229.2±472.8 g. The mean full-scale intelligence quotient was 92.89±11.90; 24.3% scored between 70 and 85 (borderline intelligence functioning). An abnormal score was noted for at least one of the variables on the attention deficit hyperactivity disorder diagnostic system for 65% of the children. Scores below borderline function for executive quotient and memory quotient were 32.4% and 24.3%, respectively. Borderline or clinically relevant internalizing problems were noted in 13.5% on the Child Behavior Check List. There were no significant associations between perinatal factors or socioeconomic status and cognitive, visual perception, executive function, or behavior outcomes.

Conclusion: Moderate to late preterm infants are at risk of developing borderline intelligence functioning and attention problems at early school age. Cognitive and executive functions that are important for academic performance must be carefully monitored and continuously followed up in moderate to late preterm infants

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Medicine (Baltimore). 2020 Jul;99:e20931.

METHYLPHENIDATE HAS MILD HYPERGLYCEMIC AND HYPOKALEMIA EFFECTS AND INCREASES LEUKOCYTE AND NEUTROPHIL COUNTS.

Charach G, Karniel E, Grosskopf I, et al.

Various psychotropic drugs may affect the hematological and biochemical profiles of plasma and its metabolism. Carbamazepine, the most well-known psychotropic drug, can cause substantial hyponatremia. Methylphenidate, a piperidine derivative structurally related to amphetamines, acts as a central nervous system stimulant. The current study evaluated whether methylphenidate affects hematological and biochemical parameters of patients diagnosed with attention deficit hyperactivity disorder.Patients undergoing treatment for attention deficit hyperactivity disorder at our Adolescent Psychiatric Clinic were enrolled in the study. Blood samples for complete blood count and common biochemical analyses were collected before patients started methylphenidate and after 3 months of continuous treatment.Participants included 64 patients comprised the study cohort. There were 48 (75%) males and 16 (25%) females, with a median age of 16 years (range 11-31). The total median potassium level decreased by 0.6 mg/dL (P < .0001), while glucose rose by 15 mg/dL (P < .0001), sodium decreased in 0.7meq/L, (P = .006). The white blood count rose by 1350 cells/μL (P < .033) due to neutrophilia, lymphocytosis and eosinophilia. Hemoglobin rose slightly by 0.1 (P = .041). Changes in calcium, phosphorus, protein, albumin, and liver enzyme levels were not significant.The results indicate that methylphenidate may cause hypokalemia and elevated glucose, leukocyte, neutrophil, lymphocyte and eosinophil counts

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NeuroImage Clin. 2020;27.

ABNORMAL MODULATION OF THETA OSCILLATIONS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Guo J, Luo X, Li B, et al.

Previous studies have found that theta activities exhibit posterior lateralized modulation as well as midfrontal event-related synchronization (ERS) during covert visual attention in adults. The present study investigated whether these theta modulations existed in children and whether they were associated with attentional problems in attention-deficit/hyperactivity disorder (ADHD). Electroencephalography signals were recorded from typically developing (TD) children and children with ADHD (TD: n = 24; ADHD: n = 22) while they performed a cued covert visual attention task. The participants responded to a target following a cue designed as human eyes that gazed to the left or right visual field (70% validity). Compared with the TD children, the children with ADHD showed increased midfrontal theta ERS and significant posterior theta lateralization in response to the cues. More importantly, we found that the stronger posterior theta lateralization in the right hemisphere exhibited a positive trial-based correlation with the larger midfrontal theta ERS and predicted lower RT variability at the trial level in the children with ADHD. We suggest that ADHD may be associated with some enhanced systems in the frontal and posterior areas via theta oscillations, which may be involved in the compensatory maturation for their attention deficits in childhood, thereby promoting the stability of behavioral responses

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NeuroImage Clin. 2020;27.

INCREASED LEFT INFERIOR FRONTO-STRIATAL ACTIVATION DURING ERROR MONITORING AFTER FMRI NEUROFEEDBACK OF RIGHT INFERIOR FRONTAL CORTEX IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Criaud M, Wulff M, Alegria AA, et al.

Attention Deficit/Hyperactivity Disorder (ADHD) is a self-regulation disorder, with impairments in error monitoring associated with underactivation of the related brain network(s). Psychostimulant medication improves ADHD symptoms and can upregulate brain function, but has side effects, with limited evidence for longer-term effects. Real-time functional magnetic resonance neurofeedback (fMRI-NF) has potential longer-term neuroplastic effects. We previously reported the effects of 11 runs of 8.5 min of fMRI-NF of the right inferior frontal cortex (rIFC) in adolescents with ADHD. This resulted in improvement of clinical symptom and enhanced rIFC activation post-pre treatment during response inhibition, when compared to a control group receiving fMRI-NF of the left parahippocampal gyrus (lPHG). In the current study we applied a novel analysis to the existing data by investigating the effects of fMRI-NF of rIFC in 16 adolescents with ADHD compared to fMRI-NF of lPHG in 11 adolescents with ADHD on the neurofunctional correlates of error monitoring during the same fMRI tracking stop task and potential associations with cognitive and clinical measures. We found stronger performance adjustment to errors in the rIFC-NF compared to the control lPHG-NF group. At the brain function level, fMRI-NF of rIFC compared to that of lPHG was associated with increased activation in error monitoring regions of the left IFC, premotor cortex, insula and putamen. The increased activation in left IFC-insular-striatal error monitoring regions in the rIFC-NF relative to the lPHG-NF group was furthermore trend-wise correlated with NF-induced ADHD symptom improvements. The findings of this study show, that during error monitoring, fMRI-NF training of rIFC upregulation elicited improvement in post-error behavioural adjustments and concomitant increased activation in left hemispheric fronto-insular-striatal and premotor regions mediating self-control and self-monitoring functions. This suggests that the administration of fMRI-NF of the rIFC may have had an impact on wider networks of self-regulation and self-monitoring in adolescents with ADHD

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NeuroImage Clin. 2020;27.

NEUROFUNCTIONAL AND BEHAVIOURAL MEASURES ASSOCIATED WITH FMRI-NEUROFEEDBACK LEARNING IN ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Lam S-L, Criaud M, Alegria A, et al.

Functional Magnetic Resonance Imaging Neurofeedback (fMRI-NF) targeting brain areas/networks shown to be dysfunctional by previous fMRI research is a promising novel neurotherapy for ADHD. Our pioneering study in 31 adolescents with ADHD showed that fMRI-NF of the right inferior frontal cortex (rIFC) and of the left parahippocampal gyrus (lPHG) was associated with clinical improvements. Previous studies using electro-encephalography-NF have shown, however, that not all ADHD patients learn to self-regulate, and the predictors of fMRI-NF self-regulation learning are not presently known. The aim of the current study was therefore to elucidate the potential predictors of fMRI-NF learning by investigating the relationship between fMRI-NF learning and baseline inhibitory brain function during an fMRI stop task, along with clinical and cognitive measures. fMRI-NF learning capacity was calculated for each participant by correlating the number of completed fMRI-NF runs with brain activation in their respective target regions from each run (rIFC or lPHG); higher correlation values were taken as a marker of better (linear) fMRI-NF learning. Linear correlations were then conducted between baseline measures and the participantsΓÇÖ capacity for fMRI-NF learning. Better fMRI-NF learning was related to increased activation in left inferior fronto-striatal regions during the fMRI stop task. Poorer self-regulation during fMRI-NF training was associated with enhanced activation in posterior temporo-occipital and cerebellar regions. Cognitive and clinical measures were not associated with general fMRI-NF learning across all participants. A categorical analysis showed that 48% of adolescents with ADHD successfully learned fMRI-NF and this was also not associated with any baseline clinical or cognitive measures except that faster processing speed during inhibition and attention tasks predicted learning. Taken together, the findings suggest that imaging data are more predictive of fMRI-NF self-regulation skills in ADHD than behavioural data. Stronger baseline activation in fronto-striatal cognitive control regions predicts better fMRI-NF learning in ADHD

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Neurology International. 2020;12:1-5.

DETERMINING THE ASSOCIATION BETWEEN POLYMORPHISMS OF THE DAT1 AND DRD4 GENES WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN FROM JAVA ISLAND.

Thursina C, Nurputra DK, Harahap ISK, et al.

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurobehavioural in the children. Genetic factor is known one of the factors which contributed in ADHD development. VNTR polymorphism in 3'UTR exon 15 of DAT1 gene and exon 3 of DRD4 gene are reported to be associated in ADHD. In this study we examine the association of ADHD with VNTR polymorphism of DAT1 and DRD4 gene in Indonesian children. Sixty-five ADHD children and 70 normal children (6- 13 years of age), were included in the study, we matched by age and gender. ADHD was diagnosed by DSM-IV. We performed a casecontrol study to found the association between ADHD and VNTR polymorphism of DAT1 and DRD4 genes. The 10-repeat allele of DAT1 and 2-repeat allele of DRD4 were higher in Indonesian children. Although the frequency of these allele was higher, but it was similar both in ADHD and control groups. Neither DAT1 nor DRD4 gene showed showed significant difference in genotype distribution and frequency allele between both groups ($p > 0.05$). No association between ADHD and VNTR polymorphism of DAT1 and DRD4 genes found in Indonesian children. This data suggest that DAT1 and DRD4 do not contribute to etiology of ADHD in Indonesian children. Further studies are needed to clarify association between VNTR polymorphism of DAT1 and DRD4 genetic with ADHD of Indonesian children in larger sample size and family based study

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Neurophotonics. 2020;7.

ACUTE ADMINISTRATION OF METHYLPHENIDATE DIFFERENTIALLY AFFECTS CORTICAL PROCESSING OF EMOTIONAL FACIAL EXPRESSIONS IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER CHILDREN AS STUDIED BY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY.

Kobayashi M, Ikeda T, Tokuda T, et al.

Significance: It has been reported that children with attention-deficit hyperactivity disorder (ADHD) have impairment in the recognition of angry but not of happy facial expressions, and they show atypical cortical activation patterns in response to facial expressions. However, little is known about neural mechanisms underlying the impaired recognition of facial expressions in school-aged children with ADHD and the effects of acute medication on their processing of facial expressions.

Aim: We aimed to investigate the possibility that acute administration of methylphenidate (MPH) affects processing of facial expressions in ADHD children.

Approach: We measured the hemodynamic changes in the bilateral temporo-occipital areas of ADHD children observing the happy and angry facial expressions before and 1.5 h after MPH or placebo administration in a randomized, double-blind, placebo-controlled, crossover design study.

Results: We found that, regardless of medication, happy expressions induced increased oxyhemoglobin (oxy-Hb) responses in the right inferior occipital region but not in the superior temporal region. For angry expressions, oxy-Hb responses increased after MPH administration, but not after placebo administration, in the left inferior occipital area, whereas there was no significant activation before MPH administration.

Conclusions: Our results suggest that (1) ADHD children consistently recruit the right inferior occipital regions to process happy expressions and (2) MPH administration to ADHD children enhances cortical activation in the left inferior occipital regions when they process angry expressions

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Neuropsychiatr Dis Treat. 2020;16:1619-43.

REVIEW OF CLINICAL OUTCOME ASSESSMENTS IN PEDIATRIC ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Markowitz JT, Oberdhan D, Ciesluk A, et al.

Purpose: Various clinical outcome assessments (COAs) are used in clinical research to assess and monitor treatment efficacy in pediatric attention-deficit/hyperactivity disorder (ADHD) trials. It is unclear whether the concepts assessed are those that are important to patients and their caregivers. The concepts measured by commonly used COAs in this population have not been explicitly compared.

Methods: We conducted reviews of the qualitative literature to extract information on pediatric ADHD-related concepts reported by pediatric patients, parents, and teachers. Using these concepts, we developed a conceptual framework of pediatric ADHD using both the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria and the additional symptoms and behavioral impacts identified in the literature. We searched for COAs that have been used in pediatric ADHD research and mapped their items based on their conceptual underpinning.

Results: Of the 27 COAs found in the empirical literature, 4 COAs assessed only DSM symptoms. The most comprehensive coverage of our conceptual framework was seen in the Swanson, Nolan, and Pelham Rating Scale DSM-IV (SNAP-IV). Eighteen COAs were used in at least 1 clinical trial: ADHD-Rating Scale-IV (ADHD-RS-IV) was used most often (n=77), followed by SNAP-IV (n=50), Swanson, Kotkin, Agler, M-Flynn, and Pelham Scale (SKAMP; n=31), Weiss Functional Impairment Rating Scale (WFIRS; n=24), and Vanderbilt ADHD Diagnostic Rating Scale (VADRS; n=15).

Conclusion: We identified symptoms and behavioral impacts from qualitative studies in pediatric ADHD that are not included in DSM-based criteria. Most COAs used in pediatric ADHD clinical trials measure only those symptoms listed in the DSM. While these COAs can measure symptom severity, they may not assess the full range of symptoms and impacts important to patients and their caregivers. Future research is needed to measure all concepts important to patients and caregivers within ADHD clinical trials

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NeuroReport. 2020;776-79.

THE PREATTENTIVE CHANGE DETECTION IN PRESCHOOL CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A MISMATCH NEGATIVITY STUDY.

Zhang J, Qiu M, Pan J, et al.

To investigate the preattentive change detection in preschool children with attention deficit hyperactivity disorder (ADHD), we compared the mismatch negativity (MMN) and P3a of event-related potentials (ERPs) between preschool ADHD and normal children using three-stimulus oddball paradigm. Analyzing MMN and P3a components, we found that MMN elicited by deviants and P3a elicited by novelty were significantly reduced in patients than in controls. In addition, the P3a amplitude was positive correlated to IQ and negatively correlated to hyperactivity, antagonistic defiance and conduct problems in Swanson, Nolan, and Pelham IV Rating Scale, parent version. These data provided new neurophysiological evidence for the dysfunction of preattentive change detection and attentional shift in ADHD children

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Nord J Psychiatry. 2020.

DIFFUSION TENSOR IMAGING FINDINGS IN CHILDREN WITH SLUGGISH COGNITIVE TEMPO COMORBID ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Unsel-Bolat G., Baytunca MB, Karda+ƒB, et al.

Objective: The construct of Sluggish Cognitive Tempo (SCT) is characterized by daydreaming, mental confusion, staring blankly and hypoactivity. Our main goal was to explore neuropsychological differences in Attention Deficit Hyperactivity Disorder-Inattentive presentation (ADHD-IA) groups with and without SCT symptoms compared to healthy controls. After detecting specific neuropsychological differences, we examined white matter microstructure using Diffusion Tensor Imaging (DTI) data obtained from 3.0 Tesla MRI scans of the cases with SCT symptoms comparing to Typically Developing (TD) controls.

Method: In this study, we included 24 cases in the ADHD-IA group with SCT symptoms, 57 cases in the ADHD-IA group without SCT symptoms and, 24 children in the TD group. We applied tract-based spatial statistics to the DTI measures for obtaining fractional anisotropy (FA), axial, radial and mean diffusivity (AD, RD, MD) to explore white matter differences for the whole brain.

Results: Omission error scores and longer reaction time scores were specifically associated with inattention symptoms. Commission error scores were significantly and specifically related to SCT symptoms. Cases with SCT symptoms presented increased FA in the bilateral anterior and posterior limb of the internal capsule, bilateral cerebral peduncle, and the fornix than TD group.

Conclusions: Neurobiological differences in ADHD cases are still relatively unexplored. We suggest that including an assessment for SCT in the neuropsychological and neuroimaging studies of ADHD may provide more consistent results

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Noropsikiyatr Ars. 2020;57:37-43.

ATTENTION DEFICIT HYPERACTIVITY DISORDER, IMPULSIVITY, ANXIETY, AND DEPRESSION SYMPTOMS MEDIATING THE RELATIONSHIP BETWEEN CHILDHOOD TRAUMA AND SYMPTOMS SEVERITY OF OBSESSIVE-COMPULSIVE DISORDER.

Coban A., Tan O.

Introduction: A growing body of research associates childhood trauma with obsessive-compulsive disorder (OCD). The aim of this study was to investigate the relationships between childhood trauma and OCD, including both its severity and OCD patients comorbid impulsivity, ADHD, anxiety, and depressive symptoms.

Methods: A convenient sample consisting of 106 patients with OCD was given the Childhood Trauma Questionnaire (CTQ), Yale-Brown Obsessive Compulsive Scale (Y-BOCS), Wender Utah Rating Scale (WURS), Hamilton Rating Scale for Depression (HAM-D), Beck Anxiety Inventory (BAI), and Barratt Impulsivity Scale-11 (BIS-11).

Results: The results showed that childhood trauma indirectly predicts the severity of OCD and directly predicts comorbidities in OCD patients, including anxiety, ADHD, WURS, and impulsivity. Patients with

childhood trauma had higher WURS, BAI, and BIS-11 scores and fewer years of education. Ongoing adult ADHD was more common in individuals with childhood trauma.
Conclusion: A history of childhood trauma in OCD patients has indirect effects on the severity of OCD and depressive symptoms and is associated with more severe anxiety, higher levels of impulsivity, higher prevalence of ADHD, and lower levels of education. More research is needed to clarify the effects of childhood trauma on OCD severity and comorbidity

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Norsk Epidemiologi. 2019;28:62.

PARENT-OFFSPRING RECURRENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Solberg BS, Hegvik T-A, et al.

Introduction: A strong recurrence risk of attention-deficit/hyperactivity disorder (ADHD) from parent to offspring has been reported, but the mechanisms and patterns of recurrence from each parent to male and female offspring are not known.
Aims: To examine the recurrence risk by parental and offspring sex and whether reproduction influences recurrence risks.
Methods: The nationwide Medical Birth Registry of Norway (MBRN) was used to identify individuals born 1967-2011. Those born 1967-1968 were followed to 2011 for their own reproduction. Individuals diagnosed with ADHD were identified using the Norwegian Prescription Database (2004-2015) or the Norwegian patient registry (2008-2015). We used Poisson regression to calculate the relative risk (RR) and adjusted prevalence for ADHD in offspring by maternal ADHD only (n=20,032; 0.8%), paternal ADHD only (n=16,952; 0.7%) or ADHD in both parents (n=1,545; 0.06%). Offspring with neither paternal nor maternal ADHD served as the reference group (n=2,447,559; 98.5%). Reproduction (the percentage of individuals born 1967-68 with offspring registered in the MBRN) were calculated for men and women with and without ADHD.
Results: Parental and offspring ADHD were strongly related. Maternal ADHD had a stronger association with offspring ADHD than paternal ADHD (RRmaternal 8.4; 95% confidence interval (CI) 8.2- 8.6 versus RRpaternal=6.2; 95% CI 6.0-6.4). The highest recurrence risk was when both parents were diagnosed with ADHD (RRboth=11.7; 95% CI 11.0-12.5). Further, the adjusted prevalence of offspring ADHD when both parents had ADHD was 41.5% in male offspring and 25.1% in female offspring. Recurrence risks from both maternal and paternal ADHD were higher in female than in male offspring. Men diagnosed with ADHD had lower reproduction than women with ADHD (75.2% versus 90.4%, respectively) and were generally older at childbirth.
Conclusions: Transgenerational ADHD recurrence risk was high and higher from maternal than paternal ADHD, regardless of offspring sex. Our results may prove helpful for health-care professionals when it comes to the identification of children at high risk of ADHD

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Nutrients. 2020;12:1-27.

ZONULIN-DEPENDENT INTESTINAL PERMEABILITY IN CHILDREN DIAGNOSED WITH MENTAL DISORDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Asbjornsdottir B, Snorradottir H, Andresdottir E, et al.

Worldwide, up to 20% of children and adolescents experience mental disorders, which are the leading cause of disability in young people. Research shows that serum zonulin levels are associated with increased intestinal permeability (IP), affecting neural, hormonal, and immunological pathways. This systematic review and meta-analysis aimed to summarize evidence from observational studies on IP in children diagnosed with mental disorders. The review follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. A systematic search of the Cochrane Library, PsycINFO, PubMed, and the Web of Science identified 833 records. Only non-intervention (i.e., observational) studies in children (<18 years) diagnosed with mental disorders, including a relevant marker of intestinal permeability, were included. Five studies were selected, with the risk of bias assessed according to the Newcastle Ottawa scale (NOS). Four articles were identified as strong and one as moderate, representing altogether 402 participants

providing evidence on IP in children diagnosed with attention deficit and hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and obsessive compulsive disorder (OCD). In ADHD, elevated serum zonulin levels were associated with impaired social functioning compared to controls. Children with ASD may be predisposed to impair intestinal barrier function, which may contribute to their symptoms and clinical outcome compared to controls. Children with ASD, who experience gastro-intestinal (GI) symptoms, seem to have an imbalance in their immune response. However, in children with OCD, serum zonulin levels were not significantly different compared to controls, but serum claudin 5, a transmembrane tight-junction protein, was significantly higher. A meta-analysis of mean zonulin plasma levels of patients and control groups revealed a significant difference between groups (p = 0.001), including the four studies evaluating the full spectrum of the zonulin peptide family. Therefore, further studies are required to better understand the complex role of barrier function, i.e., intestinal and bloodΓÇôbrain barrier, and of inflammation, to the pathophysiology in mental and neurodevelopmental disorders. This review was PROSPERO preregistered, (162208)

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Oman Medical Journal. 2018;33:59-60.

PREVALENCE AND PREDICTORS OF DEPRESSIVE SYMPTOMS AMONG CAREGIVERS OF CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER ATTENDING A TERTIARY: A CROSS-SECTIONAL ANALYTICAL STUDY FROM MUSCAT, OMAN.

Al BN, Al SM, Al-Alawi M, et al.

Objectives: This study aimed to measure the prevalence of depressive symptoms among caregivers of children with a diagnosis of attention deficit hyperactivity disorder (ADHD) attending a tertiary care child and adolescent mental health clinic in Oman. The related aims were to explore clinical and socio-demographic predictors of depressive symptoms.

Methods: A cross-sectional analytical study was conducted among a systemic random sample of caregivers of children with ADHD seeking consultation from a dedicated unit for child and adolescent mental health services in Muscat. The presence of depressive symptom was quantified using the Patient Health Questionnaire-9 (PHQ-9). A binary logistic regression model was used to find the adjusted and unadjusted odds ratios (ORs).

Results: A total of 117 caregivers participated in the study, with a response rate of 89%. The prevalence of depression symptoms was 65%. Logistic regression analysis indicated that low income, being the only caregiver in the family, and hyperactive-impulsive or combined types of ADHD were significant predictors of depression in multivariate analysis (OR = 24.98, 95% confidence interval (CI): 2.94 - 212.56, p = 0.003; OR = 14.26, 95% CI: 2.44 - 83.24, p = 0.003; OR = 6.60, 95% CI: 2.81 - 212.58, p = 0.003; and OR = 5.60; 95% CI:2.14-108.40, p = 0.007, respectively).

Conclusions: This study showed that depressive symptoms are common among caregivers of children with ADHD in urban places in Oman, especially in those with financial difficulties and being the only caregiver whom children are suffering from hyperactive-impulsive or combined types of ADHD. Therefore, detection and prompt treatment of depression among caregiver is recommended

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Pediatrics. 2020;145.

EPIDEMIOLOGICAL PROFILE OF HEALTH AND BEHAVIORS IN MIDDLE CHILDHOOD.

Parasuraman SR, Ghandour RM, Kogan MD.

OBJECTIVES: In this study, we present an epidemiological profile of middle childhood (children aged 6-11 years) using the 2016-2017 National Survey of Children's Health.

METHODS: We used data from the 2016 and 2017 National Survey of Children's Health, a national cross-sectional, address-based survey administered annually. The study sample included 21 539 children aged 6 to 11 years. Survey items chosen to create this profile of middle childhood described sociodemographic and family characteristics, health status, and behaviors. Weighted descriptive and bivariate analyses were applied to examine the population and differences by subgroups.

RESULTS: Most children aged 6 to 11 years were in excellent or very good physical health (89%) and oral health (73%). More than 20% were considered to have special health care needs, and 20% had at least 2 health conditions. Allergies and asthma were the most prevalent physical conditions, whereas attention-deficit/hyperactivity disorder and behavioral or conduct problems were the most prevalent of emotional, behavioral, and/or developmental disorders. More than half of children participated in sports or other activities for at least 60 minutes per day, whereas more than one-third of children had 4 hours of parent-reported screen time per day, and nearly two-thirds received 9 hours of sleep per night. We found several significant differences in screen time and activity behaviors as children aged and by sex.
CONCLUSIONS: The middle-childhood population is generally healthy, yet several patterns observed with respect to age and sex indicate a need to examine the emergence and progression of select health-risk behaviors. In this study, we highlight opportunities to implement targeted interventions at earlier ages and different points along the life course

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Pediatr Int. 2020;62:725-35.
ASSOCIATION OF METHYLPHENIDATE USE AND TRADITIONAL AND CYBERBULLYING IN ADOLESCENTS WITH ADHD.
Tural HoS, Kandemir G.
Background: This study aimed to determine whether there is a difference in terms of traditional/cyberbullying or victimization among adolescents receiving methylphenidate for attention-deficit/hyperactivity disorder (ADHD) and treatment-na+»ve adolescents with ADHD during a 1-year period.
Methods: The Sociodemographic Data Form, Schedule for Affective Disorders and Schizophrenia for School-Aged Children (Present and Lifetime Version), Peer Bullying Scale Adolescent Form and the Cyberbully/Victim Scale were administered to male adolescents with ADHD.
Results: Adolescents who did not receive methylphenidate during the last 1-year were exposed to higher rates of physical victimization, isolation, destroying of property by others, and sexual victimization, all of which are subtypes of traditional victimization; they also reported higher rates of destroying others' property. Furthermore, cyberbullying victimization and cyberbullying behaviors were more common in the non-treated group.
Conclusion: Effective treatment of ADHD could lessen involvement in the bullying cycle in adolescents with ADHD

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PLoS ONE. 2020;15.
STUDYING GLOBAL PROCESSING IN AUTISM AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH GAZE MOVEMENTS: THE EXAMPLE OF A COPYING TASK.
Seernani D, Ioannou C, Damania K, et al.
Recent discussions in the literature, along with the revision of the Diagnostic and Statistical Manual (DSM) (American Psychiatric Association 2013), suggest aetiological commonalities between the highly comorbid Attention-Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD). Addressing this discussion requires studying these disorders together by comparing constructs typical to each of them. In the present study, we investigate global processing, known to be difficult for participants with ASD, and Intra-Subject Variability (ISV), known to be consistently increased in participants with ADHD, in groups, aged 10-13 years, with ADHD (n = 25), ASD without comorbid ADHD (ASD-) (n = 13) and ASD with ADHD (ASD+) (n = 18) in comparison with a typically developing group (n = 22). A Copying task, typically requiring global processing and in this case particularly designed using equally complex stimuli to also measure ISV across trials, was selected. Oculomotor measures in this task proved to be particularly sensitive to group differences. While increased ISV was not observed in the present task in participants with ADHD, both ASD groups looked longer on the figure to be drawn, indicating that global processing takes longer in ASD. However, the ASD+ group fixated on the figure only between drawing movements, whereas the ASD- group did this throughout the drawing process. The present study provides evidence towards ASD and ADHD being separate, not-overlapping, disorders. Since the pure ASD- group was affected more by central coherence problems than

the ASD + group, it may suggest that neuropsychological constructs interact differently in different clinical groups and sub-groups

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PLoS ONE. 2020;15.

NEUROFEEDBACK IN ADHD: A QUALITATIVE STUDY OF STRATEGY USE IN SLOW CORTICAL POTENTIAL TRAINING.

Hasslinger J, Souto MD, Hellstadius LF, et al.

Neurofeedback (NF) as a treatment for children and adolescents with attention deficit hyperactivity disorder (ADHD) has gained growing interest in recent years. Most research has been quantitative, focusing on treatment outcomes, while qualitative approaches exploring the treatment process and participants' experiences are scarce. The objective of this study was to examine NF participants' use of cognitive and other strategies for approaching and solving NF tasks, their development over the course of the training and the influence of participants' compliance. Method We collected 130 short semi-structured interviews following treatment sessions from 30 participants with ADHD receiving NF using slow cortical potential training (SCP). The interviews were transcribed verbatim and analyzed using thematic analysis. Themes where evaluated for changes over-time and between participants with high/low treatment compliance. Interviews from 14 participants who had undergone at least five completed interviews were examined in more depths, aiming to establish typical strategy/training profiles. Results We identified 16 strategies covering four domains: Cognitive, physiological, emotional and unspecified. Typical of most strategies were that they served as a vehicle to regulate mental arousal. Overall, no clear patterns of changes over time were found. Highly compliant participants reported to use the strategies from the emotional domain and the strategy focus more frequently than neutral compliant participants did, while neutral compliant participants reported the use of the strategies muscular activity and passivity more often than participants did with high compliance. Across participants, three strategy profiles were derived, those who handled the task by manipulating their state of mind in relation to the NF task, those who were mainly manifest and concrete towards the task, and those who were mostly unaware of what they were doing. These profiles differed in self-regulatory performance, and only participants showing the state of mind profile experienced a decrease of ADHD symptoms accompanied by objectively measured improvements in self-regulation. In addition, compliance affected both how and what strategies were used. Conclusion/discussion A heterogeneous array of cognitive and other strategies is used at varying levels of training compliance by participants with ADHD during SCP that could be condensed to three prototypical profiles. Future research should take compliance and strategy/training profiles into account when evaluating NF. The latter may help to clarify which and how brain activity regulating mechanisms drive training, individual response to NF, and how they are influenced by motivational factors. Our findings might also help to facilitate more effective instructions in how to approach SCP in clinical practice

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PM R. 2018;10:S45.

DIFFERENCE IN EXERCISE TOLERANCE DURING IN-CLINIC CONCUSSION RECOVERY WORKOUTS AMONG PATIENTS WITH HISTORY OF SELF-REPORTED HEADACHE, LEARNING DISABILITY, ATTENTION DEFICIT-HYPERACTIVITY DISORDER, OR MOOD DISORDER.

Van TM, Johnson AR, Sas A, et al.

We hypothesized that positive health history of mood disorder (Anxiety/Depression), Learning Disability/Attention Deficit-Hyperactivity Disorder (LD/ADHD), or headache (HA) would negatively affect participation in exercise after concussion compared with patients without comorbid conditions. Design: Secondary analysis of a retrospective data set. Setting: Concussion clinic at a regional medical center. Participants: 122 adolescent/young adults (15.4 -¦ 2.9 years of age) diagnosed with concussion. Interventions: Patients participated in supervised exercise as a part of treatment. Heart rate, perceived exertion, and symptom self-report was monitored throughout treatment. Patients/families provided health history prior to exercise. Main Outcome Measures: Heart rate, perceived exertion (from 1-100%), symptom

self-report, and completion of exercise intervention. Results: Tolerance for exercise was high across all groups and HA, anxiety, depression were not associated with ability to complete the exercise. The heart rate at which patients reported symptoms was not associated with any diagnoses. Controlling for the effects of HA and ADHD/LD, those with anxiety achieved a lower percentage of their age-predicted maximum heart rate (APMHR) than those without anxiety (P = .048). In univariate analyses, self-reported perceived-exertion during exercise was lower for patients with history of HA (P = .017), anxiety (P = .050), and ADHD/LD (P = .011) but after controlling for all diagnoses in a multivariate model, only history of HA remained significant (P = .015). The discrepancy between perceived exertion and percentage of APMHR achieved reached near-significance in HA patients (P = .055). Conclusions: Exercise after concussion was well tolerated regardless of premorbid diagnosis or headache symptoms. Premorbid diagnosis of anxiety was related to lower APMHR during exercise. Prior history of HA reported lower rates of perceived exertion, with a tendency to underestimate exertion compared to APMHR achieved during exercise

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Progress in Brain Research. 2020.

SOCIAL ATTENTION: WHAT IS IT, HOW CAN WE MEASURE IT, AND WHAT CAN IT TELL US ABOUT AUTISM AND ADHD?

Braithwaite EK, Gui A, Jones EJH.

Neurodevelopmental disorders like autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) affect 2-10% of children worldwide but are still poorly understood. Prospective studies of infants with an elevated familial likelihood of ASD or ADHD can provide insight into early mechanisms that canalize development down a typical or atypical course. Such work holds potential for earlier identification and intervention to support optimal outcomes in individuals with neurodevelopmental disorders. Disrupted attention may be involved in developmental trajectories to ASD and ADHD. Specifically, altered attention to social stimuli has been suggested as a possible endophenotype of ASD, lying between genetic factors impacting brain development and later symptoms. Similarly, changes in domain-general aspects of attention are commonly seen in ADHD and emerging evidence suggests these may begin in infancy. Could these patterns point to a common risk factor for both disorders? Or does social attention reflect the activity of a particular network of brain systems that is distinct to those underpinning general attention skills? One challenge to addressing such questions is our lack of understanding of the relation between social and general attention. In this chapter we review evidence from infants with later ASD and ADHD that illuminates this question

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Prog Neuro-Psychopharmacol Biol Psychiatry. 2021;104.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IS CHARACTERIZED BY A DELAY IN SUBCORTICAL MATURATION.

Wang Y, Zuo C, Xu Q, et al.

Although previous studies have found that ADHD is characterized by a delay in cortical maturation, it is not clear whether this phenomenon was secondary to developmental trajectories in subcortical regions (caudate, putamen, pallidum, thalamus, hippocampus and amygdala). Using the ADHD-200 dataset, we estimated subcortical volumes in 339 individuals with ADHD and 568 typically developing controls. We defined the growth trajectory of each subcortical structure, delineating a phase of childhood increase followed by an adolescent decrease in subcortical volumes using a quadratic growth model. From these trajectories, the age of attaining peak subcortical volumes was derived and used as an index of subcortical maturation. We found that subcortical structures (caudate, putamen, pallidum, thalamus, hippocampus and amygdala) followed curvilinear trajectories similar to those reported in previous studies. The volumes of these subcortical structures in ADHD were also delayed in the developmental trajectory, which suggested that ADHD may be characterized by a delay in subcortical maturation. This delay may lead to a shift in which individuals with ADHD go through the process of pruning the nerve connections that is part of the normal maturation process during adolescence. Further, we also found that the asymmetric development of subcortical structures was abnormal in ADHD, which resulted from the imbalance of the maturation delay of bilateral subcortical

structures. The subcortical maturation delay may play an important role in the pathophysiology of ADHD. Our findings provide new potential targets to investigate the pathophysiology of ADHD

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Psychiatric Annals. 2020 Aug;50:326-33.

METABOLIC SYNDROME IN CHILD AND ADOLESCENT PSYCHIATRY.

Hyun JK, Wilson C, Timothy VD, et al.

In adults, metabolic syndrome (MetS) is defined as a constellation of at least 3 of 5 cardiometabolic risk factors: central obesity, hyperglycemia, elevated blood pressure, elevated triglycerides, and decreased high-density lipoprotein cholesterol. In pediatric populations, MetS remains a controversial topic due to lack of clear consensus regarding the definition, clinical utility, and lack of standardized guidelines. Despite these controversies, pediatric MetS is receiving increasing clinical and research attention due to the growing obesity epidemic and a substantial increase in the use of second-generation antipsychotics in recent years. Clinicians should be familiar with prevention, early identification, and management of obesity and metabolic derangements while working with youth with psychiatric disorders

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Psychiatr Invest. 2020;17:702-09.

AGE-RELATED CHANGES IN AUDITORY NOGO-N200 LATENCY IN MEDICATION-NA+»VE CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Lee YJ, Jeong MY, Park S, et al.

Objective Event-related potential (ERP) changes with brain development in healthy children and adolescents. However, few studies have focused on age-related changes in the N200 and P300 components among individuals with attention-deficit/hyperactivity disorder (ADHD). Therefore, this study aimed to assess age-related differences in the auditory nogo-N200 components in individuals with ADHD.

Methods We enrolled 46 participants with auditory nogo-N200 and nogo-P300 components. We assessed ADHD symptoms using the Advanced Test of Attention (ATA) and Korean ADHD Rating Scale-IV (K-ARS-IV). Moreover, we assessed emotional and behavioral problems using the Korean Child Behavior Checklist (K-CBCL). Further, we measured auditory ERPs.

Results There were no differences with respect to sex or ATA, K-ARS-IV, and K-CBCL scores between the groups. With a 1-year in-crease in age, the nogo-N200 latency at Fz and Cz decreased by 6.08 ms and 4.88 ms, respectively; this result was statistically significant in multivariable linear regression adjusted by sex and dominant hand.

Conclusion Our findings revealed age-related changes in nogo-N200 latency at the Fz and Cz electrodes in individuals with ADHD. Future studies should perform comparisons with healthy controls to determine whether auditory nogo-N200 can be used to evaluate the developmental level in individuals with ADHD

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Psychiatry Res. 2020;291.

THE INTERACTIVE EFFECTS OF TEST-RETEST AND METHYLPHENIDATE ADMINISTRATION ON COGNITIVE PERFORMANCE IN YOUTH WITH ADHD: A DOUBLE-BLIND PLACEBO-CONTROLLED CROSSOVER STUDY.

Horowitz I, Avirame K, Naim-Feil J, et al.

Studies have shown that Methylphenidate (MPH) affects cognitive performance on the neuropsychological tests and clinical symptoms of individuals diagnosed with attention deficit/hyperactivity disorder (ADHD). This study investigated the acute effects of MPH on neuropsychological tests to explore the interaction between MPH and test-retest effects. Twenty youths with ADHD were tested before and after MPH intake in a double-blind placebo-controlled crossover design and compared to twenty matched controls. Participants were tested on a range of standardized tasks including sustained attention to response, N-Back, and Word/Color Stroop. Identical tasks were administered twice each testing day, before and 1 hour after MPH/Placebo administration. Healthy controls were tested similarly with no intervention. Decreases in response time (RT)

variability across tasks and in commission errors were found in ADHD after MPH. Conversely, a significant increase in RT variability and increase in omission errors were observed after the placebo. In the control group, RT variability and omission errors increased whereas commission errors decreased, suggesting fatigue and practice effects, respectively. Test-retest reliability was higher in controls than ADHD. It is suggested that cognitive tests are sensitive objective measures for the assessment of responses to MPH in ADHD but are also affected by repetition and fatigue

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Psychiatry Res. 2020;291.

SEARCH FOR AN EPIGENETIC BIOMARKER IN ADHD DIAGNOSIS, BASED ON THE DAT1 GENE 5'-UTR METHYLATION: A NEW POSSIBLE APPROACH.

Lambacher G, Pascale E, Pucci M, et al.

Attention Deficit/Hyperactivity Disorder (ADHD) is the most common neuro-developmental alteration in childhood. To date, its diagnosis is exclusively clinical, however recent studies focused on searching for objective biomarkers. We recently reported a selective alteration of DNA methylation in the 5′-UTR of dopamine transporter (DAT1) gene, in a ^{1}CGG^{2}CGG^{3}CGG and a ^{5}CG^{6}CG motif, for ADHD patients (compared to controls). Presently, we looked for DNA methylation of the corresponding CpG sites but complementary on the opposite strand ("COS"). Exploiting a novel cross-correlation approach, we found a core M5 - M5 COS and M2 - M2 COS relationship with relatively free M1 and M6 COS extremes. Our data might be relevant, to find a new biomarker to diagnose ADHD in affected subjects

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Psychiatry Res. 2020;291.

CONTRASTING EFFECTS OF MUSIC ON READING COMPREHENSION IN PREADOLESCENTS WITH AND WITHOUT ADHD.

Madjar N, Gazoli R, Manor I, et al.

Children and adolescents with attention-deficit/hyperactivity disorder (ADHD) are advised to study in quiet settings; yet, many professionals assert that environments devoid of external stimulus, are often unnecessary to facilitate optimal learning conditions. Empirical controlled trials examining this assertion are scarce. This study explored whether music improves reading performance of preadolescents with ADHD compared with typically developed (TD) peers, and its correlation with changes in heart rate variability (HRV), an autonomic nervous system indicator. After a pilot phase (N = 20; age = 12.05), additional independent sample of ADHD (n = 25; age = 10.28) and TD (n = 25; age = 10.44) preadolescents completed reading tasks under four conditions: without background music, with calm music without lyrics, calm music with lyrics, and rhythmic music with lyrics. Reading comprehension and mean-levels of HRV changes (before and during each task) were assessed using validated instruments. Reading comprehension significantly improved under the music conditions in ADHD group and deteriorated among TD. Differences in HRV changes were significant between groups, and explained reading performance. These findings suggest that music may improve attentive skills of preadolescents with ADHD, but not TD, and urge the need to identify an optimal fit between individual and contextual characteristics

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Psychiatry Res. 2020;291.

EFFICACY OF PSYCHOSOCIAL INTERVENTIONS FOR CHILDREN WITH ADHD AND EMOTION DYSREGULATION: A SYSTEMATIC REVIEW.

Vacher C, Goujon A, Romo L, et al.

Attention-Deficit Hyperactivity Disorder (ADHD) is frequently associated with emotion dysregulation (ED) that is characterized by excessive and inappropriate emotional reactions. Children with ADHD and ED present significant social, academic and family functioning impairments. These findings indicate that ED should be regularly monitored in children with ADHD and should be managed with targeted therapeutic interventions. However, few studies have evaluated the efficacy of psychosocial interventions to manage ED in children

with ADHD. The aim of this systematic review was to assess the effects of psychosocial interventions for children with ADHD and ED, particularly their benefits and limitations. This review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) model. A systematic literature search of different databases in February 2018 allowed the identification of five randomized controlled trials, one quasi-experimental study, and four open-label uncontrolled studies. Analysis of the results reported in these studies suggested that psychosocial interventions can improve severe irritability and aggressive behavior in children with ADHD and ED. However, the short trial duration, the lack of follow-up and of control group in several studies, and the heterogeneity of the outcome measures affected the result interpretation. Future studies should use standardized measures of ED and larger samples

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Psychiatry Res. 2020;291.

SLEEP PROBLEMS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER: SEX DIFFERENCES AND PARENTAL STRESS.

D'Agati E, Abate R, Gialloreti LE, et al.

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Psychiatry Res. 2020;290.

PRELIMINARY EVALUATION OF THE UTILITY OF PARENTAL RATINGS IN A CHILD NETWORK.

Post RM, Rowe M, Kaplin DB, et al.

Introduction: Children in the US have a high incidence of psychiatric disorders, but the symptoms of these illnesses are often poorly recognized and treated. We thus created a Child Network for parents of children aged 2-12 to rate their child on a weekly basis on a secure website so that longitudinal ratings could be easily visualized.

Methods: After giving informed consent, parents filled out: a one-time questionnaire and a 97 item Child Checklist; and then rated the severity of depression, anxiety, ADHD, oppositional behavior, and mania each week. The new Checklist ratings were correlated with the 23 previous validated in adults (the M-3), and symptom burden was compared with diagnoses received in the community.

Results: The 23 item M-3 ratings were highly correlated with the more extensive Child Checklist. Symptom severity also corresponded to diagnoses received in the community. An example of the longitudinal weekly ratings of a child with a dysphoric mania is also presented.

Conclusions: The convergence of scores on the adult and child portions of the Child Checklist and the ease of visualization of symptoms and response to treatment suggest the utility of the ratings in the Child Network

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Psychol Assess. 2020 Jul.

ASSESSING SLUGGISH COGNITIVE TEMPO AND ADHD INATTENTION IN ELEMENTARY STUDENTS: EMPIRICAL DIFFERENTIATION, INVARIANCE ACROSS SEX AND GRADE, AND MEASUREMENT PRECISION.

Becker SP, Mossing KW, Zoromski AK, et al.

To advance the research examining the sluggish cognitive tempo (SCT) construct, a key priority has been to develop assessment tools that are reliable and valid. The current study builds upon existing work by conducting the most thorough psychometric evaluation to date of the teacher-reported Child and Adolescent Behavior Inventory (CABI) SCT and attention-deficit/hyperactivity disorder inattention (ADHD-IN) modules in a large sample of elementary students. Participants were 7,613 students (Grades 2â€“5; 50.3% boys) attending 24 elementary schools in 3 school districts. Teachers (N = 398) provided ratings of SCT, ADHD-IN, academic impairment, and social impairment. An a priori 2-factor model with cross-loadings found the SCT items to demonstrate excellent structural validity with ADHD-IN items. The measurement properties of the SCT and ADHD-IN constructs were also invariant across sex and grade. SCT and ADHD-IN were both uniquely associated with academic and social impairment. Graded response item response theory analysis indicated that the SCT and ADHD-IN scales provided a high level of information and precision. The current

study replicates and extends previous research and provides the strongest psychometric evidence to date of teacher-rated SCT using the CABI. The teacher-report CABI may be especially useful in the school-based screening of SCT and ADHD-IN. (PsycInfo Database Record (c) 2020 APA, all rights reserved) (Source: journal abstract) Impact statementPublic Significance StatementFor research investigating the sluggish cognitive tempo (SCT) construct to advance, reliable and valid assessment tools must be developed and evaluated. Using a sample of over 7,600 elementary students, the current study provides the strongest psychometric support yet for the teacher-report version of the Child and Adolescent Behavior Inventory (CABI) SCT scale

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Psychol Assess. 2020;32:698-704.

A MULTIPLE INDICATORS MULTIPLE CAUSES (MIMIC) MODEL OF FRIENDSHIP QUALITY AND COMORBIDITIES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Normand S, Mikami AY, Savalei V, et al.

The unique objectives of the current investigation were: (a) to assess the fit of a multiinformant 2-factor measurement model of friendship quality in a clinical sample of children with attention-deficit/ hyperactivity disorder (ADHD); and (b) to use a multiple indicators multiple causes approach to evaluate whether comorbid externalizing and internalizing disorders incrementally predict levels of positive and negative friendship quality. Our sample included 165 target children diagnosed with ADHD (33% girls; aged 6-11 years). Target children, their parents, their friends, and the parents of their friends independently completed a self-report measure of friendship quality about the reciprocated friendship between the target child and the friend. Results indicated that a multiinformant 2-factor measurement model with correlated positive friendship quality and negative friendship quality had good fit. The friendships of children with ADHD and a comorbid externalizing disorder were characterized by less positive friendship quality and more negative friendship quality than the friendships of children with ADHD and no externalizing disorder after controlling for the presence of a comorbid internalizing disorder. However, the presence of a comorbid internalizing disorder did not predict positive or negative friendship quality. These findings suggest that soliciting reports from parents in addition to children and friends, and measuring comorbid externalizing disorders, may be valuable evidence-based strategies when assessing friendship quality in ADHD populations. This study suggests that the friendship quality of children with attention-deficit/hyperactivity disorder is characterized by global dimensions of positive and negative friendship features, such as companionship and conflict. Soliciting reports from parents in addition to children and friends, and measuring associated oppositional and conduct problems, may represent valuable science-based strategies when assessing friendship quality in children with attention-deficit/hyperactivity disorder

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Psychol Med. 2020 Jun;50:1338-47.

DEVELOPMENTAL JOINT TRAJECTORIES OF ANXIETY-DEPRESSIVE TRAIT AND TRAIT-AGGRESSION: IMPLICATIONS FOR CO-OCCURRENCE OF INTERNALIZING AND EXTERNALIZING PROBLEMS.

Dugré JR, Dumais A, Dellazizzo L, et al.

Background In youth, anxiety-depressive traits (ADT) and trait-aggression (TA) are important risk factors of exhibiting maladaptive behaviors in adulthood (i.e. violence and substance use). However, the developmental co-occurrence of these traits in youth remains unknown. We thus sought to investigate the developmental trajectories of ADT and TA within a data-driven approach. The aim was two-fold: (i) to examine the developmental trajectories of ADT and TA in youth from ages 10 to 16, and (ii) to investigate both childhood predictors and problematic outcomes of the identified joint trajectories.

Method The sample comprised 1354 children provided from the Longitudinal Studies of Child Abuse and Neglect (LONGSCAN) Consortium. Group-based trajectory modeling was first employed to identify individual trajectory models of ADT and TA independently (from ages 10 to 16). Then, joint trajectory models were built on the found trajectories. Last, logistic regressions were used to evaluate the childhood characteristics and negative outcomes of the joint trajectory groups.

Results Our results showed five trajectory groups with varying levels of ADT and TA. A significant co-occurrence between ADT and TA was found in three of the trajectory groups. Notably, higher levels of childhood psychopathology and more severe/frequent childhood abuse were found in the groups with moderate to high ADT and high TA. The groups with higher ADT and high TA were also more likely to exhibit violence and substance use.
Conclusions This study exposes the importance of assessing ADT and TA simultaneously and early in childhood to prevent and manage the risk of problematic behaviors in adolescence

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Psychol Med. 2020 Jun;50:1278-84.

IS ASSOCIATION OF PRETERM BIRTH WITH COGNITIVE-NEUROPHYSIOLOGICAL IMPAIRMENTS AND ADHD SYMPTOMS CONSISTENT WITH A CAUSAL INFERENCE OR DUE TO FAMILIAL CONFOUNDS?

James SN, Rommel AS, Rijsdijk F, et al.

Background: Preterm birth is associated with an increased risk for cognitive-neurophysiological impairments and attention-deficit/hyperactivity disorder (ADHD). Whether the associations are due to the preterm birth insult per se, or due to other risk factors that characterise families with preterm-born children, is largely unknown.
Methods: We employed a within-sibling comparison design, using cognitive-performance and event-related potential (ERP) measures from 104 preterm-born adolescents and 104 of their term-born siblings. Analyses focused on ADHD symptoms and cognitive and ERP measures from a cued continuous performance test, an arrow flanker task and a reaction time task.
Results: Within-sibling analyses showed that preterm birth was significantly associated with increased ADHD symptoms (Î² = 0.32, p = 0.01, 95% CI 0.05 to 0.58) and specific cognitive-ERP impairments, such as IQ (Î² = âˆ’0.20, p = 0.02, 95% CI âˆ’0.40 to âˆ’0.01), preparation-vigilance measures and measures of error processing (ranging from Î² = 0.71, âˆ’0.35). There was a negligible within-sibling association between preterm birth with executive control measures of inhibition (NoGo-P3, Î² = âˆ’0.07, p = 0.45, 95% CI âˆ’0.33 to 0.15) or verbal working memory (digit span backward, Î² = âˆ’0.05, p = 0.63, 95% CI âˆ’0.30 to 0.18).
Conclusions: Our results suggest that the relationship between preterm birth with ADHD symptoms and specific cognitive-neurophysiological impairments (IQ, preparation-vigilance and error processing) is independent of family-level risk and consistent with a causal inference. In contrast, our results suggest that previously observed associations between preterm birth with executive control processes of inhibition and working memory are instead linked to background characteristics of families with a preterm-born child rather than preterm birth insult per se. These findings suggest that interventions need to target both preterm-birth specific and family-level risk factors

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Psychosomatic Medicine. 2020;82:305-15.

ADHERENCE TO LIFE-STYLE RECOMMENDATIONS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A POPULATION-BASED STUDY OF CHILDREN AGED 10 TO 11 YEARS.

Loewen OK, Maximova K, Ekwaru JP, et al.

Objective The incidence of attention-deficit/hyperactivity disorder (ADHD) among children and youth is high, and temporal increases have been paralleled by deteriorating life-styles. Poor diet quality, physical inactivity, poor sleep habits, and sedentary behaviors have all been associated with ADHD. However, no earlier prospective study has examined the independent and combined importance of meeting established life-style recommendations in childhood for ADHD in adolescence. We examined the associations of adherence to life-style recommendations with the incidence of ADHD and the utilization of health services associated with ADHD.
Methods Life-style survey among 10- and 11-year-old students (N = 3436) was linked to administrative health data. Associations between adherence to nine established life-style recommendations with ADHD diagnosis and number of physician visits for ADHD until age 14 years were examined using Cox proportional hazard and negative binomial regression.

Results Before age 14 years, 10.8% of students received an ADHD diagnosis. Meeting recommendations for vegetables and fruit, meat and alternatives, saturated fat, added sugar, and physical activity was associated with fewer ADHD diagnoses. Compared with children who met one to three recommendations, meeting seven to nine recommendations was associated with substantially lower incidence of ADHD and fewer physician visits related to ADHD (hazard ratio = 0.42 [95% confidence interval = 0.28-0.61]; rate ratio = 0.38 [95% confidence interval = 0.22-0.65]).
Conclusions Life-style recommendations exist to benefit development and physical health. Their promotion comes at no harm and may have benefits for ADHD. Experimental evidence is needed to clarify the potential bidirectional relationship between ADHD and adverse health behaviors

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Radiology: Artificial Intelligence. 2020;2.

A MULTICHANNEL DEEP NEURAL NETWORK MODEL ANALYZING MULTISCALE FUNCTIONAL BRAIN CONNECTOME DATA FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER DETECTION.

Chen M, Li H, Wang J, et al.

Purpose: To develop a multichannel deep neural network (mcDNN) classification model based on multiscale brain functional connectome data and demonstrate the value of this model by using attention deficit hyperactivity disorder (ADHD) detection as an example.
Materials and Methods: In this retrospective case-control study, existing data from the Neuro Bureau ADHD-200 dataset consisting of 973 participants were used. Multiscale functional brain connectomes based on both anatomic and functional criteria were constructed. The mcDNN model used the multiscale brain connectome data and personal characteristic data (PCD) as joint features to detect ADHD and identify the most predictive brain connectome features for ADHD diagnosis. The mcDNN model was compared with single-channel deep neural network (scDNN) models and the classification performance was evaluated through cross-validation and hold-out validation with the metrics of accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUC).
Results: In the cross-validation, the mcDNN model using combined features (fusion of the multiscale brain connectome data and PCD) achieved the best performance in ADHD detection with an AUC of 0.82 (95% confidence interval [CI]: 0.80, 0.83) compared with scDNN models using the features of the brain connectome at each individual scale and PCD, independently. In the hold-out validation, the mcDNN model achieved an AUC of 0.74 (95% CI: 0.73, 0.76).
Conclusion: An mcDNN model was developed for multiscale brain functional connectome data, and its utility for ADHD detection was demonstrated. By fusing the multiscale brain connectome data, the mcDNN model improved ADHD detection performance considerably over the use of a single scale

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Res Autism Spectr Disord. 2020;76.

TASK ENGAGEMENT DURING NARRATIVE WRITING IN SCHOOL-AGE CHILDREN WITH AUTISM SPECTRUM DISORDER COMPARED TO PEERS WITH AND WITHOUT ATTENTIONAL DIFFICULTIES.

Zajic MC, Solari EJ, McIntyre NS, et al.

Background: Children with autism spectrum disorder (ASD) demonstrate highly variable writing skills. Few studies have examined if engagement during writing assessments may differ for children with ASD and if task engagement is related to their writing assessment performance. This study examined narrative writing and broad task engagement in children with ASD compared to peers with attention-deficit/hyperactivity disorder (ADHD) and typically developing (TD) peers.
Method: Sixty children with ASD, 32 children with ADHD, and 29 TD children completed assessments of cognitive skills, symptom severity, and spontaneous narrative writing. Time spent engaged during writing was assessed during the spontaneous narrative writing task.
Results: The ASD group performed lowest on text organization and quality scores as well as word production scores while also spending the least time engaged with the writing task. Time spent engaged was most strongly associated with narrative writing scores in the ASD group and explained unique variance in text

organization and quality scores and word production scores after controlling for related age, cognitive skills, and symptom severity variables. The ADHD group showed similar associations between time spent engaged and word production scores, and time spent engaged explained unique variance in word production scores. **Conclusions**: Time spent engaged completing the writing task appeared lowest for the ASD group and may suggest writing task engagement to be a more prominent difficulty area for children with ASD compared to peers with ADHD and TD peers. Implications for better understanding and supporting the writing skills of children with ASD are discussed

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Rev Neurol. 2016;63:19-27.

EFFICACY OF LISDEXAMPHETAMINE TO IMPROVE THE BEHAVIOURAL AND COGNITIVE SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: TREATMENT MONITORED BY MEANS OF THE AULA NESPLORA VIRTUAL REALITY TEST.

Diaz-Orueta U., Fern+índez-Fern+índez MA, Morillo-Rojas MD, et al.

Introduction. Lisdexanfetamine (LDX) is the drug for attention deficit hyperactivity disorder (ADHD) undergoing the largest research volume in the latest years. However, no studies certify its usefulness for the improvement of cognitive functioning in ADHD.

Aim. To evaluate the efficacy of LDX in the behavioral and cognitive improvement of a group of patients with ADHD. Such efficacy was measured by means of the administration of AULA Nesplora virtual reality test before the prescription of pharmacological treatment and right after the treatment with LDX. Patients and methods. The sample comprised 85 patients between 6 and 16 years, with clinical diagnosis of ADHD, who attended treatment in a neuropediatrics consultation. All patients started pharmacological treatment with the proper dose of LDX after the clinical interview and the first administration of AULA test. After an average treatment of 7.5 months, AULA was administered again and the treatment progress based on cognitive and motor symptomatology was assessed.

Results. Results showed highly significant improvements in selective and sustained attention, quality of attention focus and hyperactivity; moderate improvements in impulsivity; and an incidence close to zero in processing speed.

Conclusions. LDX constitutes an adequate treatment for the substantial improvement of attention and hyperactivity; such improvement can be monitored accurately by means of AULA virtual reality test

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Rev Psiquiatr Clin. 2020;47:82-84.

SOCIAL COMMUNICATION IMPAIRMENTS AND RESTRICTED, REPETITIVE PATTERNS ("KODAWARI") CONSIDERED FROM THE "COMPREHENSION" SECTION OF THE WISC-IV IN AUTISM SPECTRUM DISORDER.

Yokoyama F, Shono N, Takasugi A, et al.

Background: Many studies have used the Wechsler Intelligence Scale (WISC) to examine the characteristics of autism spectrum disorder (ASD). However, most studies have been based on profile analysis, not on content analysis.

Objective: The objective of the present study was to apply the WISC-IV to clinical assessment of ASD and clarify how the characteristics of the disorder were reflected in specific items.

Methods: The study participants were 20 patients aged 5-16 years diagnosed with ASD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). We recruited 20 patients with attention-deficit/hyperactivity disorder (ADHD) and 20 patients with other disorders (neurotic disorders) as controls. We then compared the scores of the ninth item of the WISC-IV ("Comprehension") among the three groups.

Results: The differences observed between the ASD vs. the other disorders group were not significant by the standard scoring method. Thus, a two-level scoring method of 0 and ΓëÑ1 point was adopted. As a result, significantly more participants in the ASD group scored 0 points compared with the ADHD and other disorders groups.

Discussion: The results of the present study revealed that a characteristic of ASD appeared in the ninth item of "Comprehension" on the WISC-IV

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Scand J Public Health. 2020 Jul;48:559-66.

CAN SUBJECTIVE WELL-BEING AND BODY CONCERN IN ADOLESCENCE PREDICT PRESCRIBED MEDICATION IN ADULTHOOD? FINDINGS FROM THE NORD-TRÃ¸NDELAG HEALTH STUDY AND THE NORWEGIAN PRESCRIPTION DATABASE.

Wærholm A.C., Meland E, Kjome RLS.

Aim: To examine whether subjective well-being (SW) and body concern among adolescents aged 15-19 years has an impact on adult health, measured by medications dispensed on average 18 years later.

Methods: Data collected in the Nord-TrÃ¸ndelag Health Study (HUNT) was paired with data from the Norwegian Prescription database (NorPD). We investigated the effects of adolescent SW and body concern on total number of medications, on use of anti-infectives (ATC-group J), medication for the musculo-skeletal system (ATC-group M), anxiolytics, hypnotics and sedatives (ATC-groups N05B and N05C), and finally antipsychotics, antidepressants and psychostimulants, agents used for attention-deficit/hyperactivity disorder and nootropics (ATC-groups N05A, N06A and N06B). We used multi-variable models where we entered body dissatisfaction and SW simultaneously in the models in order to adjust for the associations between the predictors, and also adjusted for possible confounders in the models.

Results: Both body concern (dieting and dieting desire) and impaired SW predicted drug use 17-18 years after the participants were surveyed in adolescence. The impact was disease specific as body concern was the most influential predictor for drugs used for somatic diseases and complaints, whereas impaired SW was more strongly associated with drug use for mental health diseases and complaints.

Conclusions: SW and body concern are important health determinants in the transition between adolescence and adulthood

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School Psychology. 2020 Jul;35:233-42.

SOCIAL DEFICITS IN HIGH SCHOOL STUDENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND THE ROLE OF EMOTION DYSREGULATION.

Cleminshaw C, DuPaul GJ, Kipperman KL, et al.

Attention-deficit/hyperactivity disorder (ADHD) is strongly associated with social functioning deficits in adolescents. However, the factors underlying this relationship are not well understood. Prior research has established that emotion dysregulation (ED) mediates the relationship between ADHD symptoms and social skills in middle school students and that the mediational role of ED is moderated by youthâ€™s level of depression. The current study examined whether this model holds true in high school students with ADHD, despite developmental and environmental changes during maturation. Cross-sectional measures of ADHD symptoms, emotion regulation, depression, and social functioning were collected from 174 high school students with ADHD (M age = 14.51; 81.4% male). Analyses were conducted using the PROCESS macro for SPSS. Bootstrapping results of the omnibus effect of a multiple-mediational model indicated that ADHD and ED jointly account for 49% of the variance in parent-rated social skills (i.e., evidence of mediation by ED). However, counter to our hypothesis, depression did not moderate this relationship. This study provides evidence that ED accounts for the relationship between ADHD and social deficits in an older adolescent population. Results have significant implications for intervention strategies to improve emotional self-awareness and control in adolescents with ADHD. (PsycInfo Database Record (c) 2020 APA, all rights reserved) (Source: journal abstract) Impact statementImpact and Implicationsâ€”This study builds upon prior evidence that emotion dysregulation explains the relationship between ADHD symptoms and poor social functioning in adolescents. It holds important implications for assessment and treatment of social impairment during adolescence. (PsycInfo Database Record (c) 2020 APA, all rights reserved)

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Stress and Health. 2020.

SALIVARY CORTISOL AND ALPHA-AMYLASE DAILY PROFILES AND STRESS RESPONSES TO AN ACADEMIC PERFORMANCE TEST AND A MORAL COGNITION TASK IN CHILDREN WITH NEURODEVELOPMENTAL DISORDERS.

Anesiadou S, Makris G, Michou M, et al.

There is evidence that children with neurodevelopmental disorders may exhibit atypical responses to stress and alterations in concentrations and diurnal secretion of stress hormones. We assessed diurnal profiles and stress responses of salivary cortisol and alpha-amylase (sAA) in children with attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD) and specific learning disorder (SLD) compared to typically developing children (TD). A total of 157 children of both sexes, aged between 6 and 12 years old, took part in the study distributed into four groups: ADHD (N = 34), ASD (N = 56), SLD (N = 43) and TD (N = 24). Salivary samples were collected at three time points during a day, as well as before and 5 min after an academic performance test and a moral cognition task. ADHD children had lower evening and diurnal sAA levels, adjusted for age. Also, ASD children showed lower diurnal sAA secretion, adjusted for age. The mean percentage change for salivary cortisol and sAA after both tests did not differ between the groups. In conclusion, we demonstrated alterations in diurnal autonomic functioning in children with ADHD and ASD, while hypothalamicΓÇôpituitaryΓÇôadrenal axis functioning did not differ between the clinical and the comparison groups

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Transl Psychiatry. 2020;10.

MUTATIONS IN SPHINGOLIPID METABOLISM GENES ARE ASSOCIATED WITH ADHD.

Henriquez-Henriquez M, Acosta MT, Martinez AF, et al.

Attention deficit hyperactivity disorder (ADHD) is the most prevalent neurodevelopmental disorder in children, with genetic factors accounting for 75ΓÇô80% of the phenotypic variance. Recent studies have suggested that ADHD patients might present with atypical central myelination that can persist into adulthood. Given the essential role of sphingolipids in myelin formation and maintenance, we explored genetic variation in sphingolipid metabolism genes for association with ADHD risk. Whole-exome genotyping was performed in three independent cohorts from disparate regions of the world, for a total of 1520 genotyped subjects. Cohort 1 (MTA (Multimodal Treatment study of children with ADHD) sample, 371 subjects) was analyzed as the discovery cohort, while cohorts 2 (Paisa sample, 298 subjects) and 3 (US sample, 851 subjects) were used for replication. A set of 58 genes was manually curated based on their roles in sphingolipid metabolism. A targeted exploration for association between ADHD and 137 markers encoding for common and rare potentially functional allelic variants in this set of genes was performed in the screening cohort. Single- and multi-locus additive, dominant and recessive linear mixed-effect models were used. During discovery, we found statistically significant associations between ADHD and variants in eight genes (GALC, CERS6, SMPD1, SMPDL3B, CERS2, FADS3, ELOVL5, and CERK). Successful local replication for associations with variants in GALC, SMPD1, and CERS6 was demonstrated in both replication cohorts. Variants rs35785620, rs143078230, rs398607, and rs1805078, associated with ADHD in the discovery or replication cohorts, correspond to missense mutations with predicted deleterious effects. Expression quantitative trait loci analysis revealed an association between rs398607 and increased GALC expression in the cerebellum

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Trends in Psychiatry and Psychotherapy. 2020;42:190-94.

INTRAGROUP DIFFERENCES AND SIMILARITIES IN PERFORMANCE ON RAPID AUTOMATIZED NAMING TASKS IN CHILDREN WITH ADHD SYMPTOMS, CHILDREN WITH READING DISABILITIES, AND CONTROLS.

Koltermann G, Becker N, Wauke APT, et al.

Introduction: Rapid automatized naming (RAN) is the ability to name, as fast as possible, symbols such as letters, digits and figures. The present study aimed to investigate intragroup performance patterns on RAN tasks in children with attention deficit hyperactivity disorder (ADHD) symptoms alone, children with reading disability (RD) alone and controls with typical development.

Methods: A total of 216 Brazilian children between 8 to 11 years old were selected from public schools located in two Brazilian capitals, namely Porto Alegre and Belo Horizonte, to participate in the study. Mixed 3 (participant group: ADHD symptoms, RD or control group) +ù 3 (type of stimulus: letters, numbers or figures) ANOVAs were performed using response time and number of errors as dependent variables. Only intragroup comparisons are described in this paper.
Results: The groups with ADHD symptoms and RD showed similar performance results on naming speed. There were no differences between letters and numbers within each group, but we found slower responses in figure naming compared to the other tasks for both groups. Concerning accuracy, children with ADHD symptoms showed a similar number of errors in all three tasks. These patterns were distinct from the performance of the control group.
Conclusion: Results suggest a shared deficit in naming speed of alphanumeric stimuli in children with ADHD symptoms and those with RD, and impairments in naming digits correctly in children with ADHD symptoms

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World J Biol Psychiatry. 2020.
RESTING-STATE NETWORK DYSCONNECTIVITY IN ADHD: A SYSTEM-NEUROSCIENCE-BASED META-ANALYSIS.
Sutcubasi B, Metin B, Kurban MK, et al.
Objectives: Neuroimaging studies report altered resting-state functional connectivity in attention deficit/hyperactivity disorder (ADHD) across multiple brain systems. However, there is inconsistency among individual studies.
Methods: We meta-analyzed seed-based resting state studies of ADHD connectivity within and between four established resting state brain networks (default mode, cognitive control, salience, affective/motivational) using Multilevel Kernel Density Analysis method.
Results: Twenty studies with 944 ADHD patients and 1121 controls were included in the analysis. Compared to controls, ADHD was associated with disrupted within-default mode network (DMN) connectivity-reduced in the core (i.e. posterior cingulate cortex seed) but elevated in the dorsal medial prefrontal cortex sub-system (i.e. temporal pole-inferior frontal gyrus). Connectivity was elevated between nodes in the cognitive control system. When the analysis was restricted to children and adolescents, additional reduced connectivity was detected between DMN and cognitive control and affective/motivational and salience networks.
Conclusions: Our data are consistent with the hypothesis that paediatric ADHD is a DMN-dysconnectivity disorder with reduced connectivity both within the core DMN sub-system and between that system and a broad set of nodes in systems involved in cognition and motivation

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Zhongguo Dang Dai Er Ke Za Zhi. 2020 Jul;22:768-73.
MODERATED MEDIATION ANALYSIS FOR SYMPTOMS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER WITH THE SYMPTOMS OF ANXIETY IN CHILDREN.
Liu JB, Xue ZP, Lin L, et al.
Objective: To study the moderated mediation for attention deficit/hyperactivity disorder (ADHD) with the symptoms of anxiety in children.
Methods: A total of 12 271 students were included with an average age of 8.9±1.9 years, including 6 743 male students and 5 508 female students, and 20 students with missing data on gender. Child psychological trauma questionnaires (parents version) and Conners questionnaires (parent version) were completed by the parents of primary school students. The data was studied by univariate analysis, multivariate analysis and moderated mediation analysis.
Results: The results of the univariate analysis showed that in all subjects, boys, and girls, the scores of hyperactivity index and childhood trauma were positively correlated with the score of anxiety ($P<0.01$), and ADHD and childhood trauma positively predicted anxiety disorder ($P<0.001$). The results of the multivariate analysis showed that in all subjects, boys, and girls, the scores of hyperactivity index (ADHD symptoms) and childhood trauma positively predicted the score of anxiety ($P<0.001$), and both ADHD and childhood trauma positively predicted anxiety disorder ($P<0.001$). The results of the moderated mediation analysis showed that

childhood trauma was a mediating factor for the relationship between hyperactivity index and anxiety index in boys and girls (P<0.05), and sex moderated the relationship between hyperactivity index and anxiety index (P<0.001).

Conclusions: ADHD symptoms/ADHD are closely associated with anxiety symptoms/anxiety disorder. Childhood trauma exerts a mediating effect on the relationship between ADHD symptoms and anxiety symptoms, and sex moderates the relationship between ADHD symptoms and anxiety symptoms

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frontiers in Neurology

ORIGINAL RESEARCH
published: 10 July 2020
doi: 10.3389/fneur.2020.00546

Event-Related Potentials in ADHD Associated With Tuberous Sclerosis Complex: A Possible Biomarker of Symptoms Severity?

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OPEN ACCESS

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Specialty section:
This article was submitted to Pediatric Neurology, a section of the journal Frontiers in Neurology

Received: 22 March 2020
Accepted: 14 May 2020
Published: 10 July 2020

Citation:
Moavero R, Marciano S, Pro S, De Stefano D, Vigevano F, Curatolo P and Valeriani M (2020) Event-Related Potentials in ADHD Associated With Tuberous Sclerosis Complex: A Possible Biomarker of Symptoms Severity? Front. Neurol. 11:546. doi: 10.3389/fneur.2020.00546

Background and Aim: Tuberous sclerosis complex (TSC) is associated with a high rate of attention deficit-hyperactivity disorder (ADHD), usually with more severe symptoms than in idiopathic cases. Event-related potentials have been used in idiopathic ADHD, and they have been proposed as a possible biomarker of symptoms severity. Aim of this study was to investigate event-related potential (ERP) characteristics in patients with ADHD secondary to TSC, compared to patients with drug-naive idiopathic ADHD and healthy controls (HCs), to investigate whether (1) distinct clinical features can be due to different pathophysiological mechanisms, and (2) ERPs may reliably predict ADHD symptoms severity in TSC.

Materials and Methods: We enrolled 13 patients with idiopathic ADHD (iADHD), 6 patients with ADHD associated with TSC (tscADHD), and 14 age-matched HCs (7–17 years). All of them underwent ERP recording, with mismatch negativity (MMN) preceding the P300 recording. All patients underwent neurocognitive evaluations.

Results: Mismatch negativity latency was shorter in iADHD ($P = 0.04$) and tscADHD ($P = 0.06$) than in HC, with no difference between patients' groups. Mismatch negativity amplitude was significantly higher in patients (both iADHD and tscADHD) than in HC. The P300 amplitude was significantly lower in iADHD patients than in both tscADHD patients ($P = 0.03$) and HCs ($P < 0.001$). No difference was found between tscADHD patients and HCs ($P = 0.2$).

Conclusion: While patients with iADHD present lower P300 amplitude than HC, in tscADHD patients P300 amplitude was not different from that in HC, suggesting that in TSC P300 amplitude does not really reflect symptom severity.

Keywords: tuberous sclerosis complex, ADHD, ERP, MMN, P300, attention

INTRODUCTION

Tuberous sclerosis complex (TSC) is an autosomal dominant multisystem disease characterized by hamartomas in several organs and systems (1). Central nervous system involvement represents the main source of morbidity for patients affected by this complex disease and includes epilepsy and a variety of neuropsychiatric disorders (2). Attention-deficit hyperactivity disorder (ADHD) is a neuropsychiatric condition highly prevalent in the general population (3%−7%) (3, 4), but with a significantly higher ratio in patients with TSC, affecting ∼30–50% of patients (2). Attention-deficit hyperactivity disorder is characterized by inattention, hyperactivity, and impulsive behavior (5)Core symptoms of ADHD include specific deficits in executive functions, including inhibition, and in attentional processes such as vigilance, sustained, divided, and selective attention (6). Attention-deficit hyperactivity disorder occurs in up to 50% of patients with TSC, being 10 times more prevalent in TSC than in the general population (7). Despite this frequent association, the real pathophysiological mechanisms underlying this comorbidity are not completely understood, but cortical tubers, frontal epileptiform abnormalities, and the genetic mutation *per se* are believed to play a role (2, 8). In TSC, ADHD often co-occurs with other neuropsychiatric disorders, including intellectual disability and autism spectrum disorder (7). Clinical experience suggests that symptoms of ADHD in children with TSC are usually more severe and tend to present lower benefits to pharmacological and non-pharmacological treatments when compared to idiopathic ADHD.

Attention and inhibition, which are core aspects in ADHD, can be studied with neurophysiological techniques, including event-related potentials (ERPs), which in the last decades have been widely used in this population, revealing abnormalities in the attention-dependent processing (9). The P300 component is an endogenous positive potential peaking 300 ms after a stimulus and generated by several cortical and subcortical structures (10, 11). It is believed to reflect executive and attentional function, including the updating of working memory, event categorization, and attentional resource allocation, as well as attentional reorientation (12). Moreover, P300 has been proposed to reflect late-stage monitoring of outcomes related to inhibitory processes (13). Therefore, its amplitude seems to be related with the allocation of attentional resources, whereas the latency reflects the stimulus evaluation time (14). Mismatch negativity (MMN) is an ERP component occurring ∼100–200 ms after the onset of a deviant stimulus, therefore before P300 (15), and it represents an automatic cerebral discrimination process, not under attentive control (16).

Different reports suggest that children with ADHD present lower amplitude and higher latency P300 (17), so that some authors proposed to use this ERP component as a marker of disease severity (18). The available data concerning MMN are more conflicting with different studies failing to find statistically significant differences between children with ADHD and healthy subjects (19). Event-related potential components can be modified by ADHD pharmacotherapies, such as atomoxetine and methylphenidate, which increase the P300 (20) and MMN (21) amplitudes.

The aim of this study was to investigate ERP characteristics in patients with ADHD secondary to TSC, compared to patients with drug-naive idiopathic ADHD and healthy controls (HCs), to investigate whether distinct clinical features can be due to different pathophysiological mechanisms.

MATERIALS AND METHODS

Participants

We enrolled patients with idiopathic ADHD (iADHD) and with ADHD associated with TSC (tscADHD), and age-matched HCs. Inclusion criteria for patients with ADHD (with or without TSC) were diagnosis of ADHD according to the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) criteria and age 7–17 years. Moreover, iADHD patients did not have to present any other neurological or medical condition associated with ADHD. Exclusion criteria were cognitive impairment (intelligence quotient <70), psychiatric comorbidity, and sensory deficits that could interfere with behavioral performances or with electrophysiological results. If ADHD was pharmacologically treated, children were asked to withdraw medications for 48 h before the neurophysiological and neuropsychological examination. Healthy controls were children and adolescents without a history of neurological or neuropsychiatric conditions. All patients and healthy subjects had had a normal audiological evaluation before the study. All participants' caregivers signed an informed consent form. The study was approved by the local ethical board.

ERP Recording and Analysis

For ERP recording, subjects were comfortably seated in a quiet room. Mismatch negativity recording preceded the P300 recording in all our children and adolescents.

Auditory stimuli were sinusoidal tones (10-ms duration, 2-ms rise and 2-ms fall time, 85-dB SPL of intensity), presented binaurally via headphones. Frequent 750-Hz tones and deviant 500-Hz tones were delivered with a probability of 85 and 15%, respectively. A fixed interstimulus interval (ISI) of 1 s and an ISI variable between 0.8 and 1.2 s were used for MMN and P300 recording, respectively.

Event-related potentials were recorded from three scalp electrodes, located at Fz, Cz, and Pz positions of the 10–20 International System. A further electrode placed in the outer cantus of the right eye recorded the electro-oculogram (EOG). Reference was at the nose. Electroencephalogram (EEG) sampling rate was of 1,024 Hz, and the analysis time was 1,000 ms, including 100 ms of prestimulus delay. The amplifier bandpass was 0.1 to 30 Hz (24-dB roll-off). An automatic artifact-rejection system excluded from the average all runs containing transients exceeding ± 150 μV at any recording channel, including the EOG. Averages of 15 trials (deviant stimuli) were used for ERP measurements.

MMN Recording

Mismatch negativity was recorded after 100 acoustic stimuli. Children were instructed to read a novel; thus, they did not pay attention to the acoustic stimulation. They were required to summarize the novel in a short briefing following the stimulation.

P300 Recording

Children underwent a block of ∼100 acoustic stimuli. They were instructed to count the number of infrequent tones mentally. No motor response was required. Averages in which counting mistake had exceeded 10% would not have been considered in the data analysis.

ERP Analysis

The N1 and P2 latencies and the peak-to-peak N2/P2 amplitude were measured in the Cz traces recorded to deviant stimuli. For MMN labeling, difference traces, obtained by subtracting the frequent stimuli from deviant stimuli traces, were calculated. In Fz difference trace, MMN latency and amplitude were measured at the peak and from the baseline, respectively. P300 latency and amplitude were measured in the Pz trace to deviant stimuli at the peak and from the baseline, respectively.

Cognitive and Neuropsychological Examination

All patients underwent the administration of an extensive battery of tests for the assessment of cognitive functioning and neuropsychological phenotype. This battery included the following tests: (1) Wechsler Intelligence Scale for Children for the determination of the intelligence quotient; (2) Tower of London test for the assessment of planning and problem solving skills and cognitive flexibility; (3) span of forward and backward memory numbers (DSF and DSB) for the measurement of short-term verbal memory and working memory; (4) Trail-Making Test Part A and Part B for the evaluation of visual search strategies, selective and divided attention; (5) phonological (FAS) and semantic (CAT) verbal fluency test for the evaluation of verbal ability to access vocabulary by phonological and semantic means; (6) Subtest ToM and ER of the NEPSY-II battery to assess the ability to recognize one's own and others' mental states and the ability to recognize facial expressions; (7) Physical and Neurological Assessment of Subtle Signs to evaluate minor neurological signs; (8) Schedule for Affective Disorders and Schizophrenia for School-Aged Children—Present and Lifetime Version, a psychodiagnostic tool for the assessment of psychopathological symptoms in children and adolescents according to *DSM-IV Text Revision* criteria; (9) Conners' Parents and Teachers Rating Scale–Revised, questionnaires to be filled in by parents and/or teachers, used for the evaluation of ADHD from 3 to 17 years, and for externalizing disorders that can be found in comorbidities; they also provide an index (ADHD Index), which is able to differentiate subjects affected by unaffected; (10) Child Behavior Checklist for Ages 6–18, questionnaire to be filled in by parents, which assesses the presence of internalizing and externalizing symptoms in children and adolescents aged between 6 and 18 years.

Statistical Analysis

Neurophysiological Results

Mismatch negativity and P300 latencies and amplitudes were compared by means of one-way analysis of variance (ANOVA), by considering the group of subjects (iADHD, tscADHD, and HC) as the variable. Significant values underwent *post hoc* Bonferroni test. Moreover, because of the low number of tscADHD patients, as compared to iADHD patients and healthy subjects, we performed also a single-case analysis by considering patients falling within or out of a 95% confidence level interval of any ERP parameter, calculated from healthy subjects.

Neuropsychological Results

The scores obtained at the different tests were compared between iADHD and tscADHD patients by means of unpaired Student *t*-test.

Correlation Analysis

In our patients, we investigated whether there was a correlation between the ERP data and the neuropsychological results. A series of correlation analyses between the latencies and amplitudes of both the MMN and the P300 potentials and the different neuropsychological scores was performed. Pearson coefficients were computed.

The statistical significance was fixed at $P < 0.05$.

RESULTS

Demographics

We enrolled 6 patients (3 females, 6 males) with ADHD secondary to TSC, aged 8–15 years (mean = 12.6 years, median = 15 years), and 13 patients (4 females, 9 males) with idiopathic ADHD, aged 7 to 16 years (mean = 10.4 years, median = 9 years). We also included in the study 14 HCs (9 females, 5 males) aged 8 to 16 years (mean = 11.9 years, median = 12.5 years). No difference in age was found between the groups of subjects (one-way ANOVA: $F = 0.57$, $P = 0.57$).

Clinical, Neurophysiological, and Neuroimaging Data

In patients with tscADHD, we also collected additional clinical information. None of them presented with active clinical seizures at the moment of the study, and only one of them was under antiepileptic treatment (carbamazepine), with the last epileptic seizure ∼2 years before the study enrolment. All but one presented a normal EEG; the only patient with abnormal EEG presented sporadic epileptiform bilateral temporo-occipital abnormalities. All six tscADHD patients presented typical brain magnetic resonance imaging patterns with cortico/subcortical tubers, in all brain areas, including frontal and temporal lobes. None of them presented large, dysplastic, or cystic lesions. None of the patients presented brainstem lesions. They all presented white matter migration lines and subependymal nodules. Subependymal giant cell tumor was present in one patient. **Table 1** summarizes main clinical, EEG, and neuroimaging data of tscADHD patients.

TABLE 1 | Clinical, EEG, and neuroimaging characteristics of tscADHD patients enrolled in the study.

Patient	Active epilepsy	AED treatment	IED	Brain MRI			
				Tubers	RML	SEN	SEGA
1	No	No	No	Yes, diffuse	Yes, diffuse	Yes	No
2	No	No	No	Yes, diffuse	Yes, diffuse	Yes	No
3	No	No	No	Yes, diffuse	Yes, diffuse	Yes	No
4	No	No	Yes, bilateral TO	Yes, diffuse	Yes, diffuse	Yes	No
5	No	No	No	Yes, diffuse	Yes, diffuse	Yes	No
6	No	CBZ	No	Yes, diffuse	Yes, diffuse	Yes	Yes

**Active epilepsy means epileptic seizures in the last 2 years. AED, antiepileptic drugs; IED, interictal epileptiform discharges; RML, radial migration lines; SEN, subependymal nodules; SEGA, subependymal giant cell astrocytomas; MRI, magnetic resonance imaging; CBZ, carbamazepine; TO, temporo-occipital.*

ERP Results

Event-related potential values are shown in **Table 2**. N1 ($F = 1.1$, $P = 0.34$) and P2 ($F = 1.22$, $P = 0.31$) latencies and N1/P2 amplitude ($F = 0.13$, $P = 0.88$) were not different between groups.

Analysis of variance showed a significant effect of the group on both MMN latency ($F = 7.5$, $P = 0.01$) and amplitude ($F = 3.2$, $P = 0.0001$). *Post hoc* analysis showed that the MMN latency was shorter in patients than in HC, and this difference was significant for iADHD patients ($P = 0.04$) and marginally significant for tscADHD patients ($P = 0.06$). No difference was found between patients' groups ($P = 0.3$). As for the MMN amplitude, it was significantly higher in patients than in HCs ($P < 0.01$). No difference was found between patients' groups ($P = 0.32$).

One-way ANOVA showed a significant effect of the group on the P300 amplitude ($F = 13.7$, $P < 0.001$). *Post hoc* analysis showed the P300 amplitude was significantly lower in iADHD patients than in both tscADHD patients ($P = 0.03$) and HCs ($P < 0.001$). No difference was found between tscADHD patients and HCs ($P = 0.2$). As for the P300 latency, the ANOVA showed a global effect of the group ($F = 4.3$, $P = 0.02$), but the *post hoc* analysis did not show any significant difference.

Table 3 shows a single case analysis for any considered ERP value. This confirms what was found with the ANOVA.

Figure 1 shows P300 and MMN of one patient with iADHD compared with a patient with tscADHD and a control subject.

Cognitive and Neuropsychological Results

Cognition

The average intellectual quotient (IQ) values were overall lower in tscADHD than in iADHD patients, with statistically significant differences in all the quotients, so total IQ (105.9 ± 10.2 vs. 85.8 ± 16.4; $P = 0.004$), verbal IQ (113.9 ± 15.2 vs. 92.2 ± 15.9; $P = 0.016$), and performance IQ (109.1 ± 15.6 vs. 91.3 ± 12.2; $P = 0.032$) (**Table 4**).

TABLE 2 | Event-related potential amplitudes and latencies in all subjects enrolled in the study.

	N1 latency (ms)	P2 latency (ms)	N1/P2 amplitude (μV)	MMN latency (ms)	MMN amplitude (μV)	P300 latency (ms)	P300 amplitude (μV)
iADHD patients							
1	109	141	16.9	112.6	10.5	299.8	9.2
2	112.1	165.5	8.7	120.9	4	301.5	5.6
3	108	141.3	11.3	141.1	6.7	330.8	2.2
4	90.8	151.4	10.9	103.5	3.3	319.8	3.7
5	109.1	167.2	13.5	109.1	20.3	327.4	6.5
6	97.9	127	16.9	97.9	7.5	319.1	13
7	109	141.4	13.6	125	33.9	349.1	3.5
8	109.6	159.2	22.6	109.6	12.8	363.3	2.7
9	106.7	139.4	7.8	106.7	6.8	279.3	9.3
10	109	141.3	15.8	148.9	15.4	298.1	9.78
11	117.2	136	13.4	127.9	20.9	325.4	11.5
12	110.4	152.6	14.3	114.5	13	295.9	12.3
13	95	123	10.2	95	5.3	312	5.5
Mean	106	145.1	13.5	116.4	12.3	317	7.3
Standard deviation	7.4	13.5	4	16	8.7	23	3.8
tscADHD patients							
1	110.4	145.8	9.2	91.6	4.8	340.1	5.2
2	109	140.3	13.9	105.8	18.2	383.1	26.3
3	108.9	158.7	15.7	143.3	15	264.2	20.2
4	74.7	94.7	18	74.7	11	249.5	18.7
5	115	135.7	14	115	45.4	312.7	7.5
6	104	166.8	12.7	104	14.8	324.2	7
Mean	103.7	140.3	13.9	105.7	18.2	312.3	14.2
Standard deviation	14.6	25.2	3	23.1	14.1	49.4	8.7
Healthy subjects							
1	79.9	132	7.6	99.3	5.8	360.3	30.9
2	119.1	148.2	17.1	99	9.8	415	31.3
3	108	174.5	17.1	160	5	317	22.3
4	101	145	11.4	154.7	5	373.8	30.4
5	102	156.5	9.5	168	3.8	276	15.3
6	101.2	122.2	19.3	152	4.5	235	8.9
7	86	180.8	12.2	132.2	3	386	23.4
8	98.8	148	13.3	140	4.4	301.7	7.5
9	124	172.4	17.4	136	5.8	388	9
10	95	132.6	8	60	4.8	401	20
11	95	165.5	16.8	132	1.9	378.5	14.7
12	109	148.6	8	167	10.1	320	13
13	101.1	127	14.7	161.8	6.8	552	17.8
14	95	141.6	13.2	158	3.9	353.2	27.8
Mean	101.1	149.6	13.3	137.1	5.3	361.3	19.5
Standard deviation	11.6	18.3	4	31.4	2.3	75.0	8.5

Means and standard deviations in each group of subjects are also shown.

Neuropsychological Data

Performances in executive functions were globally lower in subjects with tscADHD than in iADHD patients, with statistically significant differences both in direct number span (DSF) ($P = 0.006$) and in categorical fluency (CAT) ($P = 0.018$). Although tscADHD children performed worse in all the other administered tests, no other statistical differences have been detected. **Table 5** summarizes the results of neuropsychological assessments.

Correlation Analysis

We found one significant positive correlation between the P300 amplitude and total IQ score in iADHD patients ($R^2 = 0.35$, $P = 0.03$). It means that in this group of patients the larger was the P300 amplitude, the higher was the total IQ (**Figure 2**). It is noteworthy that the same correlation was not found in tscADHD patients ($R^2 = 0.004$, $P = 0.9$). No other significant correlations were obtained.

TABLE 3 | The 95% confidence level intervals for the different ERP parameters.

	95% confidence level interval*	iADHD		tscADHD	
		In	Out	In	Out
N1 latency	91.4–110.7 ms	10	3	4	2
P2 latency	135–164.6 ms	9	4	4	2
MMN latency	**115.8–158.4 ms**	**5**	**8**	**1**	**5**
P300 latency	310.5–411.8 ms	8	5	4	2
N1/P2 amplitude	10–16.5 μV	8	5	4	2
MMN amplitude	**3.8–6.9 μV**	**4**	**9**	**1**	**5**
P300 amplitude	**13.7–25.2 μV**	**0**	**13**	**2**	**4**

The numbers of both iADHD and tscADHD patients falling within (IN) or out of (Out) each interval are indicated.
**Calculated from values recorded in healthy subjects.*
Bold characters indicate the significant differences found with the analysis of variance (ANOVA).

TABLE 4 | Mean values of total (TIQ), verbal (VIQ), and performance (PIQ) intelligent quotient in patients with idiopathic ADHD compared to patients to ADHD associated with TSC.

	iADHD	tscADHD	*P*
TIQ	105.9	85.8	0.004
VIQ	113.9	92.2	0.016
PIQ	109.1	91.3	0.032

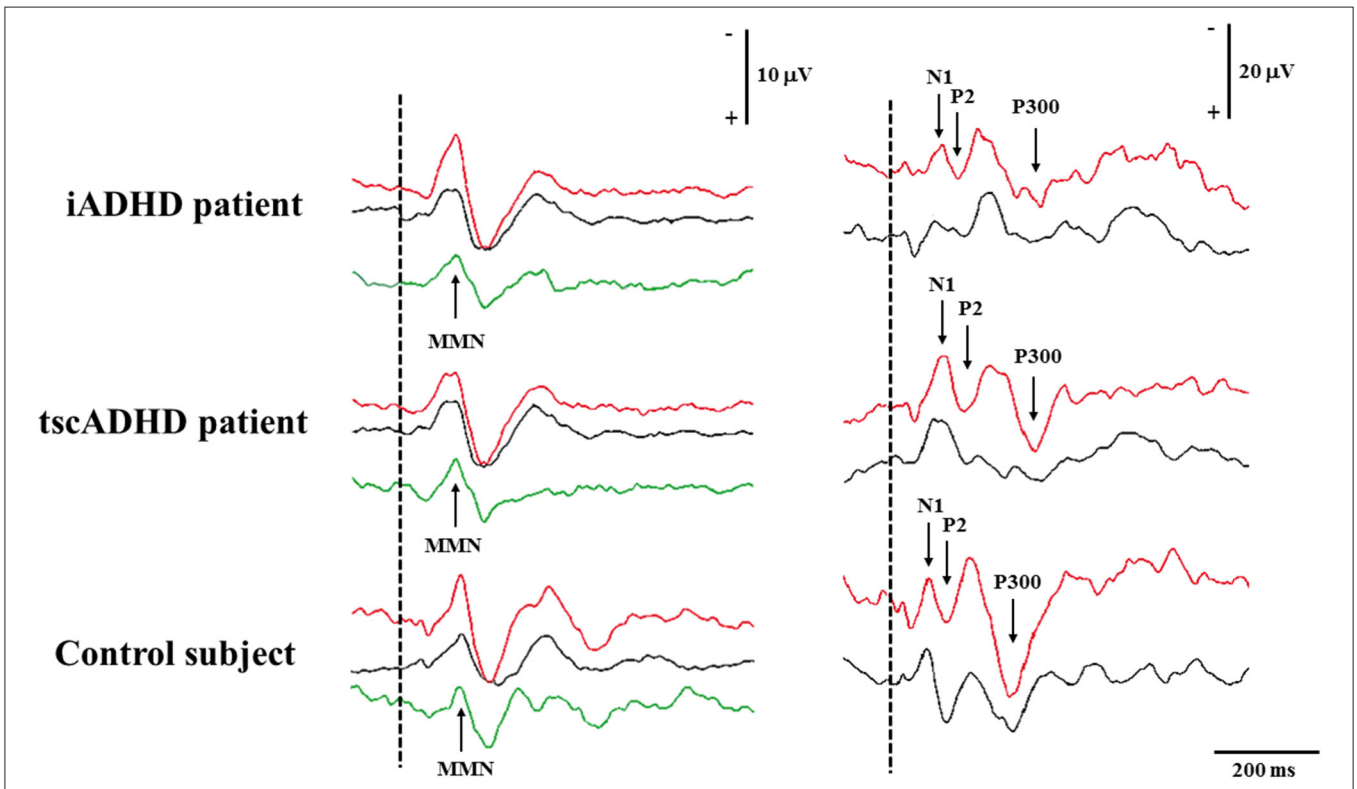

FIGURE 1 | The figure shows MMN (left) and P300 (right) recording in a patient with iADHD (upper), tscADHD (middle), and a control subject (lower). For MMN recording, the Fz traces are shown, whereas for P300 recording the traces are obtained from the Pz electrode. Recordings to frequent and deviant stimuli are in black and red color, respectively, whereas for MMN recording, the green curves are calculated by subtracting traces to frequent stimuli from those to deviant stimuli.

DISCUSSION

To the best of our knowledge, this is the first study comparing neurophysiological and neuropsychological tests between patients with iADHD and tscADHD. The main difference between the groups of patients concerned the P300 amplitude, which was lower in iADHD but not in tscADHD patients, as compared to HC. This difference allows us to speculate about the psychophysiological meaning of the P300 amplitude in different clinical contexts.

P300 Amplitude in ADHD May Depend on the Etiology

That patients with idiopathic ADHD present a significantly lower P300 amplitude than HCs, which appears to be in good agreement with previous reports (22), suggesting reduced attentional orienting to warning stimuli in patients with ADHD when compared to normal subjects. Indeed, reduced P300 amplitude has been interpreted as a failure to allocate sufficient attentional resources to stimulus evaluation processes due to reduced attentional capacity (23). On the other hand, although the mean P300 amplitude of tscADHD patients was slightly lower than that observed in healthy children, this difference did not reach the statistical significance. These results might be difficult to be interpreted, because we could expect that tscADHD patients, expressing more severe ADHD symptoms, could present more significant abnormalities. However, it is important to note that, although most of literature data suggest that children with ADHD show lower P300 amplitudes, there are some conflicting results failing to replicate these findings (24). Furthermore, in our sample of iADHD children, the P300 amplitude showed a linear correlation with the cognitive level, which was not found in subjects with TSC. Our results therefore highlight that, although ERPs are a very interesting technique to study brain functioning in neuropsychological dysfunctions, P300 amplitude might be influenced by different variables, especially by cognitive factors (20), which prevent it to be used as a reliable marker of attention at least in some neurological conditions. Although this cannot be proven, we hypothesize that the marked network dysregulation typical of children with TSC might be responsible of this lack of association and that in such a brain disease P300 amplitude might not be a real marker of attention processes. In addition, in the interpretation of these data, we cannot exclude that results might have been influenced by patients' age. Indeed, a longitudinal study showed that after the first decade of life up to young adulthood, the P300 difference between ADHD and non-ADHD groups is no longer significant (25). Seen in this light, we must underline that in our sample tscADHD patients presented a higher mean age, with only two patients younger than 10 years, as compared to

TABLE 5 | Mean values of the results obtained in neuropsychological tests administered in subjects with idiopathic ADHD and ADHD with TSC.

	iADHD	tscADHD	*P*
ToL (z)	−0.7	−1.22	0.08
DSF	−0.43	−2.15	**0.006**
DSB	−0.05	−1.22	0.05
FAS	−1.2	−1.24	0.87
CAT	−1.7	−3.51	**0.018**
TMTA (s)	62.4	81.33	0.47
TMTB (s)	148.3	114	0.32
CPRS- opp	60.76	66.83	0.43
CPRS-inatt	74.61	80.33	0.5
CPRS-hyper	68.53	70.16	0.83
CPRS-ADHD index	76.61	78.66	0.75

Significant P values in bold. ToL, Tower of London; DSF, direct number span; DSB, span of inverse numbers; FAS, phonemic fluence; CAT, categorical fluency; CAT TMTA, Trail-Making Test Part A; TMTB, Trail-Making Test Part B.

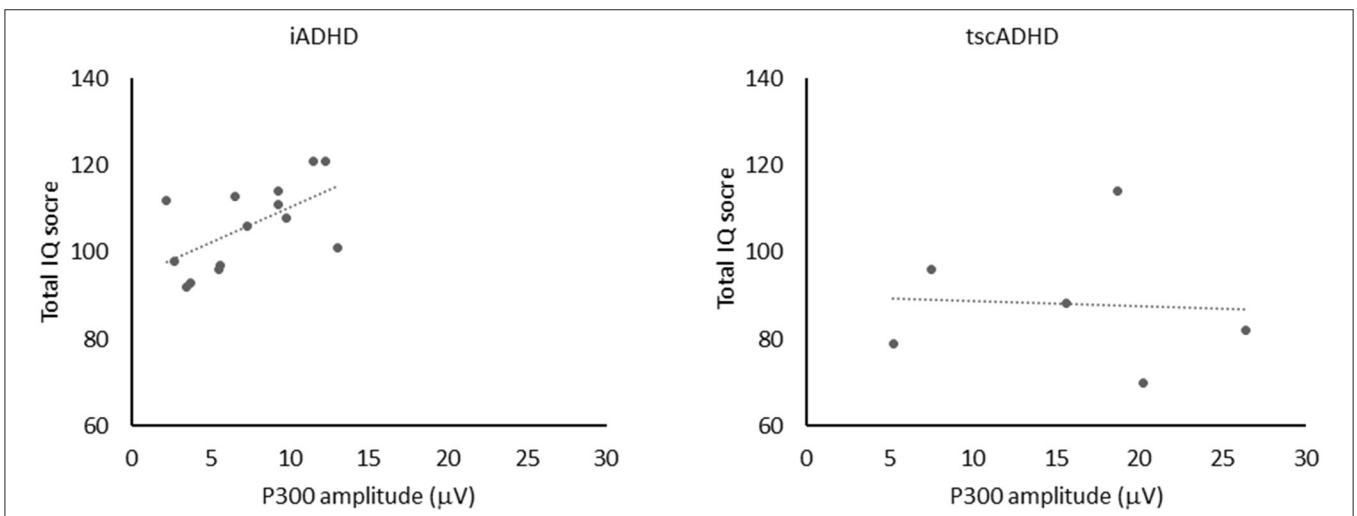

FIGURE 2 | The figure shows the positive correlation (left) between P300 amplitude and total IQ score in iADHD patients ($R^2 = 0.35$, $P = 0.03$). No significant correlation (right) between P300 amplitude and total IQ score was found in tcsADHD patients ($R^2 = 0.004$, $P = 0.9$).

iADHD patients, who included 7 of 13 subjects younger than 10 years.

MMN in ADHD

As for MMN, patients with ADHD (both with and without TSC) presented statistically significantly higher amplitudes and lower latencies, without differences between children with and without TSC. It is to be underlined that the shorter MMN latency in ADHD patients could not be attributed to a peripheral event, because both the N1 and P2 latencies were not different between our groups (iADHD and tscADHD patients and healthy subjects). Although most of literature data suggest that children with ADHD present a lower MMN amplitude and an increased MMN latency (9, 18), there are also studies revealing no significant differences (19)or an increased MMN amplitude in ADHD (26). Furthermore, similarly to what has been reported for P300, also the differences in MMN amplitude between children with ADHD and HCs tend to decrease with age (27). Whatever the reason of the disagreement between the present results and those of previous studies, it is conceivable that in patients with ADHD, who hardly keep their attention focused on one target and are easily distracted by unexpected stimuli, the MMN component shows shorter latency and higher amplitude than in HC. Mismatch negativity component is thought to reflect the preattentive detection of deviants (28). Despite MMN is mainly generated within the bilateral temporal cortex, it was shown that a further frontal source is activated when the preattentive processing of deviants is made difficult by a concomitant highly demanding task (29). This frontal contribution to the MMN building can result in a higher late MMN amplitude (29). Seen in this light, the hypothesis can be made that in ADHD patients, whose attentional resources are lower than in HC, even a simple task (reading a novel), as that used in the present study, can lead to the same result as a task requiring a far larger attentional load.

Although P300 amplitude differentiated iADHD from tscADHD patients, it is to be underlined that the MMN behavior was similar in both groups of patients. Indeed, both iADHD and tscADHD patients showed an MMN component shorter in latency and higher in amplitude as compared to HC. This finding can be relevant for two main reasons. First, from a clinical point of view, it suggests that the MMN characteristics are more dependent on the brain dynamics typical of ADHD rather than on ADHD etiology. This means that in the neurophysiological assessment and follow-up of ADHD patients MMN can provide particularly useful information. Second, the pathophysiological mechanisms of ADHD, which are far to be completely understood (30), involve the brain circuits subtending the involuntary attention, whose neurophysiological marker is represented by MMN.

Limitations of the Study

This study has some limitations that must be considered. First, we are aware that the sample studied is limited, but TSC is a rare disease, with a very high range of neuropsychiatric comorbidities; therefore, finding a homogenous sample of patients in a specific age range has been quite difficult. Furthermore, all patients with tscADHD presented structural brain lesions in both the gray and white matter, and one tscADHD patient was assuming an antiepileptic drug. We cannot exclude that these elements can have influence the ERP pattern in our tscAHDH patients. As for the typical TSC brain lesions, a control population of subjects affected by TSC but without presenting ADHD symptoms could have helped us in disentangling the contribution of ADHD and that of TSC to the observed findings. Future studies will be hopefully addressed to clarify this issue. As for the single tscADHD patient under antiepileptic treatment, it is to be underlined that his exclusion from the statistical analysis did not change our results.

Conclusions

While P300 amplitude is commonly considered a neurophysiological marker of the efficiency of the attentional processes, our data suggest that in specific clinical contexts, such as TSC patients, the impairment of the cognitive functions might not be reflected by reduced P300 amplitude. This can occur when the cortical networks underlying the attentional mechanisms are particularly disrupted, as in TSC.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary materials, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by EB of bambino gesù children's hospital. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin.

AUTHOR CONTRIBUTIONS

RM and MV: first conceptualized the work. RM and SM: enrolled the patients. SM: performed neuropsychological examinations. SM, DD, and SP: performed neurophysiological examinations. RM: wrote the first draft. PC, SP, MV, and FV: performed the corrections on the different versions of the draft, revised the literature, and updated the manuscript. All the authors approved the final version of the manuscript.

ACKNOWLEDGMENTS

The Authors would like to thank the Italian Tuberous Sclerosis Association for their contribution and support.

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Conflict of Interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Psychiatry Research 291 (2020) 113154

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Search for an epigenetic biomarker in ADHD diagnosis, based on the DAT1 gene 5'-UTR methylation: a new possible approach

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ARTICLE INFO

Keywords:
DNA opposite strand
Dopamine transporter (DAT)
CpG epigenetic marker
5'-UTR motifs

ABSTRACT

Attention Deficit/Hyperactivity Disorder (ADHD) is the most common neuro-developmental alteration in childhood. To date, its diagnosis is exclusively clinical, however recent studies focused on searching for objective biomarkers. We recently reported a selective alteration of DNA methylation in the 5′-UTR of dopamine transporter (DAT1) gene, in a ^{1}CGG^{2}CGG^{3}CGG and a ^{5}CG^{6}CG motif, for ADHD patients (compared to controls). Presently, we looked for DNA methylation of the corresponding CpG sites but complementary on the opposite strand ("COS"). Exploiting a novel cross-correlation approach, we found a core M5 - M5 COS and M2 - M2 COS relationship with relatively free M1 and M6 COS extremes. Our data might be relevant, to find a new biomarker to diagnose ADHD in affected subjects.

1. Introduction: DAT1 gene and its epigenetic modulation

Attention Deficit/Hyperactivity Disorder (ADHD) is the most common neuro-developmental alteration in childhood (Polanczyk et al., 2007; Curatolo et al., 2009; Purper-Ouakil, 2011), characterized by pervasive symptoms of inattention, hyperactivity, and impulsivity, which often lead to poor academic performance and impaired social interactions (American Psychiatric Association, 2000). Currently, ADHD diagnosis is still based on subjective observations and it is therefore of great relevance the development of a more definitively objective diagnostic system. For the identification and heritability of genes involved in ADHD, several studies have been conducted (Tistarelli et al., 2020), but to date no conclusive genetic determinants have been identified.

Recent research has focused on the dopamine transporter (DAT) (Jucaite et al., 2005; Bannon, 2005), including epigenetic regulation. The DNA methylation is mostly occurring at cytosine-phosphate-guanine (CpG) sites, where a methyl group (-CH_3) is added to the cytosines (Bird & Wolffe 1999). Xu et al. (2015), among Chinese Han children, compared 50 ADHD patients with 50 non-ADHD control subjects: they searched among19 CpG sites located in the 5'-UTR, a gene regulation area. We similarly assessed (Adriani et al., 2018) the 5'-UTR region of DAT1 gene, but addressing the nearby ^{1}CGG ^{2}CGG ^{3}CGG and ^{5}CG ^{6}CG motifs, located at +717 from TSS and onward, in the first intron.

It should be considered that fidelity for maintenance of CpG methylation is very high in hemi-methylated DNA while, on the other hand, *de novo* methylation resulted to be quite low (Riggs et al., 1998). Dnmt3a and Dnmt3b can methylate DNA *de novo*, and this occurs without regard to the methylation status of the complementary CpG position (Okano et al., 1998). It should also be considered that several enzymes (i.e. DNMT-TET-TDG) could theoretically serve cytosine modification states, within each CpG dyad, not necessarily in a symmetric form (see Wu et al., 2014). We thus thought of relevance the evaluation of the opposite reverse strand, in order to monitor for a possible differential methylation in the two strands in ADHD subjects. For this reason, by simply extending our previous work (Adriani et al., 2018), we sought at analyzing DNA methylation levels of CpG residues which are the exact *complementary on the opposite strand* ("COS") to the previous, already assessed ones (Tonelli et al., 2020).

We have been the first, to our knowledge, to perform all correlations among the original (i.e., on gene strand) and the newly assessed (i.e., dyads on COS) CpGs. Interestingly, the newly assessed CpGs (termed from M7-COS to M1-COS) correlated among them and also with the old CpGs (termed from M1 to M7). These results are shown elsewhere (Tonelli et al., 2020). Briefly, the M5-COS is correlated with M6-COS whereas the M1-COS, M2-COS and M3-COS are all strongly correlated

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https://doi.org/10.1016/j.psychres.2020.113154
Received 3 April 2020; Received in revised form 20 May 2020; Accepted 28 May 2020
Available online 30 May 2020
0165-1781/

Table 1
List of correlations we found. Each box groups all situations (couples of loci, one on gene strand and the other on COS) that correlate with one given situation (couple of loci as above, heading of that box). M means that the locus is considered as **methylation** level while D means that the locus is considered as **100-methylation** level. In panel A, the M is on gene strand and the D is on COS; in panel B, the D is on gene strand and the M is on COS. Listing of situations is divided between correlations found within the first motif (left column), within the second motif (right column), or hybrid across motifs (middle column). *Italic* highligh denotes the couples of correlations found back (see for instance the first two dyads with *italic* highlights: situation M5 - D5 COS is reported in the box among all correlations with M2 - D2 COS; accordingly, situation M2 - D2 COS is reported in the box among all correlations with M5 - D5 COS). **Bold** denotes couples of correlations where the very same CpG is involved in a same situation both as methylated and demethylated (see Discussion). Bonferroni corrected, separately within same-motif and hybrid correlations (panel B): **P < 0.10 for R > 0.6411; correlations marked with** *denote**P < 0.01 for R > 0.7604 (see text).**

CORRELATION "R" WITH ANY AMONG CpGs 1, 2 OR 3	HYBRID CORRELATION "R" OF CpG 1/2/3 WITH CpG 5/6/7	CORRELATION "R" WITH ANY AMONG CpGs 5, 6, OR 7
Gene strand M = methylated; COS strand D = de-methylated (Panel A) None of the correlations of panel A was significant, according to the Bonferroni corrected threshold. **M2 - D1 COS**		
	M3 - D5 COS at R = 0,427033824	*M5 - D5 COS 0,3977333265* ***M5 - D6 COS 0,3944721049*** **M5 - M6 COS 0,3744367799** M7 - D7 COS 0,4177846334
M2 - D2 COS		
	M3 - D5 COS 0,4266845347	*M5 - D5 COS 0,3980886016* ***M5 - D6 COS 0,393440450*** **M5 - M6 COS 0,378622174** M6 - D7 COS 0,3901105495
		M5 - D5 COS
M2 - D1 COS 0,3977333265 *M2 - D2 COS 0,3980886016* M2 - M3 COS 0,5291183531 M3 - D2 COS 0,3890903518		
		M6 – D5 COS
		M7 - D7 COS 0,5110902772
		M5 – D6 COS
M2 - D1 COS 0,3944721049 *M2 - D2 COS 0,393440450* M2 - M3 COS 0,5156527803 M3 - D2 COS 0,384019804		
		M6 - D6 COS
		M7 - D7 COS 0,4954077093
Gene strand D = de-methylated; COS strand M = methylated (Panel B)		
M1 COS - D1		
M2 COS - D2 0,67549283776 M3 COS - D3 0,74674852630 M2 COS - D3 0,75125473268		
M1 COS - D2		
M3 COS - D3 0,68977713431	M3 COS – D6 0,66771637412	M6 COS - D6 0,6660607532 M5 COS - D6 0,6692714879
M2 COS - D1		
M3 COS - D3 0,75028139158		
M2 COS - D2		
M1 COS - D1 0,67549283776 **M3 COS - D1 0,68778731299** **M3 COS - M1 0,86300208639** * (*discussed*) M3 COS - D3 0,70065853196	M3 COS - D6 0,65274369907 M5 COS - M1 0,71987992427 **M6 COS - D1 0,65307585388** **M6 COS - M1 0,76230516486** * (*discussed*) M7 COS - M1 0,76970293180 *	M6 COS - D6 0,65074117747 M5 COS - D6 0,65512958253
		M5 COS - D6
M1 COS - D2 0,66927114879		

(*continued on next page*)

Table 1 (*continued*)

CORRELATION "R" WITH ANY AMONG CpGs 1, 2 OR 3	HYBRID CORRELATION "R" OF CpG 1/2/3 WITH CpG 5/6/7	CORRELATION "R" WITH ANY AMONG CpGs 5, 6, OR 7
M2 COS - M1 0,7589999985 M2 COS - D2 0,65512958253		
		M6 COS - D6
M1 COS - D2 0,6660607532 M2 COS - M1 0,7790246170 * M2 COS - D2 0,65074117747		

one to each other. The M6-COS is negatively correlated to M6 while the M1-COS is negatively correlated to M2. The unexpected finding of a negative correlation led to the hypothesis that the opposite strand may well be de-methylated when the gene strand is methylated, and vice versa.

2. Method: A novel approach for methylation levels

Between 2010 and 2012, trained child neuro-psychiatrists (ADHD Clinical Unit, prof. Paolo Curatolo, Tor Vergata University of Rome, Italy) recruited school-aged children (6-12 years old), diagnosed by routine anamnestic and cognitive evaluation, according to DSM-IV and ICD-10 criteria plus Conners' scales and k-SADS. This study was approved by the Ethical Committee of ISS (on 15 July 2009); the parents gave their signature (i.e., written informed consent) for their child to participate in this study. The rules set by the Code of Ethics of the World Medical Association ("Declaration of Helsinki"), as printed in the British Medical Journal (18 July 1964), were fully respected.

We selected (out of the originally recruited patients) a cohort of 14 ADHD patients (half 9\10 and half 10\10 genotype), for which we assessed the other strand (Tonelli et al., 2020). By correlation with clinical scores, relatively higher levels of methylation at CpG M1 correlated negatively with CGAS (Children's Global Assessment Scale), serving an index for severity of ADHD. In contrast, relatively higher levels at CpG M6 were correlated with rescue of ADHD symptoms after six weeks of treatment (Adriani et al., 2018). The DNAs of patients were now processed to assess the region corresponding to DAT1 5'-UTR but on the other strand (Tonelli et al., 2020) and the following primers were used to amplify the region: h_SLC6A3_Rev PyroMark Custom Assay - Forward: AGGTGGAGGT-TTTAATAGGTAAT - Reverse [Biotin]-AACCACA TTT-TACTATATAAACCCA - Sequencing: AGGTAGAGTT-GGGAGAGG. All the methodological details on the sequence and the pyrosequencing assay (Hs_SLC6A3; PM00022064), used in the original study (Adriani et al., 2018), are available on the Qiagen web site.

For each dyad of CpG positions (e.g., for M1 and M1-COS), while in theory we have all four possible situations (both methylated; both de-methylated; gene-strand methylated and COS de-methylated; gene-strand de-methylated and COS methylated), the last two may be more likely. The probability of each situation can be calculated by multiplying the raw **methylation** level or the difference **(100-methylation level)**. As such, probability of the four situations is:

- both methylated, M1 \ M1 COS: M1 x M1 COS;
- both de-methylated, D1 \ D1 COS: (100-M1) x (100-M1 COS);
- gene-strand methylated & opposite de-methylated; M1 \ D1 COS: (M1) x (100-M1 COS);
- gene-strand de-methylated & opposite methylated D1 \ M1 COS: (100-M1) x (M1 COS).

For every "couple" of positions, not necessarily the dyad of two facing CpGs, we can identify the same four possible situations. For instance, together with CpG 1 we may be considering 2 COS, or together with CpG 2 we may be considering 1 COS. We termed "OMO" those situations when one locus among M1 - M7 is methylated and one locus among M1 COS - M7 COS is also methylated (or vice-versa both are de-methylated). We termed "EMI" those situations when one locus among M1 - M7 is methylated while one locus among the COS is de-methylated (therefore termed D1 COS to D7 COS); or, one locus among the gene-strand CpGs is de-methylated (therefore termed D1 to D7) while one locus among M1 COS - M7 COS is methylated.

Thus, for each couple of positions we have four possible products, and we have six times six i.e. 36 pairs of positions. We prepared a matrix with all the various 144 combinations, from (de)methylation levels of six CpGs on one strand and the corresponding complementary ones on the opposite strand.

Therefore, we decided to look for all the possible correlations, between probability of a given situation in a couple of positions and probability of a given situation in another couple of positions, being one CpG on the gene strand and one CpG on COS. In this way, we aimed at looking which setup is the most probable when considering as a whole the four CpGs (two on the gene strand and two on COS), which can each be either methylated or de-methylated.

3. Results: Interpretation and discussion

By making all correlations across all the possible series of combinations (i.e., considering probability of the 4 given situations in all couples of CpGs), we have obtained a great quantity of comparisons. It is obviously impossible to take all them into account, therefore we limited the analysis to two set-ups. In the first case (see Table 1 panel A), we start listing the correlations with the assumption of base (gene) strand methylated and opposite (COS) strand de-methylated (one of the four possibilities); in second case (see Table 1 panel B), all positions on the opposite (COS) strand are methylated and those on the base (gene) strand are de-methylated. This assumption, namely of considering as privileged the two EMI set-ups and not the other two OMO set-ups, came from the notion of a negative correlation found between the two strands (Tonelli et al., 2020).

Within a given set-up, starting from a given pair (e.g., M1 - D1 COS is the first one of the first set-up), the found correlations have been listed as sorted according to a motif-wise criterion (see Table 1). In other words, the correlations within first motif (i.e. CpGs 1, 2, 3) and within the second motif (i.e. CpGs 5, 6, also including 7) have been considered separately from "hybrid" correlations (i.e. whereby one among 1\2\3 is multiplied by one among 5\6\7). This was done for statistical reasons, as the P values associated with R values had obviously to be corrected for multiple comparisons. Within each of the three motif-wise subgroups, there is a quantity of nine pairs to correlate with (i.e., all permutations); since Bonferroni correction was applied, a significant tendency was only investigated for a threshold of $R > 0.6411$ (with 13 degrees of freedom).

3.1. First set-up: gene-strand CpG is methylated and COS is not

While a lot of correlations were found for the second set-up (see Table 1), both within and between motifs, no correlations emerged as

significant for the first set-up. However, given a functional relevance of the first set-up (see Adriani et al., 2018), we reasoned that those correlations with the highest R values deserved to be shown anyway.

It is obvious that any correlation, emerging for a given pair when looking from another pair, shall be found back and emerge again for the latter pair when looking from the former pair. This is confirming that our worksheet had no calculation error. These cases are reported in *"italic"* in panel A of Table 1. The same logic is valid for panel B (not shown). To give just an account of the few examples, we note:

1) when looking from M2 - D1 COS, a slight positive correlation with the dyad M5 - D5 COS and with the pair M5 - D6 COS was found; when looking from M5 - D5 COS and from M5 - D6 COS, the same positive correlation with the pair M2 - D1 COS was found, *indeed.*
2) when looking from M2 - D2 COS, a positive correlation of 0,3980886016 with the pair M5 - D5 COS was found; when looking from M5 - D5 COS, a positive correlation of 0,3980886016 with the pair M2 - D2 COS was found, *indeed.*

3.2. Second set-up: COS is methylated and gene-strand CpG is not

The most abundant and interesting quantity of correlations emerges when looking from **M2 COS - D2**which in itself is a relevant CpG dyad (Adriani et al., 2018). Among others:

1) a strong, positive correlation of 0,863002086390621 with the M3 COS - M1 was found. Also, a positive correlation at R value of 0,687787312995826 with the M3 COS - D1 was found.
2) a strong, positive correlation of 0,762305164861466 with the M6 COS - M1 was found. Also, a positive correlation at R value of 0,653075853880892 with the M6 COS - D1 was found.

This kind of finding may seem somewhat contradictory. How is it possible that the very same pair correlates with another pair, where the CpG 1 can, at the same time, get methylated or de-methylated? To explain this, it should be took into account that the level at CpG 1 is here multiplied by another level, measured on CpG 3 COS (line 1) or 6 COS (line 2). To keep the correlation valid, in both cases, the only explanation is that companions of the multiplication go in opposite fashion compared to CpG 1. In other words, CpG 1 *is not* independent from CpG 3 COS and from 6 COS ! Sometimes they go in the same fashion, sometimes they go in opposite fashion, but always (as a pair) correlating with the pair formed by CpG 2 and 2 COS.

The functional implication is the following: when considering CpG 1 and CpG 6 COS, they can *both of them* covary with CpG 2 together, or *either of them* may covary while the other anti-covaries ! The same notion can be inferred for relationship between CpG 1 and CpG 3 COS. Such very unsuspected conclusion is important: in particular, it means that, in the current set-up, CpG 1 on the gene-strand may well get methylated not independently from CpG 6 COS ! Either they undergo a same change together (possibly, denoting a positive link between motifs) or theyundergo opposite changes (possibly, denoting a negative link between motifs). Of note, a similar result has been obtained on a normative sample of healthy subjects (Carpentieri et al., submitted).

3.3. Possible implications drawn from this new kind of cross-correlation approach

So, in addition to previous data about simple correlations between CpGs (Tonelli et al., 2020), we presently investigated correlations between situations, whereby for "situation" we defined a couple of CpG in four possible states (Table 1). Starting from one set-up, the correlating situations are quite often from that same set-up, and not from any other of the three possible ones. This was not obvious: if one situation is in one given state, another situation (if far and independent) might well be in any of its possible four states. Therefore, as a whole, we propose the following notion: the more the COS strand gets methylated, the more the gene strand will get de-methylated.

We can observe on first set-up (Table 1 panel A) two special cases resembling the apparent contradiction seen above: both M5 - M6 COS and M5 - D6 COS are returned from M2 - D2 COS and M2 - D1 COS. Again, we can assume that, when changing states (methylation or de-methylation), simultaneous changes can be considered equally probable for CpG 5 and for CpG 6 COS; in our opinion, these two specific CpGs may change of state quite frequently and reasons for privileged interaction were already proposed in the previous commentary (Tonelli et al., 2020): note however that CpGs 5 and 6 COS are physically not so close.

Second set-up (Table 1 panel B) is similar but starting from the opposite assumption (gene strand de-methylated; COS strand methylated). As we can easily see, there are many more correlations than in the previous set-up, and they are much more stronger. A noteworthy situation can be caught by regarding, again, at the bold lines (which represent the OMO situations, where both CpGs in the pair are methylated, again emerging together with the EMI situation, where one such CpG is de-methylated). One such member of the pair is either M6 COS or M3 COS while the other member is either M1 or D1 (see bold lines in Table 1). In this set-up, therefore, there is strong ground to consider the locus CpG 1 as a "pivotal" one: starting from being de-methylated (as per assumption), it can also get methylated and, noteworthy, these changes of status (occurring at CpG 1) are not independent from those occurring in the dyad formed by CpGs 6 and 6 COS: they can either covary, or can anti-covary. Of note, a similar result has been confirmed on a normative sample of healthy subjects (Carpentieri et al., submitted). Their dynamic change, rather than their instant status, may be relevant (Zhang and Wu, 2014). As such, we can assume that the two most-sided CpGs, M6 COS and M1 (which both appear first when moving 5' to 3' in either strand), are pivotal for functional dynamics within two nearby motifs, studied here.

4. Conclusion: The future perspectives

The opposite strand, according to our opinion, could act as a control element: in order to allow the gene strand to be de-methylated, the opposite strand may need to be methylated. The transition from first to second set-up may well imply a change at the level of CpG 6 COS, transition back may well imply a change at the level of CpG 1. In other words, a crucial pivot for transition may well be the OMO situation, whereby both dyad members are methylated: while locus 2 is methylated and its sorrounding (made of 1 COS and 2 COS) is de-methylated, the gene strand changes at CpG 1; in the other case, while locus 6 is methylated, the opposite strand changes at CpG 6 COS.

Further work is warranted to ascertain whether such a dynamic is actually occurring in reality, also in other genes (D'Addario et al., 2012; D'Addario et al., 2013); purpose of this commentary is to provide a possible approach to search for new epigenetic biomarkers for diagnosis of ADHD and other conditions related to DAT, such as Parkinsonism (Tafani et al., 2020). Our data, presented recently (Tonelli et al., 2020) and here, suggest an entirely novel approach to DNA methylation analysis.

The potential conflict of interest to be disclosed

Adriani W, Laviola G, Pascale E, D'Addario C – "*Metodo per determinare il deficit di attenzione con iperattività*" (Method to determine Attention Deficit and Hyperactivity Disorder). Italian Patent Application, at no. 102016000129938 (date 22-December-2016); turned into European Patent Application, at no. 17830021.6 (date 21-December-2017).

Author contribution

WA, EP, CD conceived the study; EP, MP, CD realized the original CpG-methylation study; SM and GL described the cross-correlations on original methylation data; GL wrote a first draft with close supervision by WA; EP and CD critically commented on such draft. We are so grateful to Emilia Romano, Maria Cristina Porfirio, Grazia Giana and Miriam Troianiello, who carried out the patients' recruitment and sample assessment during years 2010 to 2012.

Contribution to the field

We suggest here for the very first time that the opposite strand of DNA may be as important as the strand where (the promoter of) a candidate gene stands, as far as epigenetic regulation through CpG methylation is concerned.

Funding statement

N/A

Acknowledgements

The study providing data for this correlation analysis was approved by the Ethical Committee of ISS (Prot. CE-ISS 09/270 of 15 July 2009). Patients were recruited between 2010 and 2012; we declare that collected biological materials were used solely to the purpose of our previous papers (Adriani et al., 2018; Tonelli et al., 2020) and that present cross-correlations are a further elaboration on already collected and fully published data. The rules set by the Code of Ethics of the World Medical Association ("Declaration of Helsinki"), which has been printed in the British Medical Journal (on 18 July 1964), were fully respected.

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Psychiatry Research 291 (2020) 113099

Contents lists available at ScienceDirect

Psychiatry Research

journal homepage: www.elsevier.com/locate/psychres

Letter to the Editor

Sleep problems in attention-deficit/hyperactivity disorder and autism spectrum disorder: Sex differences and parental stress

Sleep problems are common in children with neurodevelopmental disorders, such as Attention Deficit/Hyperactivity Disorder (ADHD) and Autism Spectrum Disorder (ASD). For example, it has been reported that up to 55% of children with ADHD may have sleep problems (Cortese et al., 2013). Furthermore, Lai et al. in a recent meta-analysis estimated an overall pooled prevalence of 13% for sleep-wake disorders in autism (Lai et al., 2019). Sleep disorders in children with ASD or ADHD are associated with poorer parent mental health and higher parenting stress. However, only a few studies have investigated sex differences in sleep problems in children with ADHD or ASD, and these yielded conflicting findings (Sivertsen et al., 2012; Mazzone et al., 2018). It should be noted that the heterogeneity found in these results could be given by the fact that all of these studies used a different measure to assess sleep problems (Sivertsen et al., 2012). Therefore, additional research on sleep problems in these clinical populations have important implications for diagnosis and treatment and may help to address existing literature gaps (Mazzone et al., 2018).

The present study aimed at describing the presence of sleep problems in a sample of drug-naïve ADHD and ASD patients without intellectual disability. Furthermore, we assessed sex differences in sleep problems in these clinical populations. Finally, we studied the relationship between sleep problems and parental stress in these clinical groups.

A total of 111 drug-naïve participants [ASD $N = 38$, 16 females (F), 22 males (M); ADHD $N = 36$, 12 F, 24 M; Typically Developing (TD) $N = 37$, 12 F, 24 M)] aged 7–13 years with an Intelligent Quotient (IQ) ≥ 85 were enrolled in the study. ADHD and ASD diagnosis were based on clinical assessment, observation, and parent interviews, and were confirmed by a senior child psychiatrist according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) criteria. Participants enrolled in the TD group were recruited in schools and none of them had a history of neurological disorders, psychiatric disorders, developmental delay, or learning disabilities.

All the participants' parents provided a written informed consent and completed the Children's Sleep Habits Questionnaire (CSHQ) and the Parenting Stress Index-Short Form (PSI-SF).

Comparisons between groups were via one-way analysis of variance (ANOVAs) followed by Tukey's contrast for multiple comparisons of means. Spearman's correlation coefficients were used to evaluate correlations between sleep problems and parental stress within the ADHD and the ASD group. Comparison between groups and sex differences within the ADHD and the ASD group on the CSHQ and the PSI-SF are reported in Table 1.

The ADHD group showed significantly higher scores on all the CSHQ and the PSI-SF subscales compared to the TD group. The ASD group showed significantly higher scores on the sleep anxiety, the night walking, and the daytime sleepiness CSHQ subscales, on the CSHQ total score, and on all the PSI-SF subscales compared to the TD group. Furthermore, the ADHD group showed more sleep problems on several CSHQ subscales and on all PSI-SF subscales compared to the ASD group.

Sex differences in the ASD group showed that females had significantly higher scores on the daytime sleepiness CSHQ subscale. Males in the ADHD group had significantly higher scores on the parasomnias CSHQ subscale. No significant sex differences were detected in the ASD group on any of the PSI-SF scales, whereas males in the ADHD group exhibited higher scores in the Difficult Child (DC) PSI-SF subscale compared to females.

In the ADHD group the highest significant correlations were found between the PSI-SF total stress index and the bedtime resistance and the daytime sleepiness CSHQ subscales. Within the ADHD group, the sleep onset delay, the sleep duration, the parasomnias, and the daytime sleepiness CSHQ subscales showed a positive correlation with the DC PSI-SF subscale, whereas the parent-child dysfunctional interaction PSI-SF subscale showed a significant positive correlation with the sleep duration and the daytime sleepiness CSHQ subscales. No statistically significant correlations have been observed between the CSHQ and the PSI-SF in the ASD group. These results confirm previous literature findings, even if the presence of parasomnias we have observed in the ADHD participants has been rarely described in previous studies. Furthermore, in our research, parents of ADHD participants showed a substantial level of stress and problematic parent-child interactions. ASD participants exhibited more anxiety problems related to falling asleep, and more night walking and daytime sleepiness compared to the TD group. Our results do not highlight the presence of bedtime resistance or sleep onset delay described in previous studies (Singh and Zimmerman, 2015).

Furthermore, the current study supports the hypothesis that there are sex differences in sleep disorders in patients with ASD or ADHD. Specifically, these findings show that males with ADHD show more parasomnias than females, whereas ASD females have more daytime sleepiness than ASD males. Sex differences in the type sleep problems in these clinical populations may be associated to underlying neurobiological processes. Further studies may help clarify the connection between these behavioral sex differences and sex specific biomarkers related to sleep disorders in these clinical populations.

Some limitations of this study should be mentioned. First, sleep problems were assessed through a parent-reported rating scale rather than objective measures. Second, participants' report of sleep problems was not collected. On the other hand, strengths of this study are the large number of subjects, the exclusion of participants with intellectual disability, and the inclusion of well screened drug-naïve participants, which eliminates drug treatments that might influence the presence of sleep disturbances. In addition, the inclusion of a representative group of females in both the ADHD and the ASD groups allowed us to consider a sex comparison. Further studies on sex differences in sleep problems in ADHD and ASD populations can help develop individualized

https://doi.org/10.1016/j.psychres.2020.113099
Received 23 March 2020; Received in revised form 11 May 2020; Accepted 11 May 2020
Available online 07 June 2020
0165-1781/

Table 1
Comparison between the ADHD, ASD, and the TD groups, and sex differences within the ASD and the ADHD group on the CSHQ and the PSI-SF.

	ADHD	ASD	TD	ADHD vs ASD*	ADHD vs TD*	ASD vs TD*	ASD M	ASD F	ASD M vs ASD F	ADHD M	ADHD F	ADHD M vs ADHD F
CSHQ												
Bedtime resistance	9.78 ± 2.71	7.68 ± 1.81	7.81 ± 2.06	***p* < .001**	***p* < .001**	*p* = .967	8.05 ± 2.01	7.19 ± 1.42	*p* = .153	9.71 ± 3.01	9.92 ± 2.10	*p* = .811
Sleep onset delay	1.86 ± 0.79	1.37 ± 0.71	1.3 ± 0.52	***p* = .007**	***p* = .002**	*p* = .895	1.59 ± 0.85	1.06 ± 0.25	*p* = .011	1.79 ± 0.83	2.00 ± 0.73	*p* = .468
Sleep duration	4.81 ± 1.80	3.79 ± 1.39	3.38 ± 0.95	***p* = .008**	***p* < .001**	*p* = .426	3.95 ± 1.49	3.56 ± 1.26	*p* = .401	5.08 ± 1.86	4.25 ± 1.60	*p* = .195
Sleep anxiety	7.42 ± 2.18	6.11 ± 1.94	4.89 ± 1.43	***p* = .009**	***p* < .001**	***p* = .016**	6.32 ± 2.05	5.81 ± 1.79	*p* = .436	7.38 ± 2.26	7.50 ± 2.11	*p* = .874
Night walking	4.31 ± 1.52	4.34 ± 1.34	3.43 ± 0.72	*p* = .991	***p*=.009**	***p* = .006**	4.59 ± 1.43	4.00 ± 1.15	*p* = .184	4.50 ± 1.56	3.92 ± 1.44	*p* = .286
Parasomnias	9.94 ± 1.63	8.26 ± 1.34	8.32 ± 1.29	***p* < .001**	***p* < .001**	*p* = .981	8.23 ± 1.41	8.31 ± 1.30	*p* = .851	10.50 ± 1.56	8.83 ± 1.19	***p* = .003**
Sleep-disordered breathing	3.89 ± 1.28	3.37 ± 0.81	3.32 ± 0.62	*p* = .051	***p* = .032**	*p* = .978	3.14 ± 0.35	3.69 ± 1.13	*p* = .078	4.04 ± 1.48	3.58 ± 0.66	*p* = .212
Daytime sleepiness	13.64 ± 4.10	16.53 ± 3.02	9.32 ± 2.09	***p* < .001**	***p* < .001**	***p* < .001**	15.41 ± 2.87	18.06 ± 2.59	***p* = .006**	14.33 ± 4.60	12.25 ± 2.49	*p* = .087
CSHQ tot	51.53 ± 11.47	48.21 ± 4.84	39.24 ± 5.13	*p* = .159	***p* < .001**	***p* < .001**	47.68 ± 5.19	48.94 ± 4.37	*p* = .425	53.46 ± 12.90	47.67 ± 6.80	*p* = .087
PSI-SF												
Parental Distress	36.06 ± 7.99	28.26 ± 9.73	18.76 ± 5.50	***p* < .001**	***p* < .001**	***p* < .001**	26.14 ± 9.60	31.19 ± 9.43	*p* = .116	36.50 ± 7.64	35.17 ± 8.93	*p* = .644
Parent-Child Dysfunctional Interaction	31.81 ± 7.75	24.53 ± 8.09	15.92 ± 3.41	***p* < .001**	***p* < .001**	***p* < .001**	22.77 ± 8.02	26.94 ± 9.60	*p* = .119	33.08 ± 8.55	29.25 ± 5.27	*p* = .165
Difficult Child characteristics	41.36 ± 9.14	32.58 ± 10.44	18.62 ± 5.61	***p* < .001**	***p* < .001**	***p* < .001**	29.95 ± 10.97	36.19 ± 8.74	*p* = .069	43.63 ± 8.97	36.83 ± 8.02	***p* = .034**
Total Stress index	97.25 ± 14.65	79.92 ± 21.36	51.00 ± 12.47	***p* < .001**	***p* < .001**	***p* < .001**	75.00 ± 22.14	86.69 ± 18.85	*p* = .096	100.25 ± 13.97	91.25 ± 14.82	*p* = .082

*Post-hoc analysis; p-values adjusted by means of Tukey contrasts for multiple comparisons of means. Bold font indicates statistical significance.

intervention models and have significant implications for early identification efforts.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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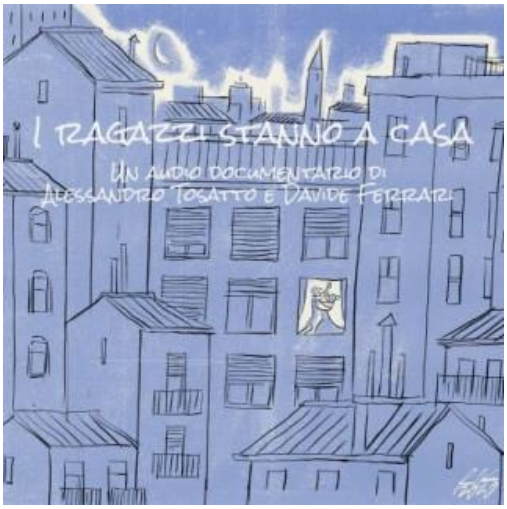
“I ragazzi stanno a casa”: gli adolescenti raccontano il loro lockdown in un podcast



È passato un quarto di secolo da quando Ligabue cantava “*I ragazzi sono in giro*”, e mai come quest'anno è stato vero il contrario. Non è un caso che ***“I ragazzi stanno a casa”*** sia il titolo scelto per il **podcast** ideato e realizzato durante il lockdown dai **giovani e dagli operatori del Centro diurno adolescenti della UONPIA** (l'Unità operativa di neuropsichiatria e psicologia per l'infanzia e l'adolescenza) dell'ospedale Policlinico di Milano. Al Centro diurno i ragazzi interagiscono con personale sanitario e medico del Policlinico e gli educatori della cooperativa del Consorzio Farsi Prossimo, che da anni lavora con personale specializzato nel campo della salute mentale, sia con preadolescenti e adolescenti, sia con adulti.

L'audio documentario, realizzato in cinque puntate, raccoglie come in un coro le voci dei ragazzi, degli educatori, dei neuropsichiatri e delle psicologhe del centro diurno accompagnando l'ascoltatore in un viaggio nel mondo degli adolescenti con disturbi neuropsichiatrici in un periodo sicuramente unico, quello in cui si sono trovati costretti “in casa”.
Una condizione che tutti hanno vissuto con disagio, e che lo è stata ancora di più per dei ragazzi che vivono già forti difficoltà in una situazione quotidiana di normalità.
Nelle cinque puntate del podcast, le voci di ragazzi, personale sanitario del Policlinico, educatori della cooperativa Filo di Arianna, raccontano **attraverso parole, poesie, musica, immagini e emozioni** i mesi in cui sono stati costretti a relazionarsi agli altri e al mondo in un modo diverso, nuovo, a causa del virus Covid-19.
Il lavoro è stato realizzato in un laboratorio “a distanza” durante il quale i ragazzi hanno aperto le proprie case e il proprio cuore con coraggio, condividendo sensazioni e stati d’animo con lo sguardo e l’onestà degli adolescenti.
L'audio documentario “I ragazzi stanno a casa” **si può ascoltare sulla piattaforma di podcast *Spreaker*** al seguente link: *www.spreaker.com/show/i-ragazzi-stanno-a-casa-presentazione*

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

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