



NEWSLETTER



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Le Monde Diplomatique Il Manifesto; n. 12, anno XXVI, dicembre 2019

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BIBLIOGRAFIA ADHD DICEMBRE 2019

Acta Med Port. 2019 Mar;32:195-201.

CLINICAL VALIDATION OF THE PORTUGUESE VERSION OF THE CHILDREN'S SLEEP HABITS QUESTIONNAIRE (CSHQ-PT) IN CHILDREN WITH SLEEP DISORDER AND ADHD.

Parreira AF, Martins A, Ribeiro F, et al.

INTRODUCTION: The Portuguese version of the Children's Sleep Habits Questionnaire showed adequate psychometric properties in a community sample but the American cut-off seemed inadequate. This study aimed to validate this questionnaire in clinical populations of children with sleep disorders and with attention deficit/ hyperactivity disorder.

MATERIAL AND METHODS: The study sample included 148 Portuguese children aged 2 to 10 years old that were divided in 3 groups: 1. Clinical group with sleep disorders (behavioral insomnias, parasomnias or sleep-related breathing disorders); 2. Clinical group with attention deficit/ hyperactivity disorder; 3.

CONTROL GROUP: The sleep habits and sleep problems were evaluated using the Children's Sleep Habits Questionnaire. Sleep-related disorders were confirmed by polysomnography.

RESULTS: The questionnaire's internal consistency (Cronbach alpha) in the clinical sample (sleep disorders and attention deficit/ hyperactivity disorder) was 0.75 and ranged from 0.55 to 0.85 for the subscales. Children with sleep disorders and attention deficit/ hyperactivity disorder had a higher sleep disturbance index (full scale score) compared to the control group. The subscales presented significant differences between the subgroups with different sleep disorders showing discriminative validity. The receiver operating characteristic analysis of the sleep disturbance index comparing the sleep disorder and control sample determined a cut-off of 48 (sensitivity 0.83; specificity 0.69).

DISCUSSION: Children with sleep disorders and attention deficit/ hyperactivity disorder evidenced higher Sleep Disturbance Index (full scale score) comparing to the control group. The subscales presented significant differences between the subgroups with different sleep disorders showing discriminative validity.

Conclusion: The Portuguese version of the Children's Sleep Habits Questionnaire showed adequate psychometric properties for children with sleep disorders and/or attention deficit/ hyperactivity disorder. The cut-off value 48 is better adjusted for the Portuguese population

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

Acta Paediatr Int J Paediatr. 2019.

WE STILL NEED TO KNOW MORE ABOUT ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER WHO UNDERGO SURGERY FOR SEVERE OBESITY.

Jarvholm K.

Alcohol Clin Exp Res. 2019.

ALCOHOL INTAKE IN EARLY PREGNANCY AND RISK OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN UP TO 19 YEARS OF AGE: A COHORT STUDY.

Weile LKK, Wu C, Hegaard HK, et al.

Background: Little is known about maternal alcohol intake in early pregnancy and the risk of attention-deficit/hyperactivity disorder (ADHD) in children beyond 5-áyears of age. We examined the association between alcohol binge drinking and weekly alcohol intake in early pregnancy and the risk of ADHD in children followed from birth to 19 years of age.

Methods: We included 48,072 children born between 1998 and 2012, whose mothers participated in the Aarhus Birth Cohort. Maternal alcohol intake was obtained from a self-administered questionnaire completed in early pregnancy. ADHD diagnoses were retrieved from the Danish Psychiatric Central Research Register and the Danish National Patient Register. Crude hazard ratio and adjusted hazard ratio (aHR) of ADHD according to alcohol binge drinking or weekly intake of alcohol were calculated using the Cox regression.

Results: Compared to children of women with no binge drinking episodes, we observed an aHR for ADHD of 0.91 (95% CI 0.76 to 1.08), 0.73 (95% CI 0.56 to 0.96), and 0.77 (95% CI 0.57 to 1.06) among children of women reporting 1, 2, and 3 or more binge drinking episodes, respectively. Among children of women drinking <1 drink per week, 1 drink per week, 2 drinks per week, and 3 or more drinks per week, we observed an aHR for ADHD of 0.87 (95% CI 0.74 to 1.03), 0.63 (95% CI 0.40 to 0.98), 1.30 (95% CI 0.89 to 1.92), and 0.78 (95% CI 0.38 to 1.59), respectively, when compared to children of women not drinking on a weekly basis.

Conclusion: We found no evidence that binge drinking or low alcohol intake in early pregnancy was associated with the risk of ADHD in children

Archives of Disease in Childhood: Fetal and Neonatal Edition. 2019.

NEURODEVELOPMENTAL IMPAIRMENT IN NECROTISING ENTEROCOLITIS SURVIVORS: SYSTEMATIC REVIEW AND META-ANALYSIS.

Matei A, Montalva L, Goodbaum A, et al.

Aim: To determine (1) the incidence of neurodevelopmental impairment (NDI) in necrotising enterocolitis (NEC), (2) the impact of NEC severity on NDI in these babies and (3) the cerebral lesions found in babies with NEC.

Methods: Systematic review: three independent investigators searched for studies reporting infants with NDI and a history of NEC (PubMed, Medline, Cochrane Collaboration, Scopus). Meta-analysis: using RevMan V.5.3, we compared NDI incidence and type of cerebral lesions between NEC infants versus preterm infants and infants with medical vs surgical NEC.

Results: Of 10 674 abstracts screened, 203 full-text articles were examined. In 31 studies (n=2403 infants with NEC), NDI incidence was 40% (IQR 28%-64%) and was higher in infants with surgically treated NEC (43%) compared with medically managed NEC (27%, p<0.00001). The most common NDI in NEC was cerebral palsy (18%). Cerebral lesions: intraventricular haemorrhage (IVH) was more common in NEC babies (26%) compared with preterm infants (18%; p<0.0001). There was no difference in IVH incidence between infants with surgical NEC (25%) and those treated medically (20%; p=0.4). The incidence of periventricular leukomalacia (PVL) was significantly increased in infants with NEC (11%) compared with preterm infants (5%; p<0.00001).

Conclusions: This study shows that a large proportion of NEC survivors has NDI. NEC babies are at higher risk of developing IVH and/or PVL than babies with prematurity alone. The degree of NDI seems to correlate

to the severity of gut damage, with a worse status in infants with surgical NEC compared with those with medical NEC.

Trial registration number: CRD42019120522

Asian J Psychiatry. 2020;48.

THE EFFICACY OF ZINC AUGMENTATION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER UNDER TREATMENT WITH METHYLPHENIDATE: A RANDOMIZED CONTROLLED TRIAL.

Noorazar SG, Malek A, Aghaei SM, et al.

Introduction: Regarding to the role of the zinc in the metabolism of the central nervous system and the correlation of zinc supplementation in the treatment of any Attention deficit hyperactivity disorder (ADHD) symptoms, this study was conducted to evaluate the complementary effects of this nutrient.

Method: This was a double-blind randomized clinical trial study and 60 children with ADHD who were treated with methylphenidate were chosen by random allocation and were divided in the two groups: 30 for the case and 30 for the control group. The treatment in case group was augmented with zinc. Duration of study was six weeks.

Result: Forty eight (80%) of participants were boy and 12 (20%) were girl. The mean age of patients was 9.6 ± 1.70 years. There was no significant difference between the two groups after the intervention in terms of total score, hyperactivity and impulsivity subscales during variance analysis, but there was a significant difference between the mean of inattention score.

Conclusion: Augmentation with zinc can enhance the improvement of inattention

Asian J Psychiatry. 2020;48.

PRE-SCHOOL ATTENTION DEFICIT HYPERACTIVITY DISORDER: 12 WEEKS PROSPECTIVE STUDY.

Vaidyanathan S, Rajan TM, Chandrasekaran V, et al .

Introduction: Extant literature lack studies on behavioural training or pharmacotherapy in Indian preschool children. With adverse long term outcomes, effective, safe and affordable early interventions for ADHD are a priority. Aim of this prospective study is to report on short term outcome of preschool ADHD with specific focus on safety and tolerability of medications.

Methods: Children with ADHD aged 2.5 to 6 years were assessed for severity and adverse events at baseline and follow-up using Conner's abbreviated rating scale and Clinical Global Impression-Severity scale. Children with Autism spectrum disorder and those with social quotient less than 50 were excluded. Statistical Analysis included descriptive statistics and Repeated measures ANOVA.

Results: Of 56 children recruited, 33.93 % (N = 19) were on behavioural interventions alone, 66.07 % (N = 37) were on a combination of medication and behavioural intervention. All children received treatment according to standard care. The most prescribed drug was clonidine (44.64%), then risperidone (28.7%), methylphenidate (10.7%) and atomoxetine (10.7%). Medication choice was determined by affordability, availability and comorbidity profile. Sedation occurred in 24 % of children on clonidine. Atomoxetine was not well tolerated in 2 children. Methylphenidate was well tolerated. Irrespective of medication choice, all children showed significant improvement at 12 weeks ($p < 0.001$).

Conclusions: Choice of interventions is largely determined by availability and affordability. There is a need for structured parent behavioural training program deliverable in low resource setting. Anti-ADHD medications should be made available under the NMHP, RBSK program and all government settings in India, to address over-prescription of antipsychotics in preschool ADHD

Aust J Gen Pract. 2018 Nov;47:776-81.

NEURODEVELOPMENTAL OUTCOME OF LATE-PRETERM INFANTS: A PRAGMATIC REVIEW.

Srinivas JR.

BACKGROUND: The number of late-preterm births (34^{0/7} to 36^{6/7} weeks of gestation at birth) has steadily increased over recent years. Recent reports suggest that late-preterm infants are at an increased risk of developing neurodevelopmental abnormalities, compared with full-term infants.

OBJECTIVES: The aim of this paper is to carry out a pragmatic review of the current evidence regarding the neurodevelopmental risks of speech delay, cerebral palsy, cognitive delay, autism spectrum disorder and attention deficit hyperactivity disorder in late-preterm infants.

DISCUSSION: Evidence from cohort studies indicates that late-preterm infants have a higher risk of speech delay in the first two years, and cognitive delay and attention problems in early childhood, compared with infants born at term. However, the results are inconsistent. Some reports indicate 'catch up' development with speech and cognition. Developmental surveillance through regular follow-up of high-risk late-preterm infants is necessary to identify risks at the earliest

Autism Res. 2019.

THE SELF-CONSTRUAL SCALE: A POTENTIAL TOOL FOR PREDICTING SUBJECTIVE WELL-BEING OF INDIVIDUALS WITH AUTISM SPECTRUM DISORDER.

Kaneko S, Kato TA, Makinodan M, et al.

Despite accumulating evidence that culture shapes the symptoms of autism spectrum disorder (ASD), no studies have yet applied the Self-Construal Scale to individuals with ASD. We compared the self-construals (measured using the Self-Construal Scale) of 31 high-functioning Japanese individuals with ASD with those of 60 typically developing (TD) individuals. We also examined how the self-construals of individuals with ASD related to their intelligence quotient, adverse childhood experiences, attention deficit hyperactivity disorder, ASD symptoms during adulthood and preschool years, and subjective well-being. Individuals with ASD were more likely to display independent self-construals than were TD individuals; unexpectedly, however, a substantial proportion of individuals with ASD (43.8%) displayed relatively interdependent self-construals. Among individuals with ASD, self-construals were significantly associated with ASD symptoms during preschool years, and with satisfaction of the need for autonomy and frustration of the need for relatedness. Evaluating self-construals can help predict the subjective well-being of high-functioning individuals with ASD. Moreover, the Self-Construal Scale may be useful for understanding the heterogeneous phenotypes of ASD, based on its association with autistic symptoms during preschool years, suggesting that the scale is a potential tool to develop efficient interventions for high-functioning individuals with ASD. Autism Res 2019. - © 2019 International Society for Autism Research, Wiley Periodicals, Inc. Lay Summary: Autism Spectrum Disorders (ASD) are a group of disorders presenting a variety of symptoms and biological origins that can complicate choosing an intervention best suited for improving well-being. Results indicate that a self-construal scale could help understand individuals with high-functioning ASD by independent and interdependent self-construals that are associated with ASD symptoms during preschool years and adult subjective well-being. Our findings suggest that this scale can help understand ASD and select appropriate interventions

Biopsychosoc Med. 2019 Nov;13.

HEMODYNAMIC RESPONSE TO FAMILIAR FACES IN CHILDREN WITH ADHD.

Shimamura K, Inoue T, Ichikawa H, et al.

Background: School-age children with attention deficit hyperactivity disorder (ADHD) have difficulties in interpersonal relationships, in addition to impaired facial expression perception and recognition. For successful social interactions, the ability to discriminate between familiar and unfamiliar faces is critical. However, there are no published reports on the recognition of familiar and unfamiliar faces by children with ADHD.

Methods: We evaluated the neural correlates of familiar and unfamiliar facial recognition in children with ADHD compared to typically developing (TD) children. We used functional near-infrared spectroscopy (fNIRS) to measure hemodynamic responses on the bilateral temporal regions while participants looked at photographs of familiar and unfamiliar faces. Nine boys with ADHD and 14 age-matched TD boys participated in the study. fNIRS data were Z-scored prior to analysis.

Results: During familiar face processing, TD children only showed significant activity in the late phase, while ADHD children showed significant activity in both the early and late phases. Additionally, the boys with ADHD did not show right hemispheric lateralization to familiar faces.

Conclusions: This study is the first to assess brain activity during familiar face processing in boys with ADHD using fNIRS. These findings of atypical patterns of brain activity in boys with ADHD may be related to social cognitive impairments from ADHD

BMC Health Serv Res. 2019 Sep;19:673.

WAITING TIMES FOR DIAGNOSIS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS REFERRED TO ITALIAN ADHD CENTERS MUST BE REDUCED.

Bonati M, Cartabia M, Zanetti M.

BACKGROUND: To investigate timely access to and the time needed to complete the diagnostic path of children and adolescents with suspected attention deficit hyperactivity disorder (ADHD) in the 18 Italian Lombardy Region ADHD reference centers.

METHODS: Data of children and adolescents enrolled in the Regional ADHD disease-oriented Registry for suspected ADHD who requested their first visit in 2013-2017 were analyzed.

RESULTS: The sample comprised 2262 children and adolescents aged 5-17 years who accessed the ADHD centers for diagnostic classification and management. The median waiting time was of 177 days (range 66-375) from the request for the initial appointment to the completion of the diagnostic path, with a three - fold difference between centers. In addition to the center, the strongest significant predictors of long waiting times were age comorbidities, the severity of the disorder, and having already completed some diagnostic procedures provided by the common standard path.

CONCLUSIONS: To guarantee an equal standard of care in ADHD centers for all children and adolescents there is a pressing need to reduce the times to complete the diagnostic path. It is the task of both policymakers and each center to optimize the quality of the service and of the care delivered

BMC Med Genet. 2019 Jun;20:101.

A NOVEL NAA10 P.(R83H) VARIANT WITH IMPAIRED ACETYLTRANSFERASE ACTIVITY IDENTIFIED IN TWO BOYS WITH ID AND MICROCEPHALY.

Ree R, Geithus AS, Topping PM, et al.

BACKGROUND: N-terminal acetylation is a common protein modification in human cells and is catalysed by N-terminal acetyltransferases (NATs), mostly cotranslationally. The NAA10-NAA15 (NatA) protein complex is the major NAT, responsible for acetylating ~ 40% of human proteins. Recently, NAA10 germline variants were found in patients with the X-linked lethal Ogden syndrome, and in other familial or de novo cases with variable degrees of developmental delay, intellectual disability (ID) and cardiac anomalies.

METHODS: Here we report a novel NAA10 (NM_003491.3) c.248G > A, p.(R83H) missense variant in NAA10 which was detected by whole exome sequencing in two unrelated boys with intellectual disability, developmental delay, ADHD like behaviour, very limited speech and cardiac abnormalities. We employ in vitro acetylation assays to functionally test the impact of this variant on NAA10 enzyme activity.

RESULTS: Functional characterization of NAA10-R83H by in vitro acetylation assays revealed a reduced enzymatic activity of monomeric NAA10-R83H. This variant is modelled to have an altered charge density in the acetyl-coenzyme A (Ac-CoA) binding region of NAA10.

CONCLUSIONS: We show that NAA10-R83H has a reduced monomeric catalytic activity, likely due to impaired enzyme-Ac-CoA binding. Our data support a model where reduced NAA10 and/or NatA activity cause the phenotypes observed in the two patients

BMC Pediatr. 2019;19.

HANDWRITING IN CHILDREN WITH ATTENTION DEFICIENT HYPERACTIVE DISORDER: ROLE OF GRAPHOLOGY.

Cohen R, Cohen-Kroitoru B, Halevy A, et al.

Background: Handwriting difficulties are common in children with attention deficient hyperactive disorder (ADHD). The aim of our study was to find distinctive characteristics of handwriting in children with ADHD by using graphology to analyze physical characteristics and patterns, and to evaluate whether graphological analysis is an effective ADHD diagnostic tool for clinicians.

Method: The cohort included 49 children aged 13-18 years attending a tertiary neurology and epilepsy center in 2016-2017; 22 had a previous DSM-IV/V diagnosis of ADHD. The children were asked to write a 10-12-line story in Hebrew on a blank sheet of paper with a blue pen over a 20-min period. The samples were analyzed by a licensed graphologist blinded to the clinical details of the children against a predetermined handwriting profile of individuals with ADHD. Each ADHD characteristic identified in each sample was accorded 1 point, up to a total of 15 points. Patients with a graphology score of 9-15 were considered to have ADHD.

Results: There were 21 boys (43%) and 28 girls (57%) in the cohort; 15 boys (71.4%) and 7 girls (25%) had a DSM-IV/V diagnosis of ADHD. The mean graphology score was significantly higher in the children who had a DSM-IV/V diagnosis of ADHD than in the children who did not (9.61 ± 3.49 vs. 5.79 ± 4.01 , $p = 0.002$, respectively). Using a score of 9 as the cutoff, in the girls, graphology had a specificity of 80% (95% CI 59.2-92.8) and a sensitivity of 71.4% for predicting ADHD. Corresponding values in the boys were 75.0 and 76.2%.

Conclusion: The handwriting of children with ADHD has specific characteristics. Graphology may serve as a clinically useful tool in the diagnosis of ADHD

Brain Dev. 2019.

CHILDREN WITH AUTISM SPECTRUM DISORDER COMORBID WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER EXAMINED BY THE WISCONSIN CARD SORTING TEST: ANALYSIS BY AGE-RELATED DIFFERENCES.

Kado Y, Sanada S, Oono S, et al.

The DSM-5 confirmed that autism spectrum disorder (ASD) might be comorbid with attention-deficit/hyperactivity disorder (ADHD). This study investigated the executive function of ASD comorbid with ADHD (ASD + ADHD), ASD, and typically developed (TD) children using the Keio version of the modified Wisconsin card sorting test (KWCST). Children with ASD + ADHD ($n = 43$), ASD ($n = 69$), and TD ($n = 69$) were examined in two age groups: 5-9 years and 10-15 years. Both of the younger clinical groups showed significantly unfavorable scores for many indices in the second step compared to the TD group. As for the older groups, the ASD children showed significantly unfavorable scores in total errors in the second step, while the ASD + ADHD children did not show significant differences in either step. However, some index scores of the two older clinical groups were comparable to the older TD group in the second step. For the cognitive differences between clinical groups, the younger ASD + ADHD showed unfavorable scores in numbers of response cards until the first category achieved in the second step, while the older ASD showed unfavorable scores in categories achieved and perseverative errors of Nelson in the first step. For the degree of improvements in the second step, the older groups did not show significant group differences, while the younger ASD group showed significantly fewer improvements compared to the TD group. Based on these results, it is presumed that younger ASD + ADHD individuals are not sufficiently able to sustain attention and/or memory, and that the older ASD patients have difficulty in terms of flexibility

Brain Imaging Behav. 2019.

DIFFERENCES IN ATTENTIONAL CONTROL AND WHITE MATTER MICROSTRUCTURE IN ADOLESCENTS WITH ATTENTIONAL, AFFECTIVE, AND BEHAVIORAL DISORDERS.

Shafer AT, Benoit JR, Brown MRG, et al.

Adolescence is a critical time of physiological, cognitive, and social development. It is also a time of increased risk-taking and vulnerability for psychopathology. White matter (WM) changes during adolescence have been better elucidated in the last decade, but how WM is impacted by psychopathology during this time remains unclear. Here, we examined the link between WM microstructure and psychopathology during adolescence. Twenty youth diagnosed with affective, attentional, and behavioral disorders (clinical sample), and 20 age-matched controls were recruited to examine group differences in WM microstructure, attentional control, and the link between them. The main results showed that clinical sample had relatively lower attentional control and fractional anisotropy (FA) in WM throughout the brain: two association tracts were identified, and many differences were found in areas rich in callosal and projection fibers. Moreover, increased FA was positively associated with attention performance in the clinical sample in structures supporting ventral WM pathways, whereas a similar link was identified in controls in dorsal WM association fibers. Overall, these results support a model of general impairment in WM microstructure combined with reliance on altered, perhaps less efficient, pathways for attentional control in youth with affective, attentional, and behavioral disorders

British Journal of Oral and Maxillofacial Surgery. 2019;57:e24-e25.

LISDEXAMFETAMINE (VYVANSE) WITHDRAWAL IN CHILDREN WITH OROFACIAL CLEFT AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Patel S, Schmidt C, Blancher A, et al.

Stimulants are the first line of therapy for attention-deficit/hyperactivity disorder (ADHD) in children 6 years and older. Vyvanse is a long acting prodrug stimulant with well-established safety, tolerability and efficacy, when compared to other stimulants such as amphetamine and methylphenidate, and non-stimulants such as atomoxetine, guanfacine, and clonidine. Treatment related adverse events for stimulant drugs in all age groups have been reported in great detail, but there is limited data available in the literature regarding withdrawal symptoms from acute cessation or dose reduction in children. In this paper, we present a case history and review of literature regarding diagnosis and treatment of acute withdrawal of stimulants in a pediatric population. The case history involves an 8 year old male with a history of ADHD and unilateral complete cleft lip and palate, who underwent a superiorly based pharyngeal flap reconstruction for velopharyngeal insufficiency. Pre-operatively his ADHD symptoms were managed with daily use of Vyvanse. Immediate post-operative period was complicated by respiratory compromise followed by complete recovery and readmission to the hospital for altered mental status, and other signs and symptoms of acute stimulant withdrawal. Children with orofacial clefts have increased diagnosis of ADHD and other psychosocial conditions. Acute cessation of chronically used long acting prodrug stimulant can cause withdrawal in children. Withdrawal symptoms in children are variable and different than in their adult counterpart. Clinicians treating children with orofacial clefts should be aware of stimulant withdrawal signs and symptoms to prevent delay in diagnosis and treatment

Chemosphere. 2020;244.

PRENATAL SERUM THALLIUM EXPOSURE AND 36-MONTH-OLD CHILDREN'S ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS: MA'ANSHAN BIRTH COHORT STUDY.

Tong J, Liang C-M, Huang K, et al.

Thallium (Tl) is a highly toxic heavy metal that has been suggested to be responsible for oxidative stress and mitochondrial dysfunction. However, few studies have focused on the relationship of prenatal Tl exposure with children's neurobehavioural development. The purpose of our study was to investigate the association between prenatal Tl exposure and attention-deficit/hyperactivity disorder (ADHD) symptoms in 36-month-old children. We used data from 2851 mother-newborn pairs from the Ma'anshan Birth Cohort Study (MABC);

serum TI concentration was assessed in the first, second and third trimesters of pregnancy as well as in the umbilical cord blood. We assessed ADHD symptoms in the children using the Chinese version of the Conners abbreviated symptom questionnaire (C-ASQ). The adjusted odds ratio (OR) for the risk of ADHD symptoms was 2.00 [95% confidence interval (CI): 1.20, 3.32] and 2.08 (95% CI: 1.26, 3.43) for the third (60.25–75.21 ng/L) and fourth quartiles of serum TI (>75.21 ng/L), respectively, in the second trimester of pregnancy, in comparison with the first quartile of serum TI (<50.86 ng/L). The risk of ADHD symptoms was elevated among boys exposed to the fourth quartile of serum TI in the second trimester of pregnancy (adjusted OR 2.08, 95% CI: 1.13, 3.83). Our results demonstrated that high levels of TI exposure in the second trimester of pregnancy were related to a higher risk of ADHD symptoms in 36-month-old children, and the association of higher serum TI exposure in the second trimester with ADHD symptoms was only found in boys

Child Psychiatry Hum Dev. 2019 Dec;50:1049-57.

SLOW PROCESSING SPEED AND SLUGGISH COGNITIVE TEMPO IN PEDIATRIC ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: EVIDENCE FOR DIFFERENTIATION OF FUNCTIONAL CORRELATES.

Cook NE, Braaten EB, Vuijk PJ, et al.

The association between slow processing speed and sluggish cognitive tempo (SCT), a phenotype described within attention-deficit/hyperactivity disorder (ADHD) samples over the past decade, remains unclear. We examined whether SCT and processing speed predict different functional correlates within children and adolescents with ADHD. Participants were 193 clinically-referred youth meeting DSM ADHD criteria without comorbid conditions (mean age = 9.9 years, SD = 2.5; age range 6–16). The incremental utility of SCT and processing speed to predict (1) adaptive functioning and (2) academic achievement, after controlling for age, sex, medication status, and ADHD symptom burden, was assessed using hierarchical multiple regressions. SCT symptoms significantly predicted adaptive functioning, accounting for 6% of the variance, but did not predict academic achievement. Processing speed did not add incrementally to the prediction of adaptive functioning, but did predict academic achievement, accounting for 4% of the variance. Results suggest that SCT and processing speed differentially predict functional abilities not accounted for by ADHD symptom burden

Child Psychiatry Hum Dev. 2019 Dec;50:918-26.

DO COMORBID OPPOSITIONAL SYMPTOMS PREDICT ADHD BEHAVIORAL TREATMENT OUTCOMES?

Elkins SR, Bond MA, Curtis DF.

Parent management training (PMT) is considered a best-practice for treating childhood ADHD. However, the magnitude of change in response to PMT differs across individuals. This study examined comorbid oppositional symptoms as a predictor of ADHD treatment outcomes. We predicted children with more severe baseline oppositionality would exhibit greater improvements in externalizing behaviors overall, including core ADHD symptoms. Participants consisted of 67 children aged 7–10 diagnosed with ADHD-Combined Type. Participants and their families received a manualized ten-session intervention, Family Skills Training for ADHD-Related Symptoms (Family STARS), combining PMT with a simultaneously occurring child skills training intervention. Pre- and post-treatment parent and teacher rating scales were collected to assess changes in ADHD and oppositional symptoms. Results demonstrated that children with more severe ratings of oppositional behaviors achieved commensurate ADHD symptom outcomes compared to those with less severe oppositionality. Implications are discussed with regard to the utilization of ADHD impairment-specific treatment targets

CNS Drugs. 2019.

PSYCHOSTIMULANTS/ATOMOXETINE AND SERIOUS CARDIOVASCULAR EVENTS IN CHILDREN WITH ADHD OR AUTISM SPECTRUM DISORDER.

Houghton R, de VF, Loss G.

Background: Psychostimulants and atomoxetine have been shown to increase blood pressure, heart rate, and QT interval in children and adolescents; however, based on current literature, it is unclear if these attention-deficit/hyperactivity disorder (ADHD) medications are also associated with serious cardiovascular (SCV) events. We addressed this question in commonly exposed groups of children and adolescents with either ADHD or autism spectrum disorder (ASD).

Methods: Using commercial (years 2000-2016) and Medicaid (years 2012-2016) administrative claims data from the United States (US), we conducted two case-control studies, nested within respective cohorts of ADHD and ASD children aged 3-18 years. We defined cases by a composite outcome of stroke, myocardial infarction, or serious cardiac arrhythmia. For each case, we matched ten controls on age, sex, and insurance type. We conducted conditional logistic regression models to test associations between SCV outcomes and a primary exposure definition of current ADHD medication use. Additionally, we controlled for resource use, cardiovascular and psychiatric comorbidities, and use of medications in a variety of sensitivity analyses.

Results: We identified 2,240,774 children for the ADHD cohort and 326,221 children for the ASD cohort. For ADHD, 33.9% of cases (63 of 186) versus 32.2% of controls (598 of 1860) were exposed, which yielded an odds ratio (OR) and 95% confidence interval (CI) of 1.08 (0.78-1.49). For ASD, 12.5% of cases (6 of 48) versus 22.1% of controls (106 of 480) were exposed [OR 0.49 (0.20-1.20)]. Covariate-adjusted results and results for individual outcomes and other exposure definitions were consistent with no increased risk of SCV events.

Conclusion: Using large US claims data, we found no evidence of increased SCV risk in children and adolescents with ADHD or ASD exposed to ADHD medications

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Codas. 2019;31:e20180197.

ORAL NARRATIVE STRUCTURE AND COHERENCE OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Zenaro MP, Rossi NF, Souza ALDM, et al .

PURPOSE: This study aimed to characterize and compare the use of typical story grammar elements and global coherence level in the oral narrative of children with Attention Deficit Hyperactivity Disorder with the narrative of children without the disorder and with typical development.

METHODS: A total of 40 children of both sexes aged 5 to 10 years who attended elementary school participated in the study, 20 of whom were diagnosed with Attention Deficit Hyperactivity Disorder (ADHD Group), and 20 with typical development (TD Group). Participants from each group were similar in sex, chronological age, schooling and socioeconomic status. The wordless picture book Frog, Where Are You? was used to elicit the oral narrative analyzed for the presence of the main typical elements of the story schema (character, theme/topic, event/plot and outcome), and afterwards their narration was classified according to four different levels of organization corresponding to the global story coherence level.

RESULTS: The ADHD Group presented lower scores on the structural elements "theme/ topic" and "outcome" and a narrative with lower degree of coherence compared to the TD Group.

CONCLUSION: The children with ADHD included in this study presented difficulties to use typical story grammar elements, mainly related to the maintenance of the central theme and outcome of the story. These elements are considered fundamental for construction of narrative coherence, which justifies the lower levels of global coherence found in the oral narrative of the ADHD Group

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Cyberpsychol Behav Soc Netw. 2019 Sep;22:588-96.

INTERACTIVE AVATAR BOOSTS THE PERFORMANCES OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER IN DYNAMIC MEASURES OF INTELLIGENCE.

Fabio RA, Capri T, Iannizzotto G, et al.

This study examined both children with attention deficit hyperactivity disorder (ADHD) and typically developing students in dynamic measures of intelligence through the use of a virtual avatar. Three conditions were compared: in the first condition, the avatar simply gave the instructions; in the second condition, the avatar presented the instructions and gave feedback on the attention of the learner; in the third condition, the avatar was not presented. Results indicated that ADHD subtypes do not differ in problem solving and the interactive avatar improved the performance of groups with ADHD in the dynamic intelligence test. Overall, these results support the hypothesis that the function of regulation and feedback of the avatar improve the attention process and, consequently, boosts performance

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Depress Anxiety. 2019 Jun;36:533-42.

THE IMPACT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN OBSESSIVE-COMPULSIVE DISORDER SUBJECTS.

Blanco-Vieira T, Santos M, Ferrao YA, et al.

BACKGROUND: Recent findings suggest an association between attention deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD). Thus, we evaluated the clinical associated features of ADHD in a large sample of adult OCD patients.

METHODS: A cross-sectional study including 955 adult patients with OCD from the Brazilian Research Consortium of Obsessive-Compulsive Spectrum Disorders (C-TOC). Clinical characteristics in adult OCD patients with and without comorbid ADHD were compared using Fisher's exact test, t-tests or Mann-Whitney tests. Bivariate analyses were followed by logistic regression analysis to identify clinical characteristics independently associated with ADHD comorbidity.

RESULTS: The lifetime prevalence of ADHD in adult OCD patients was 13.7%. The current results indicate that OCD + ADHD patients were more severe, had an earlier onset of the obsessive-compulsive symptoms, a higher history of rheumatic fever, with higher frequencies of sensory phenomena and comorbidity with Tourette syndrome. They also had an increased risk for academic impairment and suicide attempts.

CONCLUSION: Adult OCD patients with ADHD present some specific clinical features and may represent a special subgroup of adult OCD. Future studies should focus on the development of interventions more tailored to the phenotype of this subgroup of patients

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Dev Neuropsychol. 2019 Nov;44:554-65.

EVENT-, TIME- AND ACTIVITY-BASED PROSPECTIVE MEMORY IN CHILDREN WITH ADHD.

Yang Tx, Wang YY, Wang Y, et al.

We examined prospective memory (PM) function in children with attention deficit hyperactivity disorder (ADHD). A group of 28 children with ADHD and 28 typically developing children completed event-, time- and activity-based PM tasks and attention tests. ADHD children had impaired attention but intact PM performance. Both groups performed best in activity-based PM tasks, followed by event-based PM tasks, and performed worst in time-based PM tasks. ADHD children had lower ongoing task performance in the event-based PM task. The findings indicate that children with ADHD may have an intact PM, but this may be at the cost of ongoing task performance

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Drug Alcohol Depend. 2019 Jun;199:59-67.

PARENTAL VIEWS ON STATE CANNABIS LAWS AND MARIJUANA USE FOR THEIR MEDICALLY VULNERABLE CHILDREN.
Wisk LE, Levy S, Weitzman ER.

BACKGROUND: Given a rapidly changing policy landscape, we sought to characterize the effects of state marijuana laws on parents' views of marijuana use by their teenage children.

METHODS: Data are from 595 respondents to a nationally administered, web-based survey of parents of adolescents (ages 13-18 years) with any of three chronic conditions (type 1 diabetes, rheumatic disease, attention-deficit/hyperactivity disorder). Multivariate ordinal logistic regression was used to model the effects of parents' reports of state cannabis laws on their views toward marijuana use by their child.

RESULTS: While 89.9% said any marijuana use was risky for their child, 27.9% would approve of its use if prescribed as medicine. Parents reporting marijuana decriminalization (11.1%) were more amenable to teenage use, less concerned about how marijuana might impact their child's condition, more accepting of the safety of marijuana as medicine, and approved its use with a prescription. Parents reporting legal medical (35.6%) or recreational (5.7%) use were more likely to report that their child has tried or used marijuana regularly. Parents reporting legal recreational use were less likely to agree that marijuana has medical benefits for their child.

CONCLUSIONS: Among parents of medically vulnerable children, perceiving state marijuana policies as more permissive is strongly associated with lower perceived riskiness of marijuana use for their children. State marijuana policies are changing with implications for how parents of medically vulnerable youth view and potentially govern marijuana use by their medically vulnerable children

Environ Health Prev Med. 2019;24.

PRENATAL TOBACCO EXPOSURE AND ADHD SYMPTOMS AT PRE-SCHOOL AGE: THE HOKKAIDO STUDY ON ENVIRONMENT AND CHILDREN'S HEALTH.

Minatoya M, Araki A, Itoh S, et al.

Background: There have been inconsistent findings reported on maternal passive smoking during pregnancy and child risk of ADHD. In this study, ADHD symptoms at pre-school age children in association with prenatal passive and active tobacco smoke exposure determined by maternal plasma cotinine levels in the third trimester were investigated.

Methods: This was a follow-up study of the birth cohort: the Hokkaido Study on Environment and Children's Health. Children whose parents answered Strengths and Difficulties Questionnaire (SDQ) to identify child ADHD symptoms (hyperactivity/inattention and conduct problems) and total difficulties at age 5 years with available maternal plasma cotinine level at the third trimester were included (n = 3216). Cotinine levels were categorized into 4 groups; 0.21 ng/ml (non-smoker), 0.22-0.51 ng/ml (low-passive smoker), 0.52-11.48 ng/ml (high-passive smoker), and 11.49 ng/ml (active smoker).

Results: Maternal cotinine levels of active smokers were significantly associated with an increased risk of total difficulties (OR = 1.67) and maternal low- and high-passive smoking also increased the risk (OR = 1.11, 1.25, respectively) without statistical significance. Similarly, maternal cotinine levels of active smokers were associated with an increased risk of hyperactivity/inattention (OR = 1.49). Maternal low- and high-passive smoking and active smoking increased the risk of hyperactivity/inattention (OR = 1.45, 1.43, and OR = 1.59, respectively) only in boys.

Conclusion: Our findings suggested that maternal active smoking during pregnancy may contribute to the increased risk of child total difficulties and hyperactivity/inattention at pre-school age. Pregnant women should be encouraged to quit smoking and avoid exposure to tobacco smoke

Environ Res. 2019.

EXPOSURE TO AIR POLLUTION IN EARLY CHILDHOOD AND THE ASSOCIATION WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Thygesen M, Holst GJ, Hansen B, et al.

Background: Exposure to air pollution in early life has been linked to cognitive deficits and adverse neurodevelopmental effects. However, studies examining associations between air pollutants and Attention-Deficit/Hyperactivity Disorder (ADHD) have had conflicting findings.

Methods: Individuals born in Denmark 1992–2007 ($n = 809,654$) were followed for the development of ADHD from 1997 to 2013. Data on daily concentrations of nitrogen dioxide (NO₂) and fine particulate matter (PM_{2.5}) from air-modeling data at a 1 km resolution at residences within the first five years of life, was linked with population-based data from the Danish national registers, including data on clinical diagnoses of ADHD. We estimated incidence rate ratios (IRRs) with 95% confidence intervals (CI) for ADHD, according to increases in exposures, adjusting for age, year, sex, and parental education and income.

Results: Exposure to NO₂ and PM_{2.5} during early life was associated with a significantly increased risk of ADHD: IRR of 1.38 (CI: 1.35 to 1.42) per 10 $\mu\text{g}/\text{m}^3$ increase in NO₂ and an IRR of 1.51 (CI: 1.41 to 1.62) per 5 $\mu\text{g}/\text{m}^3$ increase in PM_{2.5}. In two-pollutant models, the association between NO₂ and ADHD did not change (IRR 1.35; 95% CI: 1.31 to 1.39), while the association with PM_{2.5} was substantially attenuated (IRR 1.07; 95% CI: 0.98 to 1.16), although in stratified models an elevated association with PM_{2.5} was found in the lowest quintile of NO₂ exposure.

Conclusions: In this large nationwide prospective cohort study, residential air pollution exposure, specifically NO₂, during early childhood was associated with the development of ADHD, even when adjusted for parental level of income and education

Eur Child Adolesc Psychiatry. 2019.

ADHD SYMPTOMS ACROSS ADOLESCENCE: THE ROLE OF THE FAMILY AND SCHOOL CLIMATE AND THE DRD4 AND 5-HTTLPR GENOTYPE.

Brinksma DM, Dietrich A, de BA, et al.

We examined bidirectional relations between attention-deficit/hyperactivity disorder (ADHD) symptoms and family and school climate, and the possible role of DRD4 and/or 5-HTTLPR genotypes herein. Three-wave longitudinal data of 1860 adolescents (mean ages 11, 13.5, and 16-áyears) from the general population and clinic-referred cohort of TRacking Adolescents' Individual Lives Survey were used. Using a multigroup Random Intercept Cross-Lagged Panel Model, we tested between-person (i.e., stable trait levels) and within-person (i.e., causal processes) associations across ADHD symptoms, family and school climate, and the extent to which these depended on genotype. Findings indicated no influence of genotype. Results did show significant between-person differences (ADHD symptoms with family climate $r = .38$; and school climate $r = .23$, p values $< .001$), indicating that higher stable levels of ADHD symptoms were associated with a less favorable family and school climate. Regarding within-person causal processes, ADHD symptoms predicted a less favorable family climate in early adolescence ($\beta = .16$, $p < .01$), while ADHD symptoms predicted a more favorable family climate in the later phase of adolescence ($\beta = -.11$, $p < .01$), a finding which we explain by normative developmental changes during adolescence. Overall, this study showed that negative associations between ADHD symptoms and both family and school climate are largely explained by stable between-person differences. We recommend applying the Random Intercept Cross-Lagged Path Model to developmental data to tease stable associations and change processes apart

Eur Child Adolesc Psychiatry. 2019.

DOES HELPING MOTHERS IN MULTIGENERATIONAL ADHD ALSO HELP CHILDREN IN THE LONG RUN? 2-YEAR FOLLOW-UP FROM BASELINE OF THE AIMAC RANDOMIZED CONTROLLED MULTICENTRE TRIAL.

Geissler JM, Vloet TD, Strom N, et al.

ADHD often affects multiple generations in a family. Previous studies suggested that children with ADHD benefit less from therapy if parents are also affected, since ADHD symptoms interfere with treatment implementation. This two-group randomised controlled trial examined whether targeting maternal ADHD boosts the efficacy of parent-child training (PCT) for the child's ADHD. Here, we report follow-up results 2-years from baseline. Mothers of 144 mother-child dyads (ADHD according to DSM-IV) were examined for eligibility (T1) and randomised to 12-weeks of intensive multimodal treatment comprising pharmacotherapy and DBT-based cognitive behavioural group psychotherapy (TG, n = 77) or clinical management comprising non-specific counselling (CG, n = 67) for Step 1 (concluded by T2). Subsequently, all dyads participated in 12 weekly PCT sessions for Step 2 (concluded by T3). In Step 3, participants received maintenance treatments for 6-months (concluded by T4). At 24-months after baseline (T5), we performed follow-up assessments. The primary endpoint was child ADHD/ODD score (observer blind rating). Outcomes at T5 were evaluated using ANCOVA. Assessments from 101 children and 95 mothers were available at T5. Adjusted means (m) of ADHD/ODD symptoms (range 0-26) in children did not differ between TG and CG (mean difference = 1.0; 95% CI 1.2-3.1). The maternal advantage of TG over CG on the CAARS-O:L ADHD index (range 0-36) disappeared at T5 (mean difference = 0.2; 95% CI 2.3 to 2.6). Sensitivity analyses controlling for medication and significant predictors of follow-up participation showed unchanged outcomes. Within-group outcomes remained improved from baseline. At the 24-month follow-up, TG and CG converged. The superiority of intensive treatment regarding maternal symptoms disappeared. In general, cross-generational treatment seems to be effective in the long term. (BMBF grant 01GV0605; registration ISRCTN73911400)

Eur Child Adolesc Psychiatry. 2019.

SLUGGISH COGNITIVE TEMPO AND PROCESSING SPEED IN ADOLESCENTS WITH ADHD: DO FINDINGS VARY BASED ON INFORMANT AND TASK?

Becker SP, Marsh NP, Holdaway AS, et al.

Few studies have examined whether behavioral sluggish cognitive tempo (SCT) symptoms are related to speeded task performance. Mixed findings in existing research could be due to previous studies using a broad conceptualization of processing speed, not including self-report of SCT symptoms, and relying on non-optimal measures of SCT. Using a multi-informant design with both parent- and adolescent-reported SCT symptoms, the present study provides a preliminary test of the hypothesis that SCT symptoms would be associated with slower performance on tasks having greater graphomotor and fine motor demands. Participants were 80 adolescents (ages 13-17 years; 71% male) with attention-deficit/hyperactivity disorder (ADHD). Adolescents and parents completed ratings of SCT. Adolescents were administered the Wechsler Symbol Search and Coding subtests and the Grooved Pegboard Test. When adjusting for age, sex, and ADHD symptom severity, parent-reported SCT symptoms were not significantly associated with Symbol Search or Coding scores but were significantly associated with slower Grooved Pegboard time. Adolescent-reported SCT symptoms were not significantly associated with Symbol Search but were significantly associated with lower Coding scores and slower Grooved Pegboard time. Findings provide preliminary support for the hypothesis that SCT may be more clearly associated with processing speed task performance as motor demands increase and provide a potential explanation for the mixed literature on SCT in relation to processing speed by demonstrating that the presence and magnitude of associations vary by informant and task

Eur Child Adolesc Psychiatry. 2019.

PREVALENCE, COMORBIDITIES, AND SOCIODEMOGRAPHIC PREDICTORS OF CONDUCT DISORDER: THE NATIONAL EPIDEMIOLOGY OF IRANIAN CHILDREN AND ADOLESCENTS PSYCHIATRIC DISORDERS (IRCAP).

Salmanian M, Mohammadi MR, Hooshyari Z, et al.

The aim was to evaluate the lifetime prevalence of conduct disorder according to sociodemographic characteristics, determine the sociodemographic predictors of conduct disorder, and estimate the rates of comorbidities of psychiatric disorders in children and adolescents with conduct disorder by age and gender. The National Epidemiology of Iranian Children and Adolescents Psychiatric Disorders was a cross-sectional, general population-based study on 30,532 children and adolescents aged 6-18 years from all provinces of Iran, which was done using multistage cluster sampling. Iranian citizens aged 6-18 years who resided at least 1 year in each province were included, and children and adolescents with severe physical illnesses that prevented them to participate in the study were excluded. The sample weighting adjustment was used, since we had randomly selected the equal number of 1000 participants of each province from the urban and rural areas. Trained psychologists conducted diagnostic interviews with the adolescents and the children's parents using the Persian version of the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children Present and Lifetime Version (K-SADS PL). In this study, 54 children aged 6-9 years (0.58%, CI 0.47-0.77), 64 adolescents aged 10-14 years (0.57%, CI 0.47-0.77), and 117 adolescents aged 15-18 years (1.22%, CI 0.96-1.44) met the criteria of the lifetime conduct disorder. Conduct disorder was significantly more common in boys than in girls, and was significantly less prevalent among those participants whose fathers had no history of psychiatric hospitalization. Of the participants with conduct disorder, 83.4% met the criteria for at least one other psychiatric disorder. Conduct disorder had a high rate of comorbidity with oppositional defiant disorder (54.89%, CI 48.50-61.12), attention-deficit/hyperactivity disorder (32.34%, CI 26.68-38.56), tobacco use (20.43%, CI 15.77-26.04), and depressive disorders (18.30%, CI 13.88-23.74). Because of using the diagnostic instrument, we found a low total rate of prevalence for conduct disorder; however, higher rates of it were observed among boys and adolescents. Further studies are needed to explore the nature of comorbidities of conduct disorder and to consider them in a large clinical population

Eur Neuropsychopharmacol. 2019;29:S375-S376.

P.533 SLEEP AND COGNITIVE FUNCTIONS IN TYPICALLY DEVELOPING AND DRUG-NA+»VE ADHD CHILDREN.

Darchia N, Tchintcharauli T, Basishvili T, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorder occurring in about 5 % of children. Children with ADHD often report sleep problems, sleep-wake instability and cognitive difficulties [1]. The study of sleep and cognitive profile in ADHD children remains area of a significant attention in Neuroscience and clinical research. Findings are inconclusive regarding sleep pattern differences between ADHD and control subjects. Whether or not sleep difficulties originate as a consequences of stimulant medications, is not documented. Furthermore, the impact of sleep on cognitive and behavioral functioning in ADHD children is unclear [2]. We present first time point results from the longitudinal study aimed to investigate differences in sleep architecture, sleep EEG and executive functioning measures in drug-na+»ve ADHD and typically developing children.

Method: Nine ADHD children (combined subtype according to DSM-V criteria, mean age 12.4-10.54 years) without any additional comorbid condition or sleep disordered breathing problem, and eight typically developing controls (12.1-10.37 years) were recruited. All subjects underwent an adaptation night and all night polysomnography at the Laboratory. During the week prior to recordings, actigraphy devices documented sleep-wake schedules. Cognitive performance was tested by Raven's Progressive Matrices Test and Wechsler Nonverbal Scale of Ability (WNV). Executive functioning was assessed by the Comprehensive Executive Function Inventory (CEFI, parent form). Descriptive, comparative and correlation analyses were performed. Significance was set at $p < 0.05$.

Results: Both groups showed high sleep efficiency. Total sleep time (TST) was lower in ADHD group (463.8 vs. 533.5min) but the difference did not reach significance ($p = 0.06$). No significant effect was found on sleep stages 1-3 and REM measures (% of TST). ADHD children had higher (2.64 vs. 1.97 per hour) but non-significant ($p = 0.249$) awakening index during sleep. Latency to stage 2 (ADHD = 15.3 min, control = 8.6 min) was the only measure to differ significantly ($p = 0.01$). REM latency was lower in ADHD group (70.2 vs. 81.4

min) but non-significant ($p=0.129$). Theta (4-7.91Hz) to beta (14.94-29.98Hz) ratio (power per minute in all night EEG) measured in central deviation did not differ between groups in REM sleep and approached significance in NREM sleep (11.6 vs. 14.4, $p=0.07$). ADHD children had poorer executive function behaviors on CEFI measures. All subscales and CEFI full scale was significantly ($p<0.01$ for all measures) lower in ADHD group. However, there was no difference on WNV nor on Raven's tests. Theta to beta ratio in NREM sleep was correlated with several CEFI subscales in both groups; REM latency was correlated with emotion regulation, flexibility and inhibitory control in controls. Activity counts per minute during the executive functioning measurement sessions was significantly higher in ADHD children and correlated with most of cognitive measures.

Conclusion: Drug-naïve ADHD children do not display a significant alteration in sleep parameters, and there is only weak evidence of an impact of sleep on executive functioning behavior. Follow-up results of this longitudinal study is crucial to examine the unique sleep patterns of ADHD children and to clarify the trajectory of the relationship between sleep, cognitive functioning and ADHD symptoms.

Disclosure statement: Funding: SRNSF grant_FR17_94

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P.831 METHYLPHENIDATE AND INHIBITION IN CHILDREN WITH ADHD: A META-ANALYSES ON DOSAGE EFFECTS.

Vertessen K.

Background: Attention-deficit/hyperactivity disorder (ADHD) has been associated with a broad range of neurocognitive deficits, with response inhibition as one of the most frequently reported functions playing a central role in etiological models of ADHD [1]. Methylphenidate (MPH), the preferred pharmacological treatment for ADHD in children and adolescents, is found to ameliorate neurocognitive deficits [2]. Group effects of MPH-dose on behavioral symptom reduction show a linear effect (higher dose, larger reduction) [3] although at an individual level best-dose levels are evenly distributed between low- medium and high doses [4]. For neurocognitive outcomes dose-effects are less studied and both linear and quadric dose-response curves (with the best outcomes on medium dosages) for response inhibition have been reported [5] This meta-analysis was aimed to elucidate MPH-dose effects on neurocognitive functioning in children with ADHD.

Methods: Electronic databases were searched to identify published placebo controlled trials that compared MPH (fixed) dosages with placebo on response inhibition tasks in children and adolescents (5-18 years) with a formal diagnosis of ADHD (DSM III-R, IV en 5). The fixed dosages were categorized as low, medium and high doses and compared with placebo. With low doses range: 0,10 mg/kg- 0,39 mg/kg, medium doses range: 0,40 mg/kg - 0,69 mg/kg and high dose range: 0,70 mg/kg - 0,99 mg/kg.

Results: Nineteen studies, including 34 inhibition measures, fulfilled inclusion criteria and were included in our meta-analysis. Methylphenidate was superior to placebo in all analyses: Medium doses had the strongest effects on improving inhibition with low dose: (Cohen's $d=-0,27$, 95% CI: -0,45- -0,09, $p<0,005$), medium dose: (Cohen's $d=-0,32$, 95% CI: -0,48- -0,15, $p<0,001$) high dose (Cohen's $d=-0,22$, 95% CI: -0,47- 0,03, $p<0,082$).

Conclusions: These data support potentially important dose-dependent effects of MPH on inhibition in children with ADHD. Medium doses of MPH have the largest effects on inhibition, with a decrease of the effect for the high doses. This suggest that titration with an optimal result on ADHD symptoms does not ensure an optimal effect on neurocognitive outcomes. Considering the complex relationship between ADHD symptoms, cognition and academic performance and the role of executive functioning in academic performance these findings can be clinical relevant and consideration should be given to adding cognitive outcomes to the treatment outcomes of pharmacological therapy for ADHD

Eur Neuropsychopharmacol. 2019;29:S590-S591.

C.02.01 MANAGING ADHD AND COMORBID ANXIETY DISORDERS.

Klassen L.

Individuals with ADHD are at high risk for comorbid anxiety disorders, with rates approaching 50% [1]. Individuals with anxiety disorders and comorbid ADHD tend to have more severe anxiety symptoms, an earlier age of onset for anxiety, and more frequent comorbid psychiatric conditions, including substance use [2]. The diagnosis for ADHD tends to be delayed in those with anxiety, and treatment can be more difficult for both conditions. The comorbidity of ADHD with anxiety disorders may be seen as sharing neurobiological deficits related to top-down regulation and poor prefrontal activity. The dorsolateral prefrontal cortex (dlPFC), anterior cingulate cortex (ACC), parietal cortex and insula cortex contribute to prefrontal dysfunction, and as part of the frontal-parietal executive control network they are also critically involved in executive function. Anatomical findings in children with ADHD support this model, as there is a delay in maturation of the cortex in general, with the greatest delays being in the dlPFC and ACC [3]. Diagnosis of ADHD with comorbid anxiety can also be complicated by shared symptoms. Symptoms can be attributed to a comorbid condition without considering the contribution of underlying ADHD to pathology. Similarly, treatment of one condition can ignore comorbid conditions, and contribute to a failure to achieve remission. However, treating underlying ADHD has been shown to improve the outcome of both ADHD and comorbid conditions. Early, optimized treatment of ADHD may also prevent the later development of psychiatric comorbidities [4]. Disclosure statement: Grants/Research Support: Eden Mental Health Centre, Janssen, Shire Speakers Bureau/Honoraria: Allergan, CADDRA, CPA, Janssen, Lundbeck, Otsuka, Pfizer, Purdue, Shire, Sunovion Consulting Fees: Allergan, Iron Shore, Janssen, Lundbeck, Otsuka, Pfizer, Purdue, Shire, Sunovion

Eur Neuropsychopharmacol. 2019;29:S176-S177.

P.229 CLINICAL UTILITY OF TWO SENSITIVITY/SPECIFICITY-MAXIMIZED CUT-OFF SCORES OF THE WORLD HEALTH ORGANIZATION ADHD SELF-REPORT SCALE FOR ADOLESCENTS (ASRS-A).

Fernandez-Quintana A, Olofsdotter S, Vadlin S, et al.

Introduction: Attention-deficit hyperactivity disorder (ADHD) has a lifetime prevalence of 4-11% among adolescents [1] and results in pervasive functional impairment [2]. The World Health Organization Adult Self-Report Scale (ASRS) is a valid and reliable assessment tool for screening of ADHD symptoms in adults [3]. The adolescent version consists of 18 items (ASRS-A-18) and has shown adequate psychometric properties in adolescent populations [4]. Kessler et al [5] recommended a dichotomized summation method and proposed a cut-off score of 9 for the ASRS. The clinical utility of the ASRS-A-18 may be enhanced by using the total score and several cut-off scores tailored to meet specific objectives such as high sensitivity or high specificity. Aims: To determine adequate clinical cut-off points of the ASRS-A-18 total score for the detection and identification of ADHD in psychiatrically referred adolescents.

Method: Cross-sectional, diagnostic accuracy study in a sample of adolescent psychiatric outpatients (N = 104, mean age 15.7 years, 38.5% boys). The participants reported on the ASRS-A-18 and were interviewed with the Kiddie Schedule of Affective Disorders and Schizophrenia (K-SADS), together with a parent. Receiver operating characteristic (ROC) analyses were used to identify two clinical cut-off scores, a screening cut-off (minimum sensitivity of .90), and a diagnostic cut-off (minimum specificity of .90). The K-SADS interviewers (N = 5) showed an inter-rater-reliability of 0.87 for an ADHD diagnosis. The data collection took place from September 2011 to June 2013 and the sample was recruited from two Swedish cities (Västerås and Sala).

Results: The mean age was 15.73 years old, 61.5% were girls. According to K-SADS, 53 participants (51%) met the diagnostic criteria for ADHD (52.8% were boys). The mean ASRS-A-18 score was 34.37 points (score range: 0-72). The Area Under the Curve (AUC) for ASRS-A-18 was =0.75 (95% CI= 0.66-0.85). Considering a screening cut-off score of ≥ 25 points, the ASRS-A-18 showed a sensitivity of 90.57%, specificity 37.25%, Positive Predictive Value (PPV) of 60%, Negative Predictive Value (NPV) of 79.17%, and an overall correct classification of 64.42%. Assuming a diagnostic cut-off score of ≥ 45 points, the ASRS-A-18 showed a specificity of 92.16%, sensitivity 33.96%, PPV 81.82%, NPV 57.32%, and an overall correct classification of 62.50%.

Conclusions: The clinical utility of the new identified cut-off scores of the ARSR-A-18 for the purposes of screening and identification of ADHD in adolescents is promising. The screening cut-off (≥25 score points) correctly identified 90% of adolescents with an ADHD diagnosis. The diagnostic cut-off (≥45 score points) increased the probability of an ADHD-diagnosis with 30 percentage points from 51% to 82%. Likewise, a score below the screening cut-off score decreased the probability of an ADHD-diagnosis with 30 percentage points from 51% to 21 %. In clinical settings, the screening and diagnostic cut-off scores can be combined into a tertile, three-group categorization to enhance the detection of clinical and subclinical levels of ADHD-symptoms in psychiatrically referred adolescents

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Eur Neuropsychopharmacol. 2019;29:S551-S552.

P.829 TRANSCRANIAL-DIRECT CURRENT STIMULATION ON ATTENTION AND INHIBITORY CONTROL OF CHILDREN AND ADOLESCENTS WITH ADHD: A RANDOMIZED, CROSSOVER, TRIPLE-BLIND, SHAM-CONTROLLED STUDY.

Guimaraes RSQ, Bandeira ID, Barretto BL, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is a developmental disorder characterized by inadequate levels of inattention, hyperactivity and impulsivity. According to the American Academy of Pediatrics, different areas of the child's life may be compromised as a result of ADHD, such as academic performance, interpersonal relationships and well-being, raising the need for effective treatment. The main current therapeutic strategies are based in psychostimulants and behavioral therapies. However, there have been reports in the literature of adverse effects in children and adolescents with the use of some of these medications, among them increased blood pressure and heart rate, insomnia and reduced appetite. The pilot open label trial conducted by Bandeira et al [1] showed improvement in some executive functions such as selective attention and inhibitory control using tDCS in nine children and adolescents with ADHD. However, further studies with appropriate randomization, blinding, and larger sample sizes should be performed to further investigate these findings.

Objectives: The main objective of this study is to widen the scope of the previous investigation and to prove reproducibility of the findings as well as ensure safety of the technique in this population, investigating the effect of tDCS on the performance of children and adolescents with ADHD in the neuropsychological tests of visual attention, verbal and inhibitory control.

Methodology: Triple blind, randomized, sham-controlled, cross-over trial involving tDCS in children and adolescents with ADHD. Initial screening was performed using SNAP-IV and WISC-IV Vocabulary and Cube subtests. Individuals were evaluated pre-tDCS and post-tDCS with the WISC-IV Digitus subtest, NEPSY-II Inhibiting Responses (IR) subtest, Corsi Cubes, and TAVIS-4. The sample size calculation was performed with the results obtained for the variable "errors by default of the TAVIS test" in a pilot study, using in the program WinPepi the procedure for equivalence clinical trial for paired tests and paired observations, considering the following values: 5% level of significance; 80% power; from 0 to 3.6 of negligible difference (negligible); 4.6 as the mean of the reference group; 1.2 of expected difference between means; and 1.24 standard deviation of the differences between the paired observations.

Results: A total of 15 individuals were selected, randomly assigned in two groups, 8 of whom were initially in the tDCS group and 7 in the sham group. There were no statistically significant differences between intervention and control group regarding the following scales WISC-IV Digitus subtest, NEPSY-II Inhibiting Responses (IR) subtest, and TAVIS-4. There was statistical significance only in the Corsi cubes test (direct order) in the sham group. Adverse events were mostly self-limited and characterized as mild to moderate.

Conclusion: The present study showed no difference in the neuropsychological parameters of visual attention, working memory and inhibitory control in any of the outcomes investigated, besides the subjects did not perceive benefit of the tDCS in relation to sham-tDCS

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Eur Neuropsychopharmacol. 2019;29:S178-S179.

P.232 THERE IS A CORRELATION BETWEEN PLASMA ERYTHROPOIETIN LEVELS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS.

Shim SH, Yang JC, Kim JS.

Background and Aims: Erythropoietin (EPO) is a circulating hormone that governs the rate of red blood cell production. There are a few animal models associating dopamine dysfunction with behavioral impairments that model attention deficit hyperactivity disorder (ADHD). EPO has trophic effects on dopaminergic neurons [1]. EPO concentrations in the Cerebrospinal fluid (CSF) were significantly higher in the depression patients [2]. EPO is increased in Central nervous system (CNS) to act as a neuroprotectant after the epileptic fits [3]. The aim of the present study was to examine the EPO plasma levels and determine whether there was any correlation between plasma EPO levels and clinical characteristics of ADHD.

Methods: Plasma EPO levels were measured in 78 drug-na+ve children with ADHD and 81 healthy children. The severity of ADHD symptoms was determined by scores on the Korean ADHD Rating Scale (K-ARS) in children and healthy controls.

Results: The ADHD group consisted of 64 boys and 14 girls, and the healthy control group consisted of 31 boys and 50 girls. The median plasma EPO levels in ADHD children was 12.9 mIU/mL, whereas it was 12.0 mIU/mL in the healthy controls. This difference was not statistically significant. Participants in the highest tertiles of plasma EPO had a 1.49 times higher risk of ADHD than those in the lowest tertile, and those in the second highest tertile had a 2.39 times higher risk of ADHD than those in the lowest tertile. A logistic regression showed that the plasma EPO levels were not associated with ADHD after adjusting for age and gender. Plasma EPO levels significantly correlated positively with K-ARS scores including hyperactivity impulsivity and total scores as determined by Spearman's correlation test in ADHD children and healthy controls. A linear regression analysis performed adjusting for age and gender also indicated that the significant difference in inattention score comparing participants in the highest with those in the lowest tertile of plasma EPO was 1.70. Adjusting for age and gender, a linear regression analysis showed that inattention score was significantly higher (3.04, [95% CI: 0.64, 5.44]) in the second highest tertile of plasma EPO comparing those in the lowest tertile. Hyperactivity-impulsivity score was significantly higher (2.19, [95% CI: 0.10, 4.38]) in the highest tertile of plasma EPO comparing those in the lowest tertile. And, total K-ARS scores was significantly higher (5.06, [95% CI: 0.74, 9.38]) in the second highest tertile of plasma EPO comparing those in the lowest tertile.

Conclusions: These findings suggest plasma EPO levels in untreated ADHD children did not differ with healthy controls. However, plasma EPO levels had a significant positive correlation with hyperactivity impulsivity and K-ARS total scores in ADHD children and healthy controls. Further studies are required to determine the source and role of circulating EPO in ADHD

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Eur Neuropsychopharmacol. 2019;29:S591.

C.02.02 MANAGING ADHD AND COMORBID MOOD DISORDERS.

Goodman D.

While psychiatrists and mental health professionals are comfortable with identification/diagnosis of mood disorders, ADHD in adults is much less frequently identified/diagnosed because of inadequate training internationally. Because of the symptom overlap of emotional dysregulation, cognitive symptoms, psychomotor activity, and impulsivity in mood disorders and ADHD, diagnostic differentiation is a clinical challenge. This presentation will focus on accurate diagnostic assignment of these symptoms, especially when ADHD and mood disorders co-exist. The clinical evaluation interview of presenting symptoms is diagnostically complemented with symptom age of onset, longitudinal course and family psychiatric history. Additional, observer information of historical symptoms and age of onset can be very helpful, especially when patient's recall is compromised. Understanding how to diagnostic prioritize co-morbid disorders is essential in establishing an effective pharmacologic algorithm. The goal is to treat one disorder without worsening the other conditions. While stimulant medication may be helpful for ADHD, major depression, or dysthymia, such medication have historically been avoided in the presence of bipolar disorder. In addition, a diagnosis ought not be made on the response to stimulant medication. Major depression, bipolar disorder, and dysthymia concurrent with ADHD require tracking target symptoms of each disorder through the course of

medication/treatment option trials. With medication, patient complaints need to be sorted into symptoms of a disorder vs side-effects of medication. Symptoms checklists can be complimentary to the clinical interview for symptom tracking. Presented published research will help support clinical concepts and treatment recommendations when treating mood comorbidities with adult ADHD. [17] Disclosure statement: Honoraria: WebMD, Medscape, American Professional Society of ADHD and Related Disorders, Neuroscience Education Institute, Children and Adults with ADHD Association, Global Academy for Medical Education, Global Medical Education, Canadian ADHD Resource Association Consultant: Shire, Teva Pharmaceuticals, Janssen (U.S. and Canada), Sunovion, Thomson Reuters, GuidePoint Global, Otsuka Pharmaceuticals, Ironshore Pharmaceuticals, Neos Therapeutics, Rhodes Pharmaceuticals, NLS Pharma, National Football League, Healthequity Corporation, Consumer Reports, Neuroscience Education Institute, American Professional Society for ADHD and Related Disorders Shareholder: Kempharm

Frontiers in Pediatrics. 2019;7.

INVESTIGATING THE ASSOCIATION BETWEEN EXPOSURE TO SECOND HAND SMOKE IN UTERO AND DEVELOPMENTAL COORDINATION DISORDER.

Mahlberg N, James ME, Bulten R, et al.

Background: Developmental coordination disorder (DCD) and attention-deficit hyperactivity disorder (ADHD) are highly comorbid in children. There is evidence linking second hand smoke (SHS) exposure in utero to ADHD; however, its relation to DCD is unknown. The purpose of this study was to examine the effect of SHS exposure in utero in children with and without DCD.

Methods: This study was a cross-sectional examination of 122 children from the District School Board of Niagara (72 males, 50 females, Mage = 12.9 years) who were part of a larger, prospective cohort study. Participants were assessed for motor proficiency and intelligence and were screened for symptoms of ADHD using the Bruininks-Oseretsky Test of Motor Proficiency-Short Form, the Kaufman Brief Intelligence Inventory, 2nd edition, and the Conners' Parent Rating Scales-Revised: Short Form, respectively. Parent questionnaires were used to determine SHS exposure in utero as either yes or no. Multinomial logistic regression was used to examine the relationship between SHS exposure and DCD risk.

Results: Children exposed to SHS in utero were significantly more likely to be at high risk for DCD than children who were not (OR = 3.33, $p = 0.004$), and children exposed to SHS in utero were more likely to be at moderate risk for DCD in the presence (OR = 3.57, $p = 0.025$) or absence of ADHD (OR = 2.38, $p = 0.042$). However, statistical adjustment for birth weight, socioeconomic status, age, and sex reduced this effect to non-significance in the moderate risk group.

Conclusion: Results suggest exposure to SHS during pregnancy increases the chances of a child developing high risk DCD. While SHS exposure may increase DCD risk with and without ADHD, this effect may be explained by covariates and confounding factors. Further study is needed to examine the mechanisms linking SHS exposure in utero to motor coordination problems in children

Front Psychiatry. 2019;10.

META-ANALYSIS OF SEX DIFFERENCES IN SOCIAL AND COMMUNICATION FUNCTION IN CHILDREN WITH AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Mahendiran T, Brian J, Dupuis A, et al.

Background: Sex differences in the prevalence of neurodevelopmental disorders such as autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) are well documented, but studies examining sex differences in social and communication function remain limited and inconclusive. Objectives: The objective of this study is to conduct a meta-analysis of sex differences in social-communication function in children with ASD or ADHD and typically developing controls.

Methods: Using PRISMA, a search was performed on Medline and PSYCHINFO on English-language journals (2000-2017) examining sex differences in social and communication function in ASD and ADHD compared to controls. Inclusion criteria: 1) peer reviewed journal articles, 2) diagnosis of ASD or ADHD and

controls, 3) age 6-18 years, 4) measures of social communication function, and 5) means, standard deviations, and sample sizes reported in order to calculate standardized mean differences (SMD).

Results: Eleven original/empirical studies met inclusion criteria for ASD and six for ADHD. No significant sex differences were found between ASD and controls in social (SMD = 0.43; $p = 0.5$; CI: 1.58-0.72), or communication function (SMD = 0.86; $p = 0.5$ CI: $\Gamma\hat{E}1.57\Gamma\hat{C}\hat{O}\hat{E}3.30$) and between ADHD and controls in social function (SMD = 0.68; $p = 0.7$, CI: 4.17-2.81). No studies evaluated sex differences in communication in ADHD. Significant heterogeneity was noted in all analyses. Type of measure may have partially accounted for some variability between studies.

Conclusions: The meta-analysis did not detect sex differences in social and communication function in children with ASD and ADHD; however, significant heterogeneity was noted. Future larger studies, controlling for measure and with adequate numbers of female participants are required to further understand sex differences in these domains

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Gazzetta Medica Italiana Archivio per le Scienze Mediche. 2019;178:699-705.

AN INTENSIVE LIFESTYLE INTERVENTION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Pippi R, Buratta L, Ranucci C, et al.

The present paper was a contribution on the effectiveness of a lifestyle family-based intervention for children with overweight and presenting attention-deficit/hyperactivity disorder through the exposition of the case of S., a 9-year-old boy. History of parental obesity with hypertension of grandparents on his father's side were detected. Sedentary behaviours and an excess of sugar and sweetener consumption were observed during the first counselling visit. According to EURODIS clinical model 2 weekly sessions of supervised physical activity were done in addition to an individual counselling and educational group sessions on healthy nutrition habits and psychological support for the parents. The children improved his food habits and all physical-health related capacities tested. The lifestyle intervention with a family based approach could help a child with special needs in the process of change unhealthy habits through the regulation of food intake and physical activity levels and their reciprocal connections

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Headache. 2019;59:1504-15.

ECONOMIC IMPACT OF HEADACHE AND PSYCHIATRIC COMORBIDITIES ON HEALTHCARE EXPENDITURES AMONG CHILDREN IN THE UNITED STATES: A RETROSPECTIVE CROSS-SECTIONAL STUDY.

Law EF, Palermo TM, Zhou C, et al.

Objective: To examine the annual healthcare expenditures associated with childhood headache in the United States, and to evaluate whether psychiatric comorbidities increase the impact of headache on expenditures. Background: Headache is prevalent in childhood and co-occurs with anxiety disorders, depressive disorders, and attention deficit/hyperactivity disorder (ADHD), which may increase cost of illness.

Methods: We conducted a secondary data analysis using a nationally representative sample of 34,633 children ages 2-17 from the 2012-2015 Medical Expenditure Panel Surveys (MEPS), of which 779 (weighted 2.6%) were identified as having headache based on health service use associated with headache. Using a comprehensive cost-of-illness approach, we assessed the incremental expenditures associated with headache and determined excess expenditures associated with psychiatric comorbidities using standard adjusted 2-part expenditure models.

Results: Annual total healthcare expenditures were estimated to be 24.3% higher, 95% CI [1,55], in our headache group (\$3036, 95% CI [2374,3699] vs \$2350, 95% CI [2140,2559]). Total national expenditures associated with pediatric headache in the United States were estimated at \$1.1 billion annually, 95% CI [.04, 2.2 billion]. Depression and ADHD were associated with higher incremental expenditures for the headache group (depression: \$1815, 95% CI[676,2953] vs \$1409, 95% CI[697,2112]; ADHD: \$4742, 95% CI[1659,7825] vs \$2935, 95% CI[1977,3894]); however, interactions between psychiatric comorbidities and headache did not reach statistical significance.

Conclusion: Youth with headache exert a considerable economic burden on families, healthcare systems, and society. Due to the limitations in methods used to classify youth with headache in MEPS, our findings may underestimate the true prevalence and cost of pediatric headache in the United States. Further research with larger sample sizes is needed to understand the impact of psychiatric comorbidities on healthcare expenditures in this population

Hum Brain Mapp. 2019 Dec;40:4877-87.

DISRUPTED BRAIN FUNCTIONAL NETWORKS IN DRUG-NAÏVE CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER ASSESSED USING GRAPH THEORY ANALYSIS.

Chen Y, Huang X, Wu M, et al.

Neuroimaging studies have revealed functional brain network abnormalities in attention deficit hyperactivity disorder (ADHD), but the results have been inconsistent, potentially related to confounding medication effects. Furthermore, specific topological alterations in functional networks and their role in behavioral inhibition dysfunction remain to be established. Resting-state functional magnetic resonance imaging was performed on 51 drug-naïve children with ADHD and 55 age-matched healthy controls. Brain functional networks were constructed by thresholding the partial correlation matrices of 90 brain regions, and graph theory was used to analyze network topological properties. The Stroop test was used to assess cognitive inhibitory abilities. Nonparametric permutation tests were used to compare the topological architectures in the two groups. Compared with healthy subjects, brain networks in ADHD patients demonstrated altered topological characteristics, including lower global (FDR $q = 0.01$) and local efficiency ($p = 0.032$, uncorrected) and a longer path length (FDR $q = 0.01$). Lower nodal efficiencies were found in the left inferior frontal gyrus and anterior cingulate cortex in the ADHD group (FDR both $q < 0.05$). Altered global and nodal topological efficiencies were associated with the severity of inhibitory cognitive control deficits and hyperactivity symptoms in ADHD ($p < 0.05$). Alterations in network topologies in drug-naïve ADHD patients indicate weaker small-worldization with decreased segregation and integration of functional brain networks. Deficits in the cingulo-fronto-parietal attention network were associated with inhibitory control deficits. (PsycINFO Database Record (c) 2019 APA, all rights reserved)

Indian J Pediatr. 2019 Oct;86:877-78.

AUTISM, EPILEPSY AND INTELLECTUAL DISABILITY: A CLINICAL CONUNDRUM.

Anand V, Jauhari P.

Int J Environ Res Public Health. 2019 Jul;16.

SERIOUS GAMES AND THEIR EFFECT IMPROVING ATTENTION IN STUDENTS WITH LEARNING DISABILITIES.

Garcia-Redondo P, Garcia T, Areces D, et al.

Previous studies have shown the positive effects of educational video games (serious games) in improving motivation, attention and other cognitive components in students with learning disabilities. This study analyzes the effects on attention of a serious game based on multiple intelligences in a sample of 44 students (age range = 6-16 years; experimental group = 24; control group = 20) with attention deficit hyperactivity disorder (ADHD) and specific learning disorder (SLD). Performance and observation measures of attention were used. The intervention consisted of 28 sessions (10 min each), in which the participants trained with 10 games based on multiple intelligences. A significant improvement in attention performance measures (visual attention) was found after the intervention, with the experimental and the control groups significantly differing in the posttest. These results invite consideration of the applicability of boosting different intelligences, talents

or unique abilities through educational videogames as an important bridge to improving areas of deficit-in this case attention-in students with learning disabilities

Int J Environ Res Public Health. 2019 Jun;16.

A SYSTEMATIC REVIEW OF POLYVICTIMIZATION AMONG CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY OR AUTISM SPECTRUM DISORDER.

Hellstrom L.

Children with Autism Spectrum Disorder (ASD) or Attention Deficit Hyperactivity Disorder (ADHD) have shown an increased risk for violence and victimization. However, research on exposure to multiple forms of victimization in different contexts are scarce. Hence, the current aim is to review the evidence about polyvictimization among children with ASD or ADHD. PsycInfo, ERIC, ERC, Scopus, and PubMed databases were systematically searched until 12 March 2019 to identify empirical studies with reported prevalence rates of at least four forms of victimization among children with ASD or ADHD. A total of 6/1300 articles were included in the review, ranging in sample sizes from 92 to 4114. The reported prevalence rates for polyvictimization were 1.8% and 23.1% for children with ASD and 7.3% for children with ADHD. The results emphasize the high prevalence of violence and victimization, including polyvictimization, among children with ASD or ADHD. Polyvictimization among children with ASD or ADHD is a highly under researched area. Significant knowledge gaps and important methodological considerations that provide important implications for future research include lack of information on cyber bullying, frequency or intensity of victimization, and the failure to include children as informants and to report health outcomes associated with polyvictimization

International Review of Neurobiology. 2019.

PRENATAL STRESS: EFFECTS ON FETAL AND CHILD BRAIN DEVELOPMENT.

Lautarescu A, Craig MC, Glover V.

The impact of stress on brain health begins in the womb. Both animal and human studies have found that prenatal maternal stress affects the brain and behavior of the offspring. Stressful life events, exposure to a natural disaster, and symptoms of maternal anxiety and depression increase the risk for the child having a range of emotional, behavioral and/or cognitive problems in later life. These include depression, anxiety, Attention Deficit Hyperactivity Disorder (ADHD), and/or conduct disorders. There is an increased risk for other outcomes also, including preterm delivery and reduced telomere length, possibly indicative of an accelerated life history. The causal role of prenatal maternal stress on the etiology of the neurodevelopmental disorders is supported by large population cohorts, which have controlled for a wide range of potential confounders, including postnatal maternal mood. More recently, research has begun to explore the biological correlates and mediators of these findings. These studies suggest that the hypothalamic pituitary adrenal (HPA) axis plays a role in mediating the effects of maternal stress on the fetal brain. Further, in vivo brain imaging research reports that maternal stress is associated with changes in limbic and frontotemporal networks, and the functional and microstructural connections linking them. The structural changes include cortical thinning and an enlarged amygdala. While these studies have been conducted on smaller sample sizes and could not control for many confounders, the observed brain changes do plausibly underlie many of the emotional, behavioral and cognitive changes found to be associated with prenatal stress

Int Rev Psychiatry. 2019.

PRE-SCHOOL MENTAL HEALTH DISORDERS: A REVIEW.

Zaim N, Harrison J.

Preschoolers are presenting in increasing numbers to primary care providers and mental health clinics with emotional and behavioural impairment. Preschoolers in the US have the highest rates of school expulsion of all age groups. Because young children are limited in their capacity to convey distress and internal states,

impairment is most often expressed behaviourally. Disruptive behaviour, frequently in the form of aggression or dysregulation, is a final common pathway for many disorders in this age group. Tools and training to diagnose pre-school disorders are limited, and while some effective non-medication interventions exist, the evidence base for medication use in this age group is extremely limited. This article reviews approaches to assessing common pre-school disorders including attention deficit hyperactivity disorder (ADHD), disruptive behaviour disorders, anxiety and mood disorders, perceptual disturbances and psychosis, and trauma related disorders. The evidence base for both therapeutic and psychopharmacologic interventions for these disorders is discussed

Iran J Child Neurol. 2020;14:93-103.

ATTENTION DEFICIT DISORDER WITH HYPERACTIVITY SYMPTOMS IN EARLY-TREATED PHENYLKETONURIA PATIENTS.

Beckhauser MT, Beghini M, V, Moehlecke IB, et al.

Objectives To assess the presence of symptoms consistent with Attention Deficit Disorder with Hyperactivity (ADHD) in all patients with early-treated phenylketonuria (PKU) in the State of Santa Catarina in southern Brazil.

Materials & Methods All of the patients diagnosed with PKU by newborn-screening tests, with ages varying from 6 to 18 years and who started treatment before 60 days of life and presented phenylalanine levels consistently below 6 mg/dL throughout treatment, were included. The subjects were invited to complete a questionnaire that collected sociodemographic, gestational and clinical data. ADHD symptoms were assessed using the revision of the Swanson, Nolan and Pelham Questionnaire.

Results A total of 34 patients were evaluated, who were 53% male and 94% white and had an average age of 12 years, and 15% were born premature. According to the Swanson, Nolan and Pelham Questionnaire, 13 patients (38%) met the diagnostic criteria for ADHD, with 2 patients having the inattentive type, 6 patients having the hyperactive or impulsive type and 1 patient having the oppositional defiant disorder type.

Conclusion Although the patients with PKU were regularly treated from birth, there was a high prevalence of symptoms consistent with ADHD. A pathophysiological interface that involves the dopamine metabolic pathway may exist between the two conditions

J Appl Res Intellect Disabil. 2019 Jul;32:967-80.

IMPACT OF MULTIPLE CO-OCCURRING EMOTIONAL AND BEHAVIOURAL CONDITIONS ON CHILDREN WITH AUTISM AND THEIR FAMILIES.

Dovgan K, Mazurek MO.

BACKGROUND: Comorbid conditions are very common in children and adults with autism spectrum disorder (ASD) and can affect school performance, adaptive skills and peer relationships. Comorbid conditions place strain on the family as well as the individual with ASD. This project aimed to determine the affect of comorbid conditions over and above child and family characteristics.

METHODS: The present authors examined 3,055 cases of children with ASD who had varying numbers of comorbid conditions (i.e., ADHD, depression, anxiety or behaviour problems).

RESULTS: Multiple comorbid conditions did have a unique impact on difficulties accessing services. A greater number of comorbid conditions impacted daily activity participation, but not a family's receipt of mental health care or respite, work changes or number of weekly hours dedicated to caring for a child with ASD.

CONCLUSIONS: Families, practitioners, paraprofessionals and educators of children with autism should address comorbid conditions to ensure both child and family well-being

J Autism Dev Disord. 2019 Oct;49:4170-80.

CYBERBULLYING VICTIMIZATION AND PERPETRATION IN ADOLESCENTS WITH HIGH-FUNCTIONING AUTISM SPECTRUM DISORDER: CORRELATIONS WITH DEPRESSION, ANXIETY, AND SUICIDALITY.

Hu HF, Liu TL, Hsiao RC, et al.

The present study examined the associations between cyberbullying involvement and sociodemographic characteristics, autistic social impairment and attention-deficit/hyperactivity disorder and oppositional defiant disorder (ODD) symptoms in 219 adolescents with high-functioning autism spectrum disorder (ASD). Moreover, the associations between cyberbullying involvement and depression, anxiety, and suicidality were also examined. Adolescents self-reported higher rates of being a victim or perpetrator of cyberbullying than were reported by their parents. Increased age and had more severe ODD symptoms were significantly associated with being victims or perpetrators of cyberbullying. Being a victim but not a perpetrator of cyberbullying was significantly associated with depression, anxiety, and suicidality. Cyberbullying victimization and perpetration should be routinely surveyed in adolescents with high-functioning ASD

Journal de Pédiatrie et de Puericulture. 2019.

ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN CHILDREN: MEDICAL APPROACH.

Le Heuzey MF.

Attention Deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder with an important impact on school performance, family life and social functioning. The symptomatology is characterised by inattention, impulsivity and hyperactivity. The diagnostic criteria are the same along the life (children, adolescents, adults). There are many comorbidities, and comorbidity with an autistic disorder is possible. The treatment is non pharmacological (psychoeducation, cognitive remediation, neurofeedback) and pharmacological (methylphenidate)

J Abnorm Child Psychol. 2019 Dec;47:1889-902.

REINFORCEMENT CONTINGENCY LEARNING IN CHILDREN WITH ADHD: BACK TO THE BASICS OF BEHAVIOR THERAPY.

De Meyer H, Beckers T, Tripp G, et al.

Reinforcement deficits in ADHD may affect basic operant learning processes relevant for Behavioral Treatment. Behavior acquired under partial reinforcement extinguishes less readily after the discontinuation of reinforcement than behavior acquired under continuous reinforcement, a phenomenon known as the Partial Reinforcement Extinction Effect [PREE], which has great relevance for the emergence of behavioral persistence. The present study examined acquisition and extinction of operant responding under partial and continuous reinforcement in children with and without ADHD. In addition, we evaluated the effectiveness of gradual stretching the reinforcement rate during acquisition for remedying potential acquisition or extinction deficits under partial reinforcement in ADHD. In an operant learning task designed to mimic the task confronted by an animal in a Skinner box, 62 typically developing and 49 children with ADHD (age: 8–12) were presented with a continuous, partial or gradually stretching reinforcement scheme followed by extinction. Both groups of children acquired the instrumental response more slowly and exhibited more behavioral persistence (reduced extinction) when responding was initially reinforced under partial relative to continuous reinforcement, with no differences between groups. Progressive ratio stretching resulted in faster acquisition than partial reinforcement yet promoted equal behavioral persistence, again without differences between ADHD and TD groups. Unlike suggested by previous research, children with ADHD exhibit neither an acquisition deficit under partial reinforcement nor a deficit in PREE. Of relevance for Behavioral Treatment, gradual reinforcement stretching can be used to facilitate response acquisition over purely partial reinforcement while maintaining equal behavioral persistence upon reward discontinuation

J Abnorm Child Psychol. 2019 Dec;47:1903-16.

DEPRESSION AND ADHD-RELATED RISK FOR SUBSTANCE USE IN ADOLESCENCE AND EARLY ADULTHOOD: CONCURRENT AND PROSPECTIVE ASSOCIATIONS IN THE MTA.

Howard AL, Kennedy TM, Macdonald EP, et al.

Childhood attention-deficit/hyperactivity disorder (ADHD) is prospectively linked to substance use and disorder. Depression emerging in adolescence is an understudied risk factor that may explain some of this risk. In the present study, we considered mediating and moderating roles of adolescent depression in explaining this association by using longitudinal data from the prospective 16-year follow-up of the Multimodal Treatment Study of ADHD (MTA). Participants were 547 children diagnosed with DSM-IV ADHD Combined Type, and 258 age- and sex-matched comparison children. In adolescence, depressive symptoms did not exacerbate effects of childhood ADHD on any substance use. For both groups, time-varying and average depressive symptoms were associated with more frequent use of all substances. Prospectively, we found no evidence of depression mediation to adult substance use. However, adolescent depression moderated the association between childhood ADHD and adult marijuana use. Although adults without ADHD histories used marijuana more frequently if they had elevated depressive symptoms in adolescence, marijuana use by adults with ADHD histories was independent of their adolescent depression. In adulthood, depression diagnoses and ADHD persistence continued to operate as independent, additive correlates of substance use risk. Our findings suggest a circumscribed role for depression in substance use risk that adds to, but does not alter or explain, ADHD-related risk

J Affective Disord. 2019.

PREDICTIVE POWER OF THE ADHD GWAS 2019 POLYGENIC RISK SCORES IN INDEPENDENT SAMPLES OF BIPOLAR PATIENTS WITH CHILDHOOD ADHD.

Grigoriu-Serbanescu M, Giaroli G, Thygesen JH, et al.

Background: Although there is evidence of genetic correlation between bipolar disorder (BP) and ADHD, the extent of the shared genetic risk and whether childhood ADHD (cADHD) influences the characteristics of the adult BP remain unclear.

Our objectives were: (i) to test the ability of polygenic risk scores (PRS) derived from the latest PGC ADHD-GWAS (Demontis et al., 2019) to predict the presence of cADHD in BP patients; (ii) to examine the hypothesis that BP preceded by cADHD is a BP subtype with particular clinical traits and (iii) partially shares its molecular basis with ADHD.

Method: PRS derived from the ADHD-GWAS-2019 were tested in BP patients (N = 942) assessed for cADHD with the Wender Utah Rating Scale and in controls from Romania and UK (N = 1616).

Results: The ADHD-PRS differentiated BP cases with cADHD from controls. Proband sex and BP age-of-onset significantly influenced the discriminative power of the ADHD-PRS. The ADHD-PRS predicted the cADHD score only in males and in BP cases with early age-of-onset (≤21 years). Bipolar patients with cADHD had a younger age-of-onset of mania/depression than patients without cADHD. The ADHD-PRS predicted the BP-affection status in the comparison of early-onset BP cases with controls suggesting a partial molecular overlap between early-onset BP and ADHD.

Limitations: Retrospective diagnosis of cADHD, small sample size.

Conclusions: The PRS-analysis indicated an acceptable predictive ability of the ADHD-SNP-set 2019 in independent BP samples. The best prediction of both cADHD and BP-affection status was found in the early-onset BP cases. The results may have impact on the individual disease monitoring

J Affective Disord. 2020;262:293-97.

ANTIDEPRESSANT RESISTANCE IN ADOLESCENTS WITH MAJOR DEPRESSIVE DISORDER: A NATIONWIDE LONGITUDINAL STUDY.

Chen L-C, Chen Y-H, Bai Y-M, et al.

Background: Studies have suggested that psychiatric comorbidities have major effects on antidepressant resistance in adult patients with major depressive disorder (MDD). However, the association between psychiatric comorbidities and antidepressant resistance remains unclear in adolescents with MDD.

Methods: A total of 10,624 adolescents with MDD were selected from the Taiwan National Health Insurance Research Database between 2001 and 2010 and followed for one year. Treatment-resistant depression (TRD) was defined as unresponsiveness to at least two antidepressants, and treatment resistant tendency was defined as unresponsiveness to the first antidepressant. Psychiatric comorbidities, such as anxiety disorders, substance use disorders, and attention deficit hyperactivity disorder (ADHD), were assessed as confounding factors.

Results: In our study, only 1.7% (n = 184) of adolescents with MDD met the TRD criteria but 23.3% (n = 2480) were classified as exhibiting treatment resistant tendency. Anxiety disorders (OR: 2.34, 95% CI: 1.73-3.16) and substance use disorders (OR: 2.41, 95% CI: 1.28-4.54) exhibited a correlation with TRD, and ADHD (OR: 1.34, 95% CI: 1.08-1.66) was associated with treatment resistant tendency.

Conclusions: Approximately one-fourth of adolescents with MDD respond poorly to the first antidepressant treatment. The psychiatric comorbidities of anxiety disorders, substance use disorders, and ADHD may increase the risk of treatment resistance in adolescents with MDD

J Behav Ther Exp Psychiatry. 2020;68.

REAPPRAISAL IS AN EFFECTIVE EMOTION REGULATION STRATEGY IN CHILDREN WITH TOURETTE SYNDROME AND ADHD.

Hagstrom J, Maigaard K, Pagsberg AK, et al.

Background and objectives: Difficulties in emotion regulation (ER) have been associated with several psychiatric disorders, emphasizing a need for a greater understanding of the concept and its associations with disruptive behavior. We aimed to study the ER strategy of cognitive reappraisal with an experimental test to increase our knowledge of emotional processes in child psychopathology.

Methods: In the present study, we examined emotional reactivity and cognitive reappraisal with a computer task in 160 medication-naïve children aged 8-12 comprising four groups: Fifty-eight children with Tourette syndrome (TS), 26 children with attention-deficit/hyperactivity disorder (ADHD), 19 children with TS and ADHD, and 57 typically developing controls.

Results: The use of cognitive reappraisal reduced negative affect across all participants and the ability to reappraise was positively correlated with age, whereas reactivity was not. Overall, groups did not differ in reactivity or regulation success. Looking at specific differences within groups, however, only the ADHD group did not significantly decrease negative affect when reappraising. Finally, the use of strategies considered to be efficacious was correlated with regulation success, whereas the use of a less adaptive strategy related to suppression was associated with reactivity, but not regulation of emotions. Limitations: The study was limited by small, clinical contrast groups and a lack of blinding to diagnostic status in the coding of verbal strategies employed during the task.

Conclusions: Cognitive reappraisal appears to be a beneficial ER strategy for children regardless of diagnostic status. Our findings indicate that children can learn and employ an adaptive ER strategy when instructed in the technique, even in the presence of attention problems, which is highly relevant to therapeutic approaches to dysregulated behavior

J Child Adolesc Psychopharmacol. 2019;29:730-39.

TREATMENT PATTERNS, HEALTH CARE RESOURCE UTILIZATION, AND HEALTH CARE COST ASSOCIATED WITH ATYPICAL ANTIPSYCHOTICS OR GUANFACINE EXTENDED RELEASE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN QUEBEC, CANADA.

Lachaine J, Ben AL, Pringsheim T, et al.

Objective: To assess treatment patterns, health care resource utilization, and health care costs associated with use of atypical antipsychotics (AAPs) or the nonstimulant guanfacine extended release (GXR) after stimulant therapy for attention-deficit/hyperactivity disorder (ADHD). In Canada, GXR is approved as a monotherapy for children and adolescents with ADHD or as an adjunct to stimulants, and AAPs are commonly used off-label as an adjunct to stimulants.

Methods: Health care claims data (January 1, 2007 to March 31, 2016) from Quebec's provincial health plan were assessed for individuals with ADHD, 6-17 years of age, who received 1 stimulant followed by a first AAP or GXR prescription (index medication), without a diagnosis for which AAPs are indicated.

Results: Overall, 1327 individuals were included (AAPs, 1098; GXR, 229). Rates of discontinuation, augmentation, or switching of the index medication did not differ between AAPs and GXR during the first follow-up year. Discontinuation rates were significantly lower with GXR than with AAPs during the second year (22.0% vs. 35.9%; $p = 0.03$). GXR and AAPs resulted in similar increases in total health care cost. In GXR users, the increase in prescription drug cost after 6 months was higher than in AAP users, whereas the increase in overall medical cost was higher with AAPs than GXR, owing to more psychiatric department visits.

Conclusions: In children and adolescents with ADHD who used AAPs or GXR after stimulants, secondary treatment changes were similar with both treatments after 1 year, but discontinuation rates were significantly lower with GXR than with AAPs in the second year. The greater increase in prescription cost with GXR was balanced by a greater increase in overall medical costs with AAPs, resulting in no overall difference in total health care cost between the two treatments

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J Child Fam Stud. 2019 Dec;28:3338-45.

CONFLICT BETWEEN PARENTS AND ADOLESCENTS WITH ADHD: SITUATIONAL TRIGGERS AND THE ROLE OF COMORBIDITY.

Garcia AM, Medina D, Sibley MH.

Objectives: Little is known about factors that contribute to conflict between parents and adolescents with ADHD. The current study examines the frequency and intensity of arguments between adolescents with ADHD and their parents with attention to situational triggers and adolescent and parent characteristics that predict conflict.

Method: Adolescents and parents ($N = 128$) completed a battery of rating scales at baseline intake into a randomized clinical trial.

Results: The most frequent and clinically significant argument topics identified by parent were homework problems, personal hygiene, and bedtime. Similarly, homework problems were rated by parents as the most intense sources of arguments. Adolescents with ADHD who displayed higher comorbid depressive or aggressive symptoms had the most frequent arguments with their parents.

Conclusions: Intervention and prevention programs targeting conflict between teens with ADHD and their parents might consider concurrent treatment of argument sources (i.e., disorganization, homework problems). Comorbid mood and behavior problems should also be addressed

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J Clin Exp Neuropsychol. 2019 Dec;41:1074-87.

THE EFFICACY OF A TRAINING THAT COMBINES ACTIVITIES ON WORKING MEMORY AND METACOGNITION: TRANSFER AND MAINTENANCE EFFECTS IN CHILDREN WITH ADHD AND TYPICAL DEVELOPMENT.

Capodieci A, Re AM, Fracca A, et al.

Introduction: It has been demonstrated that children with attention deficit and hyperactivity disorder (ADHD) have impairments in working memory (WM), and particularly its visuospatial component, responsible for academic underachievement. Furthermore, children with ADHD have difficulty in metacognition, and consequently use inappropriate strategies to control attention and impulsive behavior. The aim of the present study was to devise a training that combined individual exercises on visuospatial WM and group metacognitive activities capable of helping children with ADHD to ameliorate their performance in executive functioning tasks, and to contain their inattentive and hyperactive/impulsive behavior.

Method: A combined training that focused on visuospatial WM and metacognition was administered to 12 children with a diagnosis of ADHD and 15 typically-developing children. Tasks on executive functions and questionnaires for parents and teachers were administered before and at the end of the training, and one month after the post-test. Specific short- and long-term training gains and transfer effects were examined. Effects of the training on parents' and teachers' ratings were also considered.

Results: Specific gains and transfer effects were found at the post-test and long-term assessments in both typically-developing children and those with ADHD. Parents' and teachers' ratings also indicated an improvement in the symptomatic behavior of children with ADHD.

Conclusion: The results of this study have clinical and educational implications. A training that combines individual computerized visuospatial WM activities with metacognitive group reflection about useful strategies seems to produce promising results, helping children with ADHD to improve their executive functioning and behavioral problems

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J Consult Clin Psychol. 2019.

THE LONG-TERM FINANCIAL OUTCOME OF CHILDREN DIAGNOSED WITH ADHD.

Pelham WE, Page TF, Altszuler AR, et al.

Objective: Characterize the early trajectories of financial functioning in adults with history of childhood ADHD and use these trajectories to project earnings and savings over the lifetime.

Method: Data were drawn from a prospective case-control study (PALS) following participants with a rigorous diagnosis of ADHD during childhood (N = 364) and demographically matched controls (N = 240) for nearly 20 years. Participants and their parents reported on an array of financial outcomes when participants were 25 and 30 years old.

Results: At age 30, adults with a history of ADHD exhibited substantially worse outcomes than controls on most financial indicators, even when they and their parents no longer endorsed any DSM symptoms of ADHD. Between ages 25 and 30, probands had exhibited considerably slower growth than controls in positive financial indicators (e.g., monthly income) and substantially less reduction than controls in indicators of financial dependence (e.g., living with parents), indicating worsening or sustained deficits on nearly all measures. When earnings trajectories from age 25 to age 30 were extrapolated using matched census data, male probands were projected to earn \$1.27 million less than controls over their working lifetime, reaching retirement with up to 75% lower net worth.

Conclusion: The financial deficit of adults with history of childhood ADHD grows across early adulthood. Projections based on early financial trajectories suggest very large cumulative differences in earnings and savings. With or without persistence of the DSM symptoms, the adult sequela of childhood ADHD can be conceptualized as a chronic condition often requiring considerable support from others during adulthood

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J Headache Pain. 2013;14.

PRIMARY HEADACHES, ATTENTION DEFICIT DISORDER AND LEARNING DISABILITIES IN CHILDREN AND ADOLESCENTS.
Genizi J, Genizi J, Kerem NC, et al .

Background: Primary headaches and Learning difficulties are both common in the pediatric population. The goal of our study was to assess the prevalence of learning disabilities and attention deficit disorder in children and adolescents with migraine and tension type headaches.

Methods: Retrospective review of medical records of children and adolescents who presented with headache to the outpatient pediatric neurology clinics of Bnai-Zion Medical Center and Meyer Children's Hospital, Haifa, during the years 2009–2010. Demographics, Headache type, attention deficit disorder (ADHD), learning disabilities and academic achievements were assessed.

Results: 243 patients met the inclusion criteria and were assessed: 135 (55.6%) females and 108 (44.4%) males. 44% were diagnosed with migraine (35.8% of the males, 64.2% of the females, $p = 0.04$), 47.7% were diagnosed with tension type headache (50.4% of the males, 49.6% of the females). Among patients presenting with headache for the first time, 24% were formerly diagnosed with learning disabilities and 28% were diagnosed with attention deficit disorder (ADHD). ADHD was more prevalent among patients with tension type headache when compared with patients with migraine (36.5% vs. 19.8%, $p = 0.006$). Poor to average school academic performance was more prevalent among children with tension type headache, whereas good to excellent academic performance was more prevalent among those with migraine.

Conclusions: Learning disabilities and ADHD are more common in children and adolescents who are referred for neurological assessment due to primary headaches than is described in the general pediatric population. There is an association between headache diagnosis and school achievements

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Journal of Neural Engineering. 2019;16.

USE OF DEEP LEARNING TO DETECT PERSONALIZED SPATIAL-FREQUENCY ABNORMALITIES IN EEGS OF CHILDREN WITH ADHD.

Chen H, Song Y, Li X.

Objective. Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent neurobehavioral disorders. Studies have tried to find the neural correlations of ADHD with electroencephalography (EEG). Due to the heterogeneity in the ADHD population, a multivariate EEG profile is useful, and the detection of a personalized abnormality in EEG is urgently needed. Deep learning algorithms, especially convolutional neural network (CNN), have made tremendous progress recently, and are expected to solve the problem. Approach. We adopted CNN techniques and a visualization technique named gradient-weighted class activation mapping (Grad-CAM) for detecting a personalized spatial-frequency abnormality in EEGs of ADHD children. A total of 50 children with ADHD (nine girls, mean age: 10.44 0.75) and 57 controls who were matched for age and handedness were recruited. The power spectrum density of EEGs was used as input. We presented an intuitive form of representing multichannel EEG data that is trainable to CNN models. Personalized abnormalities were derived from ADHD children and were compared to the distributions of relative powers in different frequency bands. Main results. We demonstrated that applying CNN techniques to ADHD identification is feasible, with an accuracy of 90.29% 0.58%. There were major differences in personalized spatial-frequency abnormalities between individuals affected by ADHD. The abnormalities were consistent with the power distributions in both group-and individual-level. Significance. This study provided a novel method for detecting personalized spatial-frequency abnormalities of children with ADHD at a precise spatial-frequency resolution. We proposed a new form of representation of multichannel EEG data that is compatible with mainstream CNN architectures. We ensured that CNN models were interpretable and reliable relating to clinical practice by visualizing the decision-making process. We expect that detection of personalized abnormalities using deep learning techniques can facilitate the identification of potential neural pathways and the planning of targeted treatments for children with ADHD

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J Neural Transm. 2019 Dec;126:1679-93.

IMPACT OF AUTISM-ASSOCIATED GENETIC VARIANTS IN INTERACTION WITH ENVIRONMENTAL FACTORS ON ADHD COMORBIDITIES: AN EXPLORATORY PILOT STUDY.

Waltes R, Freitag CM, Herlt T, et al.

Attention-deficit/hyperactivity disorder (ADHD) is determined by genetic and environmental factors, and shares genetic risk with ASD. Functional single-nucleotide polymorphisms of the metabotropic glutamatergic signaling pathway are reported to increase the risk for ASD. The aim of this pilot study was to explore the main effects of respective ASD variants as well as their interaction effects with well-replicated ADHD environmental risk factors on the risk for ADHD, ADHD symptom severities, and comorbidities. We included 318 children with ADHD, aged 5–13 years, and their parents (N = 164 trios, N = 113 duos, N = 41 singletons). Interaction of ASD risk variants CYFIP1-rs7170637, CYFIP1-rs3693, CAMK4-rs25925, and GRM1-rs6923492 with prenatal biological and lifetime psychosocial risk factors was explored in a subsample with complete environmental risk factors (N = 139 trios, N = 83 duos, two singletons) by transmission disequilibrium test and stepwise regression analyses. We identified nominally significant ($\alpha < 0.05$) GxE interactions of acute life events with CYFIP1-rs3693 on ADHD diagnosis ($p = 0.004$; $\text{fdr} = 0.096$) but no significant association of any single marker. Further results suggest that the risk for comorbid disruptive disorders was significantly modulated by GxE interactions between familial risk factors and CAMK4-rs25925 ($p = 0.001$; $\text{fdr} = 0.018$) and prenatal alcohol exposure with CYFIP1-rs3693 ($p = 0.003$; $\text{fdr} = 0.027$); both findings survived correction for multiple testing ($\text{fdr value} < 0.05$). Nominal significant GxE interactions moderating the risk for anxiety disorders have also been identified, but did not pass multiple testing corrections. This pilot study suggests that common ASD variants of the glutamatergic system interact with prenatal and lifetime psychosocial risk factors influencing the risk for ADHD common comorbidities and thus warrants replication in larger samples

J Neurophysiol. 2019;122:2427-37.

EEG POWER SPECTRAL SLOPE DIFFERS BY ADHD STATUS AND STIMULANT MEDICATION EXPOSURE IN EARLY CHILDHOOD.

Robertson MM, Furlong S, Voytek B, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disorder characterized by hyperactivity/impulsivity and inattentiveness. Efforts toward the development of a biologically based diagnostic test have identified differences in the EEG power spectrum; most consistently reported is an increased ratio of theta to beta power during resting state in those with the disorder, compared with controls. Current approaches calculate theta/beta ratio using fixed frequency bands, but the observed differences may be confounded by other relevant features of the power spectrum, including shifts in peak oscillation frequency and altered slope or offset of the aperiodic 1/f-like component of the power spectrum. In the present study, we quantify the spectral slope and offset, peak alpha frequency, and band-limited and band-ratio oscillatory power in the resting-state EEG of 3- to 7-yr-old children with and without ADHD. We found that medication-naïve children with ADHD had higher alpha power, greater offsets, and steeper slopes compared with typically developing children. Children with ADHD who were treated with stimulants had comparable slopes and offsets to the typically developing group despite a 24-h medication-washout period. We further show that spectral slope correlates with traditional measures of theta/beta ratio, suggesting the utility of slope as a neural marker over and above traditional approaches. Taken with past research demonstrating that spectral slope is associated with executive functioning and excitatory/inhibitory balance, these results suggest that altered slope of the power spectrum may reflect pathology in ADHD

J Neurosci Rural Pract. 2019;10:617-22.

PSYCHIATRIC COMORBIDITIES IN CHILDREN WITH SPECIFIC LEARNING DISORDER-MIXED TYPE: A CROSS-SECTIONAL STUDY.

Sahu A, Patil V, Sagar R, et al.

Background Specific learning disorder (SLD) is a neurodevelopmental condition which frequently exhibits with comorbidities of other disorders, including attention deficit hyperactivity disorder (ADHD), conduct disorder, anxiety, and depression. SLD with any comorbidity may affect the expression and severity of the SLD and may make its management difficult. Thus, the present cross-sectional study was planned to examine the psychiatric comorbidities among children with SLD. Materials and

Methods The sample consisted of 41 patients aged between 7 and 12 years with a diagnosis of SLD-mixed type. Clinical and psychological assessment included the following tests for behavioral, anxiety, mood, and interpersonal problems: Child behavior checklist, Mini-international Neuropsychiatric Interview for Children and Adolescents (MINI-KID), and Conner's 3 Parent Short form-45.

Results The mean age of the participants was 9.8 years (standard deviation [SD] = 1.5). About 75.6% of participants were male, and their mean years of education was 5 years (SD = 1.5). Twenty-four percent of children had a history of delayed developmental milestones. Among comorbidities of SLD, association with attention deficit disorder (ADD)/ADHD has been found to be significant along with difficulties in executive function, peer relation, and aggression.

Conclusion Children with SLD are likely to exhibit signs of ADHD/ADD and dysfunction in executive function, peer relation, and aggression. The management of comorbid conditions is recommended along with remediation of learning problem to overall educational and behavioral achievements and development of child

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Journal of Obstetrics and Gynaecology. 2019.

THE AFFECTIVE TEMPERAMENT TRAITS AND PREGNANCY-RELATED DEPRESSION IN MOTHERS MAY CONSTITUTE RISK FACTORS FOR THEIR CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Sevincok L, et al.

We investigated whether the affective temperaments of mothers and maternal depression before and during the index pregnancy are related to the development of Attention-Deficit Hyperactivity Disorder (ADHD) in their children. One hundred and twenty children were screened for the diagnosis of ADHD. After exclusion and inclusion criteria were applied for children and their mothers, we compared the mothers of children with (n = 63) and without ADHD (n = 60) in terms of affective temperament traits, depression before and during the index pregnancy, and some environmental risk factors. The rate of boys were significantly higher among children with ADHD compared to healthy controls. The mothers of children with ADHD had significantly lower education levels, more cigarette consumption during pregnancy, and more depression rates before the pregnancy than those of healthy children. Male gender (p = .002), Hamilton Depression Rating Scale (HDRS) (p = .002), cyclothymic (p = .022), irritable (p = .035) and anxious temperament scores (p = .016) significantly predicted the association between the mothers and their children with ADHD. Our findings might suggest that male child gender, the severity of depression at index pregnancy, higher cyclothymic, irritable, and anxious temperament scores in mothers may constitute as important risk factors for the development of ADHD in their children. Impact statement What is already known on this subject? Although the effects of maternal depression on ADHD were extensively investigated, the relationship between affective temperament traits of mothers and ADHD in their children has not been sufficiently examined. To investigate the roles of maternal affective temperament traits and pregnancy-related depression on offspring ADHD would help us to understand the etiopathogenic bases of ADHD. What do the results of this study add? Cyclothymic, irritable and anxious temperaments of mothers were significantly associated with the offspring ADHD after adjusting for the gender, maternal smoking, prepartum and antenatal depression. What are the implications of these findings for clinical practice and/or further research? These findings might demonstrate that some maternal affective temperaments and depression during pregnancy are suggestive of an inherited predisposition to ADHD in offsprings. Longitudinal studies are required to demonstrate the relationship

between maternal affective temperament features and the development of affective illness in children with ADHD

Journal of Practice in Clinical Psychology. 2019;7:11-20.

EVALUATION OF THE EFFECTS OF POSITIVE PARENTING PROGRAM ON SYMPTOMS OF PRESCHOOL CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER .

Khademi M, Ayatmehr F, Mehr NK, et al.

Objective: Positive Parenting Program (Triple-P) is an approved method of parent training for reducing child behavioral problems. The present study aimed to evaluate the effectiveness of standard level of Triple-P in improving behavioral problems and core Attention Deficit Hyperactivity Disorder (ADHD) symptoms of preschool children diagnosed with ADHD.

Methods: The study was conducted on 94 mothers who had preschool children with ADHD (53 subjects and 41 controls), referred to child psychiatry clinic at Imam Hossein Hospital, Tehran, Iran. The subjects were selected by purposive sampling method. Mothers with adjusted homogeneous demographic factors responded to study questionnaires (pre-test and post-test) in both groups. The subject group received child-rearing intervention Triple-p and the control group received the routine clinical treatment. The obtained data were analyzed by analysis of covariance in SPSS.

Results: A significant decrease was observed in ADHD symptoms based on Conner's questionnaire in the subjects compared to controls ($P = 0.001$). Parent depression index in the subject group was significant compared to control group ($P = 0.005$). In addition, results related to parent problem scale in the subject group indicated a significant improvement compared to control group ($P = 0.001$).

Conclusion: Our findings suggest that the Triple-p can reduce ADHD symptoms and behavioral problems and improve the capabilities of preschool children with ADHD

J Psychopathol Behav Assess. 2019.

WORKING MEMORY CAPACITY AND ADHD SYMPTOMS IN BOYS: EXAMINING THE HETEROGENEITY OF WORKING MEMORY FUNCTIONING USING LATENT PROFILE ANALYSIS.

Campez M, Raiker JS, Sarver DE, et al.

Recent studies demonstrate that working memory (WM) is integral to etiological models of ADHD; however, significant questions persist regarding the relation between WM performance across tasks with varying cognitive demands and ADHD symptoms. The current study incorporates an individual differences approach to WM heterogeneity (i.e., latent profile analysis) to (a) identify differential profiles of WM across the phonological and visuospatial WM subsystems; and (b) characterize differences in symptom presentation among WM profiles. Parent and teacher ratings of child behavior, obtained for boys with ($n = 51$) and without ($n = 38$) a diagnosis of ADHD, were compared across latent classes of visuospatial and phonological WM performance. Latent profile analysis identified three classes of WM functioning: Low WM, Moderate WM, and High WM. Membership in the Low and Moderate WM classes was associated with greater levels of parent- and teacher-rated inattentive and hyperactive symptoms. While 84% of the ADHD group were assigned to the Low and Moderate WM classes, more than a quarter of children without ADHD exhibited Moderate WM limitations. Collectively, these findings extend prior work suggesting that there is substantial heterogeneity in WM functioning in children with and without ADHD and that these differences contribute to the expression of symptoms of inattention and hyperactivity

J Am Acad Child Adolesc Psychiatry. 2016;55:937-44.

CHILDHOOD FACTORS AFFECTING PERSISTENCE AND DESISTENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN ADULTHOOD: RESULTS-ÁFROM-ÁTHE MTA.

Roy A, Hechtman L, Roy A, et al.

Objective To determine childhood factors that predict attention-deficit/hyperactivity disorder (ADHD) persistence and desistence in adulthood.

Method Regression analyses were used to determine associations between childhood factors and adult ADHD symptom persistence in 453 participants (mean age, 25 years) from the Multimodal Treatment Study of Children with ADHD (MTA). Childhood IQ, total number of comorbidities, child-perceived parenting practices, child-perceived parent-child relationships, parental mental health problems, marital problems of parents, household income levels, and parental education were assessed at a mean age of 8 years in all participants. Adult ADHD persistence was defined using DSM-5 symptom counts either with or without impairment, as well as mean ADHD symptom scores on the Conners Adult ADHD Rating Scale (CAARS). Age, sex, MTA site, and childhood ADHD symptoms were covaried.

Results The most important childhood predictors of adult ADHD symptom persistence were initial ADHD symptom severity (odds ratio [OR]-á= 1.89, standard error [SE]-á= 0.28, p-á=.025), comorbidities (OR-á= 1.19, SE-á= 0.07, p-á=.018), and parental mental health problems (OR-á= 1.30, SE-á= 0.09, p-á=.003). Childhood IQ, socioeconomic status, parental education, and parent-áchild relationships showed no associations with adult ADHD symptom persistence.

Conclusion Initial ADHD symptom severity, parental mental health, and childhood comorbidity affect persistence of ADHD symptoms into adulthood. Addressing these areas early may assist in reducing adult ADHD persistence and functioning problems

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J Neurol Sci. 2019;405:58.

ADHD AND EPILEPSY MYTHS AND FACTS.

Wilmshurst J.

Attention deficit hyperactivity disorder (ADHD) is a common and challenging comorbidity affecting many children with epilepsy. Practitioners and caregivers are affected by contentious issues relating to the care of these children. In variance to children with ADHD in isolation, there is no increased risk of ADHD in boys who have epilepsy compared to girls with epilepsy. Maternal use of valproate in pregnancy is associated with inattentiveness and hyperactivity in offspring. The impact of early seizure onset on development of ADHD is not delineated but does become more evident with poor seizure control. Screening for ADHD is recommended from 6 years of age, or at the time of diagnosis, and repeated annually and should be reevaluated after change of antiseizure medication (ASM). Diagnosis should involve health practitioners with expert training in ADHD and the Strength and Difficulties Questionnaire screening tool is a useful aid. Behavioral problems are more likely with polytherapy than monotherapy. Valproate can exacerbate attentional issues in children with childhood absence epilepsy. Methylphenidate is tolerated and effective in children with epilepsy. This talks will address these issues and will highlight the strength of evidence to support the points raised

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J Neurol Sci. 2019;405:52.

THE RELATIONS BETWEEN ABNORMAL SENSORY PROCESSING PATTERNS AND ADHD SUBTYPES COMPARED WITH A HEALTHY CONTROL GROUP RYDER CHEN OHANA KARI AND SHAHIEN RADI.

Shahien R.

Background: ADHD is an early childhood neurodevelopmental disorder with an estimated prevalence of 5.9%-7.1%. Sensory processing disorder (SPD), another early childhood developmental disorder, received much less attention. The prevalence of SPD may be as high as ADHD in the pediatric population and it is estimated to be highly co-morbid with ADHD. Many ADHD patients who suffer from co-occurring sensory processing symptoms in adulthood do not receive an SPD diagnosis and therefore may not receive

eligible treatment. The study aimed to evaluate the co-occurrence of SPD in different modalities among different subtypes of ADHD in adult population and to compare it with a healthy control group.

Methods: A total of 60 individuals between 18 and 45 years of age, were divided into two groups: the ADHD group (n = 30) and a healthy control group (n = 30). The participants completed questionnaires regarding ADHD in adulthood and SPD symptoms and subtypes. The results of sensory profile in different subtypes of ADHD were statistically analyzed and compared with control group.

Results: Individuals suffering from combined type ADHD were found having more frequent and extreme reactions (both hyper- and hypo sensitivity) to sensory stimuli compared to healthy controls and individuals with inattentive type ADHD.

Conclusion: This study's results emphasize the importance of utilizing the SPD questionnaire among adult patients who seek neurological or mental treatment as part of the medical intake and thus should further be considered for inclusion in a standard DSM-VI adult diagnosis as a disorder whose impact continues to adulthood

Medical Acupuncture. 2019;31:334-38.

PEDIATRIC ACUPUNCTURE: A SPIRITUAL PERSPECTIVE.

Aung SKH.

Background: Approaching pediatric acupuncture from a spiritual perspective is the most effective means for providing a valuable holistic relatively noninvasive approach to pediatric acupuncture, as well as preventive treatments for the repulsion of disease and the correction of Qi (i.e., vital energy) imbalances. Objectives: Parents may be taught to apply acupressure to their children with an excellent response, especially when given with loving kindness.

Materials and Methods: Methods include the use of acupressure, laser techniques, and acupuncture for children who do not display fear toward the shallow insertion of needles.

Results: Owing to the young age of the patients, children will display fast and effective positive responses to therapy, just as they are susceptible to negative effects in similar timeframes. Children will respond faster than adults to such treatments, which can also increase immune system functionality and bolster resistance to invasive forms of Qi imbalances and disease. Such treatments will also relieve pain and distress and improve concentration and mental attitudes in children. Difficult conditions such as attention-deficit/hyperactivity disorder (ADHD) and attention deficit disorder (ADD) can also be effectively treated through a spiritual approach to pediatric acupuncture.

Conclusions: Pediatric acupuncture from a spiritual perspective provides a specific, safe, and effective therapy for a wide variety of painful and nonpainful conditions through Qi balancing in children. Moreover, parents may be taught to apply acupressure to their children with an excellent response, especially when given with loving kindness. Such techniques not only resolve acute symptoms but also provide preventive measures and enable parent-child relationships to thrive. Overall, medical acupuncture from a spiritual perspective is one of the best complementary therapies in pediatrics

Medicina (Kaunas). 2019 May;55.

CURRENT PATTERN OF PSYCHIATRIC COMORBIDITY AND PSYCHOTROPIC DRUG PRESCRIPTION IN CHILD AND ADOLESCENT PATIENTS.

Araz AM, Bozatli L, Demirci SB, et al.

Background: In recent years, patterns of the use of psychotropic drugs vary with increasing rates of psychiatric presentation and diagnosis in children and adolescents.

Purpose: In this study, we aimed to investigate distributions of current psychiatric symptoms and diagnosis, patterns of the use of psychotropic drugs, and differences according to age and gender in patients presented to a child and adolescent outpatient clinic.

Methods: All patients aged between 0 and 18 years presenting to a child and adolescent psychiatry outpatient clinic between November 1, 2017 and November 1, 2018 were included in the study. Files of all

patients were examined in detail, and patients' demographic characteristics, symptoms, psychiatric diagnoses established according to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), psychotropic drugs initiated, and side effect profiles were recorded. Psychiatric symptoms and diagnostic features of the patients were determined, and the differences were investigated according to gender. Clinical characteristics were compared between diagnosed and undiagnosed patients, and between patients with and without drug initiation.

Results: Of the 2066 patients, 1298 (62.8%) were male and the mean age was 10.14 +/- 4.42 years. The most common symptoms were hyperactivity (23.8%) and inattention (21.6%) in males, inattention (15.1%) and irritability (14.2%) in females, and 79% of the patients received one or more psychiatric diagnoses. The most common psychiatric diagnoses in both genders were attention-deficit hyperactivity disorder (ADHD), specific learning disorder (SLD), and conduct disorder, respectively. Of the patients who received a psychiatric diagnosis, 61.8% were using psychotropic drugs, with the majority of them (71.3%) receiving monotherapy. The most frequently initiated drugs included psychostimulants, antipsychotics, and antidepressants, with 28.7% of the drug user patients receiving multiple drug therapy.

Conclusion: Our study indicates that rate of presentation to child and adolescent psychiatry outpatient clinics is increasing, and rates of diagnosis and initiation of psychiatry drugs are high among the presented children. The prevalence of ADHD shows an increase in males and females in our country, and psychiatric polypharmacy has reached significant rates

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Medicina (Kaunas). 2019 Jun;55.

INTERVENTIONS BASED ON MIND-BODY THERAPIES FOR THE IMPROVEMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN YOUTH: A SYSTEMATIC REVIEW.

Barranco-Ruiz Y, Etxabe BE, Ramirez-Velez R, et al.

Background and objectives: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common psychiatric disorders in children and adolescents. Mind-body therapies (MBTs) seem to be effective for improving health in different populations; however, whether a positive effect occurs in children and adolescents with ADHD is still controversial. The main aim of this systematic review was to analyse the interventions based on MBT aimed to improve the main ADHD symptoms in children and adolescents.

Materials and Methods: A systematic review was conducted following the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines to identify MBT studies on children and adolescents (4-18 years) with a clinical diagnosis of ADHD. Study quality was evaluated by the NIH quality tool (U.S. National Institute of Health).

Results: There were positive results in eleven out of twelve included studies regarding the effect of the MBT interventions on ADHD symptoms. With respect to ADHD symptoms, we observed differences across studies. In relation to the studies' quality, eleven studies were rated "poor" and one was rated as "fair".

Conclusions: MBTs, such as yoga or mindfulness, could be positive strategies to mitigate ADHD symptoms in children and adolescents. However, further research with high-quality designs, with randomization, greater sample sizes, and more intensive supervised practice programs are needed

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Medicine (Baltimore). 2019 Nov;98:e17980.

IMPACT OF PHYSICAL EXERCISE ON CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDERS: EVIDENCE THROUGH A META-ANALYSIS.

Zang Y.

BACKGROUND: Attention deficit hyperactivity disorder (ADHD) which is characterized by developmentally inappropriate levels of attention, hyperactivity and impulsivity, is considered as the most common neurodevelopmental disorder in childhood. Physical exercise has shown to have several benefits in the improvement of children with ADHD. In this meta-analysis, we aimed to systematically show, with evidence, the impact of physical exercise on children with ADHD.

METHODS: Web of Science, MEDLINE, EMBASE, Google Scholar, Cochrane Central and <http://www.ClinicalTrials.gov> were the searched sources for studies which were based on the impact of physical exercise on children with ADHD. Relevant endpoints were assessed. This evidence based meta-analysis was carried out by the most relevant RevMan 5.3 software. Due to the involvement of continuous data (mean and standard deviation), weight mean difference (WMD) with 95% confidence intervals (CI) were used to represent the final analysis. A significant level of $P \leq .05$ was set and a fixed statistical effect model was used throughout the analysis.

RESULTS: Fourteen studies with a total number of 574 participants with ADHD were included in this evidenced based meta-analysis. Two hundred and seventy six (276) participants were assigned to the physical activity group whereas 298 participants were assigned to the control group. Results of this analysis showed that anxiety and depression were significantly improved with physical activity in these children with ADHD (WMD: -1.84; 95% CI: [-2.65 - (-1.03)], $P = .00001$). Hyperactive/impulsive symptoms (WMD: -0.01; 95% CI: [-0.32 - 0.29], $P = .93$) and inattention symptoms (WMD: -0.22; 95% CI: [-0.51 - 0.08], $P = .15$) were also improved with physical exercise but the results were not statistically significant. This evidence based analysis showed thought problems (WMD: -3.49; 95% CI: [-5.51 - (-1.47)], $P = .0007$), social problems (WMD: -5.08; 95% CI: [-7.34 - (-2.82)], $P = .0001$), and aggressive behaviors (WMD: -3.90; 95% CI: [-7.10 - (-0.70)], $P = .02$) to have significantly been improved in participants with ADHD who were assigned to physical activity group.

CONCLUSIONS: This current meta-analysis showed with evidence, that physical exercise has a major contribution owing to significant improvement in anxiety and depression, aggressive behaviors, thought and social problems among children suffering from ADHD. Therefore, physical exercise should be incorporated in the daily life of children with ADHD. Further future research should be able to confirm this hypothesis

Nat Commun. 2019 Aug;10:3529.

HAPLOINSUFFICIENCY IN THE ANKS1B GENE ENCODING AIDA-1 LEADS TO A NEURODEVELOPMENTAL SYNDROME.

Carbonell AU, Cho CH, Tindi JO, et al.

Neurodevelopmental disorders, including autism spectrum disorder, have complex polygenic etiologies. Single-gene mutations in patients can help define genetic factors and molecular mechanisms underlying neurodevelopmental disorders. Here we describe individuals with monogenic heterozygous microdeletions in ANKS1B, a predicted risk gene for autism and neuropsychiatric diseases. Affected individuals present with a spectrum of neurodevelopmental phenotypes, including autism, attention-deficit hyperactivity disorder, and speech and motor deficits. Neurons generated from patient-derived induced pluripotent stem cells demonstrate loss of the ANKS1B-encoded protein AIDA-1, a brain-specific protein highly enriched at neuronal synapses. A transgenic mouse model of Anks1b haploinsufficiency recapitulates a range of patient phenotypes, including social deficits, hyperactivity, and sensorimotor dysfunction. Identification of the AIDA-1 interactome using quantitative proteomics reveals protein networks involved in synaptic function and the etiology of neurodevelopmental disorders. Our findings formalize a link between the synaptic protein AIDA-1 and a rare, previously undefined genetic disease we term ANKS1B haploinsufficiency syndrome

Neuroimage Clin. 2019;21:101653.

QUASI-PERIODIC PATTERNS OF BRAIN ACTIVITY IN INDIVIDUALS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Abbas A, Bassil Y, Keilholz S.

Individuals with attention-deficit/hyperactivity disorder have disrupted functional connectivity in the default mode and task positive networks. Traditional fMRI analysis techniques that focus on 'static' changes in functional connectivity have been successful in identifying differences between healthy controls and individuals with ADHD. However, such analyses are unable to explain the mechanisms behind the functional connectivity differences observed. Here, we study dynamic changes in functional connectivity in individuals with ADHD through investigation of quasi-periodic patterns (QPPs). QPPs are reliably recurring low-frequency spatiotemporal patterns in the brain linked to infra-slow electrical activity. They have been shown

to contribute to functional connectivity observed through static analysis techniques. We find that QPPs contribute to functional connectivity specifically in regions that are disrupted in individuals with ADHD. Individuals with ADHD also show differences in the spatiotemporal pattern observed within the QPPs. This difference results in a weaker contribution of QPPs to functional connectivity in the default mode and task positive networks. We conclude that quasi-periodic patterns provide insight into the mechanisms behind functional connectivity differences seen in individuals with ADHD. This allows for a better understanding of the etiology of the disorder and development of effective treatments

Neuroimage Clin. 2019;21:101678.

INVESTIGATING FUNCTIONAL BRAIN NETWORK INTEGRITY USING A TRADITIONAL AND NOVEL CATEGORICAL SCHEME FOR NEURODEVELOPMENTAL DISORDERS.

Dajani DR, Burrows CA, Odriozola P, et al.

BACKGROUND: Current diagnostic systems for neurodevelopmental disorders do not have clear links to underlying neurobiology, limiting their utility in identifying targeted treatments for individuals. Here, we aimed to investigate differences in functional brain network integrity between traditional diagnostic categories (autism spectrum disorder [ASD], attention-deficit/hyperactivity disorder [ADHD], typically developing [TD]) and carefully consider the impact of comorbid ASD and ADHD on functional brain network integrity in a sample adequately powered to detect large effects. We also assess the neurobiological separability of a novel, potential alternative categorical scheme based on behavioral measures of executive function.

METHOD: Five-minute resting-state fMRI data were obtained from 168 children (128 boys, 40 girls) with ASD, ADHD, comorbid ASD and ADHD, and TD children. Independent component analysis and dual regression were used to compute within- and between-network functional connectivity metrics at the individual level.

RESULTS: No significant group differences in within- or between-network functional connectivity were observed between traditional diagnostic categories (ASD, ADHD, TD) even when stratified by comorbidity (ASD+ADHD, ASD, ADHD, TD). Similarly, subgroups classified by executive functioning levels showed no group differences.

CONCLUSIONS: Using clinical diagnosis and behavioral measures of executive function, no differences in functional connectivity were observed among the categories examined. Despite our limited ability to detect small- to medium-sized differences between groups, this work contributes to a growing literature suggesting that traditional diagnostic categories do not define neurobiologically separable groups. Future work is necessary to ascertain the validity of the executive function-based nosology, but current results suggest that nosologies reliant on behavioral data alone may not lead to discovery of neurobiologically distinct categories

Neurologia. 2019;34:563-72.

VALIDATION OF A SPANISH-LANGUAGE VERSION OF THE ADHD RATING SCALE IV IN A SPANISH SAMPLE.

Vallejo-Valdivielso M, Soutullo CA, de Castro-Manglano P, et al.

Objectives: The purpose of this study is to validate a Spanish-language version of the 18-item ADHD Rating Scale-IV (ADHD-RS-IV.es) in a Spanish sample.

Methods: From a total sample of 652 children and adolescents aged 6 to 17 years (mean age was 11.14 -1 3.27), we included 518 who met the DSM-IV-TR criteria for ADHD and 134 healthy controls. To evaluate the factorial structure, validity, and reliability of the scale, we performed a confirmatory factor analysis (CFA) using structural equation modelling on a polychoric correlation matrix and maximum likelihood estimation. The scale's discriminant validity and predictive value were estimated using ROC (receiver operating characteristics) curve analysis.

Results: Both the full scale and the subscales of the Spanish-language version of the ADHD-RS-IV showed good internal consistency. Cronbach's alpha was 0.94 for the full scale and 0.90 for the subscales, and ordinal alpha was 0.95 and 0.90, respectively. CFA showed that a two-factor model (inattention and

hyperactivity/impulsivity) provided the best fit for the data. ADHD-RS-IV.es offered good discriminant ability to distinguish between patients with ADHD and controls (AUC = 0.97).

Conclusions: The two-factor structure of the Spanish-language version of the ADHD-RS-IV (ADHD-RS-IV.es) is consistent with those of the DSM-IV-TR and DSM-5 as well as with the model proposed by the author of the original scale. Furthermore, it has good discriminant ability. ADHD-RS-IV.es is therefore a valid and reliable tool for determining presence and severity of ADHD symptoms in the Spanish population

Neurologia. 2019.

IMPULSIVENESS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AFTER AN 8-WEEK INTERVENTION WITH THE MEDITERRANEAN DIET AND/OR OMEGA-3 FATTY ACIDS: A RANDOMISED CLINICAL TRIAL.

San MM, I, Sanz RS, Gonz lez CL, et al.

Introduction: The Barratt Impulsiveness Scale (BIS) is a self-administered instrument designed to assess the personality/behavioural construct of impulsiveness. Impulsiveness has been associated with several psychiatric disorders, including attention-deficit/hyperactivity disorder (ADHD). This study assesses the progression of impulsive behaviour in children with ADHD after an 8-week dietary intervention with the Mediterranean diet and/or omega-3 fatty acid supplementation, by using a version of the 11-item BIS adapted for children (BIS-11c).

Methods: This cross-sectional study includes 60 children with ADHD from the region of Madrid, Spain. Participants were divided into 4 groups, with one control group (G1) and 3 intervention groups (Mediterranean diet [G2]; omega-3 supplementation [G3]; and Mediterranean diet plus omega-3 supplementation [G4]). A personalised Mediterranean diet was designed for members of groups 2 and 4. The BIS-11c was administered to determine the level of impulsiveness, and the KIDMED test was used to assess adherence to the Mediterranean diet.

Results: The supplementation group showed a fairly significant decrease in the total BIS-11c ($P = .049$). Total cognitive score slightly decreased in the diet and supplementation groups. Only the control group showed a considerable decrease in the total motor score. Total nonplanning scores were lower in all groups after the intervention. Baseline and final BIS-11c scores were positively correlated with treatments ($r > 0.9$).

Conclusion: An intake of 550 mg EPA fatty acid and 225 mg DHA fatty acid per day for 8 weeks is associated with less marked impulsive behaviour in children with ADHD. A Mediterranean diet may improve BIS scores, although our results are not conclusive in this population

Neurology. 2019;93:E599-E610.

MOTOR CORTEX INHIBITION AND MODULATION IN CHILDREN WITH ADHD.

Gilbert DL, Huddleston DA, Wu SW, et al.

Objective Compared to typically developing (TD) peers, children with attention-deficit/hyperactivity disorder (ADHD) consistently demonstrate impaired transcranial magnetic stimulation (TMS)-evoked short interval cortical inhibition (SICI) of motor evoked potentials (MEPs) in resting motor cortex (M1). To determine whether perturbed M1 physiology also reflects clinically relevant behavioral dysfunction, we evaluated M1 physiology during a cognitive control task taxing motor response selection/inhibition.

Methods In this case-control study, behavioral ratings, motor skill (assessed using standardized examination), and left M1 physiology were evaluated in 131 right-handed, 8-to 12-year-old children (66 ADHD: Mean 10.5 years, 43 male; 65 TD: Mean 10.6 years, 42 male). The primary outcomes were MEP amplitudes and SICI, evaluated during rest and during a modified "racecar" Slater-Hammel stop signal reaction task, with TMS pulses administered 150 ms prior to the target go action and after the dynamic stop cue.

Results Go responses were significantly slower ($p = 0.01$) and more variable ($p = 0.002$) in ADHD. Children with ADHD showed less M1 SICI at rest ($p = 0.02$) and during go ($p = 0.03$) and stop trials ($p = 0.02$). Rest M1 excitability increased during response inhibition task engagement ($p < 0.0001$). This Task-Related Up-

Modulation (TRUM) was less robust across and within groups, with diminished task upmodulation associated with significantly more severe ADHD behavioral ratings and slower stop signal reaction times.

Conclusion Children with ADHD show anomalous motor cortex physiology, with deficient SICl across behavioral states and less TRUM from rest to action selection. Associations of these physiologic measures with ADHD symptoms and cognitive control measures support further investigation into biological mechanisms

Neuropsychiatr Enfance Adolesc. 2019.

PSYCHOMOTOR THERAPY AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER: EVALUATION OF A RHYTHM-BASED THERAPEUTIC PROGRAM.

Puyjarinet F, Jeannin-Fuzier A, Blain C, et al.

Aim of the study: This study aimed at investigating the effects of a rhythm-based therapeutic program among ADHD children by assessing performance in attentional and executive domains.

Participants and method: Twenty-one children (mean age: 9.1, SD: 1.8; 3 females) who previously received a diagnosis of ADHD benefited from a rhythm-based training program (8 to 12 training sessions) delivered during a psychomotor therapy. The program consisted of rhythmic perceptuo-motor exercises, including sensorimotor synchronization to external beats (metronome, music). Attentional and executive performances were assessed with a test-retest experimental design.

Results: Attentional and executive performance improved in different domains: inhibition, cognitive impulsiveness and visuo-spatial working memory. A slight improvement was visible for divided attention, whereas sustained auditory attention, selective visual attention and delay aversion did not change after intervention.

Conclusion: These results are in favor of tight relations between a rhythmic training program and some attentional and executive functions among ADHD children, with beneficial effects of the training on a variety of cognitive performances. This study seems promising for the purpose of supplementing chemical treatments among a range of ADHD patients in cognitive domain

Neuropsychopharmacology. 2019 Jun;44:1216-23.

THE MYELOARCHITECTURE OF IMPULSIVITY: PREMATURE RESPONDING IN YOUTH IS ASSOCIATED WITH DECREASED MYELINATION OF VENTRAL PUTAMEN.

Nord CL, Kim SG, Callesen MB, et al.

Impulsivity has been suggested as a neurocognitive endophenotype conferring risk across a number of neuropsychiatric conditions, including substance and behavioural addictions, eating disorders, and attention deficit/hyperactivity disorder. We used a paradigm with interspecies translation validity (the four-choice serial reaction time task, 4CSRTT) to assess 'waiting' impulsivity in a youth sample (N = 99, aged 16-26 years). We collected magnetization prepared two rapid acquisition gradient echo (MP2RAGE) scans, which enabled us to measure R1, the longitudinal relaxation rate, a parameter closely related to tissue myelin content, as well as quantify grey matter volume. We also assessed inhibitory control (commission errors) on a Go/NoGo task and measured decisional impulsivity (delay discounting) using the Monetary Choice Questionnaire (MCQ). We found R1 of the bilateral ventral putamen was negatively correlated with premature responding, the index of waiting impulsivity on the 4CSRTT. Heightened impulsivity in youth was significantly and specifically associated with lower levels of myelination in the ventral putamen. Impulsivity was not associated with grey matter volume. The association with myelination was specific to waiting impulsivity: R1 was not associated with decisional impulsivity on the MCQ or inhibitory control on the Go/NoGo task. We report that heightened waiting impulsivity, measured as premature responding on the 4CSRTT, is specifically associated with lower levels of ventral putaminal myelination, measured using R1. This may represent a neural signature of vulnerability to diseases associated with excessive impulsivity and demonstrates the

added explanatory power of quantifying the mesoscopic organization of the human brain, over and above macroscopic volumetric measurements

Neuropsychopharmacology Reports. 2019.

LONG-TERM STUDY OF LISDEXAMFETAMINE DIMESYLATE IN JAPANESE CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Ichikawa H, Miyajima T, Yamashita Y, et al.

Aims: As an extension of a phase 2/3 study evaluating the efficacy and safety of lisdexamfetamine dimesylate (LDX) 30, 50, or 70-ámg/d for 4weeks in Japanese patients aged 6-17-áyears with attention-deficit/hyperactivity disorder (ADHD), this study evaluated its long-term safety and efficacy.

Methods: This was a multicenter, open-label study of LDX for 53weeks. Safety was assessed by regular medical examination for treatment-emergent adverse events (TEAEs); regular recording of body weight, vital signs, and laboratory test values; and completion of dependence questionnaires. Efficacy was assessed using Japanese versions of the ADHD-Rating Scale-IV (ADHD-RS-IV) and Conners' 3rd edition Parent Rating Scale (Conners 3); plus Clinical Global Impression-Improvement (CGI-I), Clinical Global Impression-Severity, and Parent Global Assessment (PGA) scales.

Results: Of 132 enrolled patients, 104 completed the trial. Most frequent treatment-related TEAEs were decreased appetite (73.5%), initial insomnia (39.4%), and weight decrease (22.0%). Most TEAEs were mild (82.6% of patients). There were no serious or severe TEAEs or deaths. No treatment-related TEAEs were associated with blood pressure or pulse rate, and no patient had a QTcF interval >500 ms. Statistically significant improvement from baseline to week 53 was observed in the mean ADHD-Rating Scale-IV total score and mean Conners 3 subscale scores. Most patients showed improvement on the CGI-I (78%) and PGA (76.5%) scales.

Conclusions: No significant safety issues were observed with LDX 30, 50, or 70-ámg/d administered for 1-áyear in Japanese children and adolescents with ADHD. LDX was associated with long-term reductions in ADHD symptoms and severity

Nord J Psychiatry. 2019 Oct;73:409-16.

QUALITY OF LIFE IN OLDER ADULTS WITH ADHD: LINKS TO ADHD SYMPTOM LEVELS AND EXECUTIVE FUNCTIONING DEFICITS.

Thorell LB, Holst Y, Sjowall D.

Purpose and aim: The overall aim of the present study was to examine quality of life in attention deficit hyperactivity disorder (ADHD) patients age ≥ 60 years. First, we compared older adults with ADHD to both healthy controls of the same age and younger adults with ADHD. Second, we examined executive functioning as a possible underlying factor for quality of life among older adults with ADHD.

Methods: The study included 158 participants in three groups: (1) older adults (60-75 years of age) with ADHD (n = 42), (2) healthy controls of the same age (n = 58), and (3) younger adults (age 18-45 years of age) with ADHD (n = 56). The patients with ADHD were clinically-referred. Quality of life was examined through self-ratings and executive functioning was examined using both self-ratings and tests.

Results: Older adults with ADHD differed significantly from controls the same age on all aspects of quality of life, with large effect sizes. However, they showed similar levels of quality of life compared to younger adults with ADHD. The exception was psychological health, for which older adults displayed better quality of life compared to younger adults with ADHD. Executive deficits measured through self-ratings, especially working memory, were related to quality of life, sometimes also beyond the influence of ADHD symptom levels.

Conclusions: Older adults with ADHD show serious impairments in quality of life, that are comparable to the levels found for younger adults. Impairments may increase further as these individuals grow older and clinics need to meet the needs of this increasingly larger group of patients

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Nord J Psychiatry. 2019.

ADHD SYMPTOMS IN RELATION TO INTERNALIZING AND EXTERNALIZING SYMPTOMS IN CHILDREN: THE MEDIATING ROLE OF SLUGGISH COGNITIVE TEMPO.

Sevincok D, Ozbay HC, Ozbek MM, et al.

Objective: Although internalizing and externalizing disorders have received considerable attention among young population, the mechanisms that explain the relationships of internalization and externalization symptoms with attention deficit/hyperactivity disorder (ADHD) in children and adolescents are not well understood. Since sluggish cognitive tempo (SCT) symptoms had significant associations with ADHD, and internalization/externalization disorders, we examined whether SCT may mediate between ADHD symptoms and internalizing/externalizing problems during childhood.

Methods: We performed a retrospective chart-review of 95 children and adolescents (76 boys and 19 girls, aged 6-16) with ADHD. The severity of ADHD was evaluated by Turgay DSM-IV-Based Disruptive Behavioral Disorders Screening and Rating Scale (T-DSMIV-S) completed by teachers. Measures of SCT, internalisation and externalisation symptoms, social, thought, and attentional problems were based on the Teacher Report Form (TRF) that was completed by subjects primary teachers.

Results: The withdrawn scores were significantly correlated with SCT scores, social problems, and ADHD-inattention. There was an inverse correlation between withdrawn and ADHD-hyperactivity/impulsivity scores. The mediation test using bootstrapping method showed that the indirect coefficient for SCT was significant, after controlling of ADHD-inattention and social problems covariates, consistent with partial mediation.

Conclusion: Our results may demonstrate that while externalization symptoms were associated with hyperactivity/impulsivity symptoms of ADHD, the internalization symptoms were significantly related to SCT in youngs with ADHD. Specifically, although social withdrawal was significantly related to ADHD-inattention, this relationship was mediated by the severity of SCT

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Pediatr Ann. 2019 Jun;48:e220-e225.

PEDIATRIC ANTI-INFLAMMATORY DIET.

Mascarenhas MR.

The anti-inflammatory diet is based on two diets that have been shown to have many positive health effects- the Mediterranean diet and the Okinawan diet. The anti-inflammatory diet is more than just a prescription for healthy food, but rather a way of life characterized by a plant-based diet and a pattern of living that includes eating a diverse range of locally grown foods eaten in season, conviviality, culinary activities, physical activity, and rest. The Mediterranean diet has been shown to reduce the burden and even prevent the development of cardiovascular disease, breast cancer, depression, colorectal cancer, diabetes, obesity, asthma, and cognitive decline in adults. In children, there is emerging evidence demonstrating beneficial effects with regard to obesity, cardiorespiratory fitness, diabetes, fatty liver, academic performance, attention-deficit/hyperactivity disorder, asthma, and allergies. Maternal ingestion of the diet during pregnancy has also been shown to have positive effects on infants and children. [Pediatr Ann. 2019;48(6):e220-e225.]

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Pediatrics. 2018;141.

COLLABORATING TO IMPROVE DIAGNOSIS AND MANAGEMENT OF CHILDREN & ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Liu D, Wuthrich A, Norlin C.

Background: Attention Deficit Hyperactivity Disorder (ADHD) is the most common neurobehavioral developmental disorder in children. Though pediatricians are called upon to serve this growing population, the percentage of pediatricians who reported treating, managing, or co-managing ADHD remained relatively unchanged in 2013 compared to 2004 at 57%. (Stein, RK. Et al. Beyond ADHD: How Well Are We Doing? Acad Pediatr. 2016 Mar;16(2):115-21. doi: 10.1016/j.acap.2015.08.012. Epub 2015 Sep 26) Purpose: To improve diagnosis and management of children and adolescents with attention deficit hyperactivity disorder (ADD/ADHD).

Methods: In collaboration with the University of Utah's Department of Psychiatry Division of Child Psychiatry, and Department of Pediatrics Division of Pediatric Psychiatry and Behavioral Health, nine primary care practice teams (consisting of treating clinicians, medical/nursing staff, and administrative personnel) enrolled in a 9-month Quality Improvement Learning Collaborative (LC) from November 2015 to September 2016. Practice teams attended a quality improvement learning session to understand the DSM-V diagnostic criteria for ADHD, and recommended treatment and management guidelines by the American Academy of Pediatrics. In addition, practice teams were taught quality improvement methods, including how to conduct rapid cycles of change through the Model for Improvement. Each practice, paired with a quality improvement specialist, selected targeted interventions to address improvement of diagnosis, treatment, and management of patients with ADD/ADHD. Each practice randomly selected a sample of 30 encounters reflecting visits from patients newly diagnosed with, or returning for follow-up care for, ADD/ADHD for the initial baseline measurements. Practice teams developed customized interventions and implemented changes with the goal of achieving 80% success for patients ages 6-18 years of age with ADD/ADHD by September 2016 in each area: 1. Percent of patients newly diagnosed with ADHD with validated screening tools from 2 or more settings 2. Percent of patients newly diagnosed with ADHD with documentation of DSM-V criteria 3. Percent of patients returning for follow-up with validated screening tools from 2 or more settings 4. Percent of patients newly diagnosed with ADHD with evaluation of co-existing conditions 5. Percent of patients started on a medication for ADHD and follow-up within 45 days 6. Percent of patients on maintenance medication for ADHD and follow-up with 6 months 7. Percent of patients returning for follow-up care reflecting: a. Weight b. Height c. Evaluation of side effects d. Evaluation of school progress e. Addressing care plan Monthly measurements of 10 randomly selected charts are currently being conducted, and practices receive regular feedback via conference calls to support continued cycles of change, discuss barriers and solutions, and monitor progress. Results of the project's aggregate data are shared with all practices monthly.

Results: As this project is still underway, full analysis of results are yet to be realized. However, aggregate baseline data is reflected in the attached table.

Conclusion: Through a 9-month Quality Improvement Learning Collaborative, clinicians and staff from various practice settings are collaborating to improve diagnosis and management of children and adolescents with attention deficit hyperactivity disorder (ADD/ADHD)

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Pediatrics. 2018;141.

A PHASE III STUDY OF HLD200 IN CHILDREN WITH ATTENTION- DEFICIT/HYPERACTIVITY DISORDER: SAFETY RESULTS.

McDonnell MA, Wigal S, Childress A, et al.

Purpose: This exploratory study consisted of a 6-week open-label, treatment optimization phase followed by a 1-week randomized, double-blind, placebo-controlled, parallel-group test phase to assess HLD200, a delayed and extended-release formulation of methylphenidate (MPH) designed to be taken in the evening, before bedtime to control early morning attention-deficit/hyperactivity disorder (ADHD) symptoms before school and throughout the day, in pediatric subjects.

Methods: Males and females with ADHD, ages 6-12 were enrolled. At baseline (visit 2 [V2]), subjects initiated HLD200 at their previous MPH dose equivalent for 1 week and were dose optimized over five weeks to achieve optimal symptom control. At V8, subjects were randomly assigned (1:1 ratio) to double-blind HLD200

or placebo treatment for a period of 1 week. Safety endpoints were treatment-emergent adverse events (TEAEs), including elicited sleep disturbance and appetite suppression, vital signs, ECG parameters, clinical laboratory tests, physical examination and the Columbia-Suicide Severity Rating Scale (C-SSRS).

Results: There were a total of 23 males and 20 females enrolled; mean age was 9.7 years. There were no reports of TEAEs leading to early withdrawal and no treatment emergent serious AEs during the course of the study. The majority of these TEAEs were judged by the Investigator as mild or moderate in severity (99%) and possibly to certainly related to the study drug (65%). During the treatment optimization phase, 121 TEAEs were reported in 38 subjects (88%). The most commonly reported TEAEs (>10% of subjects) included: decreased appetite (35%), insomnia (23%), headache (16%), abdominal pain upper (14%) and irritability (12%). Fifteen subjects (35%) experienced a total of 15 events of decreased appetite and 10 subjects (23%) experienced a total of 11 insomnia events. In the double-blind phase, a total of 7 HLD200- (32%) and 7 placebo-treated subjects (33%) reported a TEAE. These TEAEs were judged by the Investigator to be mild or moderate in severity and possibly to certainly related to the study drug in 67% and 33% of HLD200- and placebo-treated subjects, respectively. The most commonly reported TEAE was headache (HLD200: 9%; Placebo: 10%) with no other TEAE reported more than once in any subject. No subjects experienced appetiterelated TEAEs, and no HLD200-treated subjects experienced sleep-related TEAEs, whereas two placebo-treated subjects (10%) experienced insomnia-related TEAEs. Vital signs (blood pressure, temperature, respiration) were comparable between HLD200- and placebo-treated subjects. ECG measurements were within normal limits for 18 subjects in the HLD200 group and 19 subjects in the placebo group. However, there were 2 HLD200- and 1 placebo-treated subjects that demonstrated abnormal, but not clinically significant ECGs. One HLD200-treated subject experienced abnormal and clinically significant ECG results (an incomplete transient right bundle branch block).

Conclusions: When taken at bedtime, HLD200 demonstrated a favorable tolerability and safety profile in pediatric ADHD subjects

Pediatrics. 2018;141.

PARENTAL IDENTIFICATION OF A PRIMARY MEDICAL PROVIDER IS ASSOCIATED WITH IMPROVED ABILITY TO FINISH TASKS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Rubinstein M, Ruest SM, Gjelsvik A.

Background: Attention deficit hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood. Affected children often require pharmacologic and/or behavioral interventions that are overseen by a primary care provider. To date there is no literature that examines management strategies and behavioral outcomes in children with ADHD who lack regular primary care. Objective: To determine whether children with ADHD and regular primary care are more likely to be able to finish tasks than affected children without an identified primary care doctor.

Methods: A cross-sectional study was performed using data collected from the 2011-2012 National Survey of Children's Health, a national telephone survey conducted by the United States Department of Health and Human Services. Parents who identified their children as having a diagnosis of ADHD were included in the study (n=8,173). These children were further subdivided by parental identification of a regular primary care provider, number of visits for preventative care, ADHD severity, ADHD medication status, Individualized Educational Plan status, parent reported learning disability, race, income level, and insurance status. The primary outcome studied was whether the parent believes the child usually or always finishes assigned tasks. Secondary parent reported functional and academic performance measures were also examined. Multiple logistic regression was performed using STATA and adjusting for complex survey design to calculate odds ratios (OR).

Results: 8.9% of parents in the study population did not identify a source of regular primary care for their child. Having a primary provider is associated with increased likelihood of taking medication for ADHD (58.1% vs. 35.5% $p < 0.01$). Children with ADHD who lack a regular primary care provider had 53% decreased odds (95% CI .29-.77) of usually or always finishing assigned tasks when compared to the same population with a regular source of primary care, controlling for ADHD medication status and the other factors listed above. In bivariate analysis, children without a regular primary care provider were more likely to get a disciplinary call from school ($p=0.02$), less likely to care about doing well in school ($p=0.01$), and less likely to regularly

complete homework ($p=0.002$). However, in the adjusted model there was no significant difference between the two populations in any of the three domains ($p=0.54$ for school calls, $p=0.07$ for caring about school, and $p=0.06$ for regularly completing homework).

Conclusions: Having a primary care provider is associated with an increased ability to finish tasks in children with ADHD. However it is unclear if this leads to improved academic or functional outcomes. Future research should focus on the relationship between ability to finish tasks and school performance. Key Words: ADHD, Primary Care, Childhood, Task-Completion, School Performance

Pediatrics. 2018;141.

WEB-BASED PORTAL DEMONSTRATES THAT TEACHER FOLLOW-UP VANDERBILT ASSESSMENTS IMPROVE ADHD OUTCOMES.

Shapiro I, Wolz R, Munro J.

Background The American Academy of Pediatrics' clinical guideline for ADHD recognizes the importance of obtaining information about a child's symptoms and impairments from informants in more than one setting (AAP, 2011). Data from a commercially available web portal for managing patients with ADHD were used to determine whether collecting longitudinal data from more than one setting has an impact on patient outcomes as determined by the Vanderbilt total symptom score.

Methods Children with a parent-rated Vanderbilt total symptom score (TSS) at their baseline diagnostic assessment and at least one follow-up rating 120-365 days after baseline were identified from the anonymized aggregated dataset. The cohort was split into two groups according to whether or not the child had a teacher Vanderbilt completed 20-100 days postbaseline; the time-frame was selected to be during the early treatment period when medication titration was most likely to be occurring and allowed at least 20 days before parent follow-up ratings (permitting eventual treatment changes to have had an impact on TSS). Statistical analyses were performed to explore differences between the groups in terms of TSS at parent follow-up.

Results Data from 1108 children were included; mean age 9 years, 30% female. Teacher Vanderbilt scales had been completed in 80% patients at the baseline assessment and in 39% during the early treatment period. TSS at subsequent parent follow-up was significantly lower ($p < 0.001$) in the group with at least one teacher follow-up assessment. There were no significant differences between the groups in terms of age, gender, baseline TSS or presence of baseline teacher Vanderbilt assessments.

Conclusions Using data from a commercially available web portal for managing patients with ADHD, a significant benefit in outcome in terms of a reduction in Vanderbilt total symptom score was demonstrated in children who had a teacher Vanderbilt assessment completed in their early treatment period. A possible explanation for this finding is that the additional teacher assessment led to an optimization of treatment that was reflected in the subsequent parent Vanderbilt rating. The use of teacher ratings to monitor treatment outcomes is infrequent in routine clinical practice (Epstein, Kelleher, Baum, et al., 2014) and the web based tool provides substantially better collection of data from the school setting than the rates previously reported. In addition to facilitating the acquisition of information from multiple settings in accordance with best practice guidelines, the online tool also allows investigation of outcomes in ADHD. This work can be continued to further refine the schedules and methods by which monitoring ratings are collected, optimizing the care of children with ADHD. This approach is consistent with the AAP's ADHD research priorities and quality improvement initiatives. (Figure Presented)

Pediatrics. 2018;141.

IMPROVING THE APPROACH TO FOLLOW-UP CARE FOR CHILDREN WITH ADHD: A QUALITY IMPROVEMENT STUDY WITHIN THE DIVISION OF DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS.

Shabason EK, Schapiro LE, Jackel CR, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) affects 5-10% of children in the US. Practice guidelines for management of ADHD include the use of standardized rating scales (RS) to monitor treatment.

However, many subspecialty providers, including Developmental and Behavioral Pediatricians (DBP), do not use a standardized approach for follow-up management. Phase 1 of this project found that our DBP division's new visits were more likely to include documentation of parent rating scale (PRS) and teacher rating scale (TRS) data (56% and 47%) than follow-up visits (8% and 22%). Clinicians requested RS for the next visit in 22% of visits. For this project (Phase 2), we focused on follow-up visits.

Aim: To increase provider compliance with requesting and documenting RS to ≥50% of visits by June 2016.

Methods: Data from clinical record review by DBP attendings was entered into a RedCap database. Variables included clinical characteristics (treatments recommended, comorbid conditions) and RS documentation and/or request for next visit. Data was discussed at monthly division meetings, with consensus for tests of change.

Interventions: Early tests of change included increased availability of RS in clinic areas and improved access to templates for documentation and recommendations. The clinicians reached a consensus to use the NICHQ Vanderbilt Assessment Follow-up RS (VRS). Providers were surveyed about possible barriers. A 1-week trial of mailing RS to families 2 weeks ahead of appointments was completed. An electronic health record (EHR)-based flowsheet was used to facilitate tracking results of VRS. Clinicians were provided monthly group data on their frequency of requesting and documenting RS.

Results: Early tests of change resulted in a minor increase in documentation of PRS and TRS (10% and 23%) and requests for RS at the next visit (37%). Mailing RS ahead of appointments increased documentation of PRS and TRS (41% and 46%); however this intervention was not continued due to excessive personnel effort for modest gains. Continued chart reviews will monitor documentation of RS. Data review (11/2015-12/2015) revealed little change in documentation of PRS and TRS (25% and 23%). However, 15% of charts included both PRS and TRS, and 33% of charts included at least 1 RS. Clinicians requesting RS for the next visit increased to 60%.

Conclusion: Preliminary results indicated modest improvement in clinicians requesting RS for the next visit. Nevertheless, the rate of RS return for use in visits remains low, indicating barriers for parents and teachers to complete and return RS. Future interventions will include a simplified process of returning RS through the EHR. Further challenges likely include patients' medical complexity, as many have co-occurring conditions such as autism spectrum disorder, for whom RS may not accurately reflect symptoms. We will continue to use PDSA cycles to implement tests of change and monitor results

Pediatrics. 2018;141.

IMPACT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER ON ADOLESCENTS IN QATAR.

Kamal M.

Introduction Attention Deficit Hyperactivity Disorder, has negative impact on children's life, it was once thought that will be eliminated at puberty, is now established it does not go away and is seen as a lifetime neurobiological challenge. Purpose of this Study To evaluate the challenges that Adolescents with Attention Deficit Hyperactivity Disorder faces: and how it impacts their lives; academically and socially at schools in Qatar

Method A cross-sectional descriptive study using a standardized rating scale of teacher observations was conducted at Schools in Qatar; grades 7 through 12. Teachers completed the SNAP IV and 9 questions regarding academic and social function for each student in their classroom. A total 1716 students were included in this study: 673 male students and 1043 female students. Statistical analysis A two tailed t-test was used to find the confidence level. Chi-square test was used to examine an association between two or more qualitative variables and outcome measures.

Results The prevalence of symptoms of ADHD between genders varied significantly, (3.6% girls and 9.6% boys rated positive for ADHD) Male students had more academic difficulty than female students. 100% Students with ADHD showed difficulty in making and maintaining friends (26% girls, 50% boys) 100% ADHD students have had trouble getting along with others (55% girls, 78% boys) Overall boys faced more challenges than girls

Conclusion The results of this study revealed that Attention Deficit Hyperactivity Disorder is greatly associated with academic and social problems in Adolescents in Qatar. Significant differences between boys

and girls were noted. Attention Deficit Hyperactivity Disorder continues to be a concern for adolescents and that it is most likely the cause of their underperformance academically, and socially and possibly behaviorally. This study hopes to add to the limited amount of literature on adolescents and ADHD, especially in the Middle East where literature for this age group is almost totally lacking. (Figure Presented)

Pediatrics. 2019 Jul;144.

FIVE-YEAR OUTCOMES OF BEHAVIORAL HEALTH INTEGRATION IN PEDIATRIC PRIMARY CARE.

Walter HJ, Vernacchio L, Trudell EK, et al.

BACKGROUND AND OBJECTIVES: In the context of protracted shortages of pediatric behavioral health (BH) specialists, BH integration in pediatric primary care can increase access to BH services. The objectives of this study were to assess the structure and process of pediatric BH integration and outcomes in patient experience (access and quality), cost, and provider satisfaction.

METHODS: In 2013, we launched a multicomponent, transdiagnostic integrated BH model (Behavioral Health Integration Program [BHIP]) in a large pediatric primary care network in Massachusetts. Study participants comprised the first 13 practices to enroll in BHIP (Phase-1). Phase-1 practices are distributed across Greater Boston, with approximately 105 primary care practitioners serving approximately 114 000 patients. Intervention components comprised in-depth BH education, on-demand psychiatric consultation, operational support for integrated practice transformation, and on-site clinical BH service.

RESULTS: Over 5 years, BHIP was associated with increased practice-level BH integration ($P < .001$), psychotherapy ($P < .001$), and medical ($P = .04$) BH visits and guideline-congruent medication prescriptions for anxiety and depression ($P = .05$) and attention-deficit/hyperactivity disorder ($P = .05$). Total ambulatory BH spending increased by 8% in constant dollars over 5 years, mainly attributable to task-shifting from specialty to primary care. Although an initial decline in emergency BH visits from BHIP practices was not sustained, total emergency BH spending decreased by 19%. BHIP providers reported high BH self-efficacy and professional satisfaction from BHIP participation.

CONCLUSIONS: Findings from this study suggest that integrating BH in the pediatric setting can increase access to quality BH services while engendering provider confidence and satisfaction and averting substantial increases in cost

PLoS ONE. 2019;14:e0213995.

SCREEN-TIME IS ASSOCIATED WITH INATTENTION PROBLEMS IN PRESCHOOLERS: RESULTS FROM THE CHILD BIRTH COHORT STUDY.

Tamana SK, Ezeugwu V, Chikuma J, et al.

BACKGROUND: Pre-school children spend an average of two-hours daily using screens. We examined associations between screen-time on pre-school behavior using data from the Canadian Healthy Infant Longitudinal Development (CHIL) study.

METHODS: CHIL participant parents completed the Child Behavior Checklist (CBCL) at five-years of age. Parents reported their child's total screen-time including gaming and mobile devices. Screen-time was categorized using the recommended threshold of two-hours/day for five-years or one-hour/day for three-years. Multiple linear regression examined associations between screen-time and externalizing behavior (e.g. inattention and aggression). Multiple logistic regression identified characteristics of children at risk for clinically significant externalizing problems (CBCL T-score ≥ 65).

RESULTS: Screen-time was available for over 95% of children (2,322/2,427) with CBCL data. Mean screen-time was 1.4 hours/day (95%CI 1.4, 1.5) at five-years and 1.5 hours/day (95%CI: 1.5, 1.6) at three-years. Compared to children with less than 30-minutes/day screen-time, those watching more than two-hours/day (13.7%) had a 2.2-point increase in externalizing T-score (95%CI: 0.9, 3.5, $p \leq 0.001$); a five-fold increased odd for reporting clinically significant externalizing problems (95%CI: 1.0, 25.0, $p = 0.05$); and were 5.9 times more likely to report clinically significant inattention problems (95%CI: 1.6, 21.5, $p = 0.01$). Children with a DSM-5 ADHD T-score above the 65 clinical cut-off were considered to have significant ADHD type symptoms

(n = 24). Children with more than 2-hours of screen-time/day had a 7.7-fold increased risk of meeting criteria for ADHD (95%CI: 1.6, 38.1, p = 0.01). There was no significant association between screen-time and aggressive behaviors (p>0.05).

CONCLUSION: Increased screen-time in pre-school is associated with worse inattention problems

PLoS ONE. 2019;14:e0214821.

STRENGTHENING CARE FOR CHILDREN WITH COMPLEX MENTAL HEALTH CONDITIONS: VIEWS OF AUSTRALIAN CLINICIANS.

Paton K, Hiscock H.

OBJECTIVES: Improving mental health outcomes for children and young people has become a priority for policy makers in the developed world. In Australia, up to half of all children and adolescents meeting criteria for mental health disorders receive suboptimal levels of treatment (or no treatment at all) despite the availability of effective treatments. Children with complex mental health conditions are particularly at risk of inadequate treatment as optimal care requires coordination from medical, educational and social services. In Australia, clinicians including pediatricians, psychologists and child and adolescent psychiatrists deliver the bulk of mental health care for children with complex mental health conditions. We aimed to determine perspectives of these Australian clinicians on barriers and enablers within the current system and components of an optimal model of care.

METHODS: Inductive content analysis was used to analyse 30 semi-structured interviews with key clinicians managing the care of children with complex mental health conditions across Australia. Interviews were conducted using vignettes with Attention Deficit Hyperactivity Disorder (ADHD) and Autism as exemplars.

FINDINGS: Multiple barriers to optimal care exist at a systemic, clinician and family level. However, regional health systems provide an enabling environment from which metropolitan models could learn. Transitioning to adult services was highlighted as the most compromised area of care. Clinicians identified short (e.g. empowering parents to advocate for and deliver their child's care, case conferencing with schools) and long term (e.g. co-locating disciplines to deliver care, workforce training) solutions.

CONCLUSIONS: Whilst multiple barriers to optimal care for children with complex mental health conditions exist, clinicians identify several enablers including developing networks with other disciplines and empowering parents to advocate for and co-ordinate care. Systemic changes based on multidisciplinary, co-located and integrated care services should be developed as longer term solutions

Prim Care Companion CNS Disord. 2019 Jun;21.

THE PATIENT PERSPECTIVE: UNMET TREATMENT NEEDS IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Brown TE, Romero B, Sarocco P, et al.

Objective: To characterize impairments in daily life experienced by pharmacologically treated adults with attention-deficit/hyperactivity disorder (ADHD) versus adults without ADHD and to identify unmet needs in ADHD treatment from the perspective of adults with ADHD.

Methods: Adults with ADHD taking prescription medication for ≥ 6 months and adults without ADHD agreed to participate in a cross-sectional online survey during December 2016. Participants with ADHD were stratified by their current ADHD medication: long-acting (LA) once daily, short-acting (SA) ≤ 2 times/d, and augmenters (AU; LA > 1 time/d, SA > 2 times/d, or LA plus SA).

Results: A total of 616 adults with ADHD (SA: n = 166, LA: n = 201, AU: n = 249) and 200 adults without ADHD completed the survey. Even with treatment, adults with ADHD reported substantial impairments in their everyday life, particularly at home, at school/work, and in their social life and relationships. Participants with ADHD experienced impairments throughout the day, especially in the afternoon and evening. Signs or symptoms were reported when the ADHD medication was wearing off, resulting in negative effects (including school work, homework, work responsibilities, household responsibilities, emotional responses, mood, and relationships) on the daily life of adults with ADHD.

Conclusions: Adults with ADHD, despite receiving medication, experienced impairments and challenges in many aspects of their daily life. Adults with ADHD described various unmet needs, especially those relating to the duration of treatment effect. When optimizing treatment for adults with ADHD, it is important that the treatment regimen is sufficient to meet the needs of the patient throughout the day

Psychiatr Serv. 2019;70:1116-22.

A COMMERCIAL INSURANCE CLAIMS ANALYSIS OF CORRELATES OF BEHAVIORAL THERAPY USE AMONG CHILDREN WITH ADHD.

Waxmonsky JG, Baweja R, Liu G, et al.

Objective: The study examined factors associated with uptake of behavioral therapy among children with attention-deficit hyperactivity disorder (ADHD).

Methods: Insurance claims data from 2008 to 2014 (MarketScan) were reviewed to examine associations between behavioral therapy use and demographic, patient, family, and provider factors. The association between ADHD medication use and future uptake of behavioral therapy was examined with logistic regression adjusted for covariates found to affect behavioral therapy use.

Results: Among 827,396 youths with ADHD, under 50% received any billable behavioral therapy services over the 7 years. ADHD severity, gender, region of residence, assessment year, comorbid behavioral disorders, and behavioral therapy use by siblings were significantly associated with behavioral therapy use ($p < 0.001$). Parent psychopathology and sibling medication use was not. Children prescribed ADHD medication were 2.5 times less likely than those not prescribed medication to use behavioral therapy, even after adjustment for severity of behavioral health symptoms and other covariates (odds ratio [OR] = 0.41, 95% confidence interval [CI] = 0.40–0.41, $p < 0.001$). Effects of medication use were stronger for future uptake of behavioral therapy (OR = 0.25, 95% CI = 0.24–0.25, $p < 0.001$). The impact of medication use on behavioral therapy use was equally strong for children under age 6 and for older children and did not weaken after release of 2011 guidelines recommending behavioral therapy as the initial ADHD treatment for young children.

Conclusions: Multiple systems, family, patient and provider factors affected behavioral therapy uptake. ADHD medication was a robust and potentially modifiable factor. It may be advisable to engage families in behavioral therapy prior to initiation of ADHD medication

Psychiatry Res. 2019 Sep;279:370-71.

COMMENTARY ON "THE NEUROCOGNITIVE NATURE OF CHILDREN WITH ADHD COMORBID SLUGGISH COGNITIVE TEMPO: MIGHT SCT BE A DISORDER OF VIGILANCE?"

Plourde V.

Psychiatry Res. 2019 Sep;279:368-69.

REPLY TO THE LETTER.

Baytunca MB, Inci SB, Ercan ES.

Psychiatry Res. 2019.

CREATIVITY IN CHILDREN WITH ADHD: EFFECTS OF MEDICATION AND COMPARISONS WITH NORMAL PEERS.

Ten W, Tseng C-C, Chiang Y-S, et al.

This study is to identify the performance of children with and without ADHD in open-ended and closed-ended creativity assessments, and investigate the moderating effect of medicated and unmedicated Children. The

study subjects included third to sixth graders: 43 children with ADHD and 43 typically developing children. The participants with ADHD were those who were identified by local Committees of Identification, Placement and Consultation for Children with Special Needs or those who were diagnosed by medical institutions. Children with ADHD were further divided into medicated (22 participants) and unmedicated groups (21 participants) based on their current medication treatment. This study employed the New Tests of Creative Thinking to gauge the participants' open-ended creativity, while Remote Associates Test and the Insight Test were used to assess the participants' closed-ended creativity. Although previous evidence for creativity in children with ADHD have been mixed, this study includes medication as moderation variable and suggests that the performance of unmedicated children with ADHD in the open-ended creativity assessments was better than medicated children with ADHD and typically developing children. The study results can further explore the creativity characteristics of children with ADHD

Psychol Assess. 2019 Dec.

MULTIGROUP MULTILEVEL STRUCTURE OF THE CHILD AND PARENT VERSIONS OF THE POSITIVE AND NEGATIVE AFFECT SCHEDULE (PANAS) IN ADOLESCENTS WITH AND WITHOUT ADHD.

Eadeh HM, Breaux R, Langberg JM, et al.

The Positive and Negative Affect Schedule (PANAS) has been widely used to assess affect expression. Shortened and adolescent versions of the measure have been created, such as the 10-item PANAS for Children (PANAS-C). However, affect expression often involves substantial intraindividual variability, and no research has examined within-person differences using the 10-item PANAS-C. Moreover, intraindividual variability is a key characteristic of attention-deficit hyperactivity disorder (ADHD), and emotion dysregulation is a key feature of ADHD. The present study examined the factor structure of the 10-item PANAS-C in a sample of adolescents (Mage = 13.17 years) with (n = 156) and without (n = 139) ADHD. A 3-factor (Positive Affect, Fear, Distress) within and a 2-factor (Positive Affect, Negative Affect) between model was found to be best fitting using both parent and adolescent reports. The model demonstrated configural invariance for the adolescent report and scalar invariance for the parent report. These results support the multidimensionality of negative affect in youth with ADHD, even when assessed via the short-version PANAS-C. In future work, it will be important to consider the implications of more discrete types of negative affect expression (fear and distress) found across time at the individual level for assessment and intervention practice. (PsychINFO Database Record (c) 2019 APA, all rights reserved)

Public Significance Statement—This is the first evaluation of the inter- and intraindividual differences in affect as assessed by the short-version PANAS for Children and Adolescents. Moreover, this is the first study to support the multidimensional structure of negative affect in adolescents with ADHD. These youth often have increased difficulty regulating their emotions, and examining affect in this population may have important implications for treatment and assessment

Psychol Addict Behav. 2019 Dec.

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

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

This study tested whether early and developmentally atypical substance use mediates risk for adult substance use among children with attention-deficit/hyperactivity disorder (ADHD), and whether that risk is substance-specific. Participants were children with ADHD previously enrolled in a randomized controlled trial (RCT), and a demographically similar non-ADHD group, assessed at 2 through 16 years after the original RCT baseline. Self-reports of heavy drinking, marijuana use, daily smoking, and other illicit drug use were collected at follow-ups to establish atypically early and frequent use. Models estimated statistically mediated effects of childhood ADHD on adult substance use via early substance involvement, with planned comparisons to evaluate substance specificity. Results supported the mediation hypothesis, showing that childhood ADHD was associated with more frequent adult substance use via early substance involvement

for marijuana, cigarettes, illicit drugs, and to a lesser extent, alcohol. Mediation was not escalated by comorbid childhood conduct disorder or oppositional defiant disorder except for early use of nonmarijuana illicit drugs. Substance-specificity in the mediational pathway was largely absent except for cigarette use, where ADHD-related early smoking most strongly predicted adult daily smoking. Findings from this study provide new evidence that atypically early substance use associated with childhood ADHD signals important cross-drug vulnerability by early adulthood, but cigarette use at a young age is especially associated with increased risk for habitual (daily) smoking specifically. Efforts to prevent, delay, or reduce substance experimentation should occur early and focus on factors relevant to multiple drugs of abuse in this at-risk population

Res Autism Spectr Disord. 2020;69.

IDENTIFYING COMORBID ADHD IN AUTISM: ATTENDING TO THE INATTENTIVE PRESENTATION .

Rau S, Skapek MF, Tiplady K, et al.

Background: There are high rates of comorbidity between ADHD and ASD; however, there has been limited work parsing rates by ADHD presentation. In addition, commonly used questionnaires have demonstrated reduced utility in capturing ADHD symptoms in individuals with ASD. We examined the prevalence of comorbid Attention-Deficit/Hyperactivity Disorder (ADHD) parsed by DSM-5 presentation in clinic-referred youth with Autism Spectrum Disorder (ASD) without intellectual disability (ID). We compared common rating scales to determine which most effectively identified comorbid ADHD.

Method: We examined comorbid ADHD diagnoses from archival assessment data for 419 youth with ASD without ID. We examined diagnostic discriminability of the parent and teacher ADHD Rating Scale (ADHD R-S), and Attention and ADH Problems Scales of the Child Behavior Checklist and Teacher Report Form using receiver operating characteristic (ROC) curves. Hierarchical logistic regression was used to examine measures unique contribution to ADHD diagnosis.

Results: Sixty-one percent of the study sample met DSM-5 criteria for an attention disorder. ADHD, Combined (ADHD-C) represented the largest proportion of ADHD diagnoses (76.8%), followed by Inattentive (ADHD-I;19.7%), Hyperactive/Impulsive (.02%), and Un-/Other Specified (.02%). Measures provided greater diagnostic discriminability in identifying ADHD-C relative to ADHD-I. The ADHD R-S inattentive symptom count provided the greatest discriminability for both subtypes and was the only scale that provided clinically meaningful differentiation between those with ASD only and ASD + ADHD-I.

Conclusions: These results support using the ADHD R-S to capture comorbid ADHD symptoms in ASD. The findings underscore the need for more thorough examination of inattentive symptoms to rule out ADHD-I

Res Dev Disabil. 2020;97.

COMPARISON OF THE K-WISC-IV PROFILES OF BOYS WITH AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Kim H, Song D-H .

Aims: This study aimed to compare the intelligence profiles of children with autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) using the Korean Wechsler Intelligence Scale for Children-Fourth Edition (K-WISC-IV) scores to differentiate between their cognitive characteristics.

Methods: Subjects were boys with ASD (n = 49) and ADHD (n = 44). The index and subtest scores of the ASD and ADHD groups were compared using MANOVA. Repeated-measures ANOVA was performed to investigate the cognitive strengths and weaknesses within the ASD and ADHD groups.

Results: Verbal comprehension was significantly lower in the ASD group compared to the ADHD group. The ASD group also scored lower than the ADHD group on Vocabulary, Comprehension, Picture Concepts, Picture Completion, and Symbol Search. The ADHD group scored lower than the ASD group on Digit Span. The ASD group displayed slower processing speed and social judgment, while the ADHD group exhibited poor working memory and graphomotor processing.

Conclusion: The WISC-IV profiles might help distinguishing between the cognitive characteristics of ASD and ADHD boys

Res Dev Disabil. 2020;97.

MULTI-SOURCE INTERFERENCE TASK PARADIGM TO ENHANCE AUTOMATIC AND CONTROLLED PROCESSES IN ADHD.
Capri T, Santoddi E, Fabio RA.

Background: The role of automatic and controlled processes in children with Attention deficit hyperactivity disorder (ADHD) has recently been debated. Most theories on ADHD assume that core deficits are related to controlled processes and executive function.

Aims: The main aim of the present study is to examine automatic and controlled attention in children with ADHD, compared to TD subjects.

Methods and procedures: Twenty ADHD-I children, 20 with ADHD-C and 20 typical developing children performed the Block-Formed Multi-Source Interference Task (MSIT) both in incongruent and congruent conditions.

Outcome and results: Results show that clinical groups had a poorer performance than the TD group in both conditions.

Conclusions and implications: This study demonstrated that children with ADHD exhibit a deficit both in automatic and controlled processes

Scand J Psychol. 2019 Oct;60:440-46.

INTELLECTUAL FUNCTIONING AND EXECUTIVE FUNCTIONS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AND SPECIFIC LEARNING DISORDER (SLD).

Faedda N, Romani M, Rossetti S, et al .

Several studies have shown neuropsychological deficits across multiple domains in attention deficit hyperactivity disorder (ADHD) and specific learning disorder (SLD), but differences and similarities between these disorders have been little considered. We were interested in analyzing the intellectual and executive profiles in a sample of children and adolescents, divided according to the diagnosis into the ADHD group and the SLD group, and in identifying the differences and similarities between these disorders. The sample included two clinical groups: the first included 36 children and adolescents with a diagnosis of ADHD (5-15 years; mean = 9.42; SD = 2.22) while the second included 36 children and adolescents with a diagnosis of SLD (7-15 years; mean = 9.43; SD = 2.25). The WISC-IV was used to measure intellectual ability and the NEPSY-II was employed to measure executive functions. The results showed that the SLD group had significantly higher scores than the ADHD group on the NEPSY-II in the inhibition, cognitive flexibility, short-term verbal memory and verbal working memory domains. The ANCOVA showed differences regarding the FSIQ of WISC-IV, in that the SLD group obtaining higher scores than ADHD group. Findings showed that ADHD children are more impaired than SLD children, in particular in cognitive inhibition, cognitive flexibility, verbal memory, working memory and intellectual functioning. The recognition of the strengths and weaknesses of children and adolescents with ADHD and SLD allows to outline an educational and clinical intervention focused on their specific executive and intellectual functioning

Sensors (Basel). 2019 Jul;19.

USING RECURRENT NEURAL NETWORKS TO COMPARE MOVEMENT PATTERNS IN ADHD AND NORMALLY DEVELOPING CHILDREN BASED ON ACCELERATION SIGNALS FROM THE WRIST AND ANKLE.

Munoz-Org, Powell L, Heller B, et al.

Attention deficit and hyperactivity disorder (ADHD) is a neurodevelopmental condition that affects, among other things, the movement patterns of children suffering it. Inattention, hyperactivity and impulsive behaviors, major symptoms characterizing ADHD, result not only in differences in the activity levels but also

in the activity patterns themselves. This paper proposes and trains a Recurrent Neural Network (RNN) to characterize the moment patterns for normally developing children and uses the trained RNN in order to assess differences in the movement patterns from children with ADHD. Each child is monitored for 24 consecutive hours, in a normal school day, wearing 4 tri-axial accelerometers (one at each wrist and ankle). The results for both medicated and non-medicated children with ADHD, and for different activity levels are presented. While the movement patterns for non-medicated ADHD diagnosed participants showed higher differences as compared to those of normally developing participants, those differences were only statistically significant for medium intensity movements. On the other hand, the medicated ADHD participants showed statistically different behavior for low intensity movements

Sleep Med. 2019;64:S333.

ADHD SYMPTOMS AND GREATER BRAIN-BEHAVIOR VULNERABILITY TO SLEEP LOSS IN CHILDREN: LINKING REDUCED RESTING-STATE BRAIN CONNECTIVITY TO MORE SEVERE PERFORMANCE DEFICITS.

Saletin J, De Queiroz CG, Koopman-Verhoeff ME, et al.

Introduction: Sleep problems common in children with attention-deficit/hyperactivity-disorder (ADHD), yet it is unknown whether ADHD symptoms affect a child's resilience to sleep loss. We combined fMRI with a behavioral response-inhibition task in a within-subjects partial sleep restriction study to test whether ADHD symptoms are associated with greater vulnerability to brain and behavioral consequences of short sleep in children.

Materials and methods: 13 children (7F; 11.7-11.3 years) characterized for ADHD symptoms (Conners-3 T-scores) slept at home for 1 week (9.5h in bed) and two consecutive nights in the lab: baseline (9.5h in bed) and partial sleep deprivation (4h in bed). A fMRI session each morning involved a go/no-go task and a resting-state scan to assess brain connectivity. A behavioral metric of response-time variability (τ) in this task was derived by an ex-gaussian fit of reaction times for go-trials. A whole-brain index of network-connectivity (modularity) was derived from resting-state analyses. Regression assessed independent associations for ADHD symptoms, brain modularity, and response-time variability following sleep loss. Sobel-Goodman mediation tested whether neural changes after sleep loss explain associations between ADHD and response-time variability after short sleep.

Results: Whole-brain modularity was reduced after sleep loss ($t(12)=-2.79$, $p=.016$); more severe ADHD symptoms were associated with progressively greater decreases in modularity ($b=-.0036$, $p=.008$). Greater behavioral response-time variability after sleep loss was associated with ADHD symptoms ($b=3.25$, $p=.038$) and the degree of modularity reduction ($b=-839.0$, $p=.002$). Decreased modularity fully mediated (89.9%; $z=2.001$; $p=.045$) the association between ADHD symptoms and response-time variability.

Conclusions: These data indicate an ADHD symptom-brain-behavior axis of vulnerability following sleep loss in children. More severe ADHD symptoms were associated with a greater reduction in resting-state brain connectivity following sleep loss, and in turn greater behavioral performance deficits during cognitive testing. The ability of resting-state connectivity to mediate the association between ADHD symptoms and sleep loss's impact on performance indicates resting brain imaging may provide a novel tool for assessing sensitivity to sleep loss in ADHD. More generally, these preliminary results underscore the need to better understand sleep-dependent brain function in children, both in typical development, and in prevalent conditions such as ADHD.

Acknowledgements: This work was supported by K01MH109854 (JMS)

Sleep Med. 2019;64:S438.

PSYCHIATRIC SYMPTOMS IN ADOLESCENTS WITH NARCOLEPSY.

Li N, Yuan Y, Ding Y, et al.

Objective: The presence of psychiatric illness in narcolepsy patients is common. The timeline for development of psychiatric symptoms is poorly define. The influencing factors include age of onset, gender,

and duration of illness. There is suggestion that the behavioral phenotype of narcolepsy encompasses various traits of psychiatric disease. We reviewed narcolepsy comorbidity schizophrenia and clinical features.

Methods: A retrospective review of 70 patients with narcolepsy who were under the age of 25 years from the sleep center of Xuanwu Hospital during 2017-2019. Neuropsychiatric assessment of ESS, HAMA, HAMD, ADHD, RBD questionnaire, and polysomnography were performed. Multiple sleep latency test studies were also performed.

Results: A total of 70 patients were enrolled to meet the diagnostic criteria for ICSD-3 of Narcolepsy I (N1)/Narcolepsy II (N2), including 46 males and 24 females, with an onset age of 7 to 25 years, and mean age 13.27 (-12.43) years. Clinical manifestations: EDS 70/70, Sleep paralysis 17/70, Cataplexy 46/70, increased limb movement during sleep 45/70, and RBD 16/70, and main complaints of nighttime sleep continuity disorder 51/70. The main psychiatric manifestations: depression 43/70, anxiety 37/70, ADHD 21/70, 16 cases of psychotic symptoms out of total 70 patients, including hallucinations, delusions, manic episodes, behavioral abnormalities, proverbs. Regarding to the cognitive assessment, there were 14 patients with cognitive decline out of these 70 patients. We also noticed multiple sleep latency test (ML) 3.12-10.26, number of REM (R) 3.31-10.15, TST 442.92-110.11, SE 78.35-11.77, WT 114.33-19.78, and SWS 74.89-15.93. A total of 7 patients were subjected to cerebrospinal fluid orexin level measurements and the orexin levels were reduced significantly.

Discussion: Narcolepsy is a rare chronic disabling neurological sleep disorder that occurs mostly in children and adolescents. Psychiatric symptoms are common in patients with narcolepsy, especially in adolescents; however, it is often misdiagnosed and delayed. Although the exact timeline for the onset of psychotic symptoms of narcolepsy is uncertain, most patients have psychiatric symptoms that occur after 2 to 4 years showing typical symptoms such as drowsiness and tripping. The psychotic symptoms have been thought to be caused by the use of awakening agents. Our retrospective analysis suggests that this is not sufficient reason to explain the observed psychotic symptoms of narcolepsy. 16 patients have typical psychotic symptoms. Only 2 patients had short-term use of methylphenidate, and 4 had a manic episode due to the use of SNRI. Excessive sleepiness associated with narcolepsy, ADHD, and psychotic symptoms severely affected the patient's social function. Anti-stumping and awakening agents can aggravate psychotic symptoms and manic symptoms. Antipsychotic treatment exacerbates drowsiness and weight gain. The mechanism of the development of psychotic symptoms of narcolepsy is unclear. It is unresolved why mental illness occurs in adolescence. Whether narcolepsy itself is a part of mental illnesses needs to be studied. Whether the persistence of low orexin level is the main cause of comorbid psychosis symptoms is to be defined. This dilemma also generally results in challenge for patient treatment. Further large sample clinical cohort studies are needed to resolved the involved questions

Sleep Med. 2019;64:S137-S138.

GENDER DIFFERENCES IN SLEEP HYGIENE ASSOCIATED WITH POOR SLEEP IN ADOLESCENTS WITH ADHD SYMPTOMS.

Dimakos J, Somerville G, Finn C, et al.

Objective: The aim of this study was to examine gender differences in sleep hygiene and objective sleep measures in relation to symptoms of ADHD in an adolescent population. We hypothesized that adolescents with high levels of ADHD symptoms would present with more inadequate sleep, and that females would demonstrate worse sleep hygiene practices and sleep patterns.

Methods: 105 adolescents (70 females) aged between 13 and 18 years old (M=14.82, SD=1.33) participated in the study. Levels of ADHD symptoms were characterized by T-Scores on the ADHD subscale of the Youth Self Report. Sleep hygiene was measured by the Adolescent Sleep Hygiene Scale, with higher scores indicating poorer sleep hygiene, and sleep patterns were assessed using sleep variables, including sleep continuity, duration, and efficiency measured objectively using actigraphy.

Results: Correlational analyses were conducted separately for males and females. In females, higher levels of ADHD symptoms were correlated with poorer sleep hygiene ($r = .51$, $p < .001$), later bedtimes ($r = .32$, $p < .01$) and less time in bed ($r = -.32$, $p < .01$) as measured by actigraphy. In males, higher levels of ADHD symptoms were strongly correlated with daytime sleep ($r = .52$, $p < .001$) and substance abuse ($r = .54$, $p < .001$) factor scores of the sleep hygiene scale. Less time in bed ($r = -.52$, $p < .001$), shorter sleep duration ($r = -.40$, $p < .01$) and less immobile minutes ($r = -.48$, $p < .01$), as measured by actigraphy, were associated with higher levels

of ADHD symptoms in males. Fisher's r-to-z transformations were performed to compare the differences in strength between correlations in males and females. Using a one-tailed test of significance, the correlation between ADHD symptoms and adolescent sleep hygiene scale total scores ($z = 1.77$, $p < .05$), and physiological ($z = 2.14$, $p < .05$), behavioural arousal ($z = 2.38$, $p < .01$) cognitive/emotional ($z = 2.63$, $p < .01$) and sleep stability ($z = 2.1$, $p < .05$) factor scores were found to be significantly higher in females than in males. The substance factor scores were found to be significantly higher in males than females ($z = 2.2$, $p < .05$). The correlations between ADHD symptoms and sleep variables were also compared using the same method and sleep efficiency was found to be significantly higher in females than males ($z = 1.70$, $p < .05$).

Conclusion: Higher levels of ADHD symptoms were associated with poorer sleep hygiene and inadequate sleep patterns. Gender differences were also found where females practiced overall poorer sleep hygiene, as well as experienced worse sleep patterns than males. These findings support the promotion of healthy sleep hygiene practices in an adolescent population with high levels of ADHD symptoms

Sleep Medicine: X. 2019;1.

FACTOR STRUCTURE OF THE SLEEP DISTURBANCE SCALE FOR CHILDREN (SDSC) IN THOSE WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER (ADHD).

Mancini VO, Rudaizky D, Percy BT, et al.

Objective: To examine the factor structure of the Sleep Disorder Scale for Children (SDSC) in children and adolescents with attention deficit and hyperactivity disorder (ADHD).

Method: The caregivers of 307 children with ADHD completed the SDSC. Standard and bifactor confirmatory factor analysis (CFA) evaluated the goodness-of-fit of competing factor structures.

Results: The original and unidimensional factor structure produced sub-optimal fit. Bifactor exploratory factor analysis (EFA) was performed to examine the underlying structure of the SDSC. A revised bifactor solution comprising six-specific factors and a general factor was identified. A nested version of this model was deemed to be the preferred model, which also demonstrated good psychometric properties.

Conclusion: There is evidence of a general sleep difficulties factor in children with ADHD. Four of the six original factors were replicated in this study. However, the revised factor structure suggests that clinicians should be cautious of the utility of subscale scores pending further validation in ADHD samples

Stud Health Technol Inform. 2019 Aug;266:156-61.

DO DIGITAL HEALTH INTERVENTIONS IMPROVE MENTAL HEALTH LITERACY OR HELP-SEEKING AMONG PARENTS OF CHILDREN AGED 2-12 YEARS? A SCOPING REVIEW.

Peyton D, Hiscock H, Sciberras E.

BACKGROUND: Digital Health Interventions (DHIs) can improve mental health literacy (MHL) and help-seeking behaviour in teens and adults. However, it is unclear whether DHIs improve parental MHL, help-seeking behaviour or access to mental health services for their children.

OBJECTIVE: To perform a scoping review of DHIs aiming to improve MHL, help-seeking behaviour or access to mental health services among parents of 2-12-year-olds with behavioural and emotional problems (BEP).

METHOD: A search of Ovid MEDLINE found four original articles meeting inclusion criteria.

RESULTS: One of the four articles was a randomised controlled trial, which showed a significant improvement in some measures of MHL, but no change in help-seeking attitudes. The other three studies evaluated interventions, in uncontrolled pre-test and post-test evaluations, on attention-deficit/hyperactivity disorder knowledge. Two of these studies showed a significant change in ADHD knowledge. There was no consistency in MHL measures between studies.

CONCLUSIONS: There is preliminary evidence that DHIs may improve MHL in parents of children with BEP. How this translates to help seeking, access to mental health services or improved outcomes is unknown

Transl Psychiatry. 2019;9.

STRUCTURAL BRAIN ABNORMALITIES IN CHILDREN AND ADOLESCENTS WITH COMORBID AUTISM SPECTRUM DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Mizuno Y, Kagitani-Shimono K, Jung M, et al.

Autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) share high rates of comorbidity, with the Diagnostic and Statistical Manual of Mental Disorders-Fifth Edition now acknowledging the comorbid diagnosis of ASD and ADHD. Although structural abnormalities in the prefrontal cortex, cerebellum, and basal ganglia occur in both ASD and ADHD, no structural studies have focused exclusively on patients with comorbid ASD and ADHD. We thus aimed to clarify the structural features and developmental changes in patients with comorbid ASD and ADHD in a relatively large sample from two sites. Ninety-two patients were age-matched to 141 typically developing (TD) controls (age range: 5-16 years) and assessed for volumetric characteristics using structural magnetic resonance imaging (i.e. surface-based morphometry). While there were no significant differences in prefrontal cortex, cerebellum, and basal ganglia volumes, patients with ASD and ADHD exhibited significantly lower left postcentral gyrus volumes than TD controls. We observed significantly lower postcentral gyrus volumes exclusively in children and preadolescents, and not in adolescents. Our findings suggest that abnormal somatosensory, attributed to delayed maturation of the left postcentral gyrus, leads to the core symptoms experienced by patients with comorbid ASD and ADHD

Transl Psychiatry. 2019;9.

SLEEP EEG SLOW-WAVE ACTIVITY IN MEDICATED AND UNMEDICATED CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Furrer M, Jaramillo V, Volk C, et al.

Slow waves (1-4.5 Hz) are the most characteristic oscillations of deep non-rapid eye movement sleep. The EEG power in this frequency range (slow-wave activity, SWA) parallels changes in cortical connectivity (i.e., synaptic density) during development. In patients with attention-deficit/hyperactivity disorder (ADHD), prefrontal cortical development was shown to be delayed and global gray matter volumes to be smaller compared to healthy controls. Using data of all-night recordings assessed with high-density sleep EEG of 50 children and adolescents with ADHD (mean age: 12.2 years, range: 8-16 years, 13 female) and 86 age- and sex-matched healthy controls (mean age: 12.2 years, range: 8-16 years, 23 female), we investigated if ADHD patients differ in the level of SWA. Furthermore, we examined the effect of stimulant medication. ADHD patients showed a reduction in SWA across the whole brain ($\sim 20.5\%$) compared to healthy controls. A subgroup analysis revealed that this decrease was not significant in patients who were taking stimulant medication on a regular basis at the time of their participation in the study. Assuming that SWA directly reflects synaptic density, the present findings are in line with previous data of neuroimaging studies showing smaller gray matter volumes in ADHD patients and its normalization with stimulant medication

Trials. 2019;20.

RANDOMISED CONTROLLED TRIAL OF THE SHORT-TERM EFFECTS OF OROS-METHYLPHENIDATE ON ADHD SYMPTOMS AND BEHAVIOURAL OUTCOMES IN YOUNG MALE PRISONERS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (CIAO-II).

Asherson P, Johansson L, Holland R, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is a highly prevalent disorder, seen in 20-30% of young adult prisoners. Pharmacoepidemiological studies, a small randomised controlled trial and open trial data of methylphenidate suggest clinically significant reductions in ADHD symptoms, emotional dysregulation, disruptive behaviour and increased engagement with educational activities. Yet, routine treatment of ADHD in offenders is not yet established clinical practice. There is continued uncertainty about the clinical response to methylphenidate (MPH), a first-line treatment for ADHD, in offenders, who often present with an array of complex mental health problems that may be better explained by states of inattentive,

overactive, restless and impulsive behaviours. To address this problem, we will conduct an efficacy trial to establish the short-term effects of osmotic-controlled release oral delivery system (OROS)-methylphenidate (Concerta XL), an extended release formulation of MPH, on ADHD symptoms, emotional dysregulation and behaviour.

Methods: This study is a parallel-arm, randomised, placebo-controlled trial of OROS-MPH on ADHD symptoms, behaviour and functional outcomes in young male prisoners aged 16-25, meeting Diagnostic and Statistical Manual of Mental Disorders, fifth edition criteria for ADHD. Participants are randomised to 8 weeks of treatment with OROS-MPH or placebo, titrated over 5 weeks to balance ADHD symptom improvement against side effects. Two hundred participants will be recruited with a 1:1 ratio of drug to placebo. The primary outcome is change in level of ADHD symptoms after 8 weeks of trial medication.

Discussion: Potential benefits include improvement in ADHD symptoms, emotional dysregulation, attitudes towards violence and critical incidents and increased engagement with educational and rehabilitation programmes. Demonstrating the efficacy and safety of MPH on ADHD symptoms and associated impairments may provide the data needed to develop effective healthcare pathways for a significant group of young offenders. Establishing efficacy of MPH in this population will provide the foundation needed to establish long-term effectiveness studies with the potential for demonstrating significant reductions in criminal behaviour and improved health-economic outcomes

Value Health. 2019;22:S760.

PND124 A REAL-WORLD DATA STUDY TO ANALYSE THE PHARMACOLOGICAL TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN SPAIN.

Ramos-Quiroga JA, Tang JP, Solozabal M, et al.

Objectives: To better understand pharmacological treatment patterns among patients with attention deficit hyperactivity disorder (ADHD) in Spain.

Methods: The analysis was performed in the Real-World Database of clinical practice IQVIA-RWD based on electronic medical records. IQVIA-RWD contains longitudinal information of both primary and specialized care, and from 2013 to 2018 IQVIA-RWD covers an estimated population of 1,000,000 patients in Spain. Our analysis was focused on patients with ADHD, classified by ICD-9 codes 314.0 to 314.9. Socio-demographic information (age and sex), percentage of treated patients, main initial treatments, treatment patterns and specialists who initiate treatment were extracted.

Results: A total of 8,697 patients with ADHD were identified: 7,405 (85.1%) children/young adults and 1,292 (14.9%) adults. The prevalence in the database is 4% for children/young adults and 0.1% for adults. 74.1% were men and most of incident patients were diagnosed between 7-12 years. 80% of all ADHD diagnosed patients were being treated during the study period (81% of 7-12-years-old children and 73% of >30-years-old patients). Most patients (90%) were initiated with methylphenidate as first line treatment whereas only 8% with atomoxetine, maintaining the trend over the years. In 2013, the medical specialty who prescribed the first pharmacological treatment were pediatricians (40%) and psychiatrists (36%), whereas in 2018 psychiatrists (60%) prescribed most initial ADHD treatments (versus 20% of pediatricians).

Conclusions: The analysis offers detailed information about treatment patterns in ADHD patients in Spain. It confirms that Real-world data is able to provide detailed insights into disease epidemiology, medication and resource use, covering information gaps especially in diseases with scarce availability of published information

Value Health. 2019;22:S750.

PND71 EPIDEMIOLOGY OF ATTENTION DEFICIT HYPERACTIVITY DISORDERS IN SPAIN BASED ON REAL-WORLD DATA.

Ramos-Quiroga JA, Targhetta M, Gasche D, et al.

Objectives: Attention deficit hyperactivity disorder (ADHD) is a disorder of neurological development, mainly onset during childhood and characterized by developmentally inappropriate levels of inattention, hyperactivity

and impulsivity. Few epidemiological information on ADHD is published in Spain. The objective of this study is to gain a better understanding of the epidemiology of ADHD in Spain.

Methods: The analysis was performed in the Real-World Database of clinical practice IQVIA-RWD based on electronic medical records to identify prevalence and other epidemiological data in ADHD. IQVIA-RWD contains longitudinal information of both, primary and specialized care. IQVIA-RWD covers an estimated population of 1,000,000 patients in Spain. This analysis is focused on patients with ADHD, classified by ICD-9 codes 314.0 to 314.9. Prevalence was estimated based on the total number of patients diagnosed with ADHD in the database. Data from 2013 to 2018 has been considered.

Results: Prevalence has been estimated at 4% in children/young adults and at 0,1% in adults. More than 50% of the patients are being diagnosed between 7-12 years of age. Almost 80% of the patients are diagnosed by a psychiatrist or a pediatrician. 74% of overall patients with ADHD are male. With increasing age, the distribution between male and female patients becomes more balanced. In the age group of patients >30 years 58% are male and 42% female. ADHD is associated with various neurological comorbidities, being anxiety (11.1%), behavior disorders (7.3%) and substance abuse (4.2%) the most frequent ones. Most comorbidities are suffered by male patients.

Conclusions: This analysis offers detailed information about general prevalence, distribution of prevalence in different age groups, comorbidities, among other information. This confirms that Real-World Data is able to provide detailed insights into the epidemiology of pathologies, covering information gaps especially in pathologies with scarce availability of published information and facilitating a better understanding of diseases

Verhaltenstherapie. 2019;29:234-43.

IDENTIFYING SYMPTOM CRITICAL AND STRESSFUL SCHOOL SITUATIONS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: CHALLENGING CLASSROOM BEHAVIOR AND TEACHER STRAIN.

Lauth-Lebens M, Lauth G.

Background: Children with a diagnosed attention deficit hyperactivity disorder (ADHD) exhibit a generalized cluster of inattentive, hyperactive and impulsive behavior. These behavioral symptoms frequently manifest themselves in the school setting, where they are perceived as demanding conduct problems. Not surprisingly, ADHD-related behavior is associated with an increase in teacher strain.

Materials and Methods: A total of 451 class teachers rated the problematic and stress-inducing behaviors of 740 school children. They were aged 6-12 years (mean 8.45 years) and rated by their teachers with an inventory consisting of 22 typical school situations and a ten-point rating scale. Additionally, teachers administered an ADHD symptom screening and completed a rating scale for teaching self-efficacy. Children were subdivided into a clinical (diagnosed ADHD), an at-risk (challenging behavior), and a typically developed control group (N = 740).

Results: The results derived from factor analysis indicate a three-factorial solution for both the behavioral problems and the teacher strain scale. Each of the factors relates to specific behavioral conditions (interactional, instructional, and individualized demands). On both scales, interactional demands explain the majority of variance (about 53%). Essentially, the factors represent internally consistent subscales. High correlations of the two rating scales between each other ($r = 0.92$) and with the number of ADHD symptoms underscore their criterion validity ($r = 0.76$ and $r = 0.81$). Children from the clinical and the at-risk group scored significantly higher than typically developed controls on each of the three subscales. Interestingly, the highest problem behavior and teacher strain scores were reported for children from the at-risk rather than the clinical group.

Conclusion: Overall, the present inventory is characterized by sufficiently satisfying psychometric properties of discriminatory power and internal homogeneity. It can be utilized to identify critical situations in the school and develop targeted interventions (e.g., teacher counselling, teacher training, prevention of problem behavior)

Zeynep Kamil Tip Bulteni. 2019;50:35-38.

EVALUATION OF ADHD RELATED QUALITY OF LIFE IN A CLINICAL SAMPLE OF CHILDREN AND ADOLESCENTS.

Celebi F, Unald D.

Objective: Attention Deficit Hyperactivity Disorder (ADHD) is a psychiatric disorder that interrupts functionality and impairs life quality. Our aim in this study is to determine the effect of ADHD related quality of life and the factors which may be related with the quality of life in children and adolescents who have ADHD.

Material and Methods: 49 children and adolescents with a diagnosis of ADHD were included in this study. ADHD diagnosis was made in the first clinical interview according to DSM-V and Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version(K-SADS-PL) was administered to assess the ADHD subtypes and comorbid psychiatric diagnoses. Socioeconomic status was determined by using the Hollingshead-Redlich scale. To assess the quality of life, ADHD quality of life scale (ADHD QoL) was used. Conners' parent rating scale (CPRS) was filled by the parents of the children to investigate the severity of ADHD symptoms.

Results: The mean age of the patient group (12 girls/37 boys) was 11.15 (SD:1.53). Mean total score of the CPRS was 44.59 (SD:18.8). According to the ADHD QoL scale, total home subscale mean score was 57.51(SD:15.49) and total school subscale mean score was 57.97 (SD:14.51). No significant relationship was found between the quality of life and age, sex, symptom severity and psychiatric comorbidities.

Conclusion: ADHD is a chronic disorder which has negative impact on daily life. It is important for clinicians not only to consider the clinical conditions and symptom severity, but also the impact of ADHD on life comfort while evaluating children and adolescents with ADHD

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RESEARCH ARTICLE

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Waiting times for diagnosis of attention-deficit hyperactivity disorder in children and adolescents referred to Italian ADHD centers must be reduced

Maurizio Bonati^{*} , Massimo Cartabia, Michele Zanetti and the Lombardy ADHD Group

Abstract

Background: To investigate timely access to and the time needed to complete the diagnostic path of children and adolescents with suspected attention deficit hyperactivity disorder (ADHD) in the 18 Italian Lombardy Region ADHD reference centers.

Methods: Data of children and adolescents enrolled in the Regional ADHD disease-oriented Registry for suspected ADHD who requested their first visit in 2013–2017 were analyzed.

Results: The sample comprised 2262 children and adolescents aged 5–17 years who accessed the ADHD centers for diagnostic classification and management. The median waiting time was of 177 days (range 66–375) from the request for the initial appointment to the completion of the diagnostic path, with a three - fold difference between centers. In addition to the center, the strongest significant predictors of long waiting times were age comorbidities, the severity of the disorder, and having already completed some diagnostic procedures provided by the common standard path.

Conclusions: To guarantee an equal standard of care in ADHD centers for all children and adolescents there is a pressing need to reduce the times to complete the diagnostic path. It is the task of both policymakers and each center to optimize the quality of the service and of the care delivered.

Keywords: Attention-deficit hyperactivity disorder, Children, Health service, Waiting time, Italy, Epidemiology

Background

Accessibility, availability, and quality of care are important for efficient and effective healthcare systems [1, 2]. Prompt, and efficient service are the first requirements and expectations of patients who call on the National Health Service (NHS) [3]. Long waiting times are part of the structural barriers in all areas of the NHS, including mental health services, for children and adolescents, and for adults [4–6]. Patients suffering from mental health conditions who do not receive timely care, often experience a rapid decline in their conditions - with a lost opportunity for effective treatment [7, 8]. It is a challenge

for policy makers and care providers to decide on the interventions needed to make the organization more effective, also reducing waiting times, although public mental health services are still not paying enough attention [9].

Long waiting times for a first appointment at Child and Adolescent Neuropsychiatric Services (CANPS) are one of the main reasons for user dissatisfaction with them [10]. A long wait can increase the patient discomfort - and distrust, and the intensity of symptoms, with a loss of motivation, non-attendance, and premature drop-out [11]. The scarce resources for CANPS are one of the main reasons put forward to justify delays, and patients' unfulfilled expectations [12]. Large differences in access and waiting times in CANPS have been reported in a few settings [13, 14] so they are to be expected in

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centers for attention-deficit hyperactivity disorder (ADHD) too.

ADHD is one of the complex neurodevelopmental disorders causing developmentally inappropriate and impairing patterns of inattention, hyperactivity, and impulsivity [15] that can have a dramatic impact on home and family life [16]. The reported range of prevalence is very wide (from 0.2 to 34.5%) with a worldwide estimate of 5.3% [17]. In Italy, when diagnostic care definition based on clinical evaluation is used as a definition, the estimated prevalence was 1.4% (from 1.1 to 3.1%) among the children aged 5 to 17 years [18]. Thus a considerable number of children and adolescents with suspected ADHD access CANPS for diagnosis.

In the Lombardy Region, where about 15% of the Italian pediatric population live, there is a network of 18 Regional ADHD reference centers, accredited by Regional health authorities as specialized ADHD hubs (Tier 3) of the CANPS network. A Regional ADHD Registry serves as a disease-oriented registry collecting information on all patients who access ADHD centers for diagnosis of suspected ADHD [19]. The Registry is part of a wider project aimed at ensuring appropriate ADHD management for every child and adolescent once the disorder is suspected and reported, and includes commonly acknowledged diagnostic and therapeutic procedures as well as educational initiatives for health care workers (child psychiatrists and psychologists) of the Lombardy Region health care system who provide assistance to ADHD patients and their families. Initiatives focused on increasing knowledge of ADHD in parents, teachers, and family pediatricians were also part of the regional project.

The main aim of this study was to examine waiting times for ADHD assessment in the 18 Regional ADHD centers, their variables, and inter-center differences for children and adolescents enrolled in the Registry between January 2013 and December 2017 for suspected ADHD.

Methods

Data stored in ADHD Registry database were extracted and analyzed for the present study. Written informed consent was obtained for all patients before data collection. Data were anonymized prior to use for research. Formal ethical review board approval was not required for the present analysis. The study will be reported according to the published STROBE statement for prospective cohort studies (observational).

We used the methodology previously described and reporting details concerning: the local health setting [19], the characteristics of the ADHD Registry activated in Lombardy in June 2011 [20–22], the systematic work made by the 18 ADHD centers belonging to the Lombardy ADHD Group [23], the rigorous diagnostic assessment

(according to national and international guidelines, and *DSM-IV-TR*) approved by all involved clinicians [24, 25], the evaluation of follow-up and the effect size of provided care [26].

Procedures

At the end of 2018 we searched the ADHD Registry to identify children residents in the Lombardy Region who requested their first visit to one of the 18 ADHD regional centers between 1 January 2013 and 31 December 2017, and completed the diagnostic procedure. We used spatial analysis to describe the distribution and ADHD center access according to place of residence, using the five-digit ZIP code to determine the local health protection agency (ATS) and the closest ADHD center for each child and adolescent. We assessed how the ADHD center characteristics and the anamnestic and clinical characteristics of the sample population contributed to the time needed for diagnosis, starting from the first request to the ADHD center.

Statistical analyses

Geographic information system (GIS) software was used to generate maps (ArcGIS Desktop 10.3.1; Esri, Redlands, CA) that illustrate the geographic distribution of the homes of participants and the location of the ADHD center by centroid geospatial resource. The characteristics of the 18 ADHD centers were summarized using descriptive statistics.

Student's *t*, Wilcoxon, and Kruskal-Wallis tests, and analysis of variance (ANOVA) were used to determine differences in population characteristics and between groups of subjects. Spearman's rank correlation test was used to analyze the linear trend of wait times over the study period. Cross tabulations with chi-square, when appropriate, were done to explore the univariate associations.

A generalized linear model (GLM) analysis was also carried out to assess how the wait time affected completion as the diagnostic path ("estimated waiting time"). All tests were two-sided, and $p < 0.05$ was considered statistically significant. All analyses were done using SAS/STAT database (version 9.4, SAS Institute, Inc., Cary, NC, USA).

Results

A total of 2464 children and adolescents' residents in Lombardy Region required for the first time a visit for suspected ADHD during the period considered, 2262 (92%) had completed the diagnostic procedure at the time of data extraction, and were included in this study. These children and adolescents had a median age of 9 years at their first visit (range = 5–17 years; prevalence =

1.65 for 1000 residents of the same range of age), 1292 (85%) were males and 222 (15%) were females.

The estimated rate of children requiring diagnosis varied across the 8 ATS with a range of 0.68–3.17 children for 1000 residents 5–17 years old. One thousand nine hundred seventy-nine children and adolescents (88%) attended an ADHD center within their ATS, 1726 (76%) the nearest their residence house, and 1656 (73%) attended the nearest ADHD center in their ATS of residence (Fig. 1). Of the 283 children and adolescents migrating across regional ATSs mean escape proportion was 5% (109/2262) ranging from 1 to 44% between ATSs, and a capture proportion of 7% (174/2262), between ATSs range 0–27%. The attraction index (capture/escape ratio) was highly positive (> 6.5) for two ATSs, and close 1 for one ATS, suggesting a varied capability of the Regional Health Service at ATS level answering residents' requests of accessing ADHD centers.

The characteristics of the 18 referral ADHD centers for the Lombardy Region are described in Table 1. For all considered variables a wide variability between centers was found, not between years.

Children and adolescents accessed the 18 ADHD centers for a median of 112 (range 25–396) youths per center. The range of median waiting time for the first visit was 14–212 days (overall 82), and of 66–375 days (overall 177) for the time from the request to the diagnosis without statistically significant differences between investigated years. A three times difference ($F = 55.49$, $p < 0.0001$) was observed between centers for the mean waiting time for completing the diagnostic trial (min 95 days, CI 95% 78–111; max 372 days, CI 95% 322–421; Fig. 2). No statistically significant relationship was observed between the waiting time from the request to the diagnosis, the amount of annual hours of work by clinical professional staff in each ADHD center, and the number of children and adolescents who accessed the center per year (Fig. 3). However, five centers (B, E, F, H, N) were outliers the 25th or 75th percentiles of all three variables, in particular B and F with all values lower than the 25th percentiles.

Of the 2262 children and adolescents in the study 1954 (86%) were diagnosed with a psychiatric disorder, and 1553 (69%) met *Diagnostic and Statistical Manual*

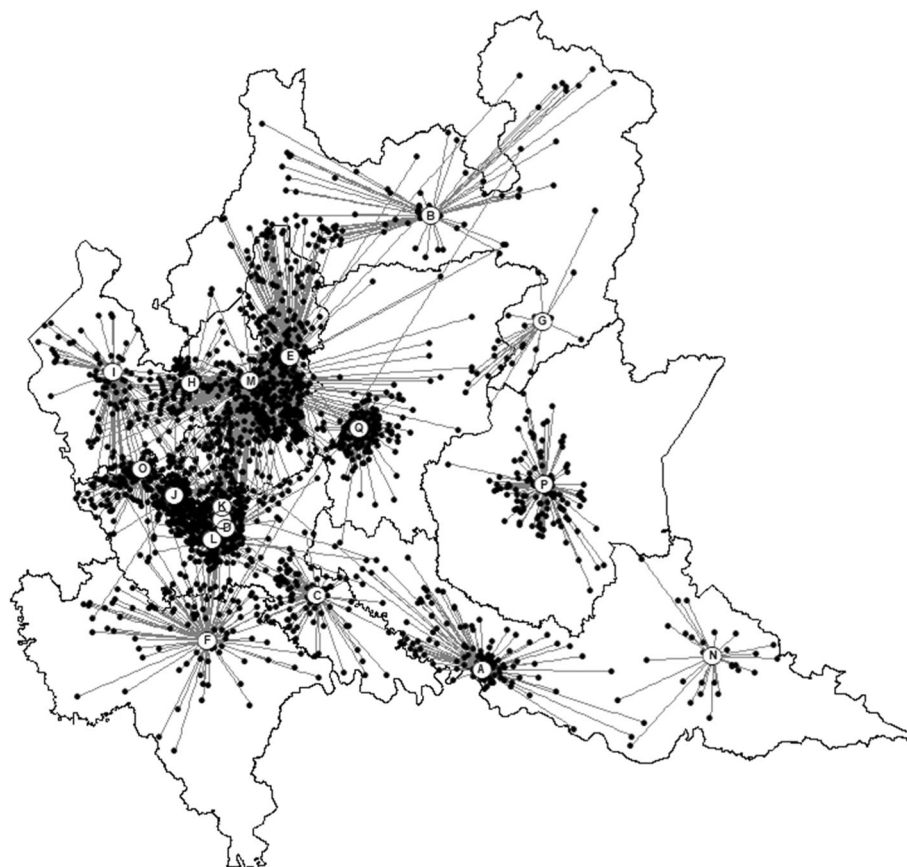


Fig. 1 Euclidian distances between house of residence and accessed ADHD center. The map of Lombardy Region is divided according to the 8 ATS

Table 1 Average characteristics of ADHD centers

Characteristics	mean (SD); median
No. of children and adolescents who accessed the Center per year	179 (90); 177
No. of children and adolescents who accessed the Center for the first time per year	35 (25); 32
No. of children and adolescents diagnosed with ADHD per year	24 (16); 20
No. of clinical staff professionals	5 (3); 5
Hours/year of work	1521 (620); 1473
Hours/year of work per children and adolescents with ≥ 1 access	11.5 (8.5); 8.3
Hours/year of work per children and adolescents with ≥ 1 access per clinical staff professionals	2.5 (1.9); 1.7
Wait time for the first visit (days)	112 (99); 82
Time from request to diagnosis (days)	204 (133); 177
No. of children and adolescents who accessed the Center per year	179 (90); 177
No. of children and adolescents who accessed the Center for the first time per year	35 (25); 32
No. of children and adolescents diagnosed with ADHD per year	24 (16); 20
No. of clinical staff professionals	5 (3); 5
Hours/year of work	1521 (620); 1473
Hours/year of work per accessed children and adolescents	11.5 (8.5); 8.3
Hours/year of work per accessed children and adolescents per clinical staff professionals	2.5 (1.9); 1.7
Wait time for the first visit (days)	112 (99); 82
Time from request to diagnosis (days)	204 (133); 177

of *Mental Disorders* (4th ed., text rev.; *DSM-IV-TR*; American Psychiatric Association [APA], 2000) criteria for ADHD diagnosis, whereas 151 (7%) had a chronic medical disease. As shown in Table 2, in addition to the difference between ADHD centers, the statistically significant characteristics of the population associated with a shorter waiting time for diagnosis by univariate analysis were: to have a younger age, a support teacher at school, a motor delay, another CANPS as referral, validated diagnostic tests already at the time of access to the center, a chronic medical disease, the access to the nearest ADHD center of the residence ATS, a middle-high CGI-S score at diagnosis. For attenders the centers with a psychiatric disorder average wait time was slightly longer than for children and adolescents without psychiatric disorders.

Using linear regression analyses to determine response variables in population characteristics and centers, 6 of 10 statistically significant characteristics from univariate analysis were confirmed (the ADHD center, to be younger, to have been sent to the ADHD center by another CANPS, to have already done a few of mandatory diagnostic evaluations, to have chronic medical diseases, or to manifest severe symptoms of a disorder (CGI-S ≥ 5 at diagnosis), besides language delay associated with a longer waiting time from asking for the first visit to complete the diagnostic path (Table 3).

Estimated waiting times values according to GLM analysis were more closed than observed (min 158 days, CI 95% 53–263; max 241 days, CI 95% 236–245; Fig. 2). No

statistically significant difference between center observed vs estimated values was found for 5 centers (G, I, K, L, N), whereas for center A and B close and similar values were maintained between center.

Discussion

To the best of our knowledge, this study, as part of a multimodal project, represents the first evaluation in a large population of the time needed to complete a diagnostic evaluation in different ADHD centers related to center and patient characteristics. To dwell on this variable (waiting time) of the care pathway is important because complex neurodevelopmental disorders (such as ADHD, autism spectrum disorders, tic disorders and Tourette's syndrome, as well as learning disorders and intellectual impairment) can have a dramatic impact on home and family life and timely access to CANPS is expected by everyone.

The major findings of the present study can be summarized as follows: despite the common work shared over time a three times difference of waiting time for the similar diagnostic pathway was observed between centers. The size of waiting times between centers can be halved weighting for a few characteristics of children and adolescents attending each center. However, between center differences remain wide.

The results therefore indicate that a critical and shared comparison of the centers organization can be done to make waiting times more homogeneous between centers. Consequently, critical points should be tackled in

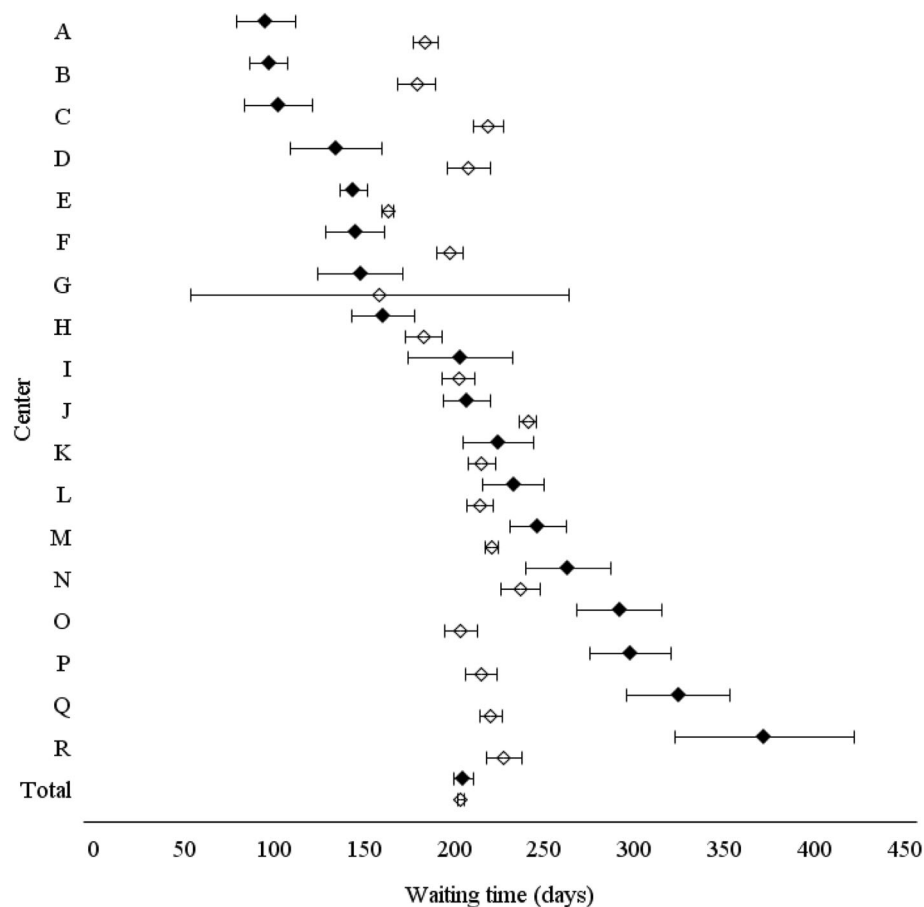


Fig. 2 Time from request to diagnosis (days) by ADHD center. Observed (•) and estimated according to a generalized linear model (GLM) analysis (◊) values (mean, CI 95%)

the individual centers through effective initiatives for improving and maintaining over time the quality of care. On the other hands at ATS level interventions for improving the effectiveness of care delivery are needed. The local distribution of ADHD centers should be reviewed by the Regional Ministry of Health since 27% of population attended a different center than that provided by the organization of regional services network. This affects the distribution of workloads of the individual centers, causes family dissatisfaction with the Health Service, and increases the costs attributable to the greater distance from residence that the family has to cope with [4–6]. It is conceivable that it is not an exclusive situation for ADHD but for also the other disorders belonging of CANPS [7, 27, 28]. So what has been done and documented here for ADHD in specialized centers should be generalized to all CANPS, at least at the regional level, so that policy makers can intervene appropriately.

The complexity of health care systems can produce inefficiencies in healthcare delivery, in particular in health areas such as mental services where organization

settings and people involved are often loosely connected. Various approaches, such as the sociotechnical system [29] or the quality assessment models [30], can be used to identify the elements cause of performance difference between centers, their interactions and their impact on quality care, as well as understanding the key adaptive role of people in the system [29]. However, sociotechnical system theory and interventions need more evaluation in child psychiatric area, as well as in Italy where a public universal health system has been up and running for decades in an efficient way. Different CANPS strategies and models of services delivery have been proposed or endorsed [11, 31–33], also for ADHD oriented services [16, 34–36], to facilitate access, reducing barriers, and improving facilitators. Signs of improvement have been seen but the rate of progress is still not good enough [14]. Waiting time reduction initiatives should be considered to answer the question “wait time to what?”, with the aim that shortened waiting time should improve the quality of delivered care, obtaining better clinical outcomes that must be monitored [37].

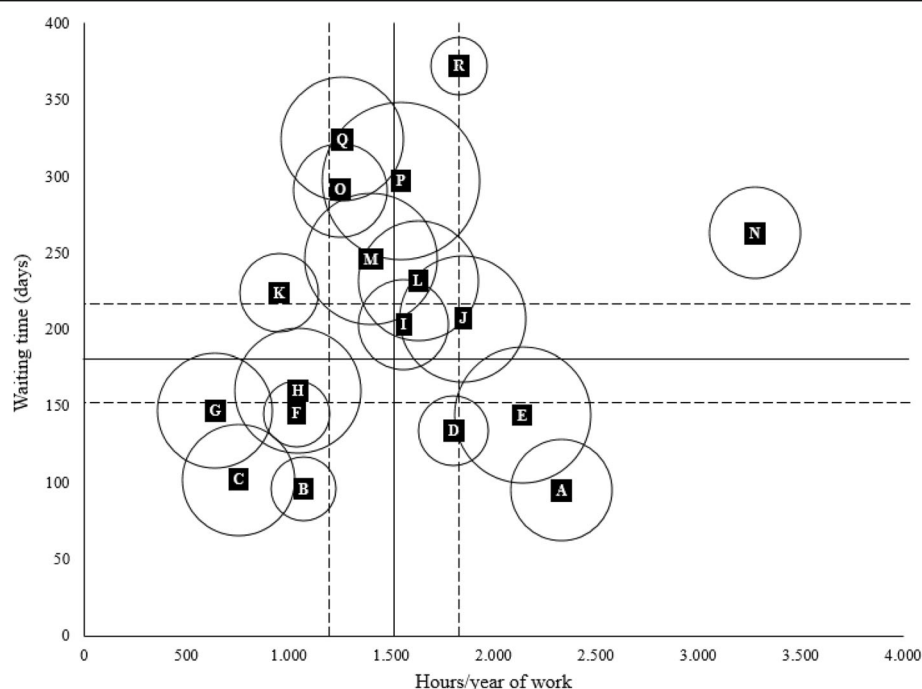


Fig. 3 Distribution of ADHD centres by waiting time from the request to the diagnosis, the hours/year of work for ADHD, and the number of children and adolescents with ≥ 1 access per year. Mean (—), CI 95% (---). Footnotes: The size of circles is proportional to the number of children and adolescents per center included in the study. Pearson's chi-squared test: $p = 0.11$; p -value = 0.6624; weighted Pearson's chi-squared: $p = 0.10$; p -value = 0.6789; Spearman's rank correlation test: $\rho = 0.01$; $p = 0.9838$

However, a mandatory intervention for each center is to manage better their available resources as suggested from not having found any association between the population size of attenders, the hours of work dedicated to ADHD diagnosis and therapeutic paths, and the waiting time.

A first and essential intervention to reduce differences between centers in the access should be the definition and utilization of common criteria of attitude and practice since the first request for an appointment. Appropriate prioritization, using different criteria (i.e. for 'emotional disorders' and for 'developmental disorders') were set up and used in a real-world setting providing effective care of ADHD [16]. Different criteria for prioritization as well as for other psychiatric disorders are required and the findings of the present study give some indication. Children and adolescents referred by another CANPS or with part of the common regional diagnostic plan already performed elsewhere had to wait less than the other attenders, suggesting that it is important to maintain and implement the relationships and information exchanges between the CANPS, as well as between professionals working in the same territory of the ADHD center. The age, language delay, or chronic medical diseases can be part of the essential points of an appropriate triage (also by phone) to better plan the

diagnostic path also in consideration of the availability and temporal possibilities of the Center.

The study setting is part of a larger, multimodal project, and represents a distinctive tool for ensuring appropriate and shared diagnostic and therapeutic pathways of care in ADHD children between the 18 participating centers. This homogeneity of the diagnostic and therapeutic practice between centers is a strength to evaluate other dependent variables, as waiting time, that can affect the care.

However, there is also the limitation that our findings refer specifically to the population accessing ADHD centers since only these hubs input data into the Registry about patients attending the center. Thus, although the 18 ADHD centers are public and cover the whole Region, it was not possible to evaluate initial appointment failures with patient losses.

It was not the aim of the study to evaluate if waiting time affected the outcome of the therapy then undertaken, although timely access to healthcare is associated with improved health outcomes [4, 38]. Besides, we know that early interventions in a period of development are crucial, and a prompt, preventive, and detection action is imperative for mental health disorders also in children and adolescents, and those with ADHD [39, 40].

Table 2 Time from request to diagnosis (days) by characteristics of the sample population

Characteristics		N	Waiting time (days) [mean (SD); median]	p-value ^a
Age at diagnosis	5–8 years	1088	194 (128); 163	0.0003
	9–17 years	1174	214 (137); 191	
Sex	Female	350	210 (136); 182	0.4110
	Male	1912	203 (132); 175	
Only child	No	1693	206 (132); 181	0.0925
	Yes	569	198 (135); 163	
Born abroad	No	2162	205 (133); 178	0.6219
	Yes	100	199 (132); 168	
Adopted	No	2190	205 (133); 178	0.2652
	Yes	71	188 (128); 157	
School repeater	No	2177	204 (133); 176	0.7265
	Yes	85	209 (138); 187	
Support teacher at school	No	2030	207 (132); 181	0.0009
	Yes	232	182 (135); 152	
Family history of ADHD	No	1873	203 (131); 173	0.2514
	Yes	389	213 (139); 193	
Born preterm or low weight	No	2029	205 (133); 178	0.2742
	Yes	233	195 (129); 167	
Motor delay	No	2146	206 (133); 180	0.0018
	Yes	116	172 (128); 130	
Language delay	No	1837	205 (132); 177	0.6040
	Yes	425	203 (136); 176	
Referral another CANPS	No	1539	229 (139); 213	< 0.0001
	Si	723	153 (100); 133	
Required assessment path done in the Center	No	1130	177 (128); 147	< 0.0001
	Yes	1132	232 (132); 210	
Optional evaluation done in the Center	No	788	208 (148); 182	0.5812
	Yes	1474	202 (124); 176	
Psychiatric disorders	No	308	187 (125); 159	0.0139
	Yes	1954	207 (134); 182	
Chronic medical diseases	No	2111	207 (134); 180	0.0010
	Yes	151	168 (110); 146	
Center in the ATS of residence and the nearest to the municipality of residence	No	625	191 (119); 163	0.0274
	Yes	1637	209 (137); 182	
CGI-S score at diagnosis	1–4	1810	208 (133); 181	0.0002
	5–7	389	183 (131); 155	

^a: Wilcoxon or Kruskal-Wallis test

SD Standard Deviation, ADHD Attention-Deficit Hyperactivity Disorder. CANPS Child and Adolescent Neuropsychiatric Services, ATS Local health protection agencies, CGI-S Clinical Global Impression–Severity

Conclusions

To guarantee an equal standard of care in ADHD centers for all children and adolescents the management of ADHD must stay within a pathway that strives for optimal care. The first step is the access to

the ADHD center, thus long waiting times for diagnosis are a sign of poor care, or at least of a questionable care, since its inception. Besides, long waiting times have a negative impact on family satisfaction, staff moral, and referrer's opinion of the service. Last

Table 3 Linear regression analysis for time from request to diagnosis (days) and characteristics of sample population

Parameter		Estimated waiting time (days) [mean (CI 95%)]	p-value ^a
Intercept		18.4 (−38.5–75.2)	0.5264
Age at diagnosis	9–17 years vs 5–8 years	20.8 (10.0–31.5)	0.0001
Sex	Female vs Male	1.8 (−12.8–16.4)	0.8092
Only child	No vs Yes	5.2 (−7.0–17.5)	0.4022
Born abroad	No vs Yes	0.6 (−30.4–31.6)	0.9701
Adopted	No vs Yes	15.5 (−20.9–51.8)	0.4048
School repeat	No vs Yes	2.5 (−25.8–30.8)	0.8634
Support teacher at school	No vs Yes	4.3 (−14.3–22.9)	0.6508
Family history of ADHD	Yes vs No	3.3 (−11.1–17.8)	0.6507
Born preterm or low weight	No vs Yes	7.0 (−10.4–24.5)	0.4285
Motor delay	No vs Yes	16.5 (−8.2–41.1)	0.1899
Language delay	Yes vs No	15.8 (1.9–29.8)	0.0262
Referred by another CANPS	No vs Yes	64.6 (52.6–76.6)	< 0.0001
Required assessment path done in the Center	Yes vs No	43.8 (32.9–54.7)	< 0.0001
Optional evaluation done in the Center	No vs Yes	5.3 (−6.1–16.8)	0.3612
Psychiatric disorders	No vs Yes	8.8 (−7.0–24.7)	0.2750
Chronic medical diseases	No vs Yes	28.5 (7.5–49.6)	0.0079
Center in the ATS of residence and the nearest to the municipality of residence	Yes vs No	7.6 (−4.3–19.5)	0.2115
CGI-S score at diagnosis	1–4 vs 5–7	25.7 (11.0–40.4)	0.0006

^a. Generalized linear model (GLM). r-squared = 0.12

CI Confidence interval, ADHD Attention-Deficit Hyperactivity Disorder, CANPS Child and Adolescent Neuropsychiatric Services, ATS Local health protection agencies, CGI-S Clinical Global Impression–Severity

but not secondary, differences in waiting times for the same needs (characteristics of children and adolescents attending the ADHD centers) are a sign of inequalities. A few critical points affecting waiting times have been highlighted in the present study. There is therefore reason and duty to intervene and improve the care.

Abbreviations

ADHD: Attention-deficit hyperactivity disorder; ANOVA: Analysis of variance; ATS: Local health protection agency; CANPS: Child and Adolescent Neuropsychiatric Services; CI: Confidence interval; DSM-IV: Diagnostic and statistical manual of mental disorders; GIS: Geographic information system; GLM: Generalized linear model; SD: Standard deviation

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Authors' contributions

MB had the idea for the study, designed it, and drafted the initial. MC and MZ managed and analyzed the data. All collected data, were analyzed monthly, and the findings were reported and periodically discussed with all 18 ADHD centers belonging to the Lombardy ADHD Group. All authors participated in study design, contributed to interpretation of data, critical review and revision of the report, and approved the final report as submitted. MB is guarantor for the study. The views expressed are those of the authors and not necessarily those of Regional Healthcare Directorate.

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Availability of data and materials

ADHD Registry database was created, developed, updated, and managed by the Authors within the project. The datasets used and/or analyzed during the current study are not public but available from the corresponding author on reasonable request for research purposes.

Ethics approval and consent to participate

This study was designed as a review of patient medical records identified from the regional ADHD Registry database. Written informed consent was obtained for all patients before collection data in the Registry. Data were anonymized prior to use for research purposes. Formal ethical review board approval was not required for the present analysis of the data.

Consent for publication

Not applicable.

Competing interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: All authors declare no financial relationships with any organizations that might have an interest in the submitted work; no other relationships or activities that could appear have influenced the submitted work.

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Interactive Avatar Boosts the Performances of Children with Attention Deficit Hyperactivity Disorder in Dynamic Measures of Intelligence

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Andrea Nucita, PhD,² and Nasrin Mohammadhasani, PhD³

Abstract

This study examined both children with attention deficit hyperactivity disorder (ADHD) and typically developing students in dynamic measures of intelligence through the use of a virtual avatar. Three conditions were compared: in the first condition, the avatar simply gave the instructions; in the second condition, the avatar presented the instructions and gave feedback on the attention of the learner; in the third condition, the avatar was not presented. Results indicated that ADHD subtypes do not differ in problem solving and the interactive avatar improved the performance of groups with ADHD in the dynamic intelligence test. Overall, these results support the hypothesis that the function of regulation and feedback of the avatar improve the attention process and, consequently, boosts performance.

Keywords: ADHD, dynamic measures, intelligence, interactive avatar, virtual avatar

Introduction

ATENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) is a highly prevalent childhood disorder and has three presentations: inattentive, hyperactive, and combined (with both inattentiveness and hyperactivity).¹ This disorder is closely linked to a series of neuropsychological deficits^{2–19} such as executive functions, working memory, variability of reaction times, emotional dysregulation, and problem solving.

New promising therapeutic approaches have recently shown that children with ADHD may take advantage of new technologies to overcome their symptoms.^{20–24} For example, the study of Mohammadhasani et al.²⁵ has investigated the use of avatars in two conditions: in the first, an avatar gives instructions to students with ADHD to learn a math task; in the second, no avatar is present and instructions are given only through computer audio. Results show that children with ADHD learned the math task faster in the first condition.

Avatars are virtual characters used in online learning environments to serve various instructional goals.²⁶ They have human-like gestures, speech, gaze, and behaviors to address some roles, such as tutor, coach, actor,^{27,28} expert, motivator, mentor, model, and virtual peer.^{29,30} Avatars can be used as a

pedagogical agent (PA) to increase learning motivation in a virtual environment. In the literature,^{31,32} PAs belong to two categories:

Conversational agents: they are interactive, capable of holding conversations with learners, and can guide their attention capacity.

Teachable agents: they are programmed to teach the students to complete various activities.²⁶

The role of the PA is supported by theories such as computers as social actors (CASA),³³ social-cognitive theories (SCTs),³⁴ and cognitive load theory (CLT)³⁵ in learning environments that emphasize the social aspect in the learning process.

CASA reveal that humans tend to respond to media in the same ways they would respond to other humans. According to this theory, an avatar can serve as a social model²⁹ in learning with computers. As Mayer³⁶ mentions, the students learn more deeply when on-screen agents display human-like gesturing, movements, eye contact, and facial expressions. Also Wang et al.³⁷ state that people learn better from on-screen multimedia programs when a gesturing PA is added to the screen, acknowledging that the social presence

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of PAs is expected to increase “learners” interest, attention, and motivation.³⁸

From the perspective of the SCT,³⁴ avatars can serve as models: the vicarious experience is very effective. The theory posits that to learn through observation, a learner must find the instruction worthy of attention, relevant, salient, and retainable, while having the self-efficacy and motivation to perform the learned action.^{34,39,40} Finally, CLT suggests that effective instructional material facilitates learning by directing cognitive resources toward activities that are relevant to learning rather than toward preliminaries to learning. CLT also provides a strong framework for the effect of attention cueing wherein a PA can effectively cope with learners’ limited cognitive resources.^{35,41}

PAs are an example of how the new technologies enhance education and help a more social behavior^{29,42,43} by providing just-in-time support or guidance, decreasing cognitive load,⁴¹ and directing the student’s attention to key elements.^{44,45} Although the effects of PAs on multimedia learning are debatable,³⁷ research has shown that using PAs can be effective for learners as they provide them with the appropriate scaffolding⁴⁶ and feedback^{37,47} and guide their attention to relevant information.^{24,25,48} PAs also showed positive effects on motivation,^{42,45,49,50} transfer,^{37,51} and collaborative learning.

This study was designed to examine both children with ADHD (belonging to all ADHD subtypes) and typically developing (TD) students, in dynamic measures of intelligence through the use of a virtual avatar as PA. Dynamic measures of intelligence are obtained by administering novel problem-solving tasks to the subjects, supplying them with gradual and balanced assistance that progressively discloses the solution of the problem, and by determining the amount of aid the learner needs to be able to solve the problem. The amount of aid is inversely proportional to the modifiability index. The modifiability index is the general propensity to change and can better measure intelligence.^{52–55} Dynamic measures are presented as an alternative or complement to the conventional static intelligence test. Many researchers approve the fundamental aims of dynamic testing.^{56–58} In contrast, some methodological aspects have been criticized.^{59,60} Most of the criticism relates to lack of standardization of tests and to inadequate validation, and to Feuerstein’s arguments against the customary psychometric procedures. However, the instruments used in this study have shown good psychometric properties and, moreover, are standardized.

The first question addressed in the study is to determine whether the different subtypes of ADHD show different levels of dynamic intelligence measures compared with TD children.

The second question is to understand whether the presence of a virtual avatar providing instruction and feedback can enhance attention and performance of children with ADHD. This study differs from the study of Moham-madhasani et al.,²⁵ since the avatar not only gives instructions but also feedback on the attention behavior of children and measures a more challenging cognitive task (complex problem solving).

The underlying logic of enhancing attention process is that the attention process significantly affects some cognitive functions such as problem solving and learning. However, the attention process does not influence all cognitive functions, for example, it does not influence routine situations or

when there is no need for adaptive changes.⁶¹ As Ropovik⁶² underlines, there are specific conditions in which the attention process plays a crucial role and these conditions involve (a) novel or unfamiliar circumstances; (b) where tasks are complex; and (c) where there is a need for integration of information such as in problem-solving tasks. The problem-solving task used in this study, as will be better specified hereunder, involves all of these three aspects.

In this study, the problem-solving task has been presented with three conditions:

In the first condition, the avatar simply gives the instructions (noninteractive avatar).

In the second condition, the avatar presents the instructions and gives feedback on the attention of the learner (interactive avatar).

In the third condition, the avatar is not present (no avatar).

The hypothesis is open; the CASA theory³³ provides evidence that individuals’ exposition to computers is fundamentally social, an avatar may be seen as a social model and students learn more efficiently when in the presence of it. Accordingly, the SCT³⁴ has found that the use of avatars can lead to better learning, increasing knowledge retention and attention, as children focus on the avatar as a model to learn from. The CLT³⁵ assumes that learning can be optimized when the learner receives effective instructions. In light of these findings, identifying the conditions that foster attention in children with ADHD in comparison with TD children in the context of interactive avatar versus no interactive avatar may help us to better understand the dynamics in human–computer interactions.

The underlying logic is summarized in Table 1.

Methods

Participants

The participants in this study were selected from a sample of 1,000 children (387 females and 613 males) attending public primary and secondary schools in Sicily. Students ranged in age from 7 to 13 years ($M=10.5$, standard deviation [SD]=4.52) and were all Italian. For all participants, their teachers completed both the Italian version of the ADHD Rating Scale for Teachers^{63–65} (SDAI) and the Disruptive Behaviour Disorder Rating Scale⁶⁶ (SCOD) aimed at assessing the possible presence of, respectively, ADHD and/or learning disabilities.

ADHD group. The first screening for ADHD diagnosis was based on SDAI scores.^{67–70} The SDAI is widely used in Italy and has been validated and standardized for the Italian population, showing an inter-rater reliability of 0.80 (inattentive subscale) and 0.74 (hyperactive/impulsive), optimal discriminatory power and concurrent validity ($r>0.95$).⁶⁵

In this experiment, inclusion in the ADHD condition was based on cutoff scores (>14) in both subscales (I and H) and on a clinical assessment carried out by a specialized psychologist. The presence of other disorders was excluded by normal SCOD scores and by the clinical interview.

TD group. The sample of the initial 1,000 children who obtained SDAI and SCOD scores in the normal range, but

TABLE 1. UNDERLYING LOGIC AND HYPOTHESES OF THE STUDY

<i>Hypothesis</i>	<i>Theory</i>
If the students with ADHD attend equally well as TD students in the noninteractive avatar condition, then the mere presence of the avatar is motivating enough to enhance their attention and consequently their problem-solving ability.	SCT, CASA, and CLT theories will be confirmed.
If the students with ADHD perform equally well as TD students in the interactive avatar condition, then the ability to provide regulation and feedback of the avatar is sufficiently motivating to improve students' attention and consequently their problem-solving ability.	SCT, CASA, and CLT do not offer appropriate tools to determine changes in children with ADHD and new tools need to be developed.

ADHD, attention deficit hyperactivity disorder; CASA, computers as social actors; CLT, cognitive load theory; SCT, social-cognitive theory; TD, typically developing.

who were not included in any clinical group, and of children diagnosed by the school psychologists without behavioral, emotional, and/or relational problems, constituted the basis to form the control group. A set of children was randomly selected from this sample to form a matched gender and age control group.

The final sample is depicted in Table 2. The sample size was set equal to 19 determined by assuming the prevalence of subjects with ADHD to be 5 percent, 95 percent confidence limit, and 5 percent marginal error.

Instruments

Dynamic test. The items in the dynamic test were selected from a standardized article of Fabio,^{53,54} which had met satisfactory criteria of statistics reliability. These items are problem-solving tasks that the child does not solve spontaneously, but during the course of a learning session and during the course of a transfer session. The test is described in Table 3.

Computerized dynamic test. A computerized version of the dynamic test has been developed, as a basis to intro-

duce the avatar in the already mentioned experimental settings. The avatar has different capabilities, depending on three different conditions, as given in Table 4. The computerized dynamic test fundamentally reproduces the items of the dynamic test, with some changes to adjust user interaction.

The computerized dynamic test is a Web application, developed using HTML5, CSS, Javascript, and Python. It is composed of two parts: the first (client side) program manages the user interface and the logic for the test interaction and the avatar; the second part is a server side program, which uses computer vision algorithms to detect whether a face focuses on the screen using the camera, and sends consequential messages through a Web socket. The client application then uses these Web socket messages to choose the corresponding avatar animation, such as recalls or rewards.

A scheme of the Web application is depicted in Figure 1.

TABLE 2. DEMOGRAPHIC CHARACTERISTICS OF THE THREE GROUPS PARTICIPATING IN THE EXPERIMENT

<i>Groups</i>	<i>Measures</i>	<i>Values</i>
ADHD-I	<i>n</i> , Boys/girls	20/4
	Age, <i>M</i> (<i>SD</i>)	10.50 (4.52)
	IQ, <i>M</i> (<i>SD</i>)	94.00 (6.50)
	Distractibility, <i>M</i> (<i>SD</i>)	19.50 (2.45)
	Hyperactivity, <i>M</i> (<i>SD</i>)	2.10 (3.01)
ADHD-C	<i>n</i> , Boys/girls	19/2
	Age, <i>M</i> (<i>SD</i>)	10.80 (4.22)
	IQ, <i>M</i> ; (<i>SD</i>)	95.00 (5.60)
	Distractibility, <i>M</i> (<i>SD</i>)	18.60 (2.50)
	Hyperactivity, <i>M</i> (<i>SD</i>)	17.10 (2.20)
TD	<i>n</i> , Boys/girls	39/6
	Age, <i>M</i> (<i>SD</i>)	9.50 (4.53)
	IQ, <i>M</i> (<i>SD</i>)	105.50 (7.95)
	Distractibility, <i>M</i> (<i>SD</i>)	2.00 (0.20)
	Hyperactivity, <i>M</i> (<i>SD</i>)	5.00 (0.31)

SD, standard deviation.

TABLE 3. DYNAMIC TEST COMPOSITION

<i>Dynamic test features</i>	<i>Description</i>
Items groups/number of items	Learning stage/7 Transfer stage/7
Typology of tasks for each item group	Completion of a series of letters Completion of a series of numbers Completion of geometrical figures Perceptive difference Mental image superimposition Chain of words Simultaneous coordination of information
Scores	The score on the single item is based on the number of prompts by experimenter, and is the other way around (e.g., 0 prompt, score 5–1 prompt, score 4–2 prompts, etc.) LMI (sum of the scores of the learning stage) TMI (sum of the scores of the transfer stage) GMI (learning stage+transfer stage)

GMI, general modifiability index; LMI, learning modifiability index; TMI, transfer modifiability index.

TABLE 4. COMPUTERIZED DYNAMIC TEST FEATURES

<i>Experimental condition</i>	<i>Avatar capabilities</i>	<i>Avatar prompts</i>
No avatar	None	None
Noninteractive avatar	Gives vocal prompts	Standardized sequence of suggestions example: (1) “pay attention to the relationship between the numbers” (2) “the relationship between the numbers refers to the sequence of three numbers” (3) “inside each series of three numbers the first figure decreases by 2 units, look at the other two figures” (4) “look at the other two figures: the second one increases by 1 unit while the third one increases by 2 units” (5) resolution of task
Interactive avatar	Gives vocal prompts Recognizes eye movements and posture of the child Draws child’s attention	Standardized sequence of suggestions “Hey friend, look at the screen!” when child is not looking at the screen “Very good!” when the child looks back at the screen

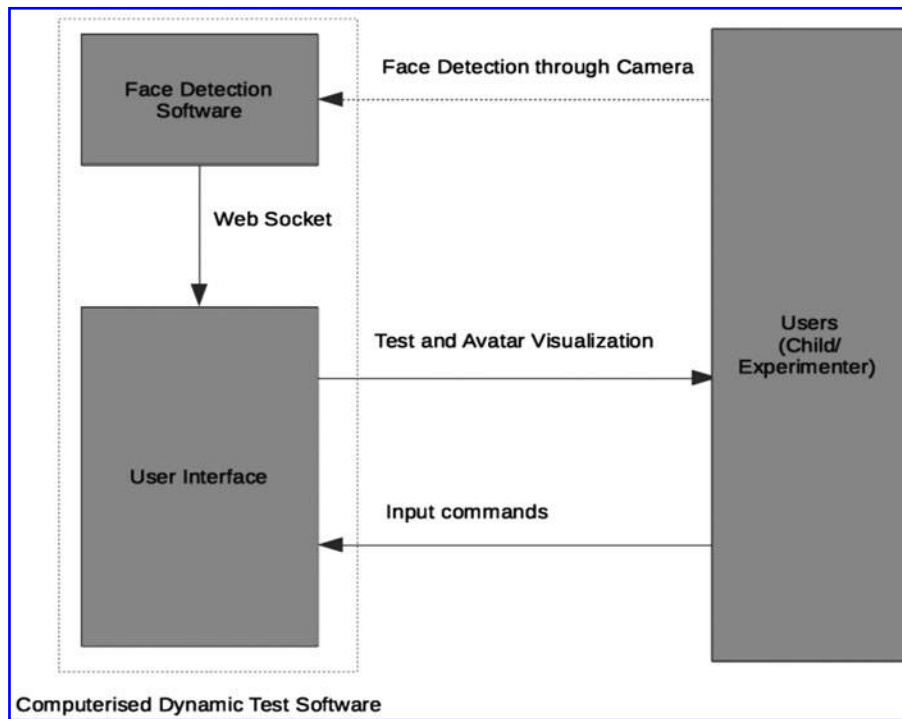


FIG. 1. Scheme of the Web application.

TABLE 5. WEB APPLICATION USER INTERACTION CONDITIONS

<i>Experimental condition</i>	<i>User</i>	<i>Interaction</i>
No avatar	Child	Mouse selection
	Experimenter	Audio for suggestions/warning/rewards Pressing keys to play audio for suggestions/warning/rewards/ and to go on with the test
Noninteractive avatar	Child	Mouse selection
	Experimenter	Video for suggestions/warning/rewards Pressing keys to play video for suggestions/warning/rewards/ and to go on with the test
Interactive avatar	Child	Mouse selection Video for suggestions/warning/rewards
	Experimenter	Face detection Pressing keys to play video for suggestions/warning/rewards/ and to go on with the test

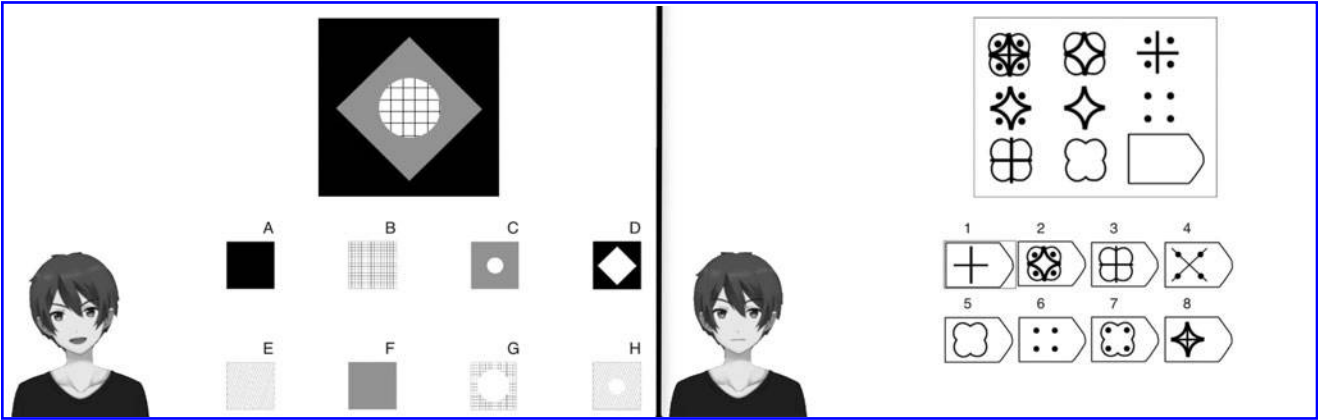


FIG. 2. Web application screenshots.

The user interface is very simple, to faithfully reproduce the original paper dynamic test. The first page of the Web application serves as a switch between the three experimental conditions, namely no avatar, noninteractive avatar, and interactive avatar. In Table 5, the different kinds of possible interaction are shown, along with the different experimental conditions and user types.

No interaction is possible through touch screen, as it may generate distractions.

The child can interact with the mouse, whereas the experimenter can control the test and the avatar through the keyboard.

In Figure 2, two screenshots of the Web application are shown, whereas in Table 6, the keyboard commands for the experimenter.

Procedure

The experiment was conducted in a quiet room of the school. The participants were randomly assigned to the three conditions. The experimenter explained that they would be completing some tasks, then he showed the first problem to the child inviting her to solve it. The child was reminded that she could ask for help, but she should try to perform the task with as little aid as possible. Once the correct solution of the first item was achieved, the same procedure was followed for all the other items: learning items first and then transfer ones.

The experimenter assigned the score (Table 3).

Statistical analyses

The data were analyzed using SPSS version 22.0 for Windows. The descriptive statistics of the dependent

variables were tabulated and examined. The alpha level was set to 0.05 for all statistical tests. In the case of significant effects, the effect size of the test was reported. The effect sizes were computed and categorized according to Cohen (1988).⁷¹ The Greenhouse–Geisser adjustment for nonsphericity was applied to probability values for repeated measures.

Results

Table 7 shows the means and SDs of the three conditions for all groups. A one-way repeated analysis of variance 3 × 3 (groups: ADHD-I, ADHD-C, and TD × conditions: noninteractive avatar, interactive avatar, and no avatar) was used to analyze the data.

With reference to “groups,” we found significant effects, $F(4, 267) = 3.14, p < 0.001$, Cohen’s $d = 0.45$. This means that groups showed different trends: the TD group showed a better performance than the groups with ADHD.

To answer the first research question, *post hoc* analysis (least significant difference of Fisher) was computed and the results of the analyses showed that there were no statistically significant differences between the groups with ADHD, $t(43) = 1.03, p < 0.25$. This result indicated that the two groups with ADHD expressed similar problem-solving performances across the dynamic test and that each of them showed significant differences with the TD group [respectively: $p < 0.01$; ADHD-I vs. TD: $t(43) = 2.31, p < 0.01, d = 0.63$; ADHD-C vs. TD: $t(43) = 2.23, p < 0.01, d = 0.62$].

With reference to the second question, significant main effects were found for the factor “conditions,” as shown in

TABLE 6. WEB APPLICATION KEYBOARD COMMANDS FOR THE EXPERIMENTER

Key	Command
1–5	Play audio/video suggestions
9	Play audio/video rewards
0	Play audio/video rewards and go on
Left arrow	Previous item
Right arrow	Next item

TABLE 7. MEANS AND (STANDARD DEVIATION) OF THE GENERAL MODIFIABILITY INDEX IN THE THREE CONDITIONS FOR ALL GROUPS

Conditions	ADHD-I	ADHD-C	TD
Interactive avatar	35.50 (15.27)	38.40 (13.20)	45.72 (10.31)
Noninteractive avatar	25.22 (6.39)	21.83 (14.83)	42.10 (15.55)
No avatar	24.14 (13.69)	21.60 (11.14)	43.06 (9.98)

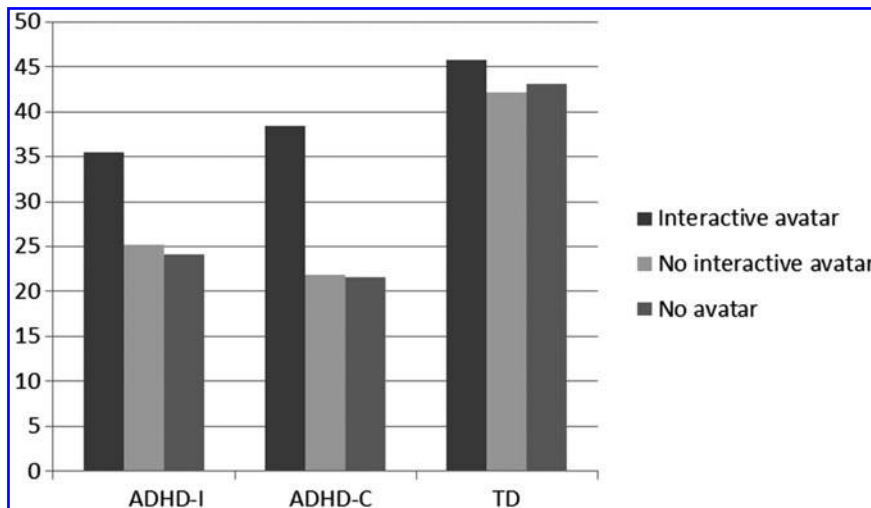


FIG. 3. Means of the general modifiability index.

Figure 3. In addition, there was an interaction between groups and condition, $F(4, 267) = 3.14$, $p < 0.001$, $d = 0.45$. This interaction indicated that the two groups with ADHD showed a better performance in the interactive avatar condition. *Post hoc* analysis (least significant difference of Fisher) was computed and the results of the analyses showed that there were statistically significant differences between the ADHD-I with interactive avatar versus ADHD-I with noninteractive avatar, $t(21) = 2.13$, $p < 0.01$, $d = 0.70$. Differences were also found between the ADHD-C with interactive avatar versus ADHD-C with noninteractive avatar, $t(21) = 2.11$, $p < 0.01$, $d = 0.7$.

Discussion

This study aimed to investigate two questions. First, whether the different subtypes of ADHD show different levels of dynamic intelligence measures compared with TD children. Second, whether the presence of a virtual avatar that gives instruction and feedback can enhance attention and performance of children with ADHD.

With reference to the first question, the experimental results show that the two groups with ADHD expressed similar levels of dynamic intelligence measures, significantly lower than those of TD children. This means that the ADHD subtypes do not differ in problem solving.

With reference to the second question, the CASA theory,³³ SCT,³⁴ and CLT³⁵ support the role of the PA in learning environments and emphasize the social aspect in the attention process. However, our experimental results indicated that only the interactive avatar improved attention and, consequently, the performance of the groups with ADHD in the dynamic intelligence test, whereas the noninteractive avatar did not produce significant improvements. This finding is in line with the CASA theory,³³ SCT,³⁴ and CLT.³⁵ This second result means that although the already mentioned theories are satisfied in their general assumptions and with reference to the TD population, they do not fit appropriately with children with ADHD, as it is necessary to propose further new tools to better check the attention process. In line with this, our avatar not only gives instructions on the problem-solving

tasks, but also helps the children to better focus attention by giving feedback on their behavior. Hence, our results indicate that an interactive avatar that helps children to better direct their attention can concretely improve cognitive performance.

We consider the findings reported in this article a relevant contribution to the introduction of a new generation of embodied interactive virtual agents (interactive avatars) aimed at supporting children with ADHD in their everyday activities. These findings can help families and educators to identify what sort of software can be effectively used to help children with ADHD, and also software designers to make good evidence-based choices to offer more focused software, capable of giving significant performance improvements.

A limitation of this research is that the graphical, behavioral, and technological characteristics of the avatar were not discussed. However, in principle it might be argued that they can influence the effectiveness of the avatar in improving the performance of the students. Some preliminary experiments have informally confirmed this hypothesis and, therefore, further work is currently in progress to investigate these aspects.

Another limitation of this study may also be related to the size of the sample. In this study, the sample size is small and there may be constraints to the generalizability of the results. However, the effect size is adequate; consequently, the results from groups can be considered reliable. Moreover, other studies on ADHD population^{72–74} have used a similar sample size to determine reliable results.

More, in general, future research is needed to understand the conditions under which a PA, such as an avatar, can enhance learning abilities and learning process in children with ADHD, involving a wider sample. Indeed, through the avatar we improve the attention process and the attention process significantly affects complex problem solving and learning.

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The efficacy of a training that combines activities on working memory and metacognition: Transfer and maintenance effects in children with ADHD and typical development

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ABSTRACT

Introduction: It has been demonstrated that children with attention deficit and hyperactivity disorder (ADHD) have impairments in working memory (WM), and particularly its visuospatial component, responsible for academic underachievement. Furthermore, children with ADHD have difficulty in metacognition, and consequently use inappropriate strategies to control attention and impulsive behavior. The aim of the present study was to devise a training that combined individual exercises on visuospatial WM and group metacognitive activities capable of helping children with ADHD to ameliorate their performance in executive functioning tasks, and to contain their inattentive and hyperactive/impulsive behavior.

Method: A combined training that focused on visuospatial WM and metacognition was administered to 12 children with a diagnosis of ADHD and 15 typically-developing children. Tasks on executive functions and questionnaires for parents and teachers were administered before and at the end of the training, and one month after the post-test. Specific short- and long-term training gains and transfer effects were examined. Effects of the training on parents' and teachers' ratings were also considered.

Results: Specific gains and transfer effects were found at the post-test and long-term assessments in both typically-developing children and those with ADHD. Parents' and teachers' ratings also indicated an improvement in the symptomatic behavior of children with ADHD.

Conclusion: The results of this study have clinical and educational implications. A training that combines individual computerized visuospatial WM activities with metacognitive group reflection about useful strategies seems to produce promising results, helping children with ADHD to improve their executive functioning and behavioral problems.

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Attention deficit and hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by inattentive, hyperactive, and impulsive behaviors. The prevalence of ADHD is around 3–7% of the general population (American Psychiatric Association [APA], 2013; Polanczyk, De Lima, Horta, Biederman, & Rohde, 2007), and it is associated with lifelong impairments (e.g., Harpin, 2005). The heritability of ADHD is now well established (e.g., Larsson, Chang, D'Onofrio, & Lichtenstein, 2014), but the genes most at risk have yet to be identified (e.g., Gizer, Ficks, & Waldman, 2009).

Although different models have been proposed in the literature (for a review, see Barkley, 2014), it is generally agreed that children with ADHD perform less well in working memory (WM) tasks than their typically-developing peers (e.g., Castellanos & Tannock, 2002). For example, the meta-analysis conducted by Willcutt, Doyle, Nigg, Faraone, and Pennington (2005) suggests that the strongest and most consistent differences

between children with and without ADHD concern measures of spatial WM (see also the meta-analysis by Martinussen, Hayden, Hogg-Johnson, & Tannock, 2005), and other components of executive functioning such as response inhibition, vigilance, and some measures of planning. Since impairments in WM have been associated with patterns of academic underachievement (e.g., Rogers, Hwang, Toplak, Weiss, & Tannock, 2011; Simone, Marks, Bédard, & Halperin, 2018), efforts have increasingly been made to target and improve WM in individuals with ADHD (see Capodiecì, Gola, Cornoldi, & Re, 2018; Gropper, Gotlieb, Kronitz, & Tannock, 2014; Mawjee, Woltering, & Tannock, 2015; Re, Capodiecì, & Cornoldi, 2015). The results have been inconsistent, however. For instance, using the computerized Cogmed WM training (CWMT) program developed by Klingberg et al. (2005), several studies reported treatment-related improvements in visuospatial and auditory verbal WM, and their generalization to other, more complex

reasoning abilities (Klingberg, 2010). These studies also suggested that WM training could improve behavioral symptoms of inattention – as reported by parents at least (Klingberg et al., 2005). Other studies that used the CWMT and a randomized controlled trial method found more limited transfer effects. Chacko et al. (2014), for example, reported some effects on short-term memory tasks (both verbal and visuospatial) in 7- to 11-year-olds with ADHD, but not on WM measures or other aspects considered (inattention, impulsivity, parents' and teachers' assessments of the children's ADHD symptoms). They consequently concluded that the CWMT is not a viable treatment for children with ADHD – to improve their WM, at least. Similar conclusions were drawn by Gray et al. (2012), who reported finding a benefit on verbal and visuospatial WM measures directly trained during the CWMT protocol in adolescents (11–17 years of age) with ADHD and learning disorders. They found no transfer effects to other measures of WM, however, nor to attention or the other domains of functioning they considered (behaviors and academic skills).

It has been suggested that the reasons for such inconsistent results might lie in the methodological differences across the studies and, more in general, in the fact that the treatments do not promote any metacognitive reflection on more appropriate strategies for controlling one's own behavior and attention (Re et al., 2015). Rote practice with the task does not seem enough to develop skills for promoting transfer. Taking a metacognitive approach enables trainees to recognize the characteristics of a given task, and also to mentally stand back and see themselves performing it. They can thus think about how best to deal with the requirements of the task. In other words, metacognition enables us to reflect on our own features and those of a given task, and on the strategies most appropriate for completing it. Feedback from the environment (e.g., from parents and teachers) on how a task might be carried out is crucial to the process of acquiring metacognitive skills. Unfortunately, children with ADHD often have difficulty registering and using feedback because of their intrinsic characteristics. They are consequently unaware that they may be failing in a task, so simply practicing with it may not be effective.

On the basis of these considerations, some studies in the literature (e.g., Capodici et al., 2018; Re et al., 2015; Tamm & Nakonezny, 2015) have focused explicitly on teaching strategies and promoting metacognitive awareness and control. With this in mind, Re et al. (2015) proposed a training program for conducting in small groups that involved tasks in game-like situations. The tasks targeted participants' control of their attention and impulsive behavior, as well as their WM,

and they were always introduced and concluded with metacognitive reflections on how the task was performed or should have been performed. The training was assessed in a sample of 26 five-year-olds with symptoms of ADHD and 26 typically-developing peers: 13 children randomly selected from each of these two groups received the training, while for the others it was 'business as usual'. The results showed that children who received the training improved in neuropsychological tasks measuring their ability to control their attention and impulsive behavior, as well as in WM (see also Capodici et al., 2018). The children with symptoms of ADHD also showed some improvements in the rating scales completed by parents and teachers. Adopting a metacognitive approach therefore enabled the benefit of WM training to be transferred to other contexts.

In the light of these results, the present study tested a combined training on metacognition (knowledge and control) and WM. To clarify the malleability of the impairments seen in WM and associated processes in children with ADHD, the training gains were compared with those obtained by typically-developing children who completed the same training protocol. The training consisted of 16 sessions administered at a rate of two a week. The first session in each week was for the activities on metacognition, administered to small groups of 4–5 children. In the second session, the children practiced doing computerized visuospatial WM exercises at home under their parents' supervision (see description of the training for details). The sessions on metacognition promoted reflection and control over the performance of the game-like tasks. To give an example, the children were asked to remember the position of hidden objects: a number of objects were placed on the table, then hidden, and the children were asked to remember which objects they had seen before, and to indicate their position. Completing this type of task involves attention and WM processes. At the end of the session, metacognitive awareness was explicitly promoted by reflecting on the characteristics of the memory task, and the importance of using strategies to aid memory, and of controlling behavior. During the individual sessions, participants practiced different types of visuospatial WM task in which both the maintenance and the control demands were manipulated (see below for a detailed description).

Training gains in the cognitive tasks were assessed in terms of specific effects, near and far transfer effects, based on the taxonomy of mental abilities proposed by Carroll (1993), who devised a framework in which abilities can be located depending on how they overlap in terms of cognitive processes. Referring to this taxonomy, Noack, Lövdén, Schmiedek, and Lindenberger

(2009) proposed its use for understanding transfer effects, and we referred to their proposal to categorize the measures included in the study (see the Procedure section).

For both groups, we expected to find an effect on visuospatial WM and sustained attention as a result of process-based activities on visuo-spatial WM. The improvement obtained was compared with standardized values for the general population, which were available for all the measures included in the study. This clarified the impact of the training in terms of expected performance, depending on the children's age. The activities on metacognition were expected to reduce the typical ADHD symptoms of inattention and hyperactivity, as rated by external observers (parents and teachers). WM performance has been found to predict inattentive behavior, as rated by parents (Lui & Tannock, 2007), and to mediate the negative effects of inattention on academic achievement (Rogers et al., 2011).

Materials and methods

Participants

The clinical diagnosis of ADHD in Italy follows the criteria proposed by the ICD-10 (World Health Organization [WHO], 2010), according to which the main symptoms are impaired attention and hyperactivity. Both of these main symptoms are necessary for a diagnosis. Impaired attention entails a lack of persistent task involvement and a tendency to move from one unfinished activity to another, while hyperactivity

is expressed in restlessness, talkativeness, noisiness and fidgeting, particularly in situations requiring calm. The ICD-10 requires that persistent behavioral symptoms developing prior to 6 years of age be apparent in two or more settings (e.g., home, classroom).

Twelve children with ADHD (9 males and 3 females; age $M = 7.25$, $SD = 0.62$), and 15 typically-developing (TD) children (12 males and 3 females; age $M = 7.2$, $SD = .41$) took part in the study. The children ranged from 6 years and 7 months to 8 years and 6 months of age. Participants with ADHD profiles had been diagnosed at a clinical center specializing in the diagnosis of children with ADHD and interventions to support them. Participants were diagnosed using clinical interviews and checklists for parents and teachers. The interviews (the ADHD Scale from the Italian battery for assessing ADHD, BIA, Marzocchi, Re, & Cornoldi, 2010) were based on the behavioral descriptors listed in the DSM-5: among the children with a diagnosis of ADHD, 9 had a combined presentation, and 3 a predominantly inattentive presentation. All participants were attending mainstream schools. The children enrolled were not receiving any kind of treatment or medication (which is very rarely prescribed for ADHD in Italy).

The two groups (ADHD and TD) were comparable in terms of nonverbal intelligence (Raven's Colored Progressive Matrices; Raven, Raven, & Court, 1998; see Table 1). Teachers and parents were invited to rate all the children (ADHD and TD) on a scale assessing the presence of attention and hyperactivity disorders and comorbidities. For both groups, children diagnosed with learning

Table 1. Descriptive statistics for the two groups on the measures obtained at the pre-test, post-test and follow-up assessments (all raw scores).

			Children with ADHD						TD children					
			Pre-test		Post-test		Follow-up		Pre-test		Post-test		Follow-up	
			M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Specific effects														
WM	Backward Corsi Blocks test**		2.83	1.34	3.33	1.16	3.33	1.07	2.27	1.03	3.07	0.96	3.87	0.92
Near transfer														
Attention	Visual search	Selective*	41.25	10.89	52.92	15.39	60.17	14.68	40.87	11.24	55.53	12.11	67.67	10.50
		Sustained*	103.92	16.19	116.75	12.58	123.67	11.02	103.67	19.89	123.07	11.65	130.47	7.51
	Auditory attention**		5.33	2.64	7.25	1.60	7.58	2.07	7.20	2.51	7.07	2.02	7.67	1.92
Far transfer														
Impulsivity	Go/No-Go*		11.08	3.61	13.50	2.43	12.83	2.17	15.73	2.60	16.67	2.32	17.27	3.08
	Matching Figure test	Errors*	24.25	12.11	16.83	6.04	15.00	5.82	11.00	7.60	7.87	4.96	7.27	4.91
		Response times	9.52	4.22	9.09	2.94	8.77	4.80	22.12	14.36	20.14	10.72	20.14	9.53
Nonverbal reasoning														
	Raven's CPM*		25.5	5.99	26.75	5.48	27.50	5.30	25.80	4.29	28.80	3.67	28.47	3.87
Ratings of behavioral symptoms														
Teachers		Hyperactivity*	15.42	8.12	14.00	8.46	13.92	8.33	2.00	4.77	1.53	3.66		
		Inattention*	17.58	4.44	16.08	3.58	15.75	3.96	4.20	6.56	3.93	6.64		
Parents		Hyperactivity*	16.67	7.60	14.50	7.24	14.08	6.80	5.40	3.29	5.67	3.16		
		Inattention*	16.83	4.53	14.83	4.02	14.50	3.66	7.53	4.75	5.67	4.17		

**Interaction between groups and sessions was significant.

*The main effect of session was significant.

disabilities, anxiety disorders, mood disorders, or pervasive developmental disorders were excluded.

Procedure

The study was approved by the Ethical Committee of the School of Psychology at Padua University, and parents' informed written consent was obtained for all participants.

The children were told they would be involved in games and activities to improve their memory and their verbal assent was required.

An ABA design (pre-test, treatment, post-test) was used to judge the efficacy of the training, and a follow-up was conducted one month after the post-test session to identify any maintenance effects. Each participant first completed the pre-test assessment, for which all tasks were presented over the course of two sessions during the same week lasting one hour each one. A measure of visuospatial WM (the Backward Corsi Blocks test) was used to analyze the specific effect of the training, because a part of it was home-based. The effect of the metacognitive activities was assessed in terms of near and far transfer effects. In particular, measures of sustained visual and auditory attention (the Bells task and the test of Auditory attention) were used to analyze near transfer effects. Measures of impulsivity and inhibition of an ongoing response (the Go/No-Go test, the Matching Figures test, the Colored Progressive Matrices), and parents' and teachers' ratings of the children's behavioral symptoms (ADHD Scales for parents and teachers) were used to analyze far transfer effects. All these effects were analyzed in terms of immediate gains measured at a post-test assessment, and long-term gains measured at a 1-month follow-up.

Within one week of completing the pre-test assessment, participants in both groups started the training activities, which took place twice a week. The time elapsing between the three assessment sessions was the same for the participants in both groups.

Tasks

Specific effects: Visuospatial WM

Backward Corsi Blocks test (Mammarella, Toso, Pazzaglia, & Cornoldi, 2008, adapted from; Corsi, 1972). This task is conducted using a set of nine blocks placed at random on a board. The cubes are numbered on the experimenter's side of the board to facilitate the test's administration. The examiner taps a number of blocks in a random sequence and the participant's task is to reproduce the sequence in reverse order. The test starts with 2 cubes being tapped in a sequence, and increases to

7. Two sequences of the same length are used for each level of difficulty. After two consecutive recall errors, the task is discontinued. A practice trial with two sequences is administered before the test starts. One point is awarded for each correctly recalled sequence. The sum of correct responses is considered as the dependent variable. The test-retest reliability reported by the manual is .74.

Near transfer effects: Visual and auditory attention control

Visual search task: The Bells task (from Biancardi & Stoppa, 1997). The task assesses visual searching ability and sustained attention. Participants are given four sheets of paper one after another, and asked to mark all the bells they find as quickly as possible. They are not told how much time they are allowed nor the number of sheets they have to complete, but the examiner allows 120 seconds to elapse for each sheet of paper and counts the number of bells marked every 30 seconds. Two main measures are calculated: speed, which is the number of bells found within the first 30 seconds (called selective attention); and accuracy, which is the total number of bells found within the 120 seconds allowed for each sheet (called sustained attention).

Auditory attention task: Test of Auditory attention – TAU (from Marzocchi et al., 2010). This task consists of 10 trials during which participants are asked to listen to a series of sounds and to count them mentally. At the end of each trial, participants have to say how many sounds they heard. The score is the total number of trials completed correctly and is considered as the dependent variable.

Far transfer effects: Impulsivity, inhibition, nonverbal reasoning, behavioral symptoms

Attention control and inhibition: GO/No-Go In this paper-and-pencil task based on the classic go/no-go procedure (from Marzocchi et al., 2010), children follow a series of directions and stop an ongoing response when a particular event (a signal) occurs. The test is conducted using two sheets of A4 paper showing a drawing of 20 steps (one step for each trial) with a little frog on the first step. The children are asked to cross out a step each time they hear the GO signal, while they have to stop every time they hear the STOP signal. The difficulty of the task lies in that the STOP signal consists of two sounds, the first of which is the same sound as the GO signal, so the children must wait to hear the whole sound before responding in order to find out whether they should GO or STOP. The score corresponds to the number of correctly performed trials. Re et al. (2015) reported a test-retest reliability of .70.

Impulsivity: The matching figures test – MF-14 This task (from Marzocchi et al., 2010) consists of 14 items comprising a target picture and six other pictures that are all similar, but only one is identical to the target. The children have to identify which picture is exactly like the target. The pictures represent objects from everyday life. The test scores concern two parameters, the number of errors and the response time for the first response (which is assumed to measure a form of impulsivity), which are considered as the dependent variables. The test-retest reliability reported by the manual is .49 for errors, and .41 for response times.

Nonverbal reasoning: Raven's colored progressive matrices – CPM In this standardized test (Raven et al., 1998), participants are presented with 36 visual patterns with one piece missing from the bottom right-hand corner. The patterns are grouped into 3 sets of 12 each (A, Ab, B). For each visual pattern, they are shown various pieces that might complete the pattern and asked to choose the right one. They are not allowed to use paper to try different solutions and they are asked to choose the piece for one pattern before moving on to the next. There are no time limits. Participants have to attempt all 36 items in the task. The final score, which is the dependent variable, is the sum of their correct answers across all three series. The test-retest reliability reported by the manual is .80.

Behavioral symptoms: ADHD scales for parents and teachers Two rating scales drawn from Marzocchi et al. (2010) were used, one for teachers and one for parents. Both scales include 18 items describing the frequency of a given type of behavior that can be rated as follows: 0 points (*never*); 1 point (*sometimes*); 2 points (*often*); or 3 points (*always*). The odd-numbered items examine the dimension of inattention, whereas even-numbered items assess hyperactivity and impulsiveness. For each scale there are two total scores, which are considered as the dependent variables in the present study: one is the sum of the scores for odd items, and thus measures inattention; the other is the sum of the scores for even items, and measures hyperactivity. A score of 14 or more is considered critical and the sign of a potential issue.

Training material

The activities took place twice a week. At the first session in a given week, activities focusing on attention control and memory were conducted in small groups (of 4 or 5 children, all either with ADHD symptoms or TD), which remained the same throughout the training. For the second session, the children were assigned computerized exercises on visuospatial WM to complete at home.

Group sessions. The training consisted of 8 sessions, each lasting 1 h, administered once a week. The training involved activities adapted from published materials (for an overview, see Re & Cornoldi, 2007; for the specific activities, see Caponi, Clama, Re, & Cornoldi, 2009). The adaptations concerned not the material itself but its order of presentation, and the choice of activities that focused mainly on attention control in the memory domain. The training was conducted by a trained psychologist (the third author, under the supervision of the second and last authors), who was not blinded to participants' diagnosis, and who monitored participants' engagement during the training in terms of their active participation and attendance. The aim of this supervision was to check on how the training was implemented in order to deal with any problems or help the trainer answer parent's questions. The trainer took notes on the activities so that the other researchers could keep track of how the training was implemented.

Each group session always followed the same routine. The trainer: commented on the goal of the day's activities during a metacognitive introduction; explained the activities to complete during the session; and gave participants instructions and a trial run with the task of the day. Then the participants practiced completing the task. Afterwards, the trainer promoted strategic reflection by asking the children to comment on the activities, and say what strategies they had used, if any, and the most useful strategies were discussed. In a feedback and self-assessment phase, participants were asked to reflect on how well they thought they had done in the task. In providing feedback, the trainer discussed the reasons for any failures and the best way to complete the task. More specifically, at the end of each session, participants were asked to assess their ability to use memory tips previously suggested by a fictional character to stimulate their awareness of the memory strategies they could use. After completing the activities, each child and the examiner separately judged how accurately the participants had completed the tasks, and the examiner gave the children feedback regarding their performance and strategy use.

The content of the sessions was organized as follows. At the first session, participants were introduced to the importance of reflecting on the characteristics of a task. They were guided to: (1) focus their attention on the task; (2) understand the objective of the task; (3) choose the most appropriate strategies for the task; and (4) keep on-line and off-line control over their performance of the task. At the next four sessions, participants were presented with different kinds of memory task. They practiced the tasks following the

above four steps, as suggested during the first session. The aim was to promote awareness and memory control, and to make it clear that this could have a positive impact on performance. At the sixth session, the children were taught how to retain recently-acquired information for a limited amount of time while performing an irrelevant task that could interfere with its recall. At the seventh the focus was on improving their ability to discriminate relevant information that was supposed to be remembered from irrelevant information. The last session was spent on promoting the importance of updating memory content depending on the requirements of a task. At the end of each session, the children were shown a metacognition sheet designed to make them aware of the strategies they had previously adopted.

It should be noted that the training did not include any activities directly related to the pre-test, post-test or follow-up measures. To promote transfer to real-life situations, the training activities reflected typical situations of recreational or school life. To give an example, the updating activities in session 8 involved preparing a backpack for the next school day, choosing the right textbooks, notebooks, pencils, and so on. Using such activities has the advantage not only of resembling the children's real-life experiences, but also of involving interaction in pairs (as the activities are conducted in groups), which promotes self-control (e.g., waiting your turn to speak or do something).

Individual sessions. A computer-based WM training was preferred for the activities to be completed at home because of its motivational value. Here again, the training consisted of 8 sessions, one a week, each lasting 30 minutes. Parents were instructed on the training schedule and monitored by means of phone calls. The exercises focused on visuospatial WM and were adapted from an existing computer-based program (Mammarella, Toso, & Caviola, 2010). The original software aims to improve visuospatial WM abilities and considers two aspects of this construct: the nature of the stimulus (visual, spatial-sequential, or spatial-simultaneous), and the level of attentional control required (low, medium, or high), based on the theoretical WM model proposed by Cornoldi and Vecchi (2003). For the purposes of the present study, only spatial-sequential and spatial-simultaneous tasks were considered. Activities were presented in the fictitious context of a *space mission*: two astronauts provided the child with information about each task, and the information to be recalled concerned the positions or movements of aliens, and

the positions and characteristics of planets or meteorites.

Each session included exercises that involved simply recalling information (a memory task requiring a low attentional control), or processing and recalling information (a memory task demanding a high attentional control). For instance, participants were asked to compare an alien's target path with other simultaneous irrelevant alien movements, and to choose the path that exactly matched the target one. In other tasks, children were shown a path and asked to reproduce the sequence of movements involved in the same or reverse order of presentation. As an example of the WM active recall tasks, several aliens occupied different positions in a grid and the children were later asked to remember the positions of only some of the aliens.

Results

One-way ANOVAs were run on the groups' pre-test performance in all tasks to identify any differences between the ADHD and TD groups. The results indicated that the children with ADHD performed less well at the baseline in the MF-14 task (errors $F_{1, 26} = 14.31$, $p = .001$, $\eta^2_p = .37$; response times $F_{1, 26} = 8.98$, $p = .006$, $\eta^2_p = .26$), and in the Go/No-Go task (errors $F_{1, 26} = 14.05$, $p = .001$, $\eta^2_p = .38$). No other differences were significant. Table 1 shows the scores obtained by the two groups for the outcome measures at pre-test, post-test and follow-up.

To identify any specific, transfer and maintenance effects, a 2×3 repeated-measures ANOVA, with Group (ADHD vs TD) as the between-group variable, and Session (pre-test, post-test, and follow-up) as a within-group factor, was run on each measure of the children's performance. The interactions were analyzed using post hoc analyzes and applying Bonferroni's adjustment for multiple comparisons. The α -value was set at 0.025 for all statistical tests and at 0.006 for interactions.

Specific effects: Visuospatial WM

Visuospatial WM: Backward Corsi block test The main effect of Session ($F_{2,50} = 19.91$, $p < .001$, $\eta^2_p = .44$) was significant, performance at pre-test being lower than at post-test ($MDiff. = -.65$, $p = .006$) or follow-up ($MDiff. = -1.05$, $p < .001$); the latter two did not differ from one another. The effect of Group ($F_{1,25} < 1$) was not significant (see Table 1).

The Session \times Group interaction was significant ($F_{2,50} = 5.73$, $p = .006$, $\eta^2_p = .19$). Post-hoc comparisons showed that TD participants performed better at

follow-up than at pre-test ($MDiff. = 1.6, p < .001$), or post-test ($MDiff. = .80, p = .004$), with no significant differences between pre- and post-test ($MDiff. = -.80, p = .011$). No other significant differences emerged (see Table 1).

Near transfer effects: Visual and auditory attention control

Visual search task: Speed score in the Bells test The main effect of Session ($F_{2,50} = 71, p < .001, \eta^2_p = .74$) was significant, with post-test ($MDiff. = 13.17, p < .001$) and follow-up ($MDiff. = 22.86, p < .001$) performance better than at pre-test; follow-up performance also differed from post-test performance ($MDiff. = 9.69, p < .001$). The effect of Group was not significant ($F < 1$), nor was the Session x Group interaction ($F_{2,50} = 2.14, p = .144$) (see Table 1).

Sustained attention: Accuracy score in the Bells test The main effect of Session ($F_{2,50} = 52.35, p < .001, \eta^2_p = .68$) was significant, performance being better at post-test ($MDiff. = 16.12, p < .001$) and follow-up ($MDiff. = 23.27, p < .001$) than at pre-test, and follow-up performance being better than post-test performance ($MDiff. = 7.16, p < .001$). The effect of Group was not significant ($F < 1$), nor was the Session x Group interaction ($F_{2,50} = 1.42, p = .249$) (see Table 1).

Auditory attention task – TAU The main effect of Session ($F_{2,50} = 4.92, p = .011, \eta^2_p = .17$) was significant, but the differences between the three assessment times were never significant. The effect of Group was not significant ($F < 1$), whereas the Session x Group interaction was ($F_{2,50} = 3.21, p = .036, \eta^2_p = .11$). No significant differences emerged from the post-hoc comparisons, however (see Table 1).

Far transfer effects: Impulsivity, inhibition, nonverbal reasoning, behavioral symptoms

Attention control and inhibition: GO/No-Go task The main effect of Session ($F_{2,50} = 4.13, p = .022, \eta^2_p = .14$) was significant, with an improvement from pre- to post-test ($MDiff. = 1.67, p = .005$), while performance at follow-up was no different from that at pre-test ($MDiff. = 1.64, p = .184$). Follow-up performance did not differ statistically from post-test performance, however ($MDiff. = .03, p = 1$). The effect of Group ($F_{1,25} = 31.25, p = .001, \eta^2_p = .56$) was significant, with the ADHD group performing less well than the TD group. The Session x Group interaction was not significant ($F_{2,50} < 1$).

Impulsivity: Error scores in the MF-14 The main effect of Session ($F_{2,50} = 13.56, p < .001, \eta^2_p = .35$) was

significant, with a better performance at post-test ($MDiff. = 5.27, p = .007$) and follow-up ($MDiff. = 6.49, p < .001$) than at pre-test; follow-up and post-test performance did not differ ($MDiff. = -1.22, p = .618$). The effect of Group ($F_{1,25} = 18.42, p < .001, \eta^2_p = .42$) was significant, with more errors in the ADHD group than in the TD group. The Session x Group interaction was not significant ($F_{2,50} = 2.38, p = .102$).

Impulsivity: Response times in the MF-14 The effect of Group ($F_{1,25} = 13.54, p = .001, \eta^2_p = .35$) was significant, the ADHD group being faster than the TD group. The main effect of Session, and the Session x Group interaction were not significant ($F_s < 1$) (see Table 1).

Nonverbal reasoning: Raven's CPM The main effect of Session ($F_{2,50} = 10.84, p < .001, \eta^2_p = .30$) was significant, with performance at post-test ($MDiff. = 2.12, p = .002$) and follow-up ($MDiff. = 2.33, p = .001$) better than at pre-test; follow-up and post-test performance did not differ from that at ($MDiff. = .20, p = 1$). Neither the main effect of Group ($F < 1$), nor the Session x Group interaction ($F_{2,50} = 1.27, p = .29$) were significant (see Table 1).

Rating of behavioral symptoms: ADHD scales for parents and teachers Due to a problem with data collection, the rating scales for the TD group at follow-up were unavailable. The first set of analyses consequently only compared the changes in the parents' and teachers' ratings from pre-test to post-test in both groups. The same ANOVA model was used, but Session had two levels. The α -value was set at 0.012 for pairwise comparisons in the case of significant interactions. Maintenance effects at follow-up were only analyzed for the ADHD group, using a repeated-measures ANOVA, with Session (pre-test, post-test, follow-up) as the within-subject factor (see Table 1 for descriptive measures).

As concerns the teachers' ratings of hyperactive/impulsive behavior, the main effect of Session ($F_{1,25} = 4.73, p = .039, \eta^2_p = .16$) was significant: overall, participants were rated as less hyperactive/impulsive at post-test ($MDiff. = .94, p = .031$) than at pre-test. The main effect of Group was significant too ($F_{1,25} = 28.45, p < .001, \eta^2_p = .53$), the ADHD group being rated as more hyperactive than the TD group. The Session x Group interaction was not significant ($F_{1,25} = 1.36, p = .26$). For the teachers' ratings of inattention, the main effect of Session ($F_{1,25} = 6.06, p = .021, \eta^2_p = .19$) was significant: overall, participants were rated as less inattentive at post-test ($MDiff. = .88, p = .014$) than at pre-test. The main effect of Group was significant too ($F_{1,25} = 35.27, p < .001, \eta^2_p = .59$), with the ADHD group rated as more inattentive than the TD group ($MDiff. = 12.76, p = .001$). The Session x Group interaction was not significant ($F_{1,25} = 3.42, p = .08$).

Turning to the parents' ratings, when impulsivity was considered the main effect of Group was significant ($F_{1,25} = 23.95$, $p < .001$, $\eta^2_p = .49$: children with ADHD were rated as more hyperactive/impulsive than the TD group. The Session \times Group interaction ($F_{1,25} = 5.02$, $p = .039$, $\eta^2_p = .17$) was significant too. Post-hoc comparisons highlighted a marked difference between the groups at both pre- and post-test ($p < .001$), but it was only the ADHD group that showed a lower frequency of hyperactive/impulsive behavior at post-test ($p = .013$) by comparison with pre-test. The effect of Session was not significant ($F_{1,25} = 2.28$, $p = .144$).

As concerns parents' ratings of inattention, the main effect of Session ($F_{1,25} = 19.60$, $p < .001$, $\eta^2_p = .44$) was significant: overall, participants were rated as less inattentive at post-test ($MDiff. = 1.93$, $p = .014$) than at pre-test. The main effect of Group was significant too ($F_{1,25} = 31.63$, $p < .001$, $\eta^2_p = .56$), with the ADHD group rated as more inattentive than the TD group ($MDiff. = 9.23$, $p < .001$). The Session \times Group interaction was not significant ($F < 1$).

No effects on the teachers' ratings of hyperactive/impulsive behavior emerged from the follow-up ratings, but teachers reported a lower frequency of inattentive behavior at follow-up than at pre-test ($F_{2,22} = 8.65$, $p = .002$, $\eta^2_p = .44$; $p = .001$). As for the parents, they rated hyperactive/impulsive behavior as being less frequent at follow-up than at pre-test ($F_{2,22} = 8.58$, $p = .002$, $\eta^2_p = .44$; $p = .001$). As regards inattention, the improvement reported by parents concerned both post-test ($p = .002$) and follow-up ($p = .002$), compared with pre-test ($F_{2,22} = 15.51$, $p < .001$, $\eta^2_p = .59$), with no differences between the post-test and follow-up ratings.

Table 2 shows the scores obtained by the two groups in most of the measures considered in the study (except for Raven's CPM and the parents' and teachers' rating scales) expressed in z-scores computed on normative data. This enabled us to use the corresponding normative data as a control measure to see how our

trained ADHD and TD samples' performance changed compared with TD children not given any such specific training. This comparison showed that the gains in performance corresponded to an improvement over the performance expected in TD children of the same age. When the same set of analyzes (2×3 repeated-measures ANOVA, with Group as the between-group variable, and Session as a within-group factor) was run using z-scores, the results overlapped those reported previously.

To establish the dimension of the immediate (pre-test vs post-test) and long-term (pre-test vs follow-up) gains obtained by our training, Cohen's d was computed for each of the two trained groups (see Table 3). The effect sizes of the two groups were compared to gain a better understanding of the effect of the two training conditions. Cohen's d values were converted into r indexes, and then compared. The size of the differences, computed by subtracting the effect sizes of the two groups, was expressed as Cohen's q , which was interpreted according to Cohen's guidelines (1988): a difference $< .1$ = no effect; from $.1$ to $.3$ = a small effect; from $.3$ to $.5$ = a medium effect; $> .5$ = a large effect.

Immediate gains

Specific effects

In the Backward Corsi Blocks test, the effect size of the training for the ADHD group was small, while for the TD group it was medium. Comparing the effect sizes showed that Cohen's d was higher for the TD group than for the ADHD group (with a small effect, $q = .16$).

Near transfer effects

In the Bells task, the effect size was large for both groups in the selective attention measure and in the sustained attention measure. Comparing the effect sizes again showed a difference, however, to the advantage of

Table 2. Performance expressed in z-scores computed on normative data for the two groups.

			Children with ADHD						TD children					
			Pre-test		Post-test		Follow-up		Pre-test		Post-test		Follow-up	
			M	SD	M	SD	M	SD	M	SD	M	SD	M	SD
Specific effects														
WM	Backward Corsi Blocks test		-0.91	1.49	-0.30	1.31	-0.28	1.29	-1.29	1.29	-0.29	1.20	0.71	1.14
Near transfer	Attention	Visual search	-0.82	1.01	0.29	1.41	0.98	1.36	-0.93	1.03	0.44	1.10	1.58	0.95
		Selective Sustained	-1.27	1.36	-0.12	1.08	0.50	1.00	-1.46	1.84	0.35	1.08	1.05	0.70
	Auditory attention		-0.80	0.96	-0.03	0.60	0.06	1.05	-0.03	0.97	-0.10	0.86	0.13	0.84
Far transfer														
	Impulsivity	Go/No-Go	-0.49	0.73	0.01	0.54	-0.13	0.45	0.48	0.63	0.68	0.53	0.81	0.66
	Matching figures *	Errors	1.24	1.25	0.35	0.67	0.07	0.53	-0.45	1.07	-0.82	0.71	-0.95	0.59
Response times		-0.62	0.42	-0.66	0.39	-0.72	0.53	0.84	1.63	0.60	1.23	0.61	1.09	

*Positive values indicate a worse performance vis-à-vis the normative data.

Table 3. Effect sizes computed for the two groups (ADHD and TD), the overall sample, and on the basis of available test-retest values.

		ADHD group		TD group		Overall sample		Normative data
		Post vs Pre	Follow-up vs Pre	Post vs Pre	Follow-up vs Pre	Post vs Pre	Follow-up vs Pre	
Backward Corsi Blocks test		0.42	0.43	0.78	1.59	0.59	0.99	2.20
Visual search	Selective	0.87	1.45	1.25	2.46			
	Sustained	0.90	1.43	1.17	1.75			
Auditory attention		0.93	0.83	-0.07	0.17			
Go/No-Go		0.76	0.58	0.33	0.48	0.46	0.43	1.96
Matching figure test*	Errors	-0.86	-1.17	-0.41	-0.57	0.51	0.51	1.12
	Response times	-0.11	-0.21	-0.16	-0.16	0.11	0.13	0.90
Raven's CPM		0.21	0.34	0.73	0.64	0.46	0.49	2.66
Ratings of behavioral symptoms*								
Teachers	Hyperactivity	-0.17	-0.18	-0.11	-			
	Inattention	-0.36	-0.42	-0.04	-			
Parents	Hyperactivity	-0.28	-0.35	0.08	-			
	Inattention	-0.45	-0.55	-0.40	-			

*Negative values indicate a better performance at post-test or follow up with respect to pre-test.

the TD group (with a small effect, $q = .17$ and $q = .11$ respectively). In the TAU, the ADHD group showed an improvement with a large effect size, whereas no improvement was seen in the TD group. Of course, the two effects differed significantly (medium effect size, $q = .42$) in favor of the ADHD group.

Far transfer effects

In the Go/No-Go task, the group with ADHD showed an improvement with a medium effect size, whereas the effect size of the improvement in the TD group was small. The difference between the d values was in the range of small effects ($q = .23$) in favor of the ADHD group. In the MF-14 task, as concerns errors, the ADHD group showed a large effect size, whereas for the TD group it was medium. The difference between the d values was in the range of small effects ($q = .22$) in favor of the ADHD group. In the case of the response times, the dimension of the differences was null for both groups. When the improvement in performance in Raven's CPM was considered, a small effect size was found for the ADHD group, and a medium one for the TD group. The difference between the d values was in the range of small effects ($q = .25$) in favor of the TD children.

Turning to the teachers' ratings, their assessment of the children's hyperactivity did not change for either group (the effect was null). In contrast, when it came to inattention, the ADHD group reportedly became less inattentive after the training, with a small effect size, while no differences emerged for the TD group. The comparison showed a clear difference between the indexes (small effect, $q = .16$) in favor of the ADHD group. As for the parents' ratings, they indicated a less hyperactive behavior at post-test (with a small effect size) in the ADHD group, while no differences emerged for the TD group. The

comparison showed a clear difference between the indexes (small effect, $q = .10$) in favor of the ADHD group. For both groups, the parents' ratings for inattention were lower at post-test than at pre-test (with a small effect), with no differences in the effect sizes.

Long-term gains

Specific effects

For what concerns the Backward Corsi blocks test the children with ADHD showed a small effect, whereas the effect was large in the group of children with TD. The comparison of the effect sizes showed that Cohen's d was higher for the TD group than for the ADHD group (with a large effect, $q = .51$).

Near transfer effects

In the Bells task, the effect was large for both groups in both the selective and the sustained attention measures. Here again, comparing the effect sizes showed a difference, however, to the advantage of the TD group (with a medium effect, $q = .34$, for the selective attention dependent variable, and a small effect, $q = .17$, for the sustained attention dependent variable). In the TAU, there was an improvement with a large effect in the ADHD group, and no improvement in the TD group. The two effects naturally differed significantly (medium effect size, $q = .32$) in favor of the ADHD group.

Far transfer effects

In the Go/No-Go task, the improvement in the group with ADHD showed a medium effect size, whereas in the TD group it was small. No differences emerged between the d values. In the MF-14 task, as concerns errors, the ADHD group showed a more marked improvement (the effect size was large for the ADHD group, medium for the TD group). The difference between the d values was in

Table 4. Number of children with ADHD showing a clinically significant improvement in terms of changes in standard deviation by comparison with normative data.

Tasks	Pre-test			Post-test			Follow-up		
	$z \leq -2$	$-2 < z \leq -1$	$z > -1$	$z \leq -2$	$-2 < z \leq -1$	$z > -1$	$z \leq -2$	$-2 < z \leq -1$	$z > -1$
Backward Corsi Blocks test	3	2	7	1	2	9	1	2	9
Visual search selective	1	5	6	0	3	9	0	0	12
Visual search sustained	3	5	4	0	4	8	1	0	11
Auditory attention	0	6	6	0	0	12	1	0	11
Go/No-Go	0	4	8	0	1	11	0	1	11
Matching figures test errors	4	2	6	0	1	11	0	1	11
Matching figures test response times	0	3	9	0	4	8	0	4	8
Raven's CPM	0	0	12	0	0	12	0	0	12

the range of small effects ($q = .27$), in favor of the ADHD group. In the case of the response times, the effect size was small for the ADHD group, and null for the TD group, with no differences in the d values. When performance in Raven's CPM was considered, a small effect size was found for the ADHD group, and a medium one for the TD group. The difference between the d values was in the range of small effects ($q = .14$) in favor of the TD group. As for the teachers' ratings, the scores for hyperactivity did not change for the ADHD group, though they were reportedly less inattentive, with a small effect size. No comparisons could be drawn with the TD group because their ratings were unavailable. The parents' ratings indicated less hyperactivity (with a small effect size) and less inattention (with a medium effect size) at post-test.

To understand whether the training produced clinically meaningful changes, we computed how many children with ADHD improved by 1 SD or more from pre- to post-test, and from pre-test to follow-up. The z -scores for the performance of most of the children with ADHD changed from -2 to -1 , or above, and this improvement was maintained over time. The z -scores were computed considering ADHD performance against normative data (Table 4).

Discussion

Ever since the first study by Klingberg, Forssberg, and Westerberg (2002), who demonstrated some positive effects of a WM training in an ADHD population, the debate on the effectiveness of WM training in children with ADHD has grown. The discussion has focused particularly on the feasibility of obtaining improvements beyond any specific training gains. Given the conflicting results reported in the literature on this issue, and the encouraging findings of some studies (i.e., Capodieci et al., 2018; Re et al., 2015) on the role of metacognition in cognitive training for such children, we explored whether both cognitive and behavioral benefits could be obtained by a training that combined specific activities on visuospatial WM

with activities to promote metacognitive reflections and control over attention and impulsivity. This training revolved around activities resembling games and related to everyday life tasks. The value of such a combined approach had already been demonstrated in TD children in other areas, such as reading comprehension (Carretti, Borella, Elosúa, Gómez-Veiga, & García-Madruga, 2017; Carretti, Caldarola, Tencati, & Cornoldi, 2014; García-Madruga et al., 2013), and problem solving (Cornoldi, Carretti, Drusi, & Tencati, 2015), as well as in executive functioning in preschoolers with symptoms of ADHD (Capodieci et al., 2018; Re et al., 2015).

The efficacy of the training was assessed in terms of specific effects, near transfer effects and far transfer effects on neuropsychological measures of WM, attention, inhibition, and reasoning, as well as on behavioral aspects (i.e., impulsivity/hyperactivity and inattention), as rated by teachers and parents. These three types of effect were analyzed in terms of immediate gains post-test, and long-term gains a month later, comparing the improvements seen in the children with ADHD with those of a group of TD children. This enabled us to examine how this type of training affected the symptoms of ADHD.

Our results showed that this combined training of WM and metacognition was effective in terms of objective measures of attention and inhibition, and of parents' and teachers' subjective ratings of the children with ADHD. In particular, analysis of variance on the specific and near effects showed an effect of Session for all measures (except the TAU, and the response times in the MF-14 task), suggesting that the training improved the performance of both TD children and those with ADHD. This better performance persisted at the follow-up in all measures (except for the Go/No-Go task). There was an improvement from post-test to follow-up for the visual search task (the Bells test) and visuospatial WM performance in the TD children too. At the follow-up, teachers' ratings indicated less inattention in the children with ADHD. Interestingly,

both teachers' and parents' ratings for inattention and hyperactivity were lower. This drop was particularly accentuated in the teachers' ratings of inattention, and in the parents' ratings of hyperactivity in the group of children with ADHD.

To better analyze the changes identified after the training, the sizes of the effects obtained in the two groups were compared using Cohen's q . As concerns immediate gains, a small difference emerged in the q value, in favor of children with ADHD, in the Go/No-Go task, the number of errors in the MF-14 task, the teachers' inattention ratings, the parents' hyperactivity ratings, and the TAU scores. The results were similar for the long-term gains, with a small difference in the q value in favor of the children with ADHD in the TAU, the number of errors in the MF-14 task, the teachers' ratings of inattention, and the parents' ratings of hyperactivity. This would suggest that the training had a positive effect on behavior observable in daily life.

Overall, our combined training procedure – based on metacognitive activities and practice with WM and attention control tasks – produced positive effects on WM and selective attention measures. The improvement related to activities involved in the training, but also to the children's control over their attention and impulsivity, their ability to inhibit irrelevant stimuli, and their nonverbal reasoning, none of which were trained explicitly. Some specific improvements emerged in the children with ADHD too, regarding their attention control, inhibition of irrelevant stimuli and symptoms typical of their disorder, with both parents and teachers observing less inattentive and hyperactive behavior. To test the clinical significance of our results, we examined the number of children progressing from a very poor performance (below 2 standard deviations) to a better level of performance (for a similar approach, see Re, Pedron, Tressoldi, & Lucangeli, 2014): it emerged that the performance of most of the children with ADHD improved, and this result was maintained over time.

Of particular importance is the improvement reported by parents and teachers, which corroborates the evidence of WM performance being associated with observers' ratings of ADHD symptoms (Lui & Tannock, 2007). For example, Rogers et al. (2011) recently reported that inattentive behavior observed in the classroom correlated with academic success through the mediation of WM performance (and the verbal-auditory component in particular) in adolescents with a profile of ADHD (Rogers et al., 2011). This finding supports the importance of strengthening the capacity and control of WM in individuals with ADHD to avoid negative school outcomes in the future.

In line with the findings of some previous studies (e.g., Capodiecici et al., 2018; Re et al., 2015), our results indicate that including activities on metacognition in training programs can promote transfer effects not seen after training activities focusing exclusively on WM. Our findings are also consistent with reports on other types of training targeting executive functions (e.g., Tamm & Nakonezny, 2015; Tamm, Nakonezny, & Hughes, 2014; Traverso, Viterbori, & Usai, 2015). Although very different training procedures were used in such studies, some common characteristics emerge. For instance, all these programs included play-based activities to sustain engagement, which is crucial to keeping children motivated to complete any type of training – and it has been claimed that a stronger motivation is associated with greater training gains (Zhao, Xu, Fu, & Maes, 2018; but see also Linares, Borella, Lechuga, Carretti, & Pelegrina, 2019). In addition, training activities strongly reliant on metacognition have been associated with a greater transfer of the strategies learned to other settings or domains (e.g., Lucangeli, Galderisi, & Cornoldi, 1995).

The present study has several limitations, meaning that caution is warranted in interpreting the results. The first, and most important limitation concerns the lack of a passive control group: demonstrating an improvement in two groups receiving the same training is clearly not enough to enable conclusions to be drawn on its efficacy. On the other hand, our use of z -scores computed on national norms enables us to speculate on the value of the training, since we were able to compare our groups' improvement with the performance seen in large groups of children of the same age, who could serve as a sort of passive control. This comparison showed that our trained groups' performance was always consistent with, or even better than the expected average performance. In an attempt overcome the limitation deriving from the lack of a passive control group, we computed Cohen's d for the overall sample (see Table 3) to ascertain whether the improvements observed over the course of the sessions went beyond the changes expected on the basis of the available test-retest indexes. Test-retest reliability has only been reported for the Backward Corsi Block test, the Go/No-Go task, the MF-14, and the CPM, but in all these cases the effect sizes for the overall sample were lower than those computed on the basis of test-retest reliability, leading us to surmise that the changes we documented were induced by the training. The improvement could be considered clinically significant for schoolchildren with ADHD, since their level of performance moved from extremely poor to within normal range. This does not mean a normalization of their performance, but does suggest an interesting

degree of malleability. The small number of participants in our groups is another limitation of this work, since it restricted the number of analyses that could be conducted. The present results can nonetheless provide the basis for future investigations. Another weakness of our study lies in that the computerized training was conducted at home. Although the experimenter was in telephone contact with the parents, it was impossible to know for sure if the activities were conducted for the established amount of time. Poor results on measures of WM, especially in children with ADHD, might have been linked to this issue. Finally, some of the TD children performed in the low-to-average or borderline range on several of the pre-test measures, highlighting the importance of taking a dimensional approach to the study of individual differences, even in the case of clinical populations such as children with ADHD (e.g., Rogers et al., 2011; Rogers, Wiener, Marton, & Tannock, 2009). A poor performance already at pre-test raises the risk of any improvement seen at post-test being due to a regression to the mean.

Despite the study's limitations, our results seem relevant for their clinical implications. As suggested by Kern et al. (2007), working with children – and not only with families and schools – can help to prevent any negative fallout of ADHD on a child's self-esteem and motivation, thereby also containing any onset of oppositional or deviant behavior. The proposed training may offer a contribution in this direction too, though this aspect was not studied directly in the present study.

In short, our findings show that it is worth investigating the opportunities afforded by combined cognitive interventions for children with ADHD. On the basis of the existing literature, it would be interesting to further analyze the impact of this kind of training on emotional and motivational variables, but also on the perceived wellbeing of children in different contexts. As already mentioned, the fact that some changes were detected by parents and teachers might be important in supporting the academic success of children with ADHD, and this issue deserves further investigation.

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Multi-Source Interference Task paradigm to enhance automatic and controlled processes in ADHD



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ABSTRACT

Background: The role of automatic and controlled processes in children with Attention deficit hyperactivity disorder (ADHD) has recently been debated. Most theories on ADHD assume that core deficits are related to controlled processes and executive function.

Aims: The main aim of the present study is to examine automatic and controlled attention in children with ADHD, compared to TD subjects.

Methods and procedures: Twenty ADHD-I children, 20 with ADHD-C and 20 typical developing children performed the Block-Formed Multi-Source Interference Task (MSIT) both in incongruent and congruent conditions.

Outcome and results: Results show that clinical groups had a poorer performance than the TD group in both conditions.

Conclusions and implications: This study demonstrated that children with ADHD exhibit a deficit both in automatic and controlled processes.

What this paper adds?

The essential contribution of the study is the demonstration that children with ADHD exhibit a deficit both in automatic and controlled processes. That is, the present study provides evidence that the executive functions alone cannot explain the ADHD symptoms, they have reinterpreted and integrated in the light of new evidence. Hence, this study supports the hypothesis that deficits in ADHD are also related to automatic processes.

1. Introduction

The dual-process theory identifies two distinctive cognitive processes, namely: controlled and automatic processes (also called controlled cognition and automatic cognition, respectively). Automatic processing is fast, effortless, autonomous, stereotypic, unavailable to conscious awareness and fairly error-free. It can be accomplished simultaneously with other cognitive processes without interference, it is not limited by attentional capacity and it can be unconscious or involuntary (Martino, Capri, Castriciano, & Fabio, 2017; Mohammadhasani, Fabio, Fardanesh, & Hatami, 2015; Mohammadhasani, Fardanesh, Hatami, Mozayani, & Fabio, 2018; Fabio & Antonietti, 2012; Fabio & Capri, 2015, 2017; Fabio et al., 2018). In contrast, controlled processing is effortful, slow, and prone to errors, but at the same time, flexible and useful to deal with novel situations (Fabio, 2017; Fabio & Capri, in press; Fabio & Urso, 2014; Moors & De Houwer, 2006). In controlled processing people carry out deliberate behaviors by retrieving information from

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memory with effort which is particularly important as it support behaviours that achieve goals and ultimately promote survival (Xu, Li, Ding, & Lu, 2014).

Visual attention allocation have been explained through automatic and controlled processing (bottom-up and top-down model, respectively). In bottom-up model, the focus of attention is considered involuntary and driven by an inherently salient or transient exogenous orienting stimulus. In this prospective, the attention is considered as a reaction to the visual properties of the stimulus confronted by the viewer, it is less susceptible to other forms of cognitive interference. Top-down model focuses on voluntary, intentional endogenous orienting of the attention to a specific location. In this model the attention is guided by a symbolic cue and is quite susceptible to cognitive interference (Toscano-Zapién, Velázquez-López, & Velázquez-Martínez, 2016).

It is important to specify that the automatic and controlled processes (also in the attention) are not two separate and dichotomous entities they are linked each other and can be active at the same time (Fabio & Capri, 2019).

Recently, it has been hypothesized that Attention Deficit Hyperactivity Disorder (ADHD), associated mainly to executive deficits, can be also characterized by an impairment in automatic processes (Fabio, 2017; Fabio & Capri, 2019; Martino et al., 2017).

ADHD is a highly prevalent childhood disorder, patients can be classified as belonging to the inattentive (ADHD-I), the hyperactive/impulsive (ADHD-H) or the combined ADHD subtype (ADHD-C) depending on symptomatology (APA, 2013).

Most research on ADHD has shown that core symptoms are related to deficits in executive functions (EFs) (Arnsten & Li, 2005; Bos et al., 2017; Doehner, Brandeis, Schneider, Drechsler, & Steinhausen, 2013; Fabio & Capri, 2015; Fabio & Urso, 2014; Fabio, Capri, & Romano, 2019; Hwang, Gau, Hsu, & Wu, 2010; Nigg et al., 2005; Nikolas & Nigg, 2013; Sonuga-Barke, Bitsakou, & Thompson, 2010). Some studies have demonstrated that children with ADHD show impairments in automatic processes, but do not exclude EF difficulties from their impairments (Fabio, Castriano, & Rondanini, 2015; Fabio, 2017; Fabio et al., 2018; Martino et al., 2017).

With reference to automatic processing, fMRI studies have demonstrated that subjects with ADHD show deficits in cortico-striatal loops (Berquin et al., 1998; Teicher et al., 2000), and consequently, an impaired performance in a set of motor and cognitive tasks, involving automatic or procedural skills, such as motor sequence tapping (Adi-Japha, Fox, & Karni, 2011; Fox, Adi-Japha, & Karni, 2014, 2016; Fox, Karni, & Adi-Japha, 2016), serial reaction time (Barnes, Howard, Howard, Kenealy, & Vaidya, 2010; Berquin et al., 1998; Prehn-Kristensen et al., 2011), probabilistic selection (Frank, Santamaria, O'Reilly, & Willcutt, 2007), visual category learning (Huang-Pollock, Maddox, & Tam, 2014), and artificial grammar learning (Laasonen et al., 2014; Rosas et al., 2010).

These observations have led some to view ADHD as a disorder that arises from a selective disruption in the automatic processing (Nicolson & Fawcett, 2007, 2011; Ullman, 2004; Ullman & Pullman, 2015). The assumption is that a selective disruption in the automatic processing leads to a fundamental impairment in the ability to “automatize” behaviors, resulting in increased demands on attentional resources (Fabio, Gangemi, Capri, Budden, & Falzone, 2018; Fabio, Magaudo, Capri, Towey, & Martino, 2018). This is manifested in a learning profile characterized by reduced resistance to interference, sensitivity to distractions, and excessive fatigue, similar to behavioral symptoms observed in ADHD.

Considering that an increasing number of studies (Batty et al., 2010; Carmona et al., 2005, 2009; Castellanos et al., 2002; Cubillo & Rubia, 2010; Krain & Castellanos, 2006; Mackie et al., 2007; Shaw et al., 2006) has found structural and functional abnormalities in both fronto-cortical and fronto-subcortical networks in children and adults with ADHD, and, considering that these circuits support both controlled and automatic processes, it is reasonable to assume that children with ADHD could show both automatic and controlled deficits. The hypothesis of an automatic deficit in ADHD has been poorly investigated (Fabio, 2017). To the best of our knowledge, few studies have examined this hypothesis. Fabio et al. (2015) tested the hypothesis that deficits in executive functioning within ADHD may be partially due to an impairment of the automatic processing. They have analyzed the characteristics of auditory vigilance in ADHD and control subjects through two tasks: Merrill, Jones, and Li's (1992) procedure on automaticity with the dual-task interference paradigm and the auditory test with automatic procedure. The results have confirmed that individuals with ADHD show deficits in auditory vigilance tests and become less careful when interference is introduced. However, this study has provided no definitive support on the role of automatic processes in children with ADHD. Another recent work by Martino et al. (2017) examined the hypothesis of an automatic deficit in ADHD. The authors have investigated the automatic processing of selective visual attention. Twelve children with ADHD, 17 with ADHD + reading disorder (RD) and 29 typically developing children (TD), matched for age and gender, performed two tasks: a Visual Information Processing Task and a Clock Test. Results indicated that ADHD and ADHD + RD groups differed from the TD group in the controlled process task, suggesting a deficit in executive functioning. All clinical groups also exhibited a lower performance in automatic processes, compared to the TD group. The results of this study have suggested that executive deficits within ADHD might be partially due to an impairment of automatic processing.

Despite the previous data, the specific research question that still needs to be answered is whether children with ADHD have deficits only in controlled attentional processing, like sustained attention, or whether deficits occur already at a very early, more automatic processing level.

The main goal of the present study is to offer a contribution to this question. The specific aim is to examine automatic and controlled attention in children with ADHD, compared to TD subjects, using the Block-Formed Multi-Source Interference Task (MSIT) (Bush & Shin, 2006). This task is presented with two conditions: a condition with congruent types of interference (CC) and a condition with incongruent types of interference (InC). The underlying logic is that the CC can be solved through an automatic process and is easy to solve, whereas the InC is more complex and the solution implies the intervention of controlled processes.

In the present study, it was hypothesized that children with ADHD show deficits in both automatic and controlled processes. More in depth, if the performance of children with ADHD is poorer than the TD group in the CC, these subjects will present difficulties in automatic processing. If the performance is also poorer than the TD group in the InC, then the subjects with ADHD will present difficulties both in the controlled and automatic processes. Whereas, if the performance was only poorer than the TD group in the InC, children with ADHD would show the classical executive deficit associated with ADHD.

2. Method

2.1. Participants

The participants in this study were selected from a sample of 650 children (212 females and 438 males) attending public primary schools in Sicily, a region of Southern Italy. Students ranged in age from 9 to 11 years ($M = 8.5$, $S.D. = 4.52$) and were all Italian. For all participants, their teachers completed both the Italian version of the Deficit Attention Teacher Scale (DATS) (Marzocchi & Cornoldi, 2000) and the Disruptive Behaviour Disorder Rating Scale (DBDRS) (Marzocchi et al., 2001) aimed at assessing the possible presence of, respectively, ADHD and/or learning disabilities (LD).

2.1.1. ADHD group

The first screening for ADHD diagnosis was based on DATS scores. Eighteen items compose DATS, corresponding to the symptom domain of ADHD as described in the Diagnostic and Statistical manual of Mental Disorders (DSM-5) (American Psychiatric Association, 2013). Two scores can be obtained: a measure of distractibility or inattention (I) and a measure of hyperactivity (H). People can meet ADHD-I criteria (inattentive subgroup), ADHD-H criteria (hyperactive subgroups) or ADHD-C criteria (combined: inattentive + hyperactive subgroups). In this experiment, inclusion in the ADHD condition was based on cut-off scores in both subscales (I and H) and on a clinical assessment carried out by a specialized psychologist. The presence of other disorders was excluded by normal DBDRS scores and by the clinical interview. No child had a history of brain damage, epilepsy, psychosis or anxiety disorders. 53 participants met cut-off criteria for ADHD based on the questionnaire, and 40 of those also had a clinical diagnosis as confirmed by a specialised psychologist. Consequently, the final ADHD group included 40 children.

2.1.2. TD group

The sample of the initial 650 children who obtained DATS and DBDRS scores in the normal range, who were not included in any clinical group, and of children not diagnosed by the school psychologists with behavioral, emotional and/or relational problems constituted the basis to form the control group, and a set of children was therefore randomly selected. Gender and age were considered so as to find students that could constitute a group whose male/female ratio and whose mean age approximately matched the male/female ratios and the mean ages of the clinical groups. Among TD children who were selected based on gender and age criteria, only children who also obtained DATS and DBDRS scores as 0 and had no clinical disorders, were included in the final TD group.

The final sample included 40 children with ADHD: 20 subtype inattentive (ADHD- I group), 20 with subtype combined (ADHD-C group) and 40 TD children (TD group) (total 80 children). We excluded 5 children who met the criteria for ADHD-H criteria, as the size of this group was too small (Table 1).

2.2. Multi-Source Interference Task (MSIT)

In this study, the cognitive paradigm Multi Source Interference Task (MSIT) was employed (Bush & Shin, 2006; Bush, Shin, Holmes, Rosen, & Vogt, 2003). This task was presented through Psychoy2 v 1.85.6. It showed a set of 3 digits on a computer screen. Participants were instructed to report the identity of the number that is different from the other 2 numbers by pressing a button on a control-pad. The task was presented in two conditions. In the CC, the distractors are zeroes and the target number (1, 2, or 3) is always placed congruently with its position on the pad (Fig. 1).

In the InC, the distractors are other numbers (1, 2, or 3), and the target number (1, 2, or 3) is never placed congruently with its position on the response pad (Fig. 2).

Correct responses (CR) and reactions time (RT) were acquired while subjects solved the task. The task was a block design that

Table 1
Demographic characteristics of the three groups participating in the experiment.

Groups	Measures	Values
ADHD-I	<i>n.</i> boys/girls	17/3
	Age. <i>M</i> (<i>SD</i>)	8.50 (4.52)
	IQ. <i>M</i> (<i>SD</i>)	95.00 (6.51)
	Distractibility. <i>M</i> (<i>SD</i>)	19.70 (2.45)
	Hyperactivity. <i>M</i> (<i>SD</i>)	3.30 (3.01)
ADHD-C	<i>n.</i> boys/girls	16/4
	Age. <i>M</i> (<i>SD</i>)	8.50 (4.51)
	IQ. <i>M</i> ; (<i>SD</i>)	96.00 (5.60)
	Distractibility. <i>M</i> (<i>SD</i>)	18.80 (2.52)
	Hyperactivity. <i>M</i> (<i>SD</i>)	16.90 (2.25)
TD	<i>n.</i> boys/girls	33/7
	Age. <i>M</i> (<i>SD</i>)	8.50 (4.53)
	IQ. <i>M</i> (<i>SD</i>)	102.50 (6.95)
	Distractibility. <i>M</i> (<i>SD</i>)	1.00 (0.20)
	Hyperactivity. <i>M</i> (<i>SD</i>)	4.0 (0.31)

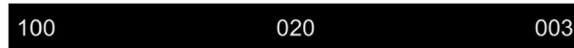


Fig. 1. Example of condition with congruent types of interference (CC).



Fig. 2. Example of condition with incongruent types of interference (InC).

consisted of five congruent condition blocks alternating with five incongruent condition blocks (total duration: 7 min and 27 s). Each block consisted of 24 trials, meaning that each subject completed a total of 120 trials per condition. The stimulus sequences were presented on a screen during 5 s with an inter-stimulus interval of 1.75 s approximately.

2.3. Procedure

The experiment was conducted in a quiet room of the COSPECS Department, University of Messina. The children performed the MSIT individually. The ADHD group and the control group were tested separately. All children were tested in the morning from 9.00 to 12.00 a.m.

2.4. Design

This study employed a mixed factorial design with one between-subjects variable (groups of participants: ADHD-I, ADHD-C, and TD) and two within-subjects variables: conditions (CC and InC) and blocks (first, second, third, fourth, fifth).

2.5. Statistical analyses

Data were analyzed using SPSS Version 24.0 for Windows. CR and RT of the MSIT were analyzed using two repeated measures ANOVA with group as a between-subjects factor and condition and blocks as within-subjects factors. In addition, we used planned comparisons to confirm that controls were significantly different from the ADHD groups. More specifically, we compared ADHD-I and TD, ADHD-C and TD and finally ADHD-I and ADHD-C.

The descriptive statistics of the dependent variables were tabulated and examined. The alpha level was set to .05 for all statistical tests. Bonferroni correction was applied for multiple comparisons. In case of significant effects, the effect size of the test was reported. More precisely, for ANOVA partial eta-squared (η^2) was used, for *t*-test Cohen's *d* was used (Cohen, 1988). The Greenhouse–Geisser adjustment for nonsphericity was applied to probability values for repeated measures.

3. Results

Table 2 shows the means and standard deviations of CR for the two conditions of the MSIT and for the overall means and standard deviations. With reference to the factor groups (ADHD-C, ADHD-I and TD), we found significant effects, $F(2, 78) = 3.21$; $p = .032$, $\eta^2 = 0.08$; this means that the three groups show general differences in the performance. More precisely, *t*-tests on the overall scores with reference to the comparison between ADHD-I and TD show significant difference, $t(58) = 3.21$, $p = .009$, $d = .88$; with reference to the comparison between ADHD-I and show significant difference, $t(38) = 2.21$, $p = .032$, $d = .78$; with reference to the comparison between ADHD-C and TD show no significant difference, $t(58) = 1.01$, $p = .32$, $d = .76$.

For multiple comparisons a Bonferroni corrected threshold of $P = 0.005$ was considered to be significant, and $p < 0.05$ was

Table 2
Means and (Standard Deviation) of CR for the two conditions of the MSIT.

MSIT	ADHD-I M (DS)	ADHD-C M (DS)	TD M (DS)
Congruent condition			
Block 1	21.38 (2.26)	23.18 (1.07)	22.57 (1.74)
Block 2	22.88 (6.52)	23.27 (6.32)	23.95 (6.27)
Block 3	22.88 (1.24)	23.64 (0.50)	23.19 (0.92)
Block 4	21.25 (2.86)	23.36 (0.92)	22.86 (1.27)
Block 5	21.63 (2.13)	22.00 (1.54)	22.86 (1.15)
Overall	21.41 (3.67)	22.60 (2.12)	22.99 (1.96)
Incongruent condition			
Block 1	10.75 (5.14)	14.45 (7.82)	16.71 (5.72)
Block 2	11.38 (4.65)	16.27 (0.78)	17.43 (0.97)
Block 3	13.25 (5.67)	16.45 (6.72)	18.76 (5.22)
Block 4	12.13 (6.85)	17.82 (6.44)	18.48 (5.18)
Block 5	12.13 (6.77)	16.91 (6.20)	18.90 (5.79)
Overall	11.88 (4.34)	16.32 (2.34)	18.62 (1.67)

Table 3
Means and (Standard Deviation) of RT for the two conditions of the MSIT.

MSIT	ADHD-I M (DS)	ADHD-C M (DS)	TD M (DS)
Congruent condition			
Block 1	0.88 (0.16)	.85 (0.13)	0.87 (0.12)
Block 2	0.91 (0.19)	0.84 (0.15)	0.83 (0.12)
Block 3	0.92 (0.18)	0.83 (0.14)	0.83 (0.11)
Block 4	0.90 (0.21)	0.88 (0.15)	0.83 (0.15)
Block 5	0.86 (0.18)	0.85 (0.14)	0.81 (0.14)
Overall	0.92 (0.10)	0.86 (0.11)	0.83 (0.11)
Incongruent condition			
Block 1	1.06 (0.15)	1.15 (0.10)	1.17 (0.14)
Block 2	1.14 (0.18)	1.15 (0.18)	1.17 (0.10)
Block 3	1.14 (0.16)	1.22 (0.09)	1.12 (0.13)
Block 4	1.11 (0.13)	1.15 (0.06)	1.16 (0.22)
Block 5	1.18 (0.07)	1.19 (0.11)	1.12 (0.13)
Overall	1.12 (0.05)	1.17 (0.09)	1.14 (0.10)

considered suggestive of evidence for a potential association.

The condition factor showed significant effects, $F(2, 78) = 15.73$; $p = .0001$, $\eta^2 = 0.68$. This result means that all the participants showed better performances in the congruent condition. The interaction Group x Condition was not significant, $F(2, 78) = 2.35$; $p = .12$, $\eta^2 = 0.05$.

With reference to the comparison between ADHD-I and TD in the congruent condition, we found no difference in the group factor, $t(58) = 1.22$, $p = .11$; With reference to the comparison between ADHD-C and TD in the congruent condition, we found no difference in the group factor, $t(58) = 0.98$, $p = .34$; With reference to the comparison between ADHD-I and ADHD-C in the congruent condition, we found no difference in the group factor, $t(38) = 0.77$, $p = .15$;

With reference to the comparison between ADHD-I and TD in the incongruent condition, we found significant difference in the group factor, $t(58) = 6.99$, $p = .001$, $d = .87$; With reference to the comparison between ADHD-C and TD in the incongruent condition, the group factor show significant effect, $t(58) = 2.88$, $p = .023$, $d = .67$. With reference to the comparison between ADHD-I and ADHD-C in the incongruent condition, the group factor do not show significant effect, $t(38) = 0.98$, $p = .15$.

With reference to the block factor (first, second, third, fourth, fifth) we found no differences between the CR to the five blocks, $F(4, 59) = 1.98$, $p = .22$; we found also no differences in the interaction block X group, $F(8, 78) = 1.34$, $p = .18$.

Table 3 shows the means and standard deviations of RT for the two conditions of the MSIT and for the overall means and standard deviations. Group showed no significant effect, $F(2, 78) = 1.091$; $p = .34$, $\eta^2 = 0.05$; as before seen Condition presented significant effects, $F(2, 78) = 42.69$; $p = .0001$, $\eta^2 = 0.82$. There was no significant interaction Group x Conditions, $F(2, 78) = 1.52$; $p = .23$, $\eta^2 = 0.05$.

With reference to the comparison between ADHD-I and TD in the congruent condition, we found significant difference in the group factor, $t(58) = 2.45$, $p = .022$, $d = .67$; With reference to the comparison between ADHD-C and TD in the congruent condition, we found no difference in the group factor, $t(58) = 0.81$, $p = .43$; With reference to the comparison between ADHD-I and ADHD-C in the congruent condition, we found no difference in the group factor, $t(58) = 1.67$, $p = .15$.

With reference to the comparison between ADHD-I and TD in the incongruent condition, we found no difference in the group factor, $t(58) = 0.41$, $p = .63$; With reference to the comparison between ADHD-C and TD in the incongruent condition, the group factor do not show significant effect, $t(58) = 0.99$, $p = .19$; With reference to the comparison between ADHD-I and ADHD-C in the incongruent condition, the group factor do not show again significant effect, $t(38) = 0.99$, $p = .17$.

With reference to the block factor we found no differences between the RT to the five blocks, $F(4, 59) = 1.38$, $p = .18$; we found also no differences in the interaction block X group, $F(8, 78) = 1.11$, $p = .21$.

4. Discussion

In the present study we examined both automatic and controlled attention in children with ADHD, compared with TD children, using MSIT paradigm. In this task, the automatic processing of stimuli is observed with the congruent condition, whereas the controlled processes are observed with the incongruent condition.

With reference to CR, the results of this study show performance differences between ADHD and TD children only in the incongruent condition. ADHD groups scored significantly lower on incongruent task, this confirms the executive deficit associated with ADHD. In the congruent condition group differences between ADHD-C and ADHD-I have been found, unexpectedly the ADHD-C group shows similar performances to TD group.

With reference to RT, only in the incongruent condition the ADHD-I group show a worse performance than TD group. They scored significantly slower on incongruent task, this suggests a deficit in automatic processing. These findings support the idea that children with ADHD also present a deficit in automatic processes (Ackerman, Anhalt, Holcomb, & Dykman, 1986; Borchardt et al., 1988; Fabio et al., 2015; Martino et al., 2017; Mohammadhasani, Capri, Nucita, Iannizzotto, & Fabio, 2019; Ott & Lyman, 1993).

Taken together the results of this study are controversial because children with ADHD do not perform equal to congruent and

incongruent trials, and indicate two directions. Firstly, the ADHD-I group is slower than TD group in the automatic processing, this means that children with ADHD are slower in terms of processing speed. Impaired performance on CC trials can be due to a baseline problem with attention. It is frequently reported that ADHD performance on simple RT tasks is lower than TD subjects, and this is interpreted as being due to lapses in on-task attention (Hervey et al., 2006; Killen, 2019; Vaurio, Simmonds, & Mostofsky, 2009). In addition ADHD-I group obtains a lower number of CR in the incongruent trials. Consequently, it is reasonable to assume that if the processing speed increases then the quality of performance (number of CR) also improves. In this scenario, it is important to consider automatic and controlled processing as two linked cognitive processes rather than as separable entities (Fabio, 2017; Kiefer & Martens, 2010; Kiefer, 2007, 2012; Leonard & Egeth, 2008; Moors & De Houwer, 2006; Naccache, Blandin, & Dehaene, 2002).

Secondly, in the congruent trials no significant group differences in terms of CR have been found. In the incongruent trials only the ADHD-I group presents a lower number of CR, as mentioned above. This inconsistency could be attributed to the heterogeneity of ADHD (Clarke et al., 2011; Loo & Makeig, 2012).

These results are in accordance with previous observations suggesting that children with ADHD show a reduced development of automatic processing (Ackerman et al., 1986; Borchardt et al., 1988; Ott & Lyman, 1993). For example, in the study of Hazell et al. (2003) 50 children with ADHD, 45 children with Specific Learning Disorder (LD), 25 children with LD and ADHD, compared to 51 TD children, completed controlled and automatic information processing tasks. The results have demonstrated that children with ADHD show a reduced performance in the automatic task compared with TD and other groups, along with deficits in the central controlled processes. Hurks et al. (2004) have examined the performance of 20 children with ADHD on semantic category fluency (SCF) versus initial letter fluency (ILF) tasks, compared to 118 children with other psychopathology and 130 TD children. The results have confirmed that children with ADHD show differences in the development of automatic skills also for processing abstract verbal information. As stated in the introduction of this paper, Fabio et al. (2015), using the Merrill et al.'s (1992) procedure on automaticity with the dual task interference paradigm, confirm that subjects with ADHD show reductions in the automatic processing, precisely in auditory vigilance, and they became less careful when the interference was introduced. Moreover, as described in the introduction, a recent study of Martino et al. has confirmed that children with ADHD present differences in the automatic processing. All these previous studies are consistent with findings from the present work indicating that children with ADHD do not perform as well as controls children in situations demanding automatic and/or more controlled processing strategies (Hazell et al., 2003; Hurks et al., 2004).

In line with aforementioned previous studies (Fabio et al., 2015; Martino et al., 2017) the present study suggests that children with ADHD have deficits both in automatic and controlled processes. However, the results of the present study should be interpreted with caution due to the controversial results. Future research on automatic deficits in ADHD are needed to improve understanding of the nature of the underlying impairments of ADHD.

This study had some limitations, we didn't consider the ADHD-H presentation, because the size of this group was too small. For this reason, caution is needed to generalise the findings of the current study to the ADHD population as a whole.

In conclusion, from a theoretical and clinical point of view, it is important to obtain a clearer picture on deficits in early bottom-up (automatic) and top-down (controlled) attention processes in ADHD.

Declaration of Competing Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

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Health and Disability

Intellectual functioning and executive functions in children and adolescents with attention deficit hyperactivity disorder (ADHD) and specific learning disorder (SLD)

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Faedda, N., Romani, M., Rossetti, S., Vigliante, M., Pezzuti, L., Cardona, F. & Guidetti, V. (2019). Intellectual functioning and executive functions in children and adolescents with attention deficit hyperactivity disorder (ADHD) and specific learning disorder (SLD). *Scandinavian Journal of Psychology*, 60, 440–446.

Several studies have shown neuropsychological deficits across multiple domains in attention deficit hyperactivity disorder (ADHD) and specific learning disorder (SLD), but differences and similarities between these disorders have been little considered. We were interested in analyzing the intellectual and executive profiles in a sample of children and adolescents, divided according to the diagnosis into the ADHD group and the SLD group, and in identifying the differences and similarities between these disorders. The sample included two clinical groups: the first included 36 children and adolescents with a diagnosis of ADHD (5–15 years; mean = 9.42; SD = 2.22) while the second included 36 children and adolescents with a diagnosis of SLD (7–15 years; mean = 9.43; SD = 2.25). The WISC-IV was used to measure intellectual ability and the NEPSY-II was employed to measure executive functions. The results showed that the SLD group had significantly higher scores than the ADHD group on the NEPSY-II in the inhibition, cognitive flexibility, short-term verbal memory and verbal working memory domains. The ANCOVA showed differences regarding the FSIQ of WISC-IV, in that the SLD group obtaining higher scores than ADHD group. Findings showed that ADHD children are more impaired than SLD children, in particular in cognitive inhibition, cognitive flexibility, verbal memory, working memory and intellectual functioning. The recognition of the strengths and weaknesses of children and adolescents with ADHD and SLD allows to outline an educational and clinical intervention focused on their specific executive and intellectual functioning.

Key words: Attention deficit hyperactivity disorder, specific learning disorder, executive functions, intellectual functioning, children, adolescents.

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INTRODUCTION

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disability that, according to the Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM 5, American Psychiatric Association [APA], 2013) occurs in about 5% of the paediatric population. ADHD is defined as a neurological deficit characterized by a persistent pattern of inattention and/or hyperactivity-impulsivity, which is developmentally inappropriate and negatively impacts psychosocial functioning (APA, 2013; von Rhein, Oldehinkel, Beckmann *et al.*, 2016). Similarly, specific learning disorder (SLD) is a neurodevelopmental disorder with biological origins, limited to school skills such as reading, writing and calculation, with onset during the school years with adequate intellectual abilities (DSM-5, APA, 2013; ICD-10, World Health Organization, 1994).

The prevalence of school-aged children with SLD is between 5–15% (APA, 2013). Regarding gender differences, ADHD and SLD are more common in males than females, female/male ratio being 2:1 for ADHD and 2–3:1 for SLD (APA, 2013). The Italian ADHD register of the *Istituto Superiore di Sanità* (Germinario, Arcieri, Marzi, Panei & Vella 2016) includes 3,271 males (88.5%) and 425 females (11.5%) with ADHD, whereas the risk for SLD in the Italian population shows a male female ratio of 2.5:1 (Consensus Conference, 2011).

Several studies of school-aged children with ADHD and SLD have highlighted neuropsychological deficits across multiple

domains, including executive functions (Cornoldi, 2007; Virgili & Tonzar, 2012). In particular, children with ADHD reported significant impairments on measures of response inhibition and working memory (e.g., Barkley, 1996; Rajendran, Rindskopf, O'Neill, Marks, Nomura & Halperin, 2013a, Rajendran, Trampush, Rindskopf, Marks O'Neill & Halperin, 2013b; Schreiber, Possin, Girard & Rey-Casserly, 2014; Shimoni, Engel-Yeger & Tirosh, 2012; Toll, Van der Ven, Kroesbergen & Van Luit, 2011; Watson, Gable & Morin, 2016; Willcutt, Doyle, Joel, Nigg, Faraone & Pennington, 2005); instead children with SLD showed deficits in central executive functioning (Landerl, Bevan & Butterworth, 2004; Pickering, 2006), in particular in working memory (Passolunghi, 2006), whereas the role of inhibition and shifting has received increased attention only in the past few years (Gilmore & Cragg, 2018).

To date, very few studies have analyzed the different neuropsychological profiles of ADHD and SLD children. For example, Willcutt, Betjemann, McGrath *et al.* (2010) showed that individuals with reading disabilities were more impaired than individuals with ADHD on measures of phonemic awareness, verbal reasoning, working memory, and rapid automated naming. The study by Korkman and Pesonen (1994) found that the children with ADHD were specifically impaired in the control and the inhibition of impulses, while the children with SLD were impaired in phonological awareness, verbal memory span, storytelling and in verbal IQ.

The NEPSY-II (Korkman, Kirk & Kemp, 2007, 2011) and the WISC-IV (Wechsler, 2003) are established, well-known and validated tests to discriminate differences in attention executive and intellectual functioning domains in children with different psychopathological diagnosis (Calderoni, Muratori, Leggero *et al.*, 2013; Rasmussen, Tamana, Baugh, Andrew, Tough & Zwaigenbaum, 2013). However, the majority of previous studies evaluated neuropsychological functioning of children and adolescents using the previous version of NEPSY (e.g., Healey, Rajendran, O'Neill, Gopin & Halperin, 2016; Rajendran *et al.*, 2013a,b; Rajendran, O'Neill, Marks & Halperin, 2015). These studies found a significant inverse correlation between NEPSY domains and ADHD symptoms (Rajendran *et al.*, 2013a, 2013b, 2015), a significantly lower scores in the reading subtests on all language subtests in children with SLD and a significantly lower scores on some subtests in the attention and executive functioning domain in children with SLD in mathematics (i.e., Inhibition, memory, visuospatial abilities) (Korkman *et al.*, 2007).

Regarding studies using WISC-IV, findings showed lower scores in Working Memory Index (WMI) and Processing Speed Index (PSI) in children with ADHD (Mayes & Calhoun, 2006) and SLD (Cornoldi, Orsini, Cianci, Giofrè & Pezzuti, 2013; De Weerd, Desoete & Roeyers, 2013; Giofrè, Stoppa, Ferioli, Pezzuti & Cornoldi, 2016; Peng, Conqying, Beilei & Sha, 2012; Schuchardt, Maehler & Hasselhorn, 2008; Toffalini, Pezzuti & Cornoldi, 2017; Willcutt *et al.*, 2010, 2013).

Therefore, although it is widely recognized that children with ADHD and SLD have impaired working memory and inhibition (e.g., Cornoldi *et al.*, 2013; Giofrè *et al.*, 2016; Toffalini *et al.*, 2017), very few studies have analyzed the different neuropsychological profiles of ADHD and SLD children, comparing intellectual functioning and executive functions to identify differences and similarities between these two disorders (e.g., Couvadelli, 2006; Healey, Marks & Halperin, 2011). In this study, we were interested in analyzing the intellectual and executive profiles in a sample of school-aged children and adolescents, divided according to their diagnosis into the ADHD group and the SLD group, and in identifying differences and similarities between these groups in order to outline interventions that are more targeted to the characteristics of individual children.

METHODS

Participants

For this study, we recruited a sample of 72 children and adolescents (aged between 5.1 and 15.4 years) who had been referred to the Department of Human Neuroscience with suspected ADHD or SLD on the recommendation of parents, teachers, or paediatricians.

All children and parents underwent an initial interview with a child neuropsychiatrist who recorded the child's history, followed by an evaluation including a large battery of neuropsychological tests and rating scales (see Appendix A), performed by a multidisciplinary team of experts comprising a neuropsychiatrist and four psychologists.

To be included in the ADHD and SLD group, patients needed to meet, respectively Diagnostic and Statistical Manual of Mental Disorder (DSM)-5 criteria for ADHD-C (APA, 2013) and DSM-5 criteria and Italian Consensus Conferences criteria for an SLD (Consensus Conference, 2007, 2011). Furthermore, besides having a diagnosis of ADHD or SLD, the

individuals included in the study were initially screened to determine their eligibility. Inclusion criteria were an FSIQ score ≥ 85 , no other disorder in comorbidity, and Italian as the mother tongue. The sample was divided into two groups: 36 patients with a diagnosis of ADHD (combined type) without comorbidities (ADHD group; mean age = 9.42, SD = 2.22; males = 88.9%, females = 11.1%) and 36 patients with SLD without comorbidities (SLD group; mean age = 9.50, SD = 2.25; males = 63.9%, females = 36.1%).

Measures

The Wechsler Intelligence Scale for Children Fourth Edition (WISC-IV, Wechsler, 2003; Italian version, Orsini, Pezzuti & Picone, 2012) is designed to assess the cognitive ability of children and adolescents by providing subtest and composite scores that represent intellectual functioning in specific cognitive domains, as well as a composite score that represents intellectual ability, Full Scale Intelligence Quotient (FSIQ). The WISC-IV comprises four indexes: Verbal Comprehension Index (VCI), a measure of crystallized intelligence (Gc) that assesses the child's ability to listen to a question, draw upon learned information from both formal and informal education, reason through an answer, and express their thoughts aloud; Perceptual Reasoning Index (PRI), a measure of non-verbal and fluid reasoning (Gv/Gf) that assesses the child's ability to examine a problem, draw upon visual-motor and visual-spatial skills, organize their thoughts, create solutions, and then test them; Working Memory Index (WMI), a measure of short-term and working memory (Gsm) that assesses the child's ability to memorize new information, hold it in their short-term memory, concentrate, and manipulate that information to produce some result or reasoning process; and Processing Speed Index (PSI), a measure of the speed regarding information processing (Gs) that assesses the child's ability to focus attention and quickly scan, discriminate between and sequentially order visual information, skills that require persistence and planning ability but are sensitive to motivation, in addition to their difficulty working under time pressure, as well as their motor coordination.

The NEPSY-II (Korkman *et al.*, 2007, 2011; Italian version, Urgesi, Campanella & Fabbro, 2011) is a multi-domain neuropsychological battery test designed to provide a comprehensive neuropsychological assessment of children aged 3–16 years. It allows for the administration of specific subtests, groups of subtests, or the entire battery (Korkman *et al.*, 2007). This battery includes many classic paradigms for testing neuropsychological functioning, and its conceptual principles can be easily understood by users with a neuropsychological background (Brooks, Sherman & Strauss, 2010). The NEPSY-II is based upon several factors including neuropsychology research, child development and child psychology, as well as early pilot studies of revisions and newly developed subtests (Korkman *et al.*, 2011). The Italian version of the NEPSY-II (Urgesi *et al.*, 2011) consists of 33 subtests (four with delayed conditions) comprising six cognitive domains:

- (1) attention and executive functioning,
- (2) language,
- (3) memory and learning,
- (4) sensorimotor functioning,
- (5) social perception, and
- (6) visuospatial processing.

For the purpose of our research, we chose to focus only on two cognitive domains:

Attention and executive functioning: this domain is composed of subtest that assesses several aspects of attention and executive functions. In particular, in this research, we considered the Inhibition subtest, comprising subtest inhibitory control (IN-I) and subtest inhibitory control and cognitive flexibility (IN-S), designed to assess the ability to inhibit automatic responses in favour of novel responses and the ability to switch between response types (Kemp & Korkman, 2010).

Memory and learning: this domain evaluates several aspects of verbal learning and memory. In particular, in this research to assess the integrity

of visuospatial and verbal long and short memory we considered: Memory for Designs (MD-Immediate = MD-Imm; MD-Delayed = MD-Del), assessing spatial memory for novel visual memory; Memory for Faces immediate (MF), to assess encoding of facial features, as well as face discrimination and recognition; Sentence Repetition (SR tot), to evaluate the ability to repeat sentences of increasing complexity and length; List Memory (LM tot), designed to assess verbal learning and memory, rate of learning, and the role of interference in recall for verbal material and Word List Interference (WL int) to assess verbal working memory, repetition, and word recall after interference.

WISC-IV (2003) and NEPSY-II (2011) were administered to all children after a written informed consent for use of the information and scores in the empirical study was obtained from parents of the evaluated children and adolescents. Strict anonymity of responses was maintained via de-identification of data, and the collected data were stored in a password-protected database. The research was conducted in accordance with the Declaration of Helsinki of 1964 (World Medical Association [WMA], 2008).

Data analysis

To compare the performance in four indexes and FSIQ of WISC-IV and in the attention and executive functioning and memory and learning domains of NEPSY-II based on diagnosis, the data were analyzed using a series of multivariate analysis of covariance (MANCOVA) and one analysis of covariance (ANCOVA) using gender and age as covariates. For the interpretation of Eta squared (η^2): $\eta^2 > 0.01$ is a small effect; $\eta^2 > 0.06$ is a medium effect; $\eta^2 > 0.14$ is a large effect.

RESULTS

To verify if the two groups were balanced by age, gender and ethnicity of the participants, we conducted an ANOVA for the age, while for the other control variables we used the chi-squared (χ^2) statistical test. The results obtained suggest that the two groups are balanced by age ($F_{(1,70)} = 0.022$, $p = 0.883$) and ethnicity ($\chi^2_{(1)} = 0.000$, $p = 1$), while for the gender the ADHD group has more males ($n = 32$) and less females ($n = 4$) than the SLD group (males = 23, females = 13) ($\chi^2_{(1)} = 6.237$, $p < 0.05$), according to prevalence data reported in Italy by ISTISAN (2016).

The ethnic composition of the sample was 97.2% Italian and only 2.8% of participants were from different ethnic groups.

The MANCOVA identified significant differences between both the two diagnostic groups (ADHD and SLD) with respect to the NEPSY-II subtest scores. In particular, the MANCOVA for the NEPSY-II subtests showed that the diagnosis is a statistically significant factor with a large effect (Wilks Lambda = 0.689, $F_{(1, 70)} = 2.555$, $p < 0.05$, $\eta^2 = 0.311$, power = 0.895). Tables 1 shows the mean (M), standard deviation (SD), F , effect size (η^2) and power for all scores obtained in each subtest for children and adolescents with ADHD and SLD.

The results show that the SLD group had significantly higher scores than the ADHD group in the following subtests: inhibitory control and cognitive flexibility (IN-C), word list interference recall, list memory total and sentence repetition total. The IN-C subtest was found to be most influenced by the presence of ADHD ($\eta^2 = 0.275$), followed by the list memory total ($\eta^2 = 0.087$) and sentence repetition total ($\eta^2 = 0.086$) and word list interference recall ($\eta^2 = 0.081$) subtests.

The MANCOVA conducted for the four indexes of WISC-IV did not show any significant differences between diagnoses (diagnostic groups: Wilks Lambda = 0.885, $F_{(1, 68)} = 2.114$, $p = 0.089$, $\eta^2 = 0.115$, power = 0.596).

The ANCOVA showed significant differences between the FSIQ obtained for the diagnostic groups, in particular SLD group obtaining higher scores than ADHD group.

Table 2 reports the mean (M), standard deviation (SD), F , effect size (η^2), and power for FSIQ obtained by children and adolescents with ADHD and SLD.

Table 2. ANCOVA: diagnostic and age groups (ADHD vs SLD) \times FSIQ

Groups	M	SD	F	p	η^2	Observed power
ADHD	94.05	16.08	7.53	0.01	0.1	0.77
SLD	103.64	15.28				

Note: For the interpretation of Eta squared (η^2): $\eta^2 > 0.01$ is a small effect; $\eta^2 > 0.06$ is a medium effect; $\eta^2 > 0.14$ is a large effect.

Table 1. MANCOVA: diagnostic groups (ADHD vs SLD) \times NEPSY-II subtests

Subtests	Groups	M	SD	F	p	η^2	Observed power
Inhibition B combined	ADHD	7.06	3.245	3.255	0.076	0.052	0.427
	SLD	8.19	1.975				
Inhibition C combined	ADHD	6.42	1.822	22.348	0.000	0.275	0.996
	SLD	8.81	2.348				
Memory for faces immediate	ADHD	9.68	3.673	1.350	0.250	0.022	0.208
	SLD	10.69	3.496				
Word list interference	ADHD	8.42	3.802	5.212	0.026	0.081	0.612
	SLD	9.91	3.216				
List memory total	ADHD	8.32	3.7	5.589	0.021	0.087	0.639
	SLD	10.53	3.027				
Memory for designs immediate	ADHD	9.35	3.292	0.309	0.581	0.005	0.085
	SLD	9.72	3.846				
Memory for designs delayed	ADHD	8.84	4.001	0.677	0.414	0.011	0.128
	SLD	9.34	3.747				
Sentence repetition	ADHD	8.19	3.081	5.541	0.022	0.086	0.639
	SLD	10.06	2.735				

Note: For the interpretation of Eta squared (η^2): $\eta^2 > 0.01$ is a small effect; $\eta^2 > 0.06$ is a medium effect; $\eta^2 > 0.14$ is a large effect.

DISCUSSION

The aim of the present study was to examine the intellectual and executive profiles in a sample of school-aged children and adolescents, divided according to the diagnosis in ADHD group and SLD group, using NEPSY-II and WISC-IV to identify differences and similarities. Analyzing the intellectual and executive profile of pure ADHD and pure SLD children and adolescents to identify the differences and similarities, it is very interesting not only in order to outline more targeted interventions to the characteristics of children, but also because often these two disorders occur in comorbidity (Reale & Bonati, 2018).

The current study presented evidence of a significant effect of ADHD diagnosis on the performance of children and adolescents in the WISC-IV and in the domains of attention, executive functions, memory, and learning of NEPSY-II, similar to that previously observed in the literature (e.g., Rohrer-Baumgartner, Zeiner, Egeland *et al.*, 2014; San Miguel Montes, Allen, Puente & Neblina, 2010; Weyandt, Oster, Dupaul & Anastopoulos, 2017). This effect was most noticeable in the NEPSY-II subtests that require inhibition of learned and automatic responses, cognitive flexibility to switch between two response set, working memory, verbal memory and learning, as well as the global intellectual functioning (FSIQ) determined by the WISC-IV. No other difference was observed between two groups for the remaining performances in the domains of NEPSY-II considered. Therefore, in our sample, children with ADHD showed a greater weakness than children with SLD, in particular in the cognitive inhibition, cognitive flexibility, verbal memory, working memory and in the intellectual functioning.

To our knowledge, only the study by Korkman and Pesonen (1994) compared 8-year-old children with ($n = 21$) pure ADHD to those with SLD ($n = 12$), using the NEPSY and the WISC-R; they found that the children with ADHD were specifically impaired in the control and the inhibition of impulses, while the children with SLD were impaired in phonological awareness, verbal memory span, and storytelling and in verbal IQ. Our results are in line with an extensive body of literature that has shown that children with ADHD experience difficulties across a wide range of executive functions (e.g., Frazier, Demaree & Youngstrom, 2004; Martinussen & Tannock, 2006). Similarly, Doyle (2006) found impaired performances on measures of response inhibition, working memory, and other aspects of executive functions in ADHD samples. Also, Schreiber *et al.* (2014) showed that ADHD children performed worse working memory compared with the controls. Therefore, as highlighted by many authors (Castellanos, Sonuga-Barke, Milham & Tannock, 2006; Nigg, 2001; Willcutt *et al.*, 2005), cognitive inhibition seems to be one of the most frequently altered executive functions in ADHD.

Consistently with the aforementioned studies, in our sample, the performance of the ADHD group in inhibition and cognitive flexibility assessing working memory, switching, cognitive flexibility and the interference effect, was within the borderline range regarding to developmental age, whereas the performance of the SLD group on the same task was within the average range.

Few studies in literature have focused on the encoding of facial features, as well as face discrimination and recognition assessed through of NEPSY-II (Collin, Bindra & Raju, 2013; Romani,

Vigliante, Faedda *et al.*, 2018). In addition to the previous results in the literature that found an impairment in facial emotion recognition in children and adolescents with ADHD, in our study, we observed that the ADHD group showed performance within the average range but lower than the SLD group in face recollection. This ability represents a cold aspect of social cognition, an issue that the previous literature studied by taking in account mainly hot aspects assessed through tasks of facial emotion recognition (e.g., Aspan, Bozsik, Gadoros *et al.*, 2014; Bora & Pantelis, 2016).

Similarly, regarding intellectual functioning, ADHD group showed lower IQ than the SLD group, although the scores of both groups were within the average range. This was probably because the ADHD group had significantly poorer performance than the SLD group in tasks assessing the ability to control the interference effect, verbal memory, inhibition, switching, and working memory, which are variables that influence intellectual functioning (e.g., Alloway, 2010).

Regarding the comparisons between the other constructs, although the ADHD group showed significantly poorer performance than the SLD group in word list interference recall, list memory total, and sentence repetition total, the performance of both groups was within the expected range for developmental age. Poor executive performance was not observed in the SLD group in our sample. This finding is in contrast with those of Watson *et al.* (2016), who found that students with SLD had significant problems with executive functions, which included working memory and inhibitions. Crews and D'Amato (2009) examined subtypes of children with reading disabilities using NEPSY (Korkman, Kirk & Kemp, 1998) and suggested that memory-related processes, not exclusively phonologically related processes, might contribute to reading difficulties. It is important to highlight that our sample was made up of children with pure SLD, so it is possible that we did not find deficits and poor executive performances in these children because the SLD core deficit is mainly represented by a characteristic and specific impairment in the reading, writing, and math domains. Our findings suggested that the main component of SLD is its "specificity" (APA, 2013; Consensus Conference, 2007, 2011). Therefore, it would be interesting to assess children with SLD and comorbidities to understand how the presence of other disorders could affect their executive and intellectual functioning. In particular Anxiety Disorder, Developmental Coordination Disorder, Language Disorder and Mood Disorder were often reported in association with SLD (Margari *et al.*, 2013).

Furthermore, it is widely recognized in literature that one of the most common comorbidities associated to SLD is really ADHD (Somale, Kondekar, Rathi & Iyer, 2016). The main findings of this current study are that children with ADHD seem to be more impaired in specific cognitive and executive functions than SLD children, in particular in working memory, inhibition, cognitive flexibility and verbal memory. However, in the other domains, children with ADHD and SLD did not show differences, in particular in spatial and content memory for novel visual material and in long-term visuospatial memory.

Consequently, it would be interesting to assess neuropsychological and executive functioning of children with both ADHD and SLD; in fact these children may show a different

intellectual and executive profile, unlike children with pure ADHD and pure SLD. Intervention strategies should be targeted on specific profile, needs and characteristic of the child, for example pure SLD typically receives intervention only at school, those with comorbid ADHD and SLD should receive intervention across several settings (DuPaul, Gormley & Laracy, 2012). Furthermore, the specific profile of the child should be considered when planning school-based interventions and educational or rehabilitation programs. Such as, since both ADHD and SLD children did not report deficits in visuospatial domain, spatial mnemonics and visual maps could help children to recall and retrieve new information, learn new vocabulary words, becoming more efficient learners.

The present study has some limitations. First of all, the use of NEPSY-II as the only test to assess executive functions in the sample made it impossible to analyze potential correlations with other executive function testing methods. Second, our sample size does not allow us to make generalizations about our findings and does not assure an adequate power to detect statistical significance between the four indexes of WISC-IV, mainly in the comparison between groups based on age. It would be desirable to continue this research in a larger sample of patients diagnosed with SLD and ADHD with different demographic characteristics and to conduct a longitudinal study to analyze the growth curves of executive functions and intellectual functioning, assessing the effectiveness of the intervention, in patients with an early and late diagnosis.

CONCLUSIONS

A global assessment of intellectual functioning and executive functions allows for the recognition of the strengths and weaknesses of children and adolescents with ADHD and SLD in order to outline a focused intervention for the improvement of cognitive and social disempowerment and to promote better clinical progress.

Furthermore, although further research including children with ADHD and SLD in comorbidity are needed, since in neurodevelopmental disorders the presence of a comorbid disorder is the rule not the exception, these results provide additional support to studies indicating more severely altered executive functioning in ADHD than in SLD and they could help to understand the specific contribution of the core deficits of two disorders on executive and intellectual domains.

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APPENDIX A

For the diagnosis the following tests were administered:

- *Wechsler Intelligence Scale for Children, fourth edition* (Wechsler, 2003) or *Wechsler Preschool and Primary Scale of Intelligence, fourth edition* Wechsler (2012a, 2012b) in order to exclude children and adolescents with intellectual disabilities and borderline functioning;
- *DDE-2 Batteria per la valutazione della Dislessia e della Disortografia evolutiva- 2* (Sartori, Job & Tressoldi, 2007) in order to evaluate dyslexia and dysorthography;
- *Prove di Lettura MT per la Scuola Elementare-2* (Cornoldi & Colpo, 1998) and *Nuove prove di lettura MT per la scuola media inferiore* (Cornoldi & Colpo, 1995) to evaluate dyslexia and reading comprehension;
- *Batteria Discalculia Evolutiva (BDE)* (Biancardi & Nicoletti, 2004) and *Batteria AC-MT* (Cornoldi, Lucangeli & Bellina, 2002) to evaluate numeracy and dyscalculia;
- *Developmental Test of Visual-Motor Integration (VMI)* (Beery, 1997), in order to evaluate the growth of visuospatial and visuomotor skills in childhood;
- *Prova per la valutazione della scrittura in età evolutiva (BHK)* (Di Brina & Rossini, 2011) to evaluate dysgraphia;
- *NEPSY-II* (Korkman et al., 2011) to evaluate the development of neuropsychological function.

Emotional and behavioral profile:

- *Big Five Questionnaire Children, self-report version* (Barbaranelli, Caprara & Rabasca, 1998);
- *Children's Depression Inventory (CDI)* (Kovacs, 1986);
- *Multidimensional Anxiety Scale for Children (MASC)* (March, Parker, Sullivan, Stallings & Conners, 1997);
- *Thematic Apperception Test (TAT)* (Murray, 1943);
- *Children's Apperception Test (CAT)* (Bellak & Bellak, 1949); and
- *Graphics Tests: Draw-a-person Test, Kinetic Family Drawing, Invented Family Drawing*.

Interviews for parents and teachers:

- *Child Behavior Checklist (CBCL 6-18) and Teacher Report Form (TRF)* (Achenbach & Rescorla, 2001);
- *Conners' Parent and Teacher Rating Scales (revised version)* (Conners, 1989);
- *Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime version (K-SADS-PL)*, adapted by Kaufman et al. (1997), Kaufman, Birmaher, Brent, Ryan and Rao (2000), Kaufman, Schweder, Hilsenroth and Segal (2004).

Al termine della lettura dell'articolo "La pillola dell'obbedienza" di Julien Brygo pubblicato sul numero di dicembre de *Le Monde diplomatique* **il manifesto** sorgono almeno due domande.

La prima. E in Italia? Nulla è detto della realtà italiana che è quella che dovrebbe interessare principalmente i lettori. L'organizzazione dei servizi di neuropsichiatria e le attitudini diagnostico-terapeutiche dei disturbi dell'età evolutiva differiscono notevolmente all'interno e tra le nazioni, non solo tra Francia e USA, ma ancor più in Italia. Una scheda o un breve articolo di contestualizzazione della realtà italiana che avesse accompagnato l'articolo francese avrebbe contribuito ad una appropriata informazione dei lettori italiani.

La seconda. Perché pubblicare un articolo di dubbia qualità informativa? Il giornalista non sembra conoscere il disturbo di cui scrive e di non essersi documentato a sufficienza. È un articolo confuso e confondente tra uso terapeutico e illecito di farmaci. Riporta di effetti drammatici raccontati e non documentati, quantificati, contestualizzati allo stato e tipo disturbo. Questo non vuol dire che si debbano negare e celare possibili effetti avversi indotti da farmaci, ma di documentarli in modo appropriato. Un articolo basato su convinzioni e non sulle evidenze scientifiche e oltretutto non aggiornato. Nessun riferimento agli esiti di altri trattamenti o del non trattamento. Per un articolo informativo e divulgativo che tratta di scienza (medicina/psichiatria) e tecnica (cure e assistenza) non sono limiti su cui soprassedere. Se si aggiunge inoltre che alcune delle note/referenze sono inaccurate e non pertinenti al testo il risultato per i lettori, sia francesi che italiani, non è dei migliori.

Il disturbo da deficit di attenzione/iperattività (ADHD) interessa 1,2% della popolazione italiana tra i 6 e i 17 anni d'età, quindi circa 80.000 bambini e adolescenti; prevalentemente maschi e nella forma combinata del disturbo (attenzione con iperattività), di gravità medio-lieve. La diagnosi si basa sulla valutazione clinica, con l'impiego di alcuni test psicologici e il coinvolgimento di genitori e insegnanti. Come per gli altri disturbi mentali e indipendentemente dall'età, nella maggioranza dei casi l'ADHD si accompagna ad altri disturbi (comorbidità) quali, per esempio: ansia, disturbi del sonno, disturbi dell'apprendimento. Il trattamento, ad eccezione delle forme

gravi, prevede interventi psicologici (per esempio, psico-comportamentali) indirizzati anche genitori e insegnanti (child, parent e teacher training). Il trattamento farmacologico rappresenta quindi una seconda scelta e, comunque, parte di una terapia “multimodale”. Queste le indicazioni essenziali riconosciute a livello internazionale dalle società scientifiche di psichiatria e neuropsichiatria con cui confrontarsi e reclamare diritti di cura.

In Italia sono disponibili solo due farmaci con indicazione specifica per l’ADHD: il metilfenidato (Ritalin®), oggi pressoché l’unico utilizzato, e l’atomoxetina. Anche per prevenire l’uso illecito del farmaco dal 2007 è stato istituito un registro nazionale che ne limita e controlla la prescrizione. In Regione Lombardia dal 2011 il Registro prevede addirittura il monitoraggio dell’intero percorso diagnostico-terapeutico, omogeneo in tutti i Centri di riferimento lombardi. Una situazione, quella italiana, unica a livello internazionale a garanzia del diritto di ottenere cure sicure ed efficaci, anche prevenendo distorsioni d’uso di farmaci particolarmente critici come gli amfetaminosimili (metilfenidato). Ecco, nonostante i limiti e le difficoltà dei servizi pubblici italiani di neuropsichiatria l’articolo di Brygo ci racconta di “altro” e i lettori non lo sanno.

Maurizio Bonati

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e segnalazioni

ALLE PAGINE 22 E 23

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Sommario
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RIUSCIRE A SCUOLA CON LA PASTIGLIA

La pillola dell’obbedienza

In origine il farmaco era destinato ai soli bambini «iperattivi», una patologia relativamente rara. Ma da qualche anno, negli Stati uniti, chiunque si mostri un po’ turbolento può vedersi prescrivere il Ritalin, un presidio vicino alle anfetamine che fa furore anche nei campus. Dopo aver inondato il mercato statunitense, la pillola miracolosa si sta diffondendo in Francia

dal nostro inviato speciale JULIEN BRYGO*

Parigi, sabato 13 aprile 2019. Claire Leblon, caposquadra in un grande albergo della regione parigina, si siede nella sala d’attesa dell’ambulatorio di psichiatria infantile con suo figlio Niels, 11 anni. Fra poco il ragazzino sarà esaminato dal medico che gli farà domande sui suoi risultati scolastici e sul suo comportamento. Dopo essere rimasto seduto per alcuni minuti, comincia ad agitarsi, si alza, si siede di nuovo, poi afferra lo smartphone della madre per scorrere foto di città, la sua passione del momento, dopo i lampadari, i bidoni della spazzatura e i camion.

E patatrac: il portatile cade a terra. Leblon si arrabbia, lo rimprovera con voce alterata. Questo episodio le appare come un’altra prova del fatto che suo figlio è diverso, incontrollabile, incorreggibile – da alcuni anni ha trovato la parola giusta: «iperattivo». Le stupidaggini che combina a casa e a scuola la esasperano.

continua alle pagine 6 e 7

* Giornalista. Coautore, con Olivier Cyran, di *Boulots de merde! Du cireur au trader, enquête sur l'utilité et la nuisance sociales des métiers*, La Découverte Poche, Parigi, 2018

LA RICETTA MEDICA PER UNA BUONA RIUSCITA SCOLASTICA

La pillola dell'obbedienza

continua dalla prima pagina

Ha bussato alla porta giusta. Il medico – la cui voce si sente dall'altra parte del muro – ha la reputazione di essere «un'autorità nel suo campo», sussurra lei. Invitato abituale alle trasmissioni radiofoniche nazionali, Gabriel Wahl pubblica regolarmente editoriali sulla stampa medica e generalista. Ha scritto una quantità di saggi sui temi che predilige, in primo luogo il fallimento scolastico, la precocità e il famoso disturbo da deficit dell'attenzione con o senza iperattività (Adhd).

Il suo rimedio miracoloso è il Ritalin, farmaco ricavato da una molecola sintetizzata nel 1944 da un chimico italiano, Leandro Panizzon. Panizzon avrebbe concepito questo prodotto per sua moglie, Margherita (detta «Rita»), che cercava di migliorare la propria concentrazione – e la rovesciata al tennis. Quel giorno, tutti i pazienti del dottor Wahl ripartiranno con la loro ricetta di farmaci psicotropi.

Il Ritalin è a base di metilfenidato cloridrato, un derivato dalle anfetamine che aumenta la produzione di dopamina nel cervello. Questa molecola sarebbe in grado di liberare gli adulti come i bambini da una lista impressionante di pecche, dalla brutta tendenza a impuntarsi di fronte a un compito fastidioso al puro e semplice rifiuto dell'autorità, passando per la mancanza di attenzione e l'incapacità di concentrarsi. È uno dei prodotti di punta di Novartis (che nel 2018 ha registrato un fatturato di 52 miliardi di dollari). Spesso chiamato *smart drug* («droga dell'intelligenza»), «pillola dell'obbedienza» o *kiddy coke* («cocaina per bambini»), questo psicostimolante dovrebbe migliorare le performance intellettuali del paziente e garantire bambini malleabili a genitori e insegnanti. «Il Ritalin non cura nulla. Non cura, sospende i sintomi dell'inattenzione, ammette il dottor Wahl. Non si guarisce dalla Adhd, un disturbo psicologico trasmesso dai geni (1).» Il Ritalin e i suoi concorrenti, in primo luogo l'Adderall (laboratorio Shire), sono classificati fra gli stupefacenti.

Niels è fra i 62mila bambini e ragazzi di meno di 20 anni in Francia – principalmente maschi fra i 6 e i 17 anni – che hanno consumato metilfenidato nel 2016 (2). Come la maggior parte dei suoi compagni «iperattivi», prende il farmaco solo nei giorni di scuola. Il meccanismo di assorbimento, a liberazione progressiva, è stato pensato per farlo agire esattamente fra le 8 e le 16 ore. «Quando c'è un allievo che disturba, la classe ne risente moltissimo», insiste il dottor Wahl. Grazie alla pozione magica, non c'è più bisogno di punizioni o di astuzie psicologiche per calmare le teste matte. Alle ragazze, educate ad avere un comportamento meno inquieto, viene in genere diagnosticato un semplice disturbo da deficit dell'attenzione, senza iperattività.

In Francia, la prescrizione di metilfenidato è in pieno boom: oggi il consumo è trenta volte superiore rispetto al 1996, anno dell'introduzione sul mercato del farmaco. Nel 2017, ne sono state vendute 810.000 confezioni, quattro volte più che nel 2005. E c'è chi pensa che il mercato non sia ancora saturo: «*Quarantamila ragazzi trattati* [nel 2014] *sono una quantità insufficiente*», scrive per esempio *Le Figaro*, per il quale «*diverse centinaia di migliaia di ragazzi non usufruiscono del trattamento necessario*» (3). E il sito *Allodocteurs.fr* allerta: «*Il Ritalin non viene prescritto a sufficienza*» (5 settembre 2017). Leblon

taglia corto: «*Noi glielo diamo per stare in pace, perché obbedisca, perché si comporti bene in classe e abbia buoni voti. Continuavano a chiamarci a scuola! Ma non fa più effetto, e a volte pare angosciato, quindi dovremo smettere.*»

«Non è facile dare anfetamine al proprio figlio»

Nessuno studio è stato dedicato agli effetti a lungo termine del metilfenidato sui minori (4). Leblon se ne preoccupa, e Wahl lo conferma, seppure con l'abituale flemma dei grandi medici: «*Sì, possono verificarsi disturbi del sonno o dell'appetito, dolori al ventre... Ma il farmaco viene prescritto in 65 paesi, ed è stato messo a punto oltre settant'anni fa. Nessuna avventura umana è priva di rischi. Non fa alcun danno e non crea alcuna dipendenza. Il metilfenidato permette di salvare vite, essenzialmente quelle delle persone che non riescono a concentrarsi e quindi vanno male a scuola.*» Ad esempio, un'allieva «*dal quoziente di intelligenza molto alto*» non riusciva a concentrarsi a sufficienza: «*da un giorno all'altro*» la media dei suoi voti è passata da 9 a 16. Un «*importante medico*» di Lione ha «*dichiarato esplicitamente che suo fi-*

la medicalizzazione dei bambini disattenti. Nel 2017, assumevano psicostimolanti oltre venti milioni di statunitensi: sedici milioni di adulti – cinque in modo illegale – e quattro milioni di bambini (6). Gli Stati dell'Ovest e del Sud, rurali e industriali, sono più toccati del resto del paese.

Domenica 29 settembre 2019, Lexington, Kentucky. Svincoli autostradali, una successione di centri commerciali e, al fondo di un quartiere di case con giardino, la biblioteca Beaumont. Jesse Dune e i suoi due figli sono venuti a prendere in prestito libri per la settimana. «*Questo record mondiale non mi stupisce affatto, dice la farmacologa 39enne, che lavora presso l'ospedale universitario. Il Kentucky è uno Stato molto conservatore; non si parla mai delle emozioni, dei sentimenti dei bambini. Si preferisce dar loro una pasticca, è più facile. In California è il contrario: essere creativi e iperattivi non suscita alcun sospetto. Qui, è un disturbo diagnosticato all'eccesso, soprattutto presso i maschi.*»

Con lei c'è Elizabeth, 11 anni, calma e tranquilla. «*Mia figlia è sempre stata precoce rispetto agli altri. Ha imparato a leggere molto presto. E passa le giornate a leggere. Ma la sera era ingestibile. Non voleva mai mangiare con tranquillità con noi genitori. Io lavoro cinquanta ore*



Pxhere

glio senza il Ritalin non avrebbe potuto studiare medicina e in seguito chirurgia». Di aneddoti, Wahl ne ha a bizzeffe. «*I miei pazienti prendono questo trattamento come si accendono i termosifoni se fa freddo, si apre un ombrello se piove o si inforcano gli occhiali se si è miopi. Andate a spiegare loro del Kentucky, delle questioni sociali, e di questo e quello... Se ne fregano.*»

Il Kentucky, perché? Perché è lo Stato americano che conta il numero più elevato di minori diagnosticati come iperattivi: il 14,8%, secondo i Centers for Disease Control and Prevention (Cdc), che si basano sulle dichiarazioni dei genitori. Uno su dieci è sotto trattamento (5). In alcune contee, come quella di Herderson, nell'ovest, per un quarto dei bambini scolarizzati è stata dichiarata alla propria scuola una diagnosi di Adhd. Lo Stato, quattro milioni e mezzo di abitanti, è dunque al primo posto mondiale per

la settimana, il lavoro mi assorbe molto e la sera sono stanchissima. In più aveva idee morbose, mi diceva cose tipo: "Mamma, vorrei non essere mai nata". Questo mi ha spezzato il cuore. Ci siamo rivolti a molti medici e, quando aveva 7 anni, le abbiamo somministrato Concerta [concorrente del Ritalin]. Da allora lo assume senza interruzioni, anche durante le vacanze e i week-end. Quando abbiamo cercato di toglierlo, i suoi voti sono precipitati. Per un genitore, è molto difficile dover dare anfetamine al proprio figlio, ma ci sembra di non avere scelta.»

Ogni mese, Dune deve prendere appuntamento con il medico per rinnovare la scorta. «*Abbiamo il diritto di tenere in casa una quantità utile per trenta giorni, poi devo tornare dallo psichiatra infantile per la ricetta. In seguito devo chiamare la farmacia, quattro giorni prima, mostrare la mia carta d'identità... Il tutto è molto*

regolamentato, perché c'è chi vende il prodotto al mercato nero agli studenti.»

Secondo uno studio condotto nel 2008 in una grande università del sud-est degli Stati Uniti, il 34% degli studenti ha già fatto ricorso al metilfenidato in occasione degli esami (7). Shannon, studi commerciali, si stupisce: «*Così pochi? Direi che sono di più, molti di più. Qui, almeno il 70%, secondo me. Tutti i miei conoscenti ne assumono.*» Nel campus dell'università del Kentucky, a Lexington, niente di più facile che trovare del metilfenidato. «*Quando assumo il Concerta, mi sento super concentrata. Ieri l'ho preso alle 14 e sono rimasta incollata allo studio fino all'una di notte, senza mangiare. Ho pagato 8 dollari per 27 milligrammi, attraverso un gruppo su Internet. Molto semplice*», assicura Maya (8), 19 anni la quale, sguardo vitreo e colorito pallido, ha appena finito l'esame di psicologia. «*Sono la prima della mia famiglia a fare l'università. Non ho scelta: devo riuscire al 100%. Vengo dal nord del Kentucky e là nessuno frequenta una facoltà, nemmeno chi è bravo a basket.*» Ogni semestre costa 13.000 dollari (11.800 euro); la ragazza non esita a «*cogliere tutte le opportunità*»

È una situazione «*pericolosa*», secondo Matthew Neltner, medico universitario che lavora presso l'unità di trattamento delle malattie mentali degli studenti dell'università. «*Affermare che gli psicostimolanti non provocano dipendenza ricorda il discorso sugli oppioidi: la crisi è cominciata proprio così! Quando non si ha il Ritalin a disposizione, ci si sente depressi, affaticati, si dorme tutto il giorno e non si ha motivazione per niente.*» Racconta che molti pazienti gli dichiarano di soffrire di Adhd: «*Nessuno viene alla visita dicendo "Sono bipolare" oppure "Sono depresso". Non è sexy. Gli studenti non vogliono sentir parlare di terapie comportamentali, che pure sono efficaci, o di soluzioni più semplici, come fare esercizio fisico. Eppure, correre, uscire all'aperto, fare sport cura l'iperattivismo.*» Neltner spiega: «*Cerco di limitare le prescrizioni: ci si basa sul Dsm-5, secondo il quale soffre di Adhd il 5% dei minori e il 2,5% degli adulti*» (9).

Negli Stati Uniti, essere affetti da Adhd è talora considerato positivo, una sorta di biglietto d'ingresso nella categoria degli iperdotati. Diverse celebrità, dal cantante Justin Timberlake all'attrice Emma Watson, passando per l'imprenditore Richard Branson, il nuotatore Michael Phelps, e in passato il musicista Kurt Cobain... e Leonardo da Vinci, hanno avuto una diagnosi di questo genere. E non si contano le odi al metilfenidato, presente nel quotidiano degli statunitensi di diversi ambienti: finanza, videogiochi, baseball, show-business, ma anche esercito o corse dei cavalli (10).

«*Mio figlio è un genio*, dice Mary Fuller Proffit, una donna di servizio di 63 anni che cresce da sola Isiac, adottato undici anni fa. È capace di disegnare con gli occhi chiusi le mappe esatte dell'Europa prima e dopo la prima guerra mondiale, e dopo la seconda.» È stata assistente sociale per malati mentali («*Dovevo occuparmi di trentotto pazienti, per un totale di 10.000 farmaci da gestire ogni mese*»), e a lungo ha rifiutato gli psicostimolanti. I medici hanno concluso molto presto che Isiac soffriva di Adhd ma secondo Proffit, diffidente, nel Kentucky si esagera con queste diagnosi. «*Isiac è nato dipendente dal crack e dall'alcol, la madre biologica ne faceva uso. Ho dovuto lasciare il mio lavoro per occuparmi di lui. Lamentele continue per il suo*

comportamento a scuola. Parla di continuo, rifiuta di sedersi, fa quel che gli pare. I suoi insegnanti hanno fatto pressione su di me per una cura. Ovviamente a loro interessa che si sieda e stia zitto.» Alla fine la madre ha ceduto: «Gli do del Concerta solo per la scuola, e i professori sono soddisfatti. Io un po' meno: sono povera, non ho una buona assicurazione e ogni mese la cura mi costa 130 dollari [118 euro].»

Nell'est del Kentucky, ai piedi degli Appalachi, la città di Hazard, cinquemila abitanti, è un susseguirsi di farmacie in drive-in, supermercati e montagne bucate dalle escavatrici che estraggono il carbone o riparano le strade. Andando verso il rettorato, che ha accettato di riceverci, ci fermiamo in una clinica, segnalata da uno schermo su strada, con la sigla «Adhd». All'interno, una pubblicità del Crossroads Health Center: «Vostro figlio non rispetta quanto gli viene assegnato e non finisce i compiti? Conoscete qualche scolaro o uno studente che abbia difficoltà a rimanere seduto o a fare la coda? Vi trovate accanto a un bambino che si agita, corre, salta ed è sempre in movimento? Conoscete qualcuno che sembra avere l'Adhd e vorrebbe un aiuto per la diagnosi? Chiamate questo numero.» Presso lo sportello informazioni, chiediamo a partire da quale età, nella regione, si può diagnosticare un bambino iperattivo: «A partire dai 18 mesi», ci risponde il medico di turno.

Nella sala riunioni della Kentucky Valley Educational Cooperative (50.000 allievi, 2.900 professori), la vicedirettrice Dessie Bowling ha convocato otto persone per rispondere alle nostre domande sull'epidemia locale di Adhd. «Fra i venti alunni della mia classe, racconta Emily K., professoressa in un grande liceo della regione, probabilmente un 30% presenta un deficit dell'attenzione, con o senza iperattività. Insegno qui da cinque anni ed è sempre stato così. Credo che tutti lo ritengano normale. Almeno la metà dei miei alunni non vive più con i genitori a causa degli oppioidi o di altre droghe, e vive con i nonni o famiglie adottive. Questo è il vero problema, nella mia classe.»

Prescrizioni «a partire dai 4 anni, se occorre»

In questa regione minata dal declino dell'industria del carbone e dal flagello della droga (essenzialmente oppiacei, metanfetamina e cocaina), gli insegnanti fanno quello che possono. «Cerchiamo di indirizzare i bambini che si distraggono facilmente al laboratorio di realtà virtuale o a quello di falegnameria, spiega Bowling. Quando costruiscono droni o stampano oggetti in 3D, non hanno alcun problema a concentrarsi. Forse semplicemente sono allievi che si trovano più a proprio agio con un motore o uno schema di montaggio che con carta e penna. Spingiamo i professori a dotare la classe di grossi palloni, sedie alte per chi vuole stare in piedi, sedie a dondolo. Soluzioni che possono evitare la somministrazione di cure farmacologiche.»

In questi venti anni, la scuola statunitense è stata oggetto di due riforme di seguito che hanno aumentato la concorrenza fra istituti, allievi, professori. No child left behind («Nessun bambino lasciato lungo il cammino»), una legge votata durante la presidenza di George W. Bush, e Race to the top («Corsa verso la cima»), un programma introdotto durante la presidenza di Barack Obama, hanno aggravato le disuguaglianze scolastiche. La scuola è forse diventata così dura che si devono drogare gli allievi affinché riescano a seguire il ritmo? «Occorre prepararli



EMANUELE SARACINO *Bubbles*

a essere adulti, membri produttivi della società, risponde Emily K. Il problema principale è che, il lunedì mattina, alcuni allievi non hanno preso il farmaco durante tutto il week-end. Iniziano la settimana agitatissimi e bisogna arrivare a martedì perché siano di nuovo operativi.»

In alto, su una montagna carbonifera, nel Primary Care Center di Hazard, il più grande della contea, la pediatra Molly O'Rourke ci apre la porta del suo studio medico. «Guardi la mia agenda: il giovedì è un giorno davvero pieno. Su ventisei pazienti, dodici sono qui per l'iperattività o per disturbi dell'attenzione. Vogliono la ricetta mensile. A volte si tratta della metà delle persone che vengono da me.» Per stabilire una diagnosi di Adhd, O'Rourke fa compilare un questionario, il Vanderbilt Adhd Diagnostic Rating Scale (Vadrs). «È soggettivo, spiega. I genitori lo compilano in funzione del comportamento dei propri figli. Se hanno gli stessi sintomi a scuola e a casa, allora si pensa al farmaco.» Il formulario comprende 47 domande. Le risposte possibili vanno da 0 («mai») a 3 («molto spesso»).

Come per il Dsm (manuale diagnostico dei disturbi mentali), si barrano le caselle e, a partire da un certo numero di punti, si viene considerati «iperattivi» o semplicemente «non attenti». Esempi: «Parla troppo.» «Dimentica spesso quello che deve fare.» «Fa fatica a organizzare i compiti.» «Interrompe sovente gli altri.» «Tende a innervosirsi.» «È già scappato di notte.» «Ha già aggredito qualcuno sessualmente.» «Litiga con gli adulti.» Le domande sono varie, ma sono tutte incentrate sulla capacità dei bambini di recare fastidio. O'Rourke prescrive Ritalin, Concerta, Focalin, Adderall o Vyvanse, «a partire dai 4 anni, se occorre. Ogni mese esce un nuovo farmaco», esclama.

L'ultimo nato, Adhansia, è stato messo a punto da Purdue Pharma, il laboratorio dell'OxyContin, considerato il principale responsabile della crisi degli oppioidi (400mila morti in venti anni) (11). «Vengo da un programma nel quale si cerca di abbassare le dosi, favorire le terapie comportamentali, smettere l'assunzione dei farmaci, prosegue O' Rourke. Il mio obiettivo è che riescano a essere dei bambini, giocare e imparare. Non ho mai visto effetti negativi nel lungo periodo, a eccezione di una crescita ansiosa. Il problema maggiore sarebbe la dipendenza, soprattutto per gli adolescenti, e la rivendita del farmaco.» Secondo la pediatra, «la televisione è la principale responsabile dell'Adhd. È la prima baby-sitter del paese.» Nella sala d'attesa, Jayden, 12 anni, «non sta fermo un attimo». Diagnosticato come iperattivo, è sotto farmaci psicotropi da quattro anni. Sua madre Tasha commenta: «Quando non li

prende è insopportabile.» La scuola? «Penso che sia noiosa, risponde Jayden. Leggere è noioso. Rimanere seduti tutto il giorno è noioso. Preferisco giocare a baseball con mio padre, o a Fortnite, Worlds of Warcraft o Nba 2K [videogiochi] con i miei amici.»

Torniamo in Francia. Nell'ufficio del dottor Wahl, Claire Leblon parla al medico con franchezza. «Diciamolo: il Ritalin è per la tranquillità della scuola. Infatti durante il week-end o le vacanze estive, non glielo diamo...» Wahl sembra irritato. Si raddrizza sulla poltrona: «Guardi, francamente non sono d'accordo con lei. L'obiettivo primario è permettere a bambini che soffrono di stare meglio, perché chi è affetto da Adhd è in uno stato di conflittualità permanente. Viene rimproverato di giorno dagli insegnanti e di sera dai genitori!» Leblon risponde: «Questo è vero, dottore. Ne abbiamo abbastanza di dover reagire continuamente così!» Lo psichiatra infantile ripete la sua dottrina: «È un disturbo biologico. In questa faccenda, voi non siete né buoni né cattivi. Non siete più responsabili del suo Adhd di quanto non lo siano i miei genitori della mia miopia.» Niels scoppia a ridere. Il dottore riprende: «Niels non ha un Adhd puro.» Eppure, ha ingurgitato sostanze psicotrope per quattro anni e oggi prova quelli che si potrebbero definire episodi di grande angoscia.

Angoscia e tentativi di suicidio

Le lunghe ore passate a guardare «Enquête exclusive», «Enquête d'action», «Enquête sous haute tension» e altre trasmissioni in forma di «reportage» sulle forze dell'ordine spiegherebbero il suo timore per un improbabile rapimento? «Purtroppo, il Ritalin cura solo l'Adhd, non l'ansia», precisa Wahl. Niels non è il primo caso di minore sotto stimolanti che viene preso da inquietudine e da angosce. Gab T., un adolescente di 14 anni, ha tentato il suicidio dopo aver iniziato ad assumere l'Adderall a 7 anni. Trey McCormick, 23 anni, lavoratore nel campo alberghiero e della ristorazione nel Kentucky, quando era più giovane di età faceva credere alla madre che prendeva le compresse ma le gettava nelle toilette, talmente gli davano «idee nere, opprimenti, visioni orribili». E l'operaio edile Joe Dazier non ha parole abbastanza forti contro il «veleno» che i genitori lo hanno «obbligato» a prendere.

Secondo uno studio pubblicato nel 2019, i bambini sotto psicostimolanti corrono il doppio del rischio di sviluppare psicosi (12). Ma il dottor Wahl non è affatto convinto: «Il Ritalin riduce

il rischio di dipendenze e, in linea di massima, limita il rischio di psicosi, perché i risultati scolastici migliorano.» Insomma: se i voti sono buoni, missione compiuta e medico soddisfatto.

Leblon ci riceve nella sua casa a Saint-Prix, nel nord di Parigi. «Quando mi ha prescritto il Ritalin, il dottor Wahl mi ha detto: “Non legga il foglietto illustrativo, la lista di effetti secondari la può impressionare!” Visto che è uno specialista importante, ho seguito il suo consiglio. Ma quello che ho letto altrove, in particolare sulla prossimità con le anfetamine, mi ha inquietata. Dopo queste scoperte, e constatando che il Ritalin non faceva più alcun effetto, abbiamo deciso di smettere. L'ha preso per quattro anni; è tanto. L'anno prossimo andrà al college. Aspettiamo.»

Nella sala da pranzo, Leblon scuote il tubetto di Ritalin, e ci allunga il bugiardino perfettamente piegato di quella che con ironia chiama «la pillolina magica». Al capitolo 4, sono elencati almeno 70 «eventuali effetti indesiderabili», dai «più frequenti» (palpitazioni, battito cardiaco irregolare, mal di testa, nervosismo, insonnie, ecc.) ai «frequentissimi» (diminuzione dell'appetito, febbre, perdita di capelli, ecc.) e ai «molto rari» (crisi cardiaca, tentativo di suicidio, pensieri anomali, assenza di sentimenti ed emozioni...). Alla voce «Altri effetti indesiderabili» si legge, fra l'altro: «Dipendenza dal farmaco.»

Niels, divertente e giocoso, racconta di essere davvero contento di aver smesso di prendere questa pillola che gli «impediva di dormire» e gli faceva «battere il cuore troppo velocemente». «Ero sicura che fosse iperattivo», confida la madre, che si chiede: «Ma non ci vergogniamo, a dare una droga ai nostri bambini?»

JULIEN BRYGO

(1) Si legga Gérard Pommier, «La medicalizzazione dell'esperienza umana», *Le Monde diplomatique/il manifesto*, marzo 2018.

(2) Cfr. «Méthylphénidate (Ritaline): dernier choix dans l'hyperactivité», *Prescrire*, 1 agosto 2017, www.prescrire.org

(3) Damien Mascret, «La Ritaline, entre sous-prescription et abus», *Le Figaro*, Parigi, 16 maggio 2017.

(4) La rivista *Prescrire*, che denuncia l'«assenza di studi a medio e lungo termine sugli effetti del metilfenidato», ha pubblicato numerosi articoli per attirare l'attenzione sugli effetti indesiderabili di questa sostanza psicotropa, «*banalizzata malgrado i pericoli*» e la cui prescrizione è vicina a un «*doping di bambini*» (*Prescrire*, n. 406, Parigi, agosto 2017).

(5) Cifre del 2011. «State profiles – Diagnosis and medication treatment among children ages 4-17 years (survey data)», Centers for Disease Control and Prevention, www.cdc.gov

(6) Amelia M. Arria e Robert L. DuPont, «Prescription stimulant use and misuse: Implications for responsible prescribing practices», *The American Journal of Psychiatry*, vol. 175, n. 8, Washington, Dc, agosto 2018.

(7) Alan De Santis e Audrey Curtis Hane, «“Adderall is definitely not a drug”: Justifications for the illegal use of Adhd stimulants», *Informa Healthcare*, 2010, www.uky.edu

(8) I nomi sono stati cambiati.

(9) Il *Diagnostic and Statistical Manual of Mental Disorders* (Dsm), realizzato dall'Associazione americana di psichiatria, stabilisce i criteri di diagnosi dei disturbi mentali, fra i quali l'Adhd.

(10) Nel 2015, in occasione di un audit del laboratorio Trusdail, gli ispettori hanno scoperto che erano stati nascosti sette casi di cavalli positivi al metilfenidato (dopante di categoria 1) nel campionato equestre.

(11) *Le Monde*, 16 ottobre 2019. L'Adhansia è uno psicostimolante i cui effetti durano sedici ore, il doppio del Ritalin. Si legga Maxime Robin, «Overdose da ricetta», *Le Monde diplomatique/il manifesto*, febbraio 2018.

(12) Edith Bracho-Sanchez, «Young people on amphetamines for Adhd have twice the psychosis risk compared to other stimulants, study says», Cable News Network (Cnn), 20 marzo 2019, <https://edition.cnn.com>

(Traduzione di Marianna De Dominicis)

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