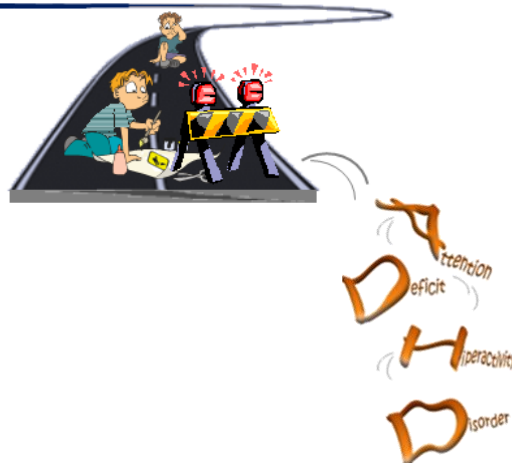




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Acta Paediatr Int J Paediatr. 2017.

BIRTH ASPHYXIA MEASURED BY THE pH VALUE OF THE UMBILICAL CORD BLOOD MAY PREDICT AN INCREASED RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Mikkelsen SH, Olsen J, Bech BH, et al.

Aim: Although birth asphyxia is a major risk factor for neonatal and childhood morbidity and mortality, it has not been investigated much in relation to attention deficit hyperactivity disorder (ADHD). We examined whether birth asphyxia measured by the pH of the blood in the umbilical artery cord was associated with childhood ADHD.

Method: A population-based cohort of 295 687 children born in Finland between 1991 and 2002 was followed until December 31, 2007. ADHD was identified by the International Classification of Diseases, 10th edition, as a diagnosis of hyperkinetic disorder. We examined the risk of ADHD with varying pH values using Cox regression, taking time trends into consideration.

Results: When compared to the reference group, a pH value below 7.10 was significantly associated with an increased risk of ADHD. The strongest risks were observed among children with a pH value <7.15 and a gestational age of <32 weeks. The pH value did not contribute much to the risk among children with an Apgar score of 0-3.

Conclusion: Birth asphyxia, defined by low pH value, may predict an increased risk of ADHD in childhood. The association between the pH value and ADHD was homogenous when stratified by gestational age and the Apgar score

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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.

ADHD Atten Deficit Hyperact Disord. 2017;1-8.

RELATIONSHIP OF SELF-MUTILATIVE BEHAVIOUR WITH HISTORY OF CHILDHOOD TRAUMA AND ADULT ADHD SYMPTOMS IN A SAMPLE OF INPATIENTS WITH ALCOHOL USE DISORDER .

Evren C, Umut G, Evren B.

The aim of the present study was to evaluate relationship of self-mutilative behaviour (SMB) with the severity of childhood trauma and adult attention-deficit/hyperactivity disorder (ADHD) symptoms in a sample of inpatients with alcohol use disorder (AUD). Participants included 188 inpatients with AUD. Participants were evaluated with the Self-mutilative Behaviour Questionnaire, the Childhood Trauma Questionnaire (CTQ-28) and the Adult ADD/ADHD DSM-IV Based Diagnostic Screening and Rating Scale (Adult ADHD Scale). Among inpatients with AUD those who have a history of SMB constituted the SMB group (n = 57, 30.3%), and those without a history of SMB constituted the group without SMB (n = 131, 69.7%). Risk of high ADHD risk was 2.5 times higher among those with SMB. Adult ADHD Scale and CTQ-28 scores were also higher in the group with SMB. In the first backward logistic regression model, the severity of ADHD symptoms predicted the presence of SMB, together with the severity of childhood trauma, whereas in the second model, physical neglect and inattentive (IN) dimension of ADHD predicted the presence of SMB. These findings suggest that the higher severity of physical neglect and adult IN dimension of ADHD may be related to SMB among inpatients with AUD

ADHD Atten Deficit Hyperact Disord. 2017;1-27.

PERCEPTION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Fuermaier ABM, et al.

A large body of research demonstrated that individuals with attention deficit hyperactivity disorder (ADHD) suffer from various neuropsychological deficits. In contrast, less is known and only divergent evidence exists on perceptual functions of individuals with ADHD. This is problematic as neuropsychological and perceptual functions are closely interrelated and are often difficult to disentangle in behavioral assessments. This study presents the conduct and results of a systematic literature review on perceptual functions in children and adults with ADHD. This review considers studies using psychophysical methods (objective measurements) and self- and informant reports (subjective measurements). Results indicate that individuals with ADHD have altered perceptual functions in various domains as compared to typically developing individuals. Increased perceptual functions in individuals with ADHD were found with regard to olfactory detection thresholds, whereas reduced perceptual functions were evident for aspects of visual and speech perception. Moreover, individuals with ADHD were found to experience discomfort to sensory stimuli at a lower level than typically developing individuals. Alterations of perceptual functions in individuals with ADHD were shown to be moderated by various factors, such as pharmacological treatment, cognitive functions, and symptom severity. We conclude by giving implications for daily life functioning and clinical practice

ADHD Atten Deficit Hyperact Disord. 2017;1-6.

RELATIONSHIP BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND SEDENTARY BEHAVIOR IN ADOLESCENCE: A CROSS-SECTIONAL STUDY.

Suchert V, Pedersen A, Hanewinkel R, et al.

Existing studies reveal that high levels of sedentary behavior are associated with more inattention and hyperactivity problems. Since most previous studies used screen time as an indicator of sedentary behavior and assessed symptoms of attention-deficit/hyperactivity disorder (ADHD) by short screening measures which do not allow to distinguish between subtypes of ADHD, the current study aimed to investigate association between different types of sedentary behavior and symptoms and subtypes of ADHD. The current cross-sectional study analyzed data of 913 students (46.1% girls) aged 13–17 years (M = 15.0, SD = 0.6). Using a self-administered questionnaire, screen-based and non-screen-based sedentary behavior and ADHD symptoms were assessed. Linear and logistic regression analyses were conducted. All analyses were adjusted for age, gender, moderate to vigorous physical activity and body mass index. Screen time was

related to the total ADHD score ($p < 0.001$) as well as to the subscales inattention ($p \leq 0.016$) and hyperactivity/impulsivity ($p \leq 0.008$). Sedentary time without screens was virtually not associated with ADHD. As far as ADHD symptoms are considered as a correlate of sedentary behavior, the type of activity which is pursued sedentarily seems to matter: screen time, but not other non-screen-based sedentary activities should be considered as being a risk factor for ADHD

Am J Hum Genet. 2017 Apr;100:650-58.

DE NOVO TRUNCATING MUTATIONS IN THE LAST AND PENULTIMATE EXONS OF PPM1D CAUSE AN INTELLECTUAL DISABILITY SYNDROME.

Jansen S, Geuer S, Pfundt R, et al.

Intellectual disability (ID) is a highly heterogeneous disorder involving at least 600 genes, yet a genetic diagnosis remains elusive in approximately 35%-40% of individuals with moderate to severe ID. Recent meta-analyses statistically analyzing de novo mutations in >7,000 individuals with neurodevelopmental disorders highlighted mutations in PPM1D as a possible cause of ID. PPM1D is a type 2C phosphatase that functions as a negative regulator of cellular stress-response pathways by mediating a feedback loop of p38-p53 signaling, thereby contributing to growth inhibition and suppression of stress-induced apoptosis. We identified 14 individuals with mild to severe ID and/or developmental delay and de novo truncating PPM1D mutations. Additionally, deep phenotyping revealed overlapping behavioral problems (ASD, ADHD, and anxiety disorders), hypotonia, broad-based gait, facial dysmorphisms, and periods of fever and vomiting. PPM1D is expressed during fetal brain development and in the adult brain. All mutations were located in the last or penultimate exon, suggesting escape from nonsense-mediated mRNA decay. Both PPM1D expression analysis and cDNA sequencing in EBV LCLs of individuals support the presence of a stable truncated transcript, consistent with this hypothesis. Exposure of cells derived from individuals with PPM1D truncating mutations to ionizing radiation resulted in normal p53 activation, suggesting that p53 signaling is unaffected. However, a cell-growth disadvantage was observed, suggesting a possible effect on the stress-response pathway. Thus, we show that de novo truncating PPM1D mutations in the last and penultimate exons cause syndromic ID, which provides additional insight into the role of cell-cycle checkpoint genes in neurodevelopmental disorders

Am J Psychiatry. 2017 Apr;174:341-48.

THE RISK OF TREATMENT-EMERGENT MANIA WITH METHYLPHENIDATE IN BIPOLAR DISORDER.

Viktorin A, Ryden E, Thase ME, et al.

OBJECTIVE: The authors sought to determine the risk of treatment-emergent mania associated with methylphenidate, used in monotherapy or with a concomitant mood-stabilizing medication, in patients with bipolar disorder.

METHOD: Using linked Swedish national registries, the authors identified 2,307 adults with bipolar disorder who initiated therapy with methylphenidate between 2006 and 2014. The cohort was divided into two groups: those with and those without concomitant mood-stabilizing treatment. To adjust for individual-specific confounders, including disorder severity, genetic makeup, and early environmental factors, Cox regression analyses were used, conditioning on individual to compare the rate of mania (defined as hospitalization for mania or a new dispensation of stabilizing medication) 0-3 months and 3-6 months after medication start following nontreated periods.

RESULTS: Patients on methylphenidate monotherapy displayed an increased rate of manic episodes within 3 months of medication initiation (hazard ratio=6.7, 95% CI=2.0-22.4), with similar results for the subsequent 3 months. By contrast, for patients taking mood stabilizers, the risk of mania was lower after starting methylphenidate (hazard ratio=0.6, 95% CI=0.4-0.9). Comparable results were observed when only hospitalizations for mania were counted.

CONCLUSIONS: No evidence was found for a positive association between methylphenidate and treatment-emergent mania among patients with bipolar disorder who were concomitantly receiving a mood-stabilizing

medication. This is clinically important given that up to 20% of people with bipolar disorder suffer from comorbid ADHD. Given the markedly increased hazard ratio of mania following methylphenidate initiation in bipolar patients not taking mood stabilizers, careful assessment to rule out bipolar disorder is indicated before initiating monotherapy with psychostimulants

Am J Med Genet Part B Neuropsychiatr Genet. 2017.

GENETIC AND ENVIRONMENTAL CONTRIBUTIONS TO THE ASSOCIATION BETWEEN ADHD AND AFFECTIVE PROBLEMS IN EARLY CHILDHOOD-A SWEDISH POPULATION-BASED TWIN STUDY.

Rydell M, Taylor MJ, Larsson H.

Few twin studies have explored the relative contribution of genetic and environmental factors to the association between attention deficit hyperactivity disorder (ADHD) and affective problems, and no study has focused on preschool children. We used the classical twin design to explore the genetic and environmental overlap between ADHD symptoms and affective problems in preschool children, based on 879 five-year-old twin pairs born in Sweden 2004-2005. Questionnaire-based parent-ratings were used to measure ADHD symptoms and affective problems. A bivariate twin design was used to decompose variance in ADHD and affective problems into genetic and environmental components, and to test the degree to which these components overlapped across the two traits. Our results showed that there was a significant correlation of 0.34 (95% Confidence Interval [CI] 0.29-0.38) between ADHD and affective problems. This correlation was mostly explained by additive genetic factors (64%, 95%CI 37-93%), and to a lesser extent by shared environmental factors (35%, 95%CI 10-59%). Nonshared environmental factors did not contribute to the correlation between ADHD and affective problems (0%, 95%CI -9 to 10%). These findings show that there is a significant association between ADHD and affective problems in preschool children that is mostly explained by genetic influences. This adds important knowledge about the etiology of both ADHD and affective problems by indicating that these phenotypes are linked from as early as preschool years. This also needs to be taken into consideration when diagnosing young children and clinicians should consider assessing both affective problems and ADHD if one is present

Am J Psychiatry. 2017;174:387-96.

IDENTIFICATION OF TWO HERITABLE CROSS-DISORDER ENDOPHENOTYPES FOR TOURETTE SYNDROME.

Darrow SM, Hirschtritt ME, Davis LK, et al.

Objective: Phenotypic heterogeneity in Tourette syndrome is partly due to complex genetic relationships among Tourette syndrome, obsessive-compulsive disorder (OCD), and attention deficit hyperactivity disorder (ADHD). Identifying symptom-based endophenotypes across diagnoses may aid gene-finding efforts.

Method: Assessments for Tourette syndrome, OCD, and ADHD symptoms were conducted in a discovery sample of 3,494 individuals recruited for genetic studies. Symptom-level factor and latent class analyses were conducted in Tourette syndrome families and replicated in an independent sample of 882 individuals. Classes were characterized by comorbidity rates and proportion of parents included. Heritability and polygenic load associated with Tourette syndrome, OCD, and ADHD were estimated.

Results: The authors identified two cross-disorder symptom-based phenotypes across analyses: symmetry (symmetry, evening up, checking obsessions; ordering, arranging, counting, writing-rewriting compulsions, repetitive writing tics) and disinhibition (uttering syllables/words, echolalia/palilalia, coprolalia/copropraxia, and obsessive urges to offend/mutilate/ be destructive). Heritability estimates for both endophenotypes were high and statistically significant (disinhibition factor=0.35, SE=0.03; symmetry factor=0.39, SE=0.03; symmetry class=0.38, SE=0.10). Mothers of Tourette syndrome probands had high rates of symmetry (49%) but not disinhibition (5%). Polygenic risk scores derived from a Tourette syndrome genome-wide association study (GWAS) were significantly associated with symmetry, while risk scores derived from an OCD GWAS were not. OCD polygenic risk scores were significantly associated with disinhibition, while Tourette syndrome and ADHD risk scores were not.

Conclusions: The analyses identified two heritable endophenotypes related to Tourette syndrome that cross traditional diagnostic boundaries. The symmetry phenotype correlated with Tourette syndrome polygenic load and was present in otherwise Tourette-unaffected mothers, suggesting that this phenotype may reflect additional Tourette syndrome (rather than OCD) genetic liability that is not captured by traditional DSM-based diagnoses

Am J Addict. 2017;26:240-41.

ATTENTION DEFICIT HYPERACTIVITY DISORDER AND SUBSTANCE USE DISORDERS ASSOCIATION: A FAMILIAL RISK ANALYSIS.

Yule A, Martelon MK, Faraone S, et al.

This research examines the familial relationship between substance use disorders (SUDs) and attention deficit hyperactivity disorder (ADHD) through two longitudinal case controlled family studies of ADHD. There are various pathways involved in the transmission of SUD in ADHD families including: the risk associated with SUD itself, the risk conferred by ADHD, and the risk conferred by the cosegregation of ADHD and SUD. The presence of multiple etiological pathways emphasizes the complexity of the risk for SUD in individuals with ADHD and their family members, and begins to explain the elevated risk of SUDs in youth with ADHD. Since ADHD typically onsets at least a decade before the onset of SUD, ADHD children and their siblings should benefit from preventive and early intervention strategies aimed at mitigating this risk. Background: A significant and bidirectional association between ADHD and SUDs has been well documented in clinical and epidemiological studies. While these findings suggest that the two disorders are linked, the nature of the association remains unclear. To date there have been a limited number of family studies investigating the relationship between ADHD and SUD. The results of this familial study will help clinicians understand why ADHD is a risk factor for developing a SUD and may lead to preventive and early intervention strategies to decrease the risk for developing a SUD in ADHD children and their siblings. Methods: Subjects were derived from two longitudinal case-control family studies of probands aged 6 to 17 years with and without DSM-III-R ADHD of both sexes and their first degree relatives followed from childhood onto young adult years. Cox proportional hazard models were used to estimate rates of ADHD and SUDs (any SUD, alcohol dependence, and drug dependence). Logistic regression was used to test both cosegregation and assortative mating. Results: Our sample included 404 probands (ADHD: 112 boys and 96 girls; Control: 105 boys and 91 girls) and their 1,336 relatives. ADHD and SUDs (any SUD, alcohol dependence, and drug dependence) in the proband were consistently associated with a significantly increased risk for the same and the opposite substance use disorder (drug or alcohol) in relatives. There was also evidence that even in the absence of a SUD in the proband, ADHD by itself increased the risk of SUDs in relatives. Proband sex did not moderate the familial relationship between ADHD and SUDs. There was evidence of cosegregation between ADHD and SUD. Conclusions: Findings indicate that various independent pathways are involved in the transmission of SUD in ADHD and that these risks were not moderated by proband sex. Educational Objectives: At the conclusion of this activity, participants should be able to: 1. Summarize the familial relationship between ADHD and SUD 2. Assess the impact of proband sex on the familial relationship between ADHD and SUD

Appl Neuropsychol Child. 2017 Apr;6:172-79.

COMPARISON BETWEEN OBJECTIVE MEASURES AND PARENTAL BEHAVIORAL RATING SCALES OF MEMORY AND ATTENTION IN PEDIATRIC ENDOCRINOLOGY PATIENTS.

Limbers C, Young D, Jernigan S, et al.

Behavioral rating scales represent one potential method for screening of cognitive functioning in routine clinical care. It is not yet known if objective performance based measures and behavioral rating scales of cognitive functioning completed by parents yield similar information in pediatric endocrinology patients. The purpose of the present study was to evaluate the associations between performance-based measures and behavioral rating scales of memory and attention/concentration completed by parents of pediatric patients with Type 1 Diabetes or obesity. The sample consisted of 73 pediatric patients with Type 1 Diabetes or

obesity (BMI > 95th percentile) ages 6-16 years (mean age = 12.29 years) referred to an outpatient pediatric endocrinology clinic. Youth were administered the Wide Range Assessment of Memory and Learning (WRAML-2). Parents completed the Child Behavior Checklist (CBCL) and the PedsQL Cognitive Functioning Scale. Pearson's Product Moment Correlations were examined among the performance-based measures and behavioral rating scales. RESULTS: All intercorrelations between the performance-based measures and behavioral rating scales completed by parents were in the small range. The only statistically significant ($P < 0.05$) and approaching medium correlation was between the PedsQL Cognitive Functioning Scale and WRAML-2 Verbal Memory Index ($r = 0.28$). On behavioral rating scales and performance-based measures of visual memory and attention/concentration, our sample exhibited greater difficulties than healthy youth from previously published data ($P < 0.05$). One possible explanation for our findings is that behavioral rating scales of attention/concentration and memory completed by parents measure different aspects of cognitive functioning than performance based measures in pediatric patients with Type 1 Diabetes or obesity

Arch Clin Neuropsychol. 2017 Mar;32:168-83.

NORMATIVE DATA FOR A COMPREHENSIVE NEUROPSYCHOLOGICAL TEST BATTERY USED IN THE ASSESSMENT OF SPORTS-RELATED CONCUSSION.

Merritt VC, Meyer JE, Cadden MH, et al.

Objective: The use of normative data is a hallmark of the neuropsychological assessment process. Within the context of sports-related concussion, utilizing normative data is especially essential when individualized baseline data are unavailable for comparison. The primary purpose of this study was to establish normative data for a comprehensive neuropsychological test battery used in the assessment of sports-related concussion. A secondary aim was to provide normative data for pertinent demographic variables relevant to the assessment of college athletes, including sex, previous head injuries (PHI), and history of attention deficit hyperactivity disorder (ADHD)/learning disability (LD).

Method: Participants included male and female college athletes ($N = 794$) who were involved in a concussion management program at an NCAA Division I university between 2002 and 2015. Athletes were administered a comprehensive neuropsychological test battery at baseline designed to assess the following cognitive domains: learning and memory, attention and concentration, processing speed, and executive functioning. The test battery primarily comprises paper-and-pencil measures.

Results: Normative data are presented for the overall athlete sample. Additional sub-norms are then provided for specified demographic populations (i.e., sex, PHIs, and history of ADHD/LD). Findings indicate that there are mild cognitive differences between men and women, as well as between those athletes with and without a history of ADHD/LD. Given these findings, additional norms are provided for men and women with and without a history of ADHD/LD.

Conclusions: In the absence of baseline testing, the normative data presented here can be used clinically to assess athletes' cognitive functioning post-concussion

Asian J Psychiatry. 2017;28:73-77.

THYROID AND CORTISOL HORMONES IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CASE-CONTROL STUDY.

Kuppili PP, Pattanayak RD, Sagar R, et al.

Aim There is paucity of research in the putative role of hormonal biomarkers in Attention Deficit Hyperactivity Disorder (ADHD). The current study aimed to analyze the clinical profile, socio-demographic status, co-morbidity, hormonal biomarkers namely Thyroid hormones and Cortisol in children with ADHD and compare them with healthy controls and to explore the association of the hormonal biomarkers with severity of ADHD.

Methods Thirty children with DSM-IV TR diagnosis of ADHD were assessed using semi structured proforma, Conners' Parent Rating Scale revised short (CPRS – RS), Mini international neuropsychiatric interview for children and adolescents and Childrens' Global Assessment Scale as well as serum levels of total Triiodothyronine (T3), total Thyroxine (T4), Thyroid Stimulating Hormone (TSH) and Cortisol using chemiluminescent immunometric assay and compared with 30 age- and gender -matched controls.

Results The typical profile of cases of ADHD was of a male with mean age of 9.47 years (S.D.=2.43) belonging to Hyperactive subtype of ADHD. Serum T4 was significantly lower in cases compared to controls. No significant difference was found in serum T3, TSH and Cortisol levels. No significant correlation between the CPRS R-S scores and the hormonal biomarkers.

Conclusions There is need for exploration of Serum T4 as putative biomarker for ADHD with replication in future studies. It may also be important to report the negative finding of Cortisol as a biomarker of ADHD in the context of effective utilization of resources for research with special relevance to resource deficit developing countries

Autism Res. 2017.

AUDITORY SPATIAL ATTENTION TO SPEECH AND COMPLEX NON-SPEECH SOUNDS IN CHILDREN WITH AUTISM SPECTRUM DISORDER.

Soskey LN, Allen PD, Bennetto L.

One of the earliest observable impairments in autism spectrum disorder (ASD) is a failure to orient to speech and other social stimuli. Auditory spatial attention, a key component of orienting to sounds in the environment, has been shown to be impaired in adults with ASD. Additionally, specific deficits in orienting to social sounds could be related to increased acoustic complexity of speech. We aimed to characterize auditory spatial attention in children with ASD and neurotypical controls, and to determine the effect of auditory stimulus complexity on spatial attention. In a spatial attention task, target and distractor sounds were played randomly in rapid succession from speakers in a free-field array. Participants attended to a central or peripheral location, and were instructed to respond to target sounds at the attended location while ignoring nearby sounds. Stimulus-specific blocks evaluated spatial attention for simple non-speech tones, speech sounds (vowels), and complex non-speech sounds matched to vowels on key acoustic properties. Children with ASD had significantly more diffuse auditory spatial attention than neurotypical children when attending front, indicated by increased responding to sounds at adjacent non-target locations. No significant differences in spatial attention emerged based on stimulus complexity. Additionally, in the ASD group, more diffuse spatial attention was associated with more severe ASD symptoms but not with general inattention symptoms. Spatial attention deficits have important implications for understanding social orienting deficits and atypical attentional processes that contribute to core deficits of ASD

BMC Psychiatry. 2017;17.

DOES A CHILD'S LANGUAGE ABILITY AFFECT THE CORRESPONDENCE BETWEEN PARENT AND TEACHER RATINGS OF ADHD SYMPTOMS?

Gooch D, Maydew H, Sears C, et al.

Background: Rating scales are often used to identify children with potential Attention-Deficit/Hyperactivity Disorder (ADHD), yet there are frequently discrepancies between informants which may be moderated by child characteristics. The current study asked whether correspondence between parent and teacher ratings on the Strengths and Weakness of ADHD symptoms and Normal behaviour scale (SWAN) varied systematically with child language ability.

Method: Parent and teacher SWAN questionnaires were returned for 200 children (aged 61-81 months); 106 had low language ability (LL) and 94 had typically developing language (TL). After exploring informant correspondence (using Pearson correlation) and the discrepancy between raters, we report inter-class correlation coefficients, to assess inter-rater reliability, and Cohen's kappa, to assess agreement regarding possible ADHD caseness.

Results: Correlations between informant ratings on the SWAN were moderate. Children with LL were rated as having increased inattention and hyperactivity relative to children with TL; teachers, however, rated children with LL as having more inattention than parents. Inter-rater reliability of the SWAN was good and there were no systematic differences between the LL and TL groups. Case agreement between parent and teachers was fair; this varied by language group with poorer case agreement for children with LL.

Conclusion: Children's language abilities affect the discrepancy between informant ratings of ADHD symptomatology and the agreement between parents and teachers regarding potential ADHD caseness. The assessment of children's core language ability would be a beneficial addition to the ADHD diagnostic process

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BMC Psychiatry. 2017 Mar;17.

ALLERGIC DISEASES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Miyazaki C, Koyama M, Ota E, et al.

Background: Reports of frequent manifestation of allergic diseases in children with attention deficit hyperactivity disorder (ADHD) have been the subject of mounting clinical interest. However, evidence supporting the association between ADHD and allergies is inconsistent and has yet to be systematically reviewed. The objective of this study was to compile and assess available studies on the association between ADHD and allergic diseases in children.

Methods: A comprehensive search using MEDLINE, EMBASE, the Cochrane library, and CINAHL databases was completed in 23 November 2015. The inclusion criteria for studies were that the research assessed allergic diseases in children, 18 years of age and younger, with a diagnosis of ADHD and that a distinct comparison group was incorporated. Any comparative studies, encompassing both randomized controlled trials and observational studies, were considered for inclusion. Two review authors independently assessed the quality of the selected studies by the use of validated assessment tools, performed data extraction and conducted meta-analysis according to Cochrane Collaboration guidelines.

Results: Five eligible studies were included in this systematic review. Of these studies, three were case-control and two were cross sectional studies. A majority of information from the five studies was classified as having low or unclear risk of bias. The meta-analysis showed an association between children with ADHD and asthma compared with the control groups (OR: 1.80, 95% CI: 1.57-2.07; five studies, low quality of evidence), but did not indicate an association between food allergy and ADHD (OR: 1.13, 95% CI: 0.88-1.47; three studies very low quality of evidence). The odds of experiencing allergic rhinitis, atopic dermatitis, and allergic conjunctivitis were slightly higher in children with ADHD compared with control groups, though a substantial statistical heterogeneity was notable in the overall effect estimates.

Conclusions: The findings from this review and meta-analysis show that children with ADHD are more likely to have asthma, allergic rhinitis, atopic dermatitis, and allergic conjunctivitis than their counterparts. Interventions including strategies for managing allergies in children with ADHD would be beneficial

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BMC Psychiatry. 2017;17.

THE INFLUENCE OF PARTICIPATION IN TARGET-SHOOTING SPORT FOR CHILDREN WITH INATTENTIVE, HYPERACTIVE AND IMPULSIVE SYMPTOMS - A CONTROLLED STUDY OF BEST PRACTICE.

Månsson AG, Elmose M, Dalsgaard S, et al.

Background: Practising target-shooting sport requires focused attention and motoric steadiness. A previous non-controlled pilot study suggests that children with impairing symptoms of attention-deficit/hyperactivity disorder (ADHD) benefit from participating in target-shooting sport in local shooting associations, as rated by parents and teachers. This study aims at examining if, and to which extent, target-shooting sport reduces parent- and teacher-reported severity of inattentiveness, hyperactivity, and impulsivity in children with attention difficulties, and if, and to which extent, target-shooting sport improves the children's wellbeing and quality of life.

Methods: A mixed method approach is applied. A non-blinded, waiting list controlled study is combined with a case study, consisting of interviews and observations. The intervention consists of children practising target-shooting sport, by attending a local shooting association, once a week for six months, during regular school hours. Data from questionnaires (ADHD-RS, SDQ, Kidscreen-27), as well as a computerized continued performance test (Qb test), measure the children's activity and attention. The study includes 50 children in an intervention group and 50 children in a waiting list control group. The Qb test collects data from

at least 20 children from the intervention group and at least 20 children from the waiting list control group. Data from the questionnaires and Qb-test is collected at baseline, and six months post intervention. In addition, a case study is carried out, consisting of interviews of at least five children from the intervention group, their parents, teachers and shooting instructors. Observations are carried out, when children are in school and while they are attending the local shooting association. The case study adds to an in-depth understanding of children's participation in target-shooting sports.

Discussion: At present, little is known about the effects and influence of practising target-shooting sport for children experiencing difficulties with inattentiveness, hyperactivity and impulsivity. This study is expected to contribute to an understanding of the influence of participating in target-shooting sports on inattentive, hyperactive and impulsive symptoms, and the effects on the children's psychological wellbeing and quality of life.

Trial registration: Current Controlled Trials NCT02898532. Retrospectively registered 14 September 2016

BMC Psychiatry. 2017;17.

WORKING MEMORY TRAINING IN CHILDREN WITH NEUROPSYCHIATRIC DISORDERS AND MILD TO BORDERLINE INTELLECTUAL FUNCTIONING, THE ROLE OF COACHING; A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL.

Roording-Ragelie S, Klip H, Buitelaar J, et al.

Background: Working memory training (WMT) has been shown to offer therapeutic benefits to both patients with Attention-Deficit Hyperactivity Disorder (ADHD) and patients with mild to borderline Intellectual Disabilities (MBID; $60 < IQ < 85$). However, robust evidence for transfer effects and treatment benefits of WMT over placebo training are lacking. Owing to the nature of double-blind research designs in RCTs, children have received non-specific coaching not based on their actual training performance. Active coaching based on individual training results (such as in clinical practice) might enhance the efficacy of Cogmed WMT. Furthermore, clinical experience and the general treatment approach to these vulnerable children has shown that the intensity and duration of WMT is often too stressful. This study therefore investigated the efficacy of a less intensive, but more prolonged Cogmed WMT (including active personalized coaching and feedback) in reducing behavioral symptoms and improving neurocognitive functioning and academic achievements in children with MBID and neuropsychiatric disorders.

Methods/design: A double-blind RCT with children (age 10.0-13.11) with neuropsychiatric disorders (ADHD and/or autism spectrum disorder (ASD)) and MBID ($IQ: 60 < IQ < 85$). Two groups (each $n = 26$) will receive Cogmed WMT (version R/M) at home or at school for 8 weeks, 4 days a week, at 30 min a day. One group will receive active personalized coaching and feedback based on their actual individual performance during Cogmed training. The other group will only receive general non-personalized coaching (i.e. no receive personalized coaching and feedback). Both groups will undergo a neurocognitive assessment (working memory, executive functioning, academic achievements) before and after training and complete several questionnaires (behavioral problems, parenting style) with a 6 months follow-up.

Discussion: This study will add to the literature since the role of coaching in Cogmed WMT has not been studied before. It will also provide opportunities to investigate an alternative version of WMT in a large group of vulnerable children, for whom few evidence-based treatments are available. Ultimately, this will allow us to advise mental health care professionals and special education schools about the use of this type of intervention for children with MBID and neuropsychiatric disorders.

Trial registration: Dutch Trial Register. NTR5223. Registration date 06-09-2015

BMJ Open. 2017;7.

DOES A BRIEF, BEHAVIOURAL INTERVENTION, DELIVERED BY PAEDIATRICIANS OR PSYCHOLOGISTS IMPROVE SLEEP PROBLEMS FOR CHILDREN WITH ADHD? PROTOCOL FOR A CLUSTER-RANDOMISED, TRANSLATIONAL TRIAL.

Sciberras E, Mulraney M, Heussler H, et al.

Introduction: Up to 70% of children with attention deficit/hyperactivity disorder (ADHD) experience sleep problems. We have demonstrated the efficacy of a brief behavioural intervention for children with ADHD in a

large randomised controlled trial (RCT) and now aim to examine whether this intervention is effective in real-life clinical settings when delivered by paediatricians or psychologists. We will also assess the costeffectiveness of the intervention. Methods and analysis: Children aged 5-12 years with ADHD (n=320) are being recruited for this translational cluster RCT through paediatrician practices in Victoria and Queensland, Australia. Children are eligible if they meet criteria for ADHD, have a moderate/severe sleep problem and meet American Academy of Sleep Medicine criteria for either chronic insomnia disorder or delayed sleep-wake phase disorder; or are experiencing sleep-related anxiety. Clinicians are randomly allocated at the level of the paediatrician to either receive the sleep training or not. The behavioural intervention comprises 2 consultations covering sleep hygiene and standardised behavioural strategies. The primary outcome is change in the proportion of children with moderate/severe sleep problems from moderate/severe to no/mild by parent report at 3 months postintervention. Secondary outcomes include a range of child (eg, sleep severity, ADHD symptoms, quality of life, behaviour, working memory, executive functioning, learning, academic achievement) and primary caregiver (mental health, parenting, work attendance) measures. Analyses will address clustering at the level of the paediatrician using linear mixed effect models adjusting for potential a priori confounding variables.

Ethics and dissemination: Ethics approval has been granted. Findings will determine whether the benefits of an efficacy trial can be realised more broadly at the population level and will inform the development of clinical guidelines for managing sleep problems in this population. We will seek to publish in leading international paediatric journals, present at major conferences and through established clinician networks.

Trial registration number: ISRCTN50834814, Pre-results

Brain Connectivity. 2017;7:106-14.

STRUCTURAL AND FUNCTIONAL ABNORMALITIES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A FOCUS ON SUBGENUAL ANTERIOR CINGULATE CORTEX.

Zhan C, Liu Y, Wu K, et al.

Attention-deficit/hyperactivity disorder (ADHD), characterized by developmentally inappropriate inattention, hyperactivity/impulsivity, or a combination of both, is a major public health problem. Neuroimaging studies have revealed associations of these cognitive impairments with structural and functional deficits all over the brain. Existing findings are not fully consistent because of the heterogeneity of study samples and diversity of research techniques. In this study, we propose to utilize a multimodal magnetic resonance imaging (MRI) approach to study the structural and functional brain networks in children with ADHD-combined type (ADHD-C) with a focus on the subgenual anterior cingulate cortex (sgACC). Diffusion tensor imaging (DTI) and resting-state functional MRI (rs-fMRI) data from 32 children with ADHD-C and 32 group-matched controls were involved. Network-based statistic analysis of the rs-fMRI data revealed a disconnected functional network between the sgACC and multiple regions in the occipital lobe and cerebellum, whereas the DTI data showed disrupted white matter integrity in the subgenual cingulum bundle (sgCB). Post hoc region of interest (ROI)-based analyses showed significantly increased fluctuation of the spontaneous brain activity in the sgACC and higher radial diffusivity in the sgCB in the ADHD group. Both the rs-fMRI and DTI ROI-based measures were significantly correlated with clinical measures that examine behavioral capacities of attention and inhibitory control. Findings of this study suggest that functional alterations in the sgACC and white matter under development in the sgCB may impact each other, and together contribute to impaired attention and inhibitory control function in children with ADHD

Brain Imaging Behav. 2017;1-14.

TREATMENT EFFECT OF METHYLPHENIDATE ON INTRINSIC FUNCTIONAL BRAIN NETWORK IN MEDICATION-NA+»VE ADHD CHILDREN: A MULTIVARIATE ANALYSIS.

Yoo JH, Kim D, Choi J, et al.

Methylphenidate is a first-line therapeutic option for treating attention-deficit/hyperactivity disorder (ADHD); however, elicited changes on resting-state functional networks (RSFNs) are not well understood. This study

investigated the treatment effect of methylphenidate using a variety of RSFN analyses and explored the collaborative influences of treatment-relevant RSFN changes in children with ADHD. Resting-state functional magnetic resonance imaging was acquired from 20 medication-naïve ADHD children before methylphenidate treatment and twelve weeks later. Changes in large-scale functional connectivity were defined using independent component analysis with dual regression and graph theoretical analysis. The amplitude of low frequency fluctuation (ALFF) was measured to investigate local spontaneous activity alteration. Finally, significant findings were recruited to random forest regression to identify the feature subset that best explains symptom improvement. After twelve weeks of methylphenidate administration, large-scale connectivity was increased between the left fronto-parietal RSFN and the left insula cortex and the right fronto-parietal and the brainstem, while the clustering coefficient (CC) of the global network and nodes, the left fronto-parietal, cerebellum, and occipital pole-visual network, were decreased. ALFF was increased in the bilateral superior parietal cortex and decreased in the right inferior fronto-temporal area. The subset of the local and large-scale RSFN changes, including widespread ALFF changes, the CC of the global network and the cerebellum, could explain the 27.1% variance of the ADHD Rating Scale and 13.72% of the Conner's Parent Rating Scale. Our multivariate approach suggests that the neural mechanism of methylphenidate treatment could be associated with alteration of spontaneous activity in the superior parietal cortex or widespread brain regions as well as functional segregation of the large-scale intrinsic functional network

Child Adolesc Psychiatry Ment Health. 2017;11.

PREVALENCE AND ASSOCIATED FACTORS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AMONG UGANDAN CHILDREN; A CROSS-SECTIONAL STUDY.

Wamulugwa J, Kakooza A, Kitaka SB, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is a common neuropsychiatric disorder among the children. The burden of ADHD or its associated factors in Uganda are not known. The objective of this study was to determine the prevalence and the associated factors of ADHD among children attending the neurology and psychiatry clinics at Mulago National Referral Hospital.

Methods: Using the disruptive behavior scale (45 items), we investigated the presence of ADHD symptoms among children attending Mulago Hospital. Questionnaires were administered to the primary care-takers of the study participants to gather information on the factors associated with ADHD. All children were subject to a clinical examination. Children presumed to have ADHD, using the aforementioned rating scale were further assessed by a child psychiatrist to confirm the diagnosis and associated co-morbid conditions.

Results: The estimated prevalence of DSM-IV ADHD symptoms was 11%. Children aged less than 10 years were four times likely to have ADHD (OR 4.1, 95% CI 1.7-9.6, $p < 0.001$). The demographic factors independently associated with ADHD were age less than 10 years, male gender, history of maternal abnormal vaginal discharge during pregnancy, and no formal education or the highest level of education being primary school.

Conclusion: The prevalence of ADHD among children attending the pediatric neurology and psychiatry clinics is high in our settings and is associated with delayed milestones. Early identification and addressing the co-morbid conditions associated with ADHD such as epilepsy, autism spectrum of disorder, conduct disorder, opposition defiant disorder and intellectual disability in our setting is needed

Child Adolesc Psychiatry Ment Health. 2017 Mar;11.

IDENTIFYING CROSS-CULTURAL VARIATIONS IN PSYCHOSTIMULANT USE FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER USING LINKED DATA.

Ghosh M, Holman CD, Preen DB.

Background: To validate the association between country-of-birth and disparities in the stimulant use for ADHD among individuals in Western Australia.

Methods: Using linked data, a population-based retrospective cohort of individuals admitted to hospital before age 25 years was followed through to identify having stimulants for ADHD in 2003–2007. Multivariate logistic and linear regressions were used to characterise associations between stimulants and country-of-birth, geographical remoteness and socioeconomic status.

Results: Of 679,645 individuals, 14,122 (2.1%) had a record of having stimulants for ADHD. Of these, 205 (1.5%) were born in Africa, Asia, Middle-East or South America, while 13,664 (96.8%) were born in Australia/New Zealand, Europe or North America. Individuals with traditionally non-Anglophonic backgrounds were around one-half as likely to have stimulants as individuals with Anglophonic backgrounds (OR = 0.53, 95% CI 0.46–0.61, $p < 0.001$). Non-Anglophones were an average of 2.7 years older than Anglophones at onset of having stimulants. Individuals from remote and disadvantaged backgrounds had stimulants at younger ages than individuals living in metropolitan areas and with least disadvantage.

Conclusions: The results highlight the importance of identifying factors underlying cultural differences in stimulant treatment for ADHD. Improving awareness of cultural variations may foster trust and rapport between patients and clinicians, and so better facilitate the appropriate and effective treatment of ADHD for each patient

Child Neuropsychol. 2017;1-19.

CLINICAL AND FUNCTIONAL CORRELATES OF PROCESSING SPEED IN PEDIATRIC ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Cook NE, Braaten EB, Surman CBH.

It is well established that processing speed is negatively impacted in children and adolescents with Attention-Deficit/Hyperactivity Disorder (ADHD). Unfortunately, exactly how processing speed vulnerabilities manifest in daily functioning has not been well established. To support clinical care of youth with ADHD, it is important to better understand the functional consequences and relevant outcomes associated with processing speed deficits. This systematic review and meta-analysis sought to identify the association between processing speed and clinical or functional correlates among children or adolescents diagnosed with ADHD. A total of 409 abstracts were screened, of which, 60 full-text articles were identified as potentially relevant, and 8 of these studies met inclusion criteria. Domains evaluated across these studies included reading skills, mathematics skills, written expression, anxiety, self-appraisals of competence, and adaptive functioning. Six studies reported an association between processing speed and reading skills, allowing for meta-analysis. Processing speed difficulties among youth with ADHD appear strongly associated with several clinical and functional correlates including weaker academic skills, poorer adaptive skills, increased self-reported anxiety, and overestimates of social competence. Meta-analytic results for studies reporting the association between processing speed and reading skills indicate a medium overall weighted mean effect size ($r = -0.33$, 95% CI -0.28 – -0.39) with minimal heterogeneity ($I^2 = 0.17$). Clinical implications of these findings, limitations in the current knowledge base, and suggestions for future research are discussed

Child Psychiatry Hum Dev. 2017 Apr;48:283-97.

ASSOCIATION OF REACTIVE–PROACTIVE AGGRESSION AND ANXIETY SENSITIVITY WITH INTERNALIZING AND EXTERNALIZING SYMPTOMS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Bilgiç A, Tufan AE, Yilmaz S, et al.

This study evaluates the associations among the symptoms of anxiety, depression, and disruptive behavioral disorders (DBD) in the context of their relationships with reactive–proactive aggression and anxiety sensitivity in children with attention-deficit/hyperactivity disorder (ADHD). The sample consisted of 342 treatment-naïve children with ADHD. The severity of ADHD and DBD symptoms were assessed via parent- and teacher-rated inventories. Anxiety sensitivity, reactive–proactive aggression and severity of anxiety and depression symptoms of children were evaluated by self-report inventories. According to structural equation modeling, depression and anxiety scores had a relation with the DBD scores through reactive–proactive aggression. Results also showed a negative relation of the total scores of anxiety sensitivity on DBD scores, while conduct

disorder scores had a positive relation with anxiety scores. This study suggests that examining the relations of reactive–proactive aggression and anxiety sensitivity with internalizing and externalizing disorders could be useful for understanding the link among these disorders in ADHD

Clinical Laboratory. 2017;63:435-43.

VITAMIN D DEFICIENCY AND A BLUNTED PARATHYROID HORMONE RESPONSE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Avcil S, Uysal P, Yilmaz M, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is the most frequently diagnosed neuropsychiatric disorder of childhood. The etiopathogenesis of ADHD has not been fully defined. Recent evidence has suggested a pathophysiological role of Vitamin D deficiency in ADHD. In this study, we evaluated the serum levels of 25-hydroxy Vitamin D (25(OH)D), parathyroid hormone (PTH), calcium (Ca), phosphate (P), and alkaline phosphatase (ALP) in children with ADHD.

Methods: The study group consisted of 105 children diagnosed with ADHD according to DSM-IV-TR criteria. A control group, matched for age and gender, was composed of 95 healthy children. Venous blood samples were collected, and 25(OH)D, PTH, Ca, P, and ALP levels were measured.

Results: The mean serum 25(OH)D, Ca, and P levels of the children with ADHD were significantly lower than those of the healthy controls. There were no significant differences between the groups regarding PTH and ALP. Serum PTH levels were found to be normal, but Vitamin D deficiency, hypocalcemia, and hypophosphatemia were observed in children with ADHD. There was no correlation between serum PTH and Ca levels in children with ADHD, whereas, there was a negative correlation between serum PTH and Ca levels in healthy controls. There was no correlation between serum 25(OH)D and PTH levels in children with ADHD, whereas, there was a negative correlation between serum 25(OH)D and PTH levels in healthy controls. There were no significant differences in all parameters' levels among the subtypes of ADHD.

Conclusions: The findings suggest that ADHD is associated with Vitamin D deficiency, blunted PTH response, and impaired Ca homeostasis in children

Clin Neuropharmacol. 2017;40:93-94.

THE EFFECT OF ATOMOXETIN USE IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ON THE SYMPTOMS OF RESTLESS LEGS SYNDROME: A CASE REPORT.

Baykal S, Karakurt MN.

Attention-deficit/hyperactivity disorder (ADHD) is frequently accompanied with sleep disorders such as obstructive sleep apnea, periodic limb movement disorder, restless legs syndrome (RLS), and circadian rhythm disorder. We have limited information about the effects of medical therapies used in the treatment of ADHD on RLS. This article discusses the effects of atomoxetine treatment on both disorders in a patient followed by diagnoses of ADHD and RLS

Cogn Process. 2017 May;18:183-93.

DYSFUNCTIONAL PERSONALITY TRAITS IN ADOLESCENCE: EFFECTS ON ALERTING, ORIENTING AND EXECUTIVE CONTROL OF ATTENTION.

Casagrande M, Marotta A, Canepone V, et al.

The present study examined attentional networks performance in 39 adolescents with dysfunctional personality traits, split into two groups, Group < 10 and Group ≥ 10, according to the number of criteria they met at the Structured Clinical Interview for DSM-IV Axis II Personality Disorders. The attentional performance has been tested by means of a modified version of the Attentional Network Test (ANTI-V) which allows testing both phasic and tonic components of the alerting system, the exogenous aspect of the orienting system, the executive network and their interactions. Results showed that the orienting costs of having an invalid spatial

cue were reduced in the Group ≥ 10 criteria compared to the Group < 10 . Moreover, adolescents included in the Group ≥ 10 showed lower conflict when attention was cued to the target location (valid trials) but showed normal interference when there was no overpowering focus of attention (invalid trials). The results found with ANOVA after splitting the sample into two categorical groups were also observed in a complementary correlation analysis keeping intact the continuous nature of such variables. These findings are consistent with the notion that dysfunctional features of personality disorders may represent the psychological manifestations of a neuropsychological abnormality in attention and executive functioning. Finally, we discuss the implications of this attentional anomaly for dysfunctional personality traits and behaviour

Compr Psychiatry. 2017;76:1-10.

PHENOMENOLOGY OF HOARDING IN CHILDREN WITH COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD): THE PERCEPTIONS OF PARENTS.

Lynch FA, Moulding R, McGillivray JA.

Individuals with ADHD and comorbid hoarding disorder are vulnerable to severe consequences from hoarding symptoms. Despite this, and the early onset of hoarding disorder, the nature of hoarding symptoms in children with comorbid ADHD is unknown. We therefore explored the phenomenology of hoarding symptoms among ten 8–12-year olds with ADHD and clinically significant hoarding symptoms through parental perceptions. Parents completed in-depth semi-structured interviews. The data was analyzed using Interpretative Phenomenological Analysis. Six superordinate themes were identified: emotional distress; parental avoidance and accommodating behaviors; family impacts of hoarding; excessive acquisition and saving; executive functioning; parental insight and intervention. In contrast to previous suggestions that emotional distress was not associated with hoarding in ADHD, these findings highlight that emotional distress appeared to be core to the hoarding disorder profile of the present sample of children with ADHD. This has important implications for health practitioners who may consider conceptualizing, assessing, and treating hoarding symptoms in children with comorbid ADHD using a cognitive behavioral model of hoarding disorder

Dermatol Surg. 2017 Apr;43:534-40.

EFFECT OF GENERAL ANESTHESIA ON NEURODEVELOPMENTAL ABNORMALITIES IN CHILDREN UNDERGOING TREATMENT OF VASCULAR ANOMALIES WITH LASER SURGERY: A RETROSPECTIVE REVIEW.

Terushkin V, Brauer J, Bernstein L, et al.

BACKGROUND: Multiple exposures to general anesthesia may be neurotoxic to the developing brain. This relationship has not been evaluated in children undergoing laser surgery for vascular anomalies.

OBJECTIVE: To evaluate the prevalence of neurodevelopmental abnormalities in children who received multiple laser procedures under general anesthesia before the age of 4 years for the treatment of vascular anomalies.

METHODS AND MATERIALS: Retrospective chart review of patients with contact of parents for telephone interview. **RESULTS:** Thirty-three patients were eligible. Average age at the time of survey was 7.8 years. Twenty-three (84.8%) patients were female, with average age at the time of first treatment at 1.9 years. Average number of treatments received before the age of 4 years was 6.7. Anesthetics included inhalational nitrous oxide and isoflurane and intravenous propofol. Seven patients carried one or more of the following diagnoses: attention-deficit hyperactivity disorder (3.0%), anxiety (6.1%), behavioral disorder (3.0%), language disorder (3.0%), speech disorder (3.0%), and motor disorder (6.1%). These prevalence rates are similar to those found in the US population.

CONCLUSION: This is the first report on the prevalence of neurodevelopmental disorders in children undergoing multiple laser treatments under general anesthesia. Although the study sample is small, no increased risks when comparing with prevalence rates reported in the literature were noted

Dev Med Child Neurol. 2017 May;59:544-49.

AUTISM SPECTRUM DISORDER AND OTHER NEUROBEHAVIOURAL COMORBIDITIES IN RARE DISORDERS OF THE RAS/MAPK PATHWAY.

Garg S, Brooks A, Burns A, et al.

AIM: To investigate the cognitive and behavioural phenotype in rare disorders of the Ras/MAPK pathway, namely Noonan, cardiofaciocutaneous (CFC), and Costello syndromes, particularly prevalence of autism spectrum disorder (ASD) and attention-deficit-hyperactivity disorder (ADHD).

METHOD: Fifty children were recruited over 10 months through the regional genetics service and advertisements. A range of parent, child, and observational measures were administered including Autism Diagnostic Interview-Revised and Autism Diagnostic Observation Scale.

RESULTS: Using the Collaborative Programme for Excellence in Autism criteria, 12 out of 40 children with Noonan syndrome (30%) showed ASD, and 12 out of 40 (30%) with partial ASD features and 16 out of 40 (40%) showed non-ASD. The Noonan syndrome ASD group showed male dominance in a ratio of 5:1. In the CFC group, eight out of nine children met the criteria for ASD, with equal sex distribution. Additionally 19 out of 40 (48%) of the Noonan syndrome group and eight out of nine (88.9%) of the CFC group scored met clinical criteria for ADHD. Only one child was in the Costello syndrome group.

INTERPRETATION: This is the first systematic study to suggest a high prevalence of ASD in Noonan and CFC syndromes, and thus offers crucial evidence to support the importance of the Ras/MAPK pathway in the aetiology of ASD. Limitations include the inevitable possibility of a sampling bias in a rare disorder study of this kind

Environ Int. 2016.

MATERNAL CELL PHONE USE DURING PREGNANCY AND CHILD BEHAVIORAL PROBLEMS IN FIVE BIRTH COHORTS.

Birks L, Guxens M, Papadopoulou E, et al.

Introduction: Previous studies have reported associations between prenatal cell phone use and child behavioral problems, but findings have been inconsistent and based on retrospective assessment of cell phone use. This study aimed to assess this association in a multi-national analysis, using data from three cohorts with prospective data on prenatal cell phone use, together with previously published data from two cohorts with retrospectively collected cell phone use data.

Methods: We used individual participant data from 83,884 mother-child pairs in the five cohorts from Denmark (1996-2002), Korea (2006-2011), the Netherlands (2003-2004), Norway (2004-2008), and Spain (2003-2008). We categorized cell phone use into none, low, medium, and high, based on frequency of calls during pregnancy reported by the mothers. Child behavioral problems (reported by mothers using the Strengths and Difficulties Questionnaire or Child Behavior Checklist) were classified in the borderline/clinical and clinical ranges using validated cut-offs in children aged 5-7. years. Cohort specific risk estimates were meta-analyzed.

Results: Overall, 38.8% of mothers, mostly from the Danish cohort, reported no cell phone use during pregnancy and these mothers were less likely to have a child with overall behavioral, hyperactivity/inattention or emotional problems. Evidence for a trend of increasing risk of child behavioral problems through the maternal cell phone use categories was observed for hyperactivity/inattention problems (OR for problems in the clinical range: 1.11, 95%CI 1.01, 1.22; 1.28, 95%CI 1.12, 1.48, among children of medium and high users, respectively). This association was fairly consistent across cohorts and between cohorts with retrospectively and prospectively collected cell phone use data.

Conclusions: Maternal cell phone use during pregnancy may be associated with an increased risk for behavioral problems, particularly hyperactivity/inattention problems, in the offspring. The interpretation of these results is unclear as uncontrolled confounding may influence both maternal cell phone use and child behavioral problems

Epidemiol Psychiatr Sci. 2017;1-5.

OPTIMISING TREATMENT STRATEGIES FOR ADHD IN ADOLESCENCE TO MINIMISE 'ÇYLOST IN TRANSITION' TO ADULTHOOD.

Buitelaar JK.

The persistence of attention-deficit hyperactivity disorder (ADHD) from adolescence to adulthood is not matched by continuity of care in this transition period. Many adolescents with ADHD have poor medication adherence or even stop medication treatment, and use of behavioural interventions is also suboptimal. The present commentary focuses on treatment strategies that might improve effects of ADHD medication treatment by improving adherence in adolescents with ADHD and/or optimise behavioural interventions for ADHD in adolescence. Most treatment strategies in adolescents with ADHD are merely copied from treatments offered to children. Instead however treatment should be focused on what makes adolescents special and vulnerable, such as poor insight into own functioning and poor decision making. Techniques that offer promise for adolescents are motivational interviewing, use of ecological momentary assessments and interventions, mindfulness-based training and serious games. Systematic studies into the effects of these techniques alone and in combination with medication are lacking

Eur Arch Psychiatry Clin Neurosci. 2017;1-10.

BINOCULAR RIVALRY TRANSITIONS PREDICT INATTENTION SYMPTOM SEVERITY IN ADULT ADHD.

Jusyte A, Zaretskaya N, H+Åhnle NM, et al.

Attention deficit and hyperactivity disorder (ADHD) is a prevalent childhood disorder that is often maintained throughout the development and persists into adulthood. Established etiology models suggest that deficient inhibition underlies the core ADHD symptoms. While experimental evidence for impaired motor inhibition is overwhelming, little is known about the sensory inhibition processes, their changes throughout the development, and the relationship to ADHD symptoms. Here, we used the well-established binocular rivalry (BR) paradigm to investigate for the very first time the inhibitory processes related to visual perception in adults with ADHD. In BR, perception alternates between two dichoptically presented images throughout the viewing period, with shorter dominant percept durations and longer transition periods indicating poorer suppression/inhibition. Healthy controls (N = 28) and patients with ADHD (N = 32) were presented with two dissimilar images (orthogonal gratings) separately to each eye through a mirror stereoscope and asked to report their perceptual experiences. There were no differences between groups in any of the BR markers. However, an association between transition durations and symptom severity emerged in the ADHD group. Importantly, an exploratory multiple regression analysis revealed that inattention symptoms were the sole predictor for the duration of transition periods. The lack of impairments to sensory inhibition in adult, but not pediatric ADHD may reflect compensatory changes associated with development, while a correlation between inhibition and inattention symptoms may reveal an invariant core of the disorder

Eur Child Adolesc Psychiatry. 2017 Feb;26:139-41.

COMBINING EPIDEMIOLOGICAL AND NEUROBIOLOGICAL PERSPECTIVES TO CHARACTERIZE THE LIFETIME TRAJECTORIES OF ADHD.

Shaw P, Polanczyk GV.

This editorial discusses the combining epidemiological and neurobiological perspectives to characterize the lifetime trajectories of ADHD. The concept of ADHD as a neurodevelopmental disorder has emerged from a large number of studies from convergent perspectives pointing all to that direction. Recent studies published in the European Child and Adolescent Psychiatry support this notion. Adult ADHD cases without a history of childhood ADHD were not fully explained by comorbidities, subthreshold symptoms, and information bias. Possible explanations for these findings are that subthreshold cases in childhood emerge as cases in adulthood when demands exceed capacities. Epidemiological studies are providing strong evidence for the

possibility of adult-onset ADHD. We now turn to neurobiology to determine whether adult onset represents the late expression of early onset neurogenetic risk factors or if it constitutes a novel diagnostic entity

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Eur Child Adolesc Psychiatry. 2017;1-13.

AN INTERNATIONAL QUALITATIVE STUDY OF ABILITY AND DISABILITY IN ADHD USING THE WHO-ICF FRAMEWORK.

Mahdi S, Viljoen M, Massuti R, et al.

This is the third in a series of four cross-cultural empirical studies designed to develop International Classification of Functioning, Disability and Health (ICF, and Children and Youth version, ICF(-CY) Core Sets for Attention-Deficit Hyperactivity Disorder (ADHD). To explore the perspectives of individuals diagnosed with ADHD, self-advocates, immediate family members and professional caregivers on relevant areas of impairment and functional abilities typical for ADHD across the lifespan as operationalized by the ICF(-CY). A qualitative study using focus group discussions or semi-structured interviews of 76 participants, divided into 16 stakeholder groups. Participants from five countries (Brazil, India, Saudi Arabia, South Africa and Sweden) were included. A deductive qualitative content analysis was conducted to extract meaningful functioning and disability concepts from verbatim material. Extracted concepts were then linked to ICF(-CY) categories by independent researchers using a standardized linking procedure. In total, 82 ICF(-CY) categories were identified, of which 32 were related to activities and participation, 25 to environmental factors, 23 to body functions and 2 to body structures. Participants also provided opinions on experienced positive sides to ADHD. A high level of energy and drive, creativity, hyper-focus, agreeableness, empathy, and willingness to assist others were the most consistently reported strengths associated with ADHD. Stakeholder perspectives highlighted the need to appraise ADHD in a broader context, extending beyond diagnostic criteria into many areas of ability and disability as well as environmental facilitators and barriers. This qualitative study, along with three other studies (comprehensive scoping review, expert survey and clinical study), will provide the scientific basis to define ICF(-CY) Core Sets for ADHD, from which assessment tools can be derived for use in clinical and research setting, as well as in health care administration

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Eur Child Adolesc Psychiatry. 2017;1-9.

ADDITIVE EFFECT OF CONGENITAL HEART DISEASE AND EARLY DEVELOPMENTAL DISORDERS ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER: A NATIONWIDE POPULATION-BASED LONGITUDINAL STUDY.

Tsao P-C, Lee Y-S, Jeng M-J, et al.

In this retrospective nationwide population-based case-control study, we investigated the impact of congenital heart disease (CHD) on the development of attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD), which remains unclear. Children aged <18 years that were diagnosed with CHD (n = 3552) between January 1, 1997 and December 31, 2009 were identified from the National Health Insurance Research Database in Taiwan. Non-CHD controls (n = 14,208) matched for age and sex (1:4) were selected from the same dataset. All subjects were observed until December 31, 2011 or their death. Comorbid perinatal conditions and early developmental disorders (EDD) that were diagnosed before ADHD and ASD diagnosis were also analyzed. The incidence rates of perinatal comorbidities, EDD, ADHD, and ASD were higher in the CHD group than in the control group. Multivariate Cox regression analysis revealed that the CHD group had an increased risk of developing ADHD (adjusted hazard ratio [aHR] 2.52, 95% confidence interval CI 1.96–3.25) and ASD (aHR 1.97, 95% CI 1.11–3.52) after adjusting for confounding comorbidities. EDD, but not perinatal comorbidities were also independent risk factors for ADHD and ASD after adjustment. Subgroup analysis indicated that the risk for ADHD (HR 16.59, 95% CI 12.17–22.60) and ASD (HR 80.68, 95% CI 39.96–176.12) was greatly increased in CHD subjects with EDD than in non-CHD subjects without EDD. These findings suggested that CHD at birth and EDD during early childhood were two independent risk factors for ADHD and ASD and that concurrent CHD and EDD might additively increase these risks

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Eur Child Adolesc Psychiatry. 2017;1-25.

SYSTEMATIC REVIEW OF QUALITY OF LIFE AND FUNCTIONAL OUTCOMES IN RANDOMIZED PLACEBO-CONTROLLED STUDIES OF MEDICATIONS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Coghill DR, Banaschewski T, Soutullo C, et al.

Children, adolescents and adults with attention-deficit/hyperactivity disorder (ADHD) experience functional impairment and poor health-related quality of life (HRQoL) in addition to symptoms of inattention/hyperactivity-impulsivity. To synthesize qualitatively the published evidence from randomized, double-blind, placebo-controlled trials of the effectiveness of pharmacotherapy on functional impairment or HRQoL in patients with ADHD, a systematic PubMed searching and screening strategy was designed to identify journal articles meeting pre-specified criteria. Post hoc analyses and meta-analyses were excluded. HRQoL outcomes, functional outcomes and the principal ADHD symptom-based outcome were extracted from included studies. An effect size of 0.5 versus placebo was used as a threshold for potential clinical relevance (unreported effect sizes were calculated when possible). Of 291 records screened, 35 articles describing 34 studies were included. HRQoL/functioning was usually self-rated in adults and proxy-rated in children/adolescents. Baseline data indicated substantial HRQoL deficits in children/adolescents. Placebo-adjusted effects of medication on ADHD symptoms, HRQoL and functioning, respectively, were statistically or nominally significant in 18/18, 10/12 and 7/9 studies in children/adolescents and 14/16, 9/11 and 9/10 studies in adults. Effect sizes were ≥ 0.5 versus placebo for symptoms, HRQoL and functioning, respectively, in 14/16, 7/9 and 4/8 studies in children/adolescents; and 6/12, 1/6 and 1/8 studies in adults. Effect sizes were typically larger for stimulants than for non-stimulants, for symptoms than for HRQoL/functioning, and for children/adolescents than for adults. The efficacy of ADHD medication extends beyond symptom control and may help reduce the related but distinct functional impairments and HRQoL deficits in patients with ADHD

Eur J Paediatr Neurol. 2017;21:593.

RESPONSE TO "SLEEP AND EXECUTIVE FUNCTIONS IN CHILDREN WITH ADHD ".

Sanchez-Carpintero R.

Hum Brain Mapp. 2017.

REAL-TIME fMRI NEUROFEEDBACK IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Alegria AA, Wulff M, Brinson H, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is associated with poor self-control, underpinned by inferior fronto-striatal deficits. Real-time functional magnetic resonance neurofeedback (rtfMRI-NF) allows participants to gain self-control over dysregulated brain regions. Despite evidence for beneficial effects of electrophysiological-NF on ADHD symptoms, no study has applied the spatially superior rtfMRI-NF neurotherapy to ADHD. A randomized controlled trial tested the efficacy of rtfMRI-NF of right inferior prefrontal cortex (rIFG), a key region that is compromised in ADHD and upregulated with psychostimulants, on improvement of ADHD symptoms, cognition, and inhibitory fMRI activation. To control for region-specificity, an active control group received rtfMRI-NF of the left parahippocampal gyrus (IPHG). Thirty-one ADHD boys were randomly allocated and had to learn to upregulate their target brain region in an average of 11 rtfMRI-NF runs over 2 weeks. Feedback was provided through a video-clip of a rocket that had to be moved up into space. A transfer session without feedback tested learning retention as a proximal measure of transfer to everyday life. Both NF groups showed significant linear activation increases with increasing number of runs in their respective target regions and significant reduction in ADHD symptoms after neurotherapy and at 11-month follow-up. Only the group targeting rIFG, however, showed a transfer effect, which correlated with ADHD symptom reductions, improved at trend level in sustained attention, and showed

increased IFG activation during an inhibitory fMRI task. This proof-of-concept study demonstrates for the first time feasibility, safety, and shorter- and longer-term efficacy of rtfMRI-NF of rIFG in adolescents with ADHD

Indian Journal of Clinical Biochemistry. 2017;32:239-42.

DRD4 AND DAT1 VNTR GENOTYPING IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Stanley A, Chavda K, Subramanian A, et al.

The dopamine receptor-D4 and the dopamine transporter have been investigated for their role in attention deficit hyperactivity disorder (ADHD) in children. Reports of their genetic association with ADHD have shown mixed results. The aim of the study was to evaluate the association of variable number tandem repeats (VNTRs) of the DRD4 and DAT1 genes with ADHD in children. A pilot 1:1 case control study, with 44 clinically confirmed ADHD cases and 44 age/gender matched healthy controls, was conducted at a tertiary care centre in Mumbai. Variable number tandem repeats of DRD4 exon 3, DAT1 intron 8 and 3'UTR were genotyped by PCR-AGE. Several allele repeats of the genes were observed in the screened subjects. Statistical significance was observed for the 10R/10R genotype of the DAT1 3'UTR VNTR between cases and controls

Int J Psychol. 2017 Apr;52:106-15.

PREDICTORS OF CHANGES IN CHILD BEHAVIOUR FOLLOWING PARENT MANAGEMENT TRAINING: CHILD, CONTEXT, AND THERAPY FACTORS.

Hagen KA, Ogden T.

This non-randomised study examined a set of predictive factors of changes in child behaviour following parent management training (PMTO). Families of 331 Norwegian girls (26%) and boys with clinic-level conduct problems participated. The children ranged in age from 3 to 12 years (Mage = 8.69). Retention rate was 72.2% at post-assessment. Child-, parent- and therapy-level variables were entered as predictors of multi-informant reported change in externalising behaviour and social skills. Behavioural improvements following PMTO amounted to 1 standard deviation on parent rated and (1/2) standard deviation on teacher rated externalising behaviour, while social skills improvements were more modest. Results suggested that children with higher symptom scores and lower social skills score at pre-treatment were more likely to show improvements in these areas. According to both parent- and teacher-ratings, girls tended to show greater improvements in externalising behaviour and social skills following treatment and, according to parents, ADHD symptomology appeared to inhibit improvements in social skills. Finally, observed increases in parental skill encouragement, therapists' satisfaction with treatment and the number of hours spent in therapy by children were also positive and significant predictors of child outcomes

Int J Psychol. 2017 Apr;52:96-105.

SQUEEZING OBSERVATIONAL DATA FOR BETTER CAUSAL INFERENCE: METHODS AND EXAMPLES FOR PREVENTION RESEARCH.

Garcia-Huidobro D, Michael OJ.

Randomised controlled trials (RCTs) are typically viewed as the gold standard for causal inference. This is because effects of interest can be identified with the fewest assumptions, especially imbalance in background characteristics. Yet because conducting RCTs are expensive, time consuming and sometimes unethical, observational studies are frequently used to study causal associations. In these studies, imbalance, or confounding, is usually controlled with multiple regression, which entails strong assumptions. The purpose of this manuscript is to describe strengths and weaknesses of several methods to control for confounding in observational studies, and to demonstrate their use in cross-sectional dataset that use patient registration data from the Juan Pablo II Primary Care Clinic in La Pintana-Chile. The dataset contains responses from 5855 families who provided complete information on family socio-demographics, family functioning and

health problems among their family members. We employ regression adjustment, stratification, restriction, matching, propensity score matching, standardisation and inverse probability weighting to illustrate the approaches to better causal inference in non-experimental data and compare results. By applying study design and data analysis techniques that control for confounding in different ways than regression adjustment, researchers may strengthen the scientific relevance of observational studies

Int Clin Psychopharmacol. 2017.

THE EFFECT OF METHYLPHENIDATE ON ANXIETY AND DEPRESSION SYMPTOMS IN PATIENTS WITH ASPERGER SYNDROME AND COMORBID ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Golubchik P, Rapaport M, Weizman A.

The objective of this study was to assess the response of anxiety and depression symptoms to methylphenidate (MPH) treatment in patients with Asperger syndrome (AS) combined with attention deficit/hyperactivity disorder (ADHD). A group of 12 patients with AS/ADHD, aged 8–18 years, received 12 weeks of MPH treatment. The severities of ADHD, anxiety, and depression symptoms were assessed by means of the ADHD Rating Scale (ADHD-RS), Screen for Child Anxiety Related Emotional Disorders, and the Children's Depression Inventory. The severity of ADHD and depression symptoms was reduced significantly ($P < 0.0003$ and $P = 0.046$, respectively). No improvement in total anxiety symptoms was found, but a significant reduction was obtained in the school-related subscale of the Screen for Child Anxiety Related Emotional Disorders ($P = 0.0054$). A positive correlation was found between the reductions in ADHD-RS and Children's Depression Inventory scores ($r = 0.59$, $P = 0.039$). MPH treatment may be safe, tolerable, and effective in alleviating depression and school-related anxiety symptoms in patients with AS and ADHD

Int J Pediatr Otorhinolaryngol. 2017;97:240-44.

LEFT AND RIGHT REACTION TIME DIFFERENCES TO THE SOUND INTENSITY IN NORMAL AND AD/HD CHILDREN.

Baghdadi G, Towhidkhah F, Rostami R.

Objectives Right hemisphere, which is attributed to the sound intensity discrimination, has abnormality in people with attention deficit/hyperactivity disorder (AD/HD). However, it is not studied whether the defect in the right hemisphere has influenced on the intensity sensation of AD/HD subjects or not. In this study, the sensitivity of normal and AD/HD children to the sound intensity was investigated.

Methods Nineteen normal and fourteen AD/HD children participated in the study and performed a simple auditory reaction time task. Using the regression analysis, the sensitivity of right and left ears to various sound intensity levels was examined.

Results The statistical results showed that the sensitivity of AD/HD subjects to the intensity was lower than the normal group ($p < 0.0001$). Left and right pathways of the auditory system had the same pattern of response in AD/HD subjects ($p > 0.05$). However, in control group the left pathway was more sensitive to the sound intensity level than the right one ($p = 0.0156$).

Conclusions It can be probable that the deficit of the right hemisphere has influenced on the auditory sensitivity of AD/HD children. The possible existent deficits of other auditory system components such as middle ear, inner ear, or involved brain stem nuclei may also lead to the observed results. The development of new biomarkers based on the sensitivity of the brain hemispheres to the sound intensity has been suggested to estimate the risk of AD/HD. Designing new technique to correct the auditory feedback has been also proposed in behavioral treatment sessions

International Journal of Play Therapy. 2017 Apr;26:73-83.

THE EFFECTS OF CHILD-CENTERED PLAY THERAPY ON THE BEHAVIORAL PERFORMANCE OF THREE FIRST GRADE STUDENTS WITH ADHD.

Robinson A, Simpson C, Hott BL.

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J Atten Disord. 2017 May;21:561-66.

EVALUATING PARENTAL DISAGREEMENT IN ADHD DIAGNOSIS: CAN WE RELY ON A SINGLE REPORT FROM HOME?

Caye A, Machado JD, Rohde LA.

OBJECTIVE: Few studies assessed factors associated with the agreement/disagreement between fathers and mothers when rating ADHD symptoms of their offspring. **METHOD:** Teachers and both parents assessed a referred sample of 98 children and adolescents aged 6 to 16 years (M age = 9.79, SD = 2.59) using the Swanson, Nolan, and Pelham (SNAP-IV) rating scale. The agreement was assessed for each of the items of the scale and correlated with variables measuring children's features, socioeconomic adversity, family functioning, and parental psychopathology.

RESULTS: Mean agreement between parents was moderate for the inattentive and good for the hyperactive-impulsive construct. Mothers tended to report more symptoms than fathers. The agreement was lower in those families where parents had discrepant educational levels.

CONCLUSION: Our findings suggest a significant cross-informant disagreement between parents on symptoms of ADHD. Discrepant parental education has a relevant role in explaining parental disagreement in reporting ADHD symptoms

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J Atten Disord. 2017 May;21:600-09.

DOES GENDER MODERATE THE RELATIONS BETWEEN EXTERNALIZING BEHAVIOR AND KEY EMERGENT LITERACY ABILITIES? EVIDENCE FROM A LONGITUDINAL STUDY.

Allan NP, Joye SW, Lonigan CJ.

OBJECTIVE: There is a significant negative relation between externalizing behavior and emergent literacy skills among preschool children.

METHOD: The purpose of this study was to examine the impact of gender on the predictive relation of externalizing behavior and emergent literacy in a group of 178 preschool children (mean age = 48.50 months, SD = 3.66; 48% boys).

RESULTS: Externalizing behaviors predicted emergent literacy over time. Distinct patterns of predictive associations dependent on gender were found. Girls with higher levels of externalizing behaviors experienced less change in their vocabulary skills compared with the vocabulary change shown by girls with lower levels of these problem behaviors.

CONCLUSION: The results suggest that early identification programs that include externalizing behavior problems and their relation with emergent literacy development should account for potential gender differences. A theoretical framework in which girls with behavior problems receive less opportunity for vocabulary acquisition is presented

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J Atten Disord. 2017 May;21:554-60.

DIAGNOSTIC AND DEMOGRAPHIC DIFFERENCES BETWEEN INCARCERATED AND NONINCARCERATED YOUTH (AGES 6-15) WITH ADHD IN SOUTH CAROLINA.

Soltis SL, Probst J, Xirasagar S, et al.

OBJECTIVE: Analyze diagnostic and demographic factors to identify predictors of delinquency resulting in incarceration within a group of children/adolescents diagnosed with ADHD.

METHOD: The study followed a cohort of 15,472 Medicaid covered children/adolescents with ADHD, ages 6 to 15 inclusive, between January 1, 2003, and December 31, 2006. The Diagnostic and Statistical Manual

of Mental Disorders (4th ed., text rev. [DSM-IV-TR]), 2000 Codes were used for qualifying diagnosis codes. Available demographic characteristics included race, sex, and residence. The outcome was incarceration at the South Carolina Department of Juvenile Justice during 2005-2006.

RESULTS: Among youth with ADHD, incarceration was more likely among black, male, and urban youth. Children/adolescents with comorbid ODD and/or CD were at greater risk compared with those with ADHD alone.

CONCLUSION: Within ADHD-diagnosed youth, comorbid conditions and demographic characteristics increase the risk of incarceration. Intervention and treatment strategies that address behavior among youth with these characteristics are needed to reduce incarceration

J Atten Disord. 2017 May;21:587-99.

ASSESSMENT OF ADHD SYMPTOMS AND THE ISSUE OF CULTURAL VARIATION: ARE CONNERS 3 RATING SCALES APPLICABLE TO CHILDREN AND PARENTS WITH MIGRATION BACKGROUND?

Schmidt M, Reh V, Hirsch O, et al.

OBJECTIVE: The objective was to evaluate whether Conners 3 (Conners 3rd edition) ratings of ADHD symptoms are robust to distortion by cultural variation when applied to children with migration background living in Germany.

METHOD: From 2010 to 2011, Conners 3 data (self-rating, parent rating, and teacher rating) of 243 children with Turkish migration background, aged 6 to 16 years, were collected in various German schools. Allocation of items to latent factors was tested with confirmatory analyses. Reliability and validity of resulting factors was calculated and influence of acculturation, gender, and age on rating-modalities was examined.

RESULTS: Confirmatory factor analyses showed high model fits for all rating-modalities. Resulting scales had good reliability and validity. There was a small influence of acculturation on parent ratings of oppositional defiant disorder but not on ADHD core symptoms.

CONCLUSION: Conners 3 ratings seem to be robust against influences of cultural variation. Their German translation can be utilized for children with Turkish migration background without limitation

JAMA Psychiatry. 2017;74:422-23.

CHILD VS ADULT ONSET OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-REPLY.

Arseneault L, Agnew-Blais J, Moffitt TE.

JAMA Psychiatry. 2017;74:421.

CHILD VS ADULT ONSET OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Solanto MV.

J Abnorm Child Psychol. 2017 Apr;45:471-84.

ADHD AND DEPRESSION SYMPTOMS IN PARENT COUPLES PREDICT RESPONSE TO CHILD ADHD AND ODD BEHAVIOR.

Wymbs BT, Dawson AE, Egan TE, et al.

Parents of children with attention-deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) often have elevated ADHD and depressive symptoms, both of which increase the risk of ineffective parenting and interparental discord. However, little is known about whether child ADHD/ODD behavior and parent ADHD or depressive symptoms uniquely or synergistically predict the quality of parenting and interparental communication during triadic (mother-father-child) interactions. Ninety parent couples, including

51 who have children diagnosed with ADHD, were randomly assigned to interact with a 9–12 year-old confederate child (84 % male) exhibiting either ADHD/ODD-like behavior or typical behavior. Parents reported their own ADHD and depressive symptoms, and parents and observers rated the quality of parenting and interparental communication during the interaction. Actor-partner interdependence modeling indicated that child ADHD/ODD behavior predicted less positive and more negative parenting and communication, independent of adult ADHD and depressive symptoms. Parent couples including two parents with elevated ADHD communicated more positively while managing children exhibiting ADHD/ODD behavior than couples managing children behaving typically or couples with only one parent with elevated ADHD symptoms. Couples including one parent with, and one parent without, elevated ADHD or depressive symptoms parented less positively and more negatively, and communicated more negatively, when managing children exhibiting ADHD/ODD behavior than when managing children behaving typically. Taken together, depending on the similarity of ADHD and depressive symptom levels in parent couples, adults managing children exhibiting ADHD/ODD behavior may parent or communicate positively or negatively. Findings highlight the need to consider the psychopathology of both parents when treating children with ADHD in two-parent homes

J Abnorm Child Psychol. 2017 Apr;45:501-17.

PARENT ADHD AND EVIDENCE-BASED TREATMENT FOR THEIR CHILDREN: REVIEW AND DIRECTIONS FOR FUTURE RESEARCH.

Chronis-Tuscano A, Wang CH, Woods KE, et al.

One fourth to one half of parents of children with attention-deficit/hyperactivity disorder (ADHD) have ADHD themselves, complicating delivery of evidence-based child behavioral and pharmacological treatments. In this article, we review the literature examining the relation between parent ADHD and outcomes following behavioral and pharmacological treatments for children with ADHD. We also review research that has incorporated treatment of parent ADHD (either alone or in combination with child treatment) with the goal of improving parenting and child outcomes. Finally, we offer recommendations for future research on the relation between parent ADHD and evidence-based treatment outcomes for their children, with the purpose of advancing the science and informing clinical care of these families

J Abnorm Child Psychol. 2017 Apr;45:415-27.

THE CONTRIBUTION OF MATERNAL ADHD SYMPTOMATOLOGY, MATERNAL DAT1, AND HOME ATMOSPHERE TO CHILD ADHD SYMPTOMATOLOGY AT 7 YEARS OF AGE.

Auerbach JG, Zilberman-Hayun Y, Atzaba-Poria N, et al.

Children of mothers with attention-deficit/hyperactivity disorder (ADHD) have an increased genetic and environmental risk for ADHD. The unique and interactive contributions of a maternal dopamine receptor gene (DAT1), maternal ADHD symptoms (hyperactive- impulsive, inattentive), and home atmosphere to the prediction of ADHD symptoms (hyperactive- impulsive, inattentive) in 7- year-old boys (N = 96) were examined using data from a longitudinal study of familial risk for ADHD. During the first 6 months of the study, mothers and their spouses completed a questionnaire about the mother's ADHD symptoms. Home atmosphere questionnaire data were collected 4 years later. At the 7-year assessment, mothers reported on their child's ADHD symptoms. Negative home atmosphere was significantly associated with child hyperactive-impulsive and inattentive symptoms. Maternal inattentive symptoms were significantly correlated with both child symptom dimensions. Regression models, with child genotype and maternal education controlled, showed main effects for maternal inattentive symptoms, maternal DAT1 10/10 genotype, and home atmosphere in the prediction of child inattentive symptoms. Only home atmosphere predicted child hyperactive-impulsive symptoms. There was a significant home atmosphere x maternal hyperactive-impulsive symptoms interaction in the prediction of child hyperactive-impulsive symptoms. Boys with higher levels of symptoms came from homes characterized by higher levels of negative atmosphere and had mothers with higher levels of hyperactive-impulsive symptoms. There was also a trend ($p = 0.075$) for a maternal DAT1 x home atmosphere interaction. Boys with higher levels of inattentive symptoms came from

homes with higher levels of negative atmosphere and had mothers with the homozygous 10/10 genotype. The maternal heterozygous 9/10 genotype did not predict child symptoms.

J Abnorm Child Psychol. 2017 Apr;45:429-42.

DRD4 VARIANTS MODERATE THE IMPACT OF PARENTAL CHARACTERISTICS ON CHILD ATTENTION-DEFICIT HYPERACTIVITY DISORDER: EXPLORATORY EVIDENCE FROM A MULTIPLEX FAMILY DESIGN.

Nikolas MA, Momany AM.

Parental ADHD symptomatology and related impairments have been robustly associated with youth ADHD across decades of work. Notably, these factors may impede typical development of child self-regulation capabilities through both neurobiological and interpersonal processes. High heritability of estimates for the disorder further suggest that these effects are likely genetically-mediated, at least in part. Variation within the dopamine D4 receptor gene (DRD4) has been shown to moderate parental influences on youth ADHD. Use of a multiplex family design (i.e., samples of families that included multiple affected members) may facilitate identification of additional gene variants of interest and advance understanding of gene-environment interplay in regard to parenting. Thirty multiplex families consisting of 114 individuals (66 youth, 48 parents) completed a multi-stage, multi-informant diagnostic and neurocognitive assessment, measures of parenting, and provided saliva samples for DNA analyses. Sanger sequencing of the DRD4 gene yielded 16 rare variants; a polygenic risk score was computed for both parents and youth. Generalized estimating equations (GEE) examined the predictive effects of parental ADHD symptoms, parental neurocognitive functioning, and poor parenting dimensions on youth ADHD as well as moderation of these effects by parental and youth DRD4 variants. Findings indicated that parental DRD4 variants moderated the impact of parental ADHD and neurocognitive functioning on youth ADHD symptoms. Youth DRD4 variants moderated the impact of parental inconsistent discipline on child ADHD. In all cases, stronger associations were observed for those individuals with more risk variants. These exploratory findings highlight the potential utility of a multiplex family design for examining the interplay between parent and child characteristics in predicting youth outcomes

J Abnorm Child Psychol. 2017 Apr;45:457-70.

EXTERNALIZING OUTCOMES OF YOUTH WITH AND WITHOUT ADHD: TIME-VARYING PREDICTION BY PARENTAL ADHD AND MEDIATED EFFECTS.

Moroney E, Tung I, Brammer WA, et al.

Although parental attention-deficit/hyperactivity disorder (ADHD) is a risk factor for multiple negative youth outcomes, it is unknown how change in parental ADHD symptoms over time affects change in child ADHD symptoms; moreover, mediators of these predictions are largely unknown. Parents of 230 5–10 year-old children (68 % male) with (n = 120) and without ADHD (n = 110) were followed prospectively for 6–7 years across three separate waves. Parents self-reported their ADHD and depression symptoms and similarly rated offspring ADHD, oppositional defiant disorder (ODD), and conduct disorder (CD) symptoms; youth self-reported their substance use. Temporally-ordered mediators consisted of parental expressed emotion (EE), derived from the Five Minute Speech Sample, and self-reported positive and negative parenting behavior. Controlling for key demographics and parental depression symptoms, increasing parental ADHD symptoms were a time-varying predictor of worsening youth ADHD and ODD, although it was unrelated to change in CD and alcohol/substance use. Next, although EE facets (i.e., criticism, emotional over-involvement) did not mediate these predictions, negative parenting behavior significantly mediated predictions of youth ADHD (and marginally in predictions of ODD) from parental ADHD symptoms. These quasi-experimental findings suggest that parental ADHD symptoms are a potential unique causal risk factor for offspring ADHD and ODD; also, preventing negative parenting behavior secondary to parental ADHD symptoms is critical to improve

trajectories of youth ADHD and ODD. We consider parental ADHD symptoms and family factors underlying emergent externalizing problems utilizing a developmental psychopathology framework, including implications for intervention and prevention

J Abnorm Child Psychol. 2017 Apr;45:443-56.

MEDIATORS AND MODERATORS OF THE RELATION BETWEEN PARENTAL ADHD SYMPTOMATOLOGY AND THE EARLY DEVELOPMENT OF CHILD ADHD AND ODD SYMPTOMS.

Breaux RP, Brown HR, Harvey EA.

The present study examined mediators and moderators of the relation between parental ADHD symptomatology and the development of child attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD) symptoms across the preschool years. Participants included 258 (138 boys) 3-year-old children ($M = 44.13$ months, $SD = 3.39$) with and without behavior problems and their parents who took part in a 3-year longitudinal study. Maternal ADHD symptoms predicted later ADHD symptoms in children, controlling for early child symptomatology. Both family history of ADHD and paternal comorbid psychopathology predicted later child ADHD and ODD symptoms, but they did not account for the association between maternal and child ADHD symptoms. Although paternal ADHD symptoms were associated with age 3 child ADHD symptoms, they did not significantly predict later child ADHD symptoms controlling for early symptomatology. Family adversity moderated the relation between maternal ADHD and child ADHD symptoms, such that the relation between maternal and child ADHD symptoms was stronger for families with less adversity. Maternal overreactive parenting mediated the relation between maternal ADHD symptoms and later child ADHD and ODD symptoms. Our findings suggest that targeting paternal comorbid psychopathology and maternal parenting holds promise for attenuating the effects of parental ADHD on children's ADHD

J Abnorm Child Psychol. 2017 Apr;45:485-500.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN MOTHERS AND FATHERS: FAMILY LEVEL INTERACTIONS IN RELATION TO PARENTING.

Williamson D, Johnston C, Noyes A, et al.

Previous studies linking parent ADHD symptoms to parenting have typically focused on each parent individually. To provide a broader understanding of family context, in this study, levels of inattention and hyperactivity-impulsivity in mothers and fathers were examined, both individually and in combination, in relation to negative parenting and child-rearing disagreements. Two-parent families of 5 to 13 year old boys (126 with ADHD and 53 typically developing) participated. Parents reported their own ADHD symptoms and their perceptions of child-rearing disagreements. Parenting was measured using self-, partner-, and child-reports as well as observations. Controlling for child ADHD symptoms, inattention symptoms in fathers predicted parenting difficulties. For mothers, inattention symptoms were linked to parenting problems only when fathers also had high levels of inattention. In contrast, parenting was most problematic for both mothers and fathers in families in which fathers had higher and mothers had lower levels hyperactivity-impulsivity symptoms. These results remained essentially unchanged when child externalizing behavior and mother depression and hostility were controlled, but father depression reduced the significance of some interactions. The results highlight the importance of the match between father and mother levels of symptoms, and point to differential relations of parenting to inattention and hyperactivity-impulsivity symptoms in parents

J Abnorm Child Psychol. 2017 Apr;45:519-25.

PARENTS' AND CHILDREN'S ADHD IN A FAMILY SYSTEM.

Deater-Deckard K.

ADHD symptoms 'run in families'. However, relatively little is known about the ways in which parents' symptoms might additively and interactively work with the parenting environment, to influence (and be influenced by) the developmental trajectory of symptoms in children and adolescents. In this commentary on the special section addressing this gap in knowledge, emphasis is placed on the importance of replicating and extending family-wide studies of ADHD symptoms and etiology. The current papers exemplify the leading-edge of such efforts, demonstrating the feasibility and rigor with which studies are being conducted, utilizing longitudinal and experimental designs. Families and parenting environments operate as a system in which individuals influence each other's symptoms and functioning. In so doing, parents produce tremendous variability within (as well as between) each family in individuals' ADHD symptoms from childhood through adulthood, via gene-environment transactions that may even begin during prenatal development.

J Abnorm Child Psychol. 2017 Apr;45:625-41.

EXPLORATION OF THE FACTOR STRUCTURE OF ADHD IN ADOLESCENCE THROUGH SELF, PARENT, AND TEACHER REPORTS OF SYMPTOMATOLOGY.

Nichols JQ, Shoulberg EK, Garner AA, et al.

Factor analytic studies of attention-deficit/hyperactivity disorder (ADHD) in children and adults have shown that second-order and bifactor models better represent ADHD symptoms than two- or three-factor models, yet there is far less evidence for a bestfitting model of ADHD in adolescence. Thus, the current study examined the factor structure of ADHD in adolescence and further evaluated the external validity of the best fitting model. Participants were 588 adolescents (22 % female; 366 with a childhood ADHD diagnosis; mean age 15.9 years) from the 8-year assessment of the Multimodal Treatment Study of Children with ADHD (MTA). ADHD symptoms were assessed via adolescent self-report, parent report, and teacher report on the SNAP-IV scale. Potential factor structures for the 18 symptoms of ADHD were tested for each informant, which included traditional one-factor, two-factor, and three-factor models of ADHD, as well as second-order factor (specific factors loading onto general factor) and bifactor (items loading onto both specific and general factors) models. Unique associations between external criteria and the identified factors of each informant's best fitting model were examined. Although several of the proposed models exhibited good fit, the second-order two-factor model best accounted for ADHD in adolescence according to self-report and parent report, and the second-order three-factor model was optimal according to teacher report. Several key measurement issues emerged for the hierarchical bifactor models, such as numerous Heywood cases and out-of-bound parameter estimates, which rendered them unfit as optimal representations of ADHD in adolescence. These findings and the implications of the best fitting model of ADHD in adolescence suggest that a possible reorganization of this disorder may eventually aid clinicians in the accurate diagnosis of ADHD in adolescents

Journal of Applied School Psychology. 2017 Apr;33:136-70.

THE EFFECT OF PHYSICAL ACTIVITY ON CHILDREN WITH ADHD: A QUANTITATIVE REVIEW OF THE LITERATURE.

Cornelius C, Fedewa AL, Ahn S.

Research on the effects of physical activity on children with attention deficit hyperactivity disorder is promising, yet no attempt has been made to integrate current findings using meta-analytic techniques. Using a meta-regression, the present study examined the effectiveness of physical activity for children with attention deficit hyperactivity disorder on a number of cognitive, behavioral, and emotional outcomes. From 20 empirical studies, 164 effect sizes quantifying the effectiveness of physical activity for children with attention deficit hyperactivity disorder were extracted from 22 independent samples. Results indicated an overall

moderate-to-large effect for physical activity on children with attention deficit hyperactivity disorder, with a significant effect for emotion/mood. Limitations of the study, future directions, and implications for school professionals are discussed

J Atten Disord. 2017 Feb;21:190-99.

CEREBELLAR SYMPTOMS ARE ASSOCIATED WITH OMISSION ERRORS AND VARIABILITY OF RESPONSE TIME IN CHILDREN WITH ADHD.

Goetz M, Schwabova J, Hlavka Z, et al.

Objective: We examined the presence of cerebellar symptoms in ADHD and their association with behavioral markers of this disorder.

Method: Sixty-two children with ADHD and 62 typically developing (TD) children were examined for cerebellar symptoms using the ataxia rating scale and tested using Conners' Continuous Performance Test.

Results: Children with ADHD had significantly more cerebellar symptoms compared with the TD children. Cerebellar symptom scores decreased with age in the ADHD group; in the TD group remained stable. In both groups, cerebellar symptoms were associated with parent-rated hyperactive/impulsive symptoms, variability of response time standard error (RT-SE) and increase of RT-SE as the test progresses. More variables were associated with cerebellar symptoms in the ADHD group including omission errors, overall RT-SE and its increase for prolonged interstimulus intervals.

Conclusion: Our results highlight the importance of research into motor functions in children with ADHD and indicate a role for cerebellar impairment in this disorder

J Atten Disord. 2017 Feb;21:200-08.

SIGNIFICANCE OF DOPAMINERGIC GENE VARIANTS IN THE MALE BIASNESS OF ADHD.

Das Bhowmik A, Sarkar K, Ghosh P, et al.

Objective: ADHD is frequently detected in boys though there is no established cause. One possibility is that genes predisposing to ADHD have sexually dimorphic effects. With an aim to find out the reason for this male biasness, contribution of 14 functional polymorphisms was investigated in ADHD subjects.

Method: Genomic DNA of probands, their parents, and ethnically matched controls was subjected to analysis of single-nucleotide polymorphisms and variable number of tandem repeats (VNTRs).

Results: Case-control analysis revealed significant higher occurrence of DAT1 intron 8 VNTR '5R' allele ($p = .028$), DBH rs1108580 'A' allele ($p = .027$), and MAOA-u VNTR-rs6323 3R-T haplotype ($p = .007$) in male probands. Family-based analysis showed significant preferential transmission of Dopamine receptor D4 exon 3 VNTR-rs1800955 7R-T haplotype from parents to male probands ($p = .008$). Interaction between DBH gene variants and low enzymatic activity was also noticed, especially in male probands.

Conclusion: Data obtained may partly answer the male biasness of ADHD

J Atten Disord. 2017 Feb;21:209-18.

DIMINISHED INFANT P50 SENSORY GATING PREDICTS INCREASED 40-MONTH-OLD ATTENTION, ANXIETY/DEPRESSION, AND EXTERNALIZING SYMPTOMS.

Hutchison AK, Hunter SK, Wagner BD, et al.

Objective: When behavioral problems resulting from attentional difficulties present, often in preschool, it is unknown whether these problems represent preexisting altered brain development or new brain changes. This study examines whether infant sensory gating of auditory evoked potentials predicts parent-reported behavior at 40 months.

Method: P50 sensory gating, an auditory evoked potential measure reflective of inhibitory processes in the brain, was measured in 50 infants around 70 days old. Parents, using the Child Behavior Checklist, reported on the child's behavior at 40 months.

Results: Controlling for gender, infants with diminished sensory gating had more problems later with externalizing behavior ($F = 4.17$, $ndf = 1$, $ddf = 46$, $p = .047$), attentional problems ($F = 5.23$, $ndf = 1$, $ddf = 46$, $p = .027$), and anxious/ depressed symptoms ($F = 5.36$, $ndf = 1$, $ddf = 46$, $p = .025$).

Conclusion: Diminished infant P50 sensory gating predicts attention symptoms 3 years later. These results support the hypothesis that preschool attentional dysfunction may relate to altered brain development that is detectable years prior to symptom onset

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J Atten Disord. 2017 Feb;21:219-27.

COMORBIDITY OF ALLERGIC AND AUTOIMMUNE DISEASES AMONG PATIENTS WITH ADHD: A NATIONWIDE POPULATION-BASED STUDY.

Chen MH, Su TP, Chen YS, et al.

Objective: Patients with ADHD have been suggested to have increased risks of allergic diseases but without consistent results, and limited studies about the association between ADHD and autoimmune diseases were noted in the literature.

Method: Utilizing the Taiwan National Health Insurance Research Database, ADHD patients were identified and compared with age- and gender-matched controls (1:4).

Results: In all, 8,201 participants were identified as having ADHD, and an increased prevalence of allergic diseases, including asthma (odds ratio [OR] = 1.53), allergic rhinitis (OR = 1.59), atopic dermatitis (OR = 1.53), and urticaria (OR = 1.39), compared with the control group. Although the comorbidity of autoimmune diseases with ADHD was low, ADHD patients had a significantly greater prevalence of ankylosing spondylitis (OR = 2.78), ulcerative colitis (OR = 2.31), and autoimmune thyroid disease (OR = 2.53) than the controls.

Conclusion: Our results supported the association between ADHD and allergic/autoimmune diseases. The further studies will be required to clarify the underlying mechanisms

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J Atten Disord. 2017 Mar;21:405-15.

COMPARATIVE VALIDITY OF DSM-IV AND ALTERNATIVE EMPIRICALLY DERIVED APPROACHES FOR THE ASSESSMENT OF ADHD.

Shemmassian SK, Lee SS.

Objective: To identify ADHD symptoms that are most highly predictive of ADHD diagnostic status and compare them against Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV) algorithms in predictions of functional impairment.

Method: Parent and teacher ratings of ADHD were obtained from an ethnically diverse (46% non-White) sample of 151 five- to ten-year-old children (27% female) with ($n = 76$) and without ($n = 75$) DSM-IV ADHD. We calculated total predictive values to estimate how ratings of each ADHD symptom predicted ADHD diagnostic status based on a structured parent diagnostic interview. Optimal symptom thresholds (i.e., not at all, just a little, pretty much, very much) for predicting ADHD caseness differed for inattention and hyperactivity and parents versus teachers. Algorithms consisting of highly predictive symptoms were then created and compared against DSM-IV-based algorithms to predict independent measures of functional impairment.

Results: Several empirically derived symptom algorithms were more strongly associated with functional impairment than DSM-IV-based algorithms.

Conclusion: These preliminary findings suggest that alternative methods to aggregating ADHD symptoms may improve predictions of impairment

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J Atten Disord. 2017 Mar;21:372-80.

DIAGNOSTIC UTILITY OF THE PEDIATRIC ATTENTION DISORDERS DIAGNOSTIC SCREENER.

Newman E, Reddy LA.

Objective: The Pediatric Attention Disorders Diagnostic Screener (PADDS) is an evidence-based screener of attention and executive functioning that combines computer-based Target Tests of Executive Function (TTEFs; Target Recognition, Target Sequencing, and Target Tracking) with parent and teacher behavioral reports to efficiently screen children ages 6 to 12 for ADHD. The present study is the first to examine the utility of the TTEFs in predicting ADHD status.

Method: The PADDS TTEFs were administered to 76 children (age = 6-12) with ADHD and 76 matched controls. Logistic regression and diagnostic efficiency statistics were used to evaluate the ability of the three TTEFs to predicted ADHD status.

Results: All three TTEFs significantly discriminated ADHD participants from controls, but each had a different diagnostic efficiency profile. Classification accuracy was improved when results of all three TTEFs were combined.

Conclusion: The PADDS is a promising tool for quickly and reliably screening for ADHD in clinic and school settings

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J Atten Disord. 2017 Feb;21:254-61.

THE TREND IN MORNING LEVELS OF SALIVARY CORTISOL IN CHILDREN WITH ADHD DURING 6 MONTHS OF METHYLPHENIDATE TREATMENT.

Wang LJ, Huang YS, Hsiao CC, et al.

Objective: To determine the trend in cortisol levels in children with ADHD treated with methylphenidate (MPH) and nontreated healthy controls over a 6-month period.

Method: The morning salivary cortisol levels of 50 patients with ADHD (40 boys and 10 girls, mean age = 7.6 years) and 50 age- and gender-matched healthy controls were measured at baseline and at 1, 3, and 6 months from baseline. The neuropsychological performance of the ADHD patients was measured via administration of the Continuous Performance Test.

Results: The cortisol levels of ADHD patients increased significantly after 1 month of MPH treatment before decreasing to an intermediate level, but were significantly positively correlated with neuropsychological performance throughout the 6-month treatment period. The cortisol levels of the controls did not change significantly over the 6-month period.

Conclusion: MPH administration appears to positively influence the functioning of the hypothalamic–pituitary–adrenal axis in ADHD patients

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J Atten Disord. 2017 Feb;21:228-39.

ATTENTIONAL NETWORKS IN BOYS WITH ADHD OR AUTISM SPECTRUM DISORDER AND THE RELATIONSHIP WITH EFFORTFUL CONTROL.

Samyn V, Roeyers H, Bijttebier P, et al.

Objective: The present study investigated differences in attentional networks in typically developing (TD) boys and boys with ADHD or autism spectrum disorder (ASD). In addition, we investigated the relationship between networks and the relationship with effortful control (EC).

Method: An Attention Network Test was used to assess alerting, orienting, and executive attention in 25 TD boys, 25 boys with ADHD, and 25 boys with ASD.

Results: In the absence of warning signals, boys with ADHD performed poorer than other children. In all groups, the orienting and executive control networks and the alerting and orienting networks interacted. Executive attention and EC were unrelated.

Conclusion: Results provided evidence of impaired tonic alertness in ADHD and support the idea of functional integration of attentional networks. Finally, findings suggest that the link between EC reports and

indices of neural systems involved in the effortful regulation of behavior may not be as unambiguous as previously thought

J Child Adolesc Psychopharmacol. 2017;27:112-16.

A SYSTEMATIC REVIEW OF THE USE OF BUPROPION FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS.

Ng QX.

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is one of the most prevalent neuropsychiatric disorders of childhood and adolescence. Stimulants are usually the first choice of drug; however, as many as 20% of patients do not respond to them. Stimulants may also worsen comorbid sleep, mood, and anxiety disorders, and they are associated with problems of misuse and diversion. Bupropion, a dopamine and norepinephrine reuptake inhibitor, is a promising nonstimulant alternative with reports of positive outcomes for ADHD management in both adolescent and adult populations. This study systematically reviews clinical trials on the subject.

Methods: Using the keywords bupropion or Wellbutrin or Zyban or Elontril and attention deficit hyperactivity disorder or ADHD or ADDH, a preliminary search on the PubMed and Ovid databases yielded 25,455 articles published in English between January 1, 1988 and May 1, 2016. Of these, there were only six articles on clinical trials involving children. Full articles were also reviewed for references of interest.

Results: All available open, controlled, and randomized trials demonstrated bupropion's efficacy in improving ADHD symptoms. The three head-to-head trials found that bupropion had efficacy comparable to methylphenidate ($p > 0.05$). However, a large double-blind, placebo-controlled multicenter study of bupropion found smaller effect sizes for bupropion, as quantified using teacher and parent ratings of ADHD symptoms, than methylphenidate. In terms of tolerability, a head-to-head trial found that headache was observed more frequently in the methylphenidate-treated group than in the bupropion-treated group, whereas the frequency of other side effects did not differ significantly.

Conclusion: Current findings should be interpreted with caution because of the very limited database. Bupropion should be considered for pharmacological management of childhood and adolescent ADHD, but more randomized controlled trials with larger sample sizes are warranted. There is also some evidence of its benefits in children with comorbid ADHD and conduct, substance use, or depressive disorders

J Child Adolesc Psychopharmacol. 2017;27:117-24.

RISPERIDONE ADDED TO PSYCHOSTIMULANT IN CHILDREN WITH SEVERE AGGRESSION AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: LACK OF EFFECT ON ATTENTION AND SHORT-TERM MEMORY.

Farmer CA, Epstein JN, Findling RL, et al.

Objective: Professionals have periodically expressed concern that atypical antipsychotics may cause cognitive blunting in treated patients. In this study, we report data from a double-blind, randomized, controlled study of stimulant plus placebo versus combined stimulant and risperidone to evaluate the effects of the atypical antipsychotic on attention and short-term memory.

Methods: A total of 165 ($n = 83$ combined treatment; $n = 82$ stimulant plus placebo) children with attention-deficit/hyperactivity disorder and severe physical aggression, aged 6-12 years, were evaluated with Conners' Continuous Performance Test (CPT-II) and the Wechsler Intelligence Scale for Children-III (WISC) Digit Span subscale at baseline, after 3 weeks of stimulant-only treatment, and after six additional weeks of randomized treatment (stimulant+placebo vs. stimulant+risperidone).

Results: At 3 weeks, improvement on CPT-II performance (Commissions and Reaction Time Standard Error; $p < 0.001$) and on Digit Span memory performance ($p < 0.006$) was noted for the full sample. At study week 9, no difference in CPT-II or Digit Span performance was observed between the randomized groups ($ps = 0.41$ to 0.83).

Conclusions: Similar to other studies, we found no deleterious effects on attention and short-term memory associated with short-term use of risperidone. NCT00796302

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J Child Adolesc Psychopharmacol. 2017;27:177-84.

THE PREVALENCE OF STIMULANT AND ANTIDEPRESSANT USE BY AUSTRALIAN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND MAJOR DEPRESSIVE DISORDER: A NATIONAL SURVEY.

Sawyer MG, Reece CE, Sawyer ACP, et al.

Objectives: To identify the prevalence of stimulant and antidepressant medication use by children and adolescents with symptoms meeting the criteria for attention-deficit/hyperactivity disorder (ADHD) and major depressive disorder (MDD) in Australia. To identify factors associated with stimulant and antidepressant use by children and adolescents in Australia.

Methods: Data are from a nationally representative sample of 4- to 17-year-olds (n = 6310). Parents completed the Diagnostic Interview Schedule for Children - Version IV (DISC-IV) and the Strengths and Difficulties Questionnaire. Eleven- to 17-year-olds completed a self-report version of the DISC-IV MDD module. Interviewers recorded prescribed medications used by participants in the previous 2 weeks.

Results: During a 2-week period, 1.3% of all 4- to 17-year-olds and 13.7% of those with symptoms meeting the criteria for ADHD had used stimulant medication, while 0.9% of all 4- to 17-year-olds and 13.4% with MDD had used antidepressants. In total, 22.6% of those using stimulant medications and 57.7% using antidepressant medications did not have symptoms meeting criteria for ADHD or MDD, respectively. Among 11- to 17-year-olds, 5.6% of those with adolescent-only-reported MDD, 10.9% of those with parent/carer-only-reported MDD, and 25.7% of those with MDD reported by both parents/carers and adolescents were using antidepressant medications.

Conclusions: Only a minority of 4- to 17-year-olds with ADHD and MDD were being treated with stimulant or antidepressant medication. The percentage of adolescents with MDD using antidepressant medications varied depending on whether adolescents, parents/carers, or both identified the presence of MDD. This highlights the importance of using information from both these informants when assessing and treating adolescent depressive disorder

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J Child Adolesc Psychopharmacol. 2017;27:216-22.

PHARMACOKINETICS OF A NOVEL AMPHETAMINE EXTENDED-RELEASE ORALLY DISINTEGRATING TABLET IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Stark JG, Engelking D, McMahon R, et al.

Background: A novel formulation for treating attention-deficit/hyperactivity disorder (ADHD) has recently been developed - amphetamine extended-release orally disintegrating tablets (AMP XR-ODTs). In this study, we assessed the rate of absorption and exposure of AMP XR-ODT under fasted conditions in children with ADHD. **Methods:** Children (6-12 years) with ADHD were enrolled in a single-dose, open-label, single-period pharmacokinetic (PK) study. Patients were stratified by age (6-7, 8-9, and 10-12 year olds) and were dosed with 18.8-mg AMP XR-ODT under fasted conditions. Plasma samples were analyzed for d- and l-amphetamine. Maximum plasma concentration (C_{max}), time to maximum plasma concentration (T_{max}), area under the concentration-time curve from time zero-infinity (AUC_{inf}), weight-normalized clearance (CL/F), and weight-normalized volume of distribution (V_z/F) were assessed. The geometric mean and 95% confidence intervals (CIs) were calculated for weight-normalized CL/F and V_z/F in each age group to determine if the 95% CIs were within the target range of 60%-140%. **Results:** A total of 28 children completed the study. The 95% CIs for the geometric mean CL/F/kg and V_z/F/kg for both d- and l-amphetamine fell within the target range of 60%-140% for each age group, thus meeting the primary end point. Four participants experienced treatment-related adverse events, including vomiting (n = 3), abdominal pain (n = 2), dry mouth

(n = 1), and insomnia (n = 1). Conclusions: AMP XR-ODT, a novel formulation that does not require swallowing an intact tablet or capsule, was well tolerated and demonstrated a PK profile consistent with once-daily dosing in children with ADHD

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J Child Adolesc Psychopharmacol. 2017;27:234-42.

CAREGIVER TREATMENT PREFERENCES FOR CHILDREN WITH A NEW VERSUS EXISTING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DIAGNOSIS.

DosReis S, Park A, Ng X, et al.

Objectives: Parental experiences with managing their child's attention-deficit/hyperactivity disorder (ADHD) can influence priorities for treatment. This study aimed to identify the ADHD management options caregivers most prefer and to determine if preferences differ by time since initial ADHD diagnosis.

Methods: Primary caregivers (n = 184) of a child aged 4-14 years old in care for ADHD were recruited from January 2013 through March 2015 from community-based pediatric and mental health clinics and family support organizations across the state of Maryland. Participants completed a survey that included child/family demographics, child clinical treatment, and a Best-Worst Scaling (BWS) experiment to elicit ADHD management preferences. The BWS comprised 18 ADHD management profiles showing seven treatment attributes, where the best and worst attribute levels were selected from each profile. A conditional logit model using effect-coded variables was used to estimate preference weights stratified by time since ADHD diagnosis.

Results: Participants were primarily the mother (84%) and had a college or postgraduate education (76%) with 75% of the children on stimulant medications. One-on-one caregiver behavior training, medication use seven days a week, therapy in a clinic, and an individualized education program were most preferred for managing ADHD. Aside from caregiver training and monthly out-of-pocket costs, caregivers of children diagnosed with ADHD for less than two years prioritized medication use lower than other care management attributes and caregivers of children diagnosed with ADHD for two or more years preferred school accommodations, medication, and provider specialty.

Conclusions: Preferences for ADHD treatment differ based on the duration of the child's ADHD. Acknowledging that preferences change over the course of care could facilitate patient/family-centered care planning across a range of resources and a multidisciplinary team of professionals

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J Child Adolesc Psychopharmacol. 2017;27:250-57.

PARENT-REPORTED IMPROVEMENTS IN FAMILY FUNCTIONING IN A RANDOMIZED CONTROLLED TRIAL OF LISDEXAMFETAMINE FOR TREATMENT OF PARENTAL ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Babinski DE, Waxmonsky JG, Waschbusch DA, et al.

Objective: This study examines the effects of parental stimulant medication treatment on parent ratings of parent-child functioning. Ratings of parent-child functioning in the home setting and immediately following a laboratory-based parent-child interaction were collected.

Method: Participants were 20 parents who along with their children (ages 5-12 years) were diagnosed with Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) attention-deficit/hyperactivity disorder (ADHD). Parents completed an open-label titration to determine their optimal dose of lisdexamfetamine (30, 50, or 70 mg/day) and then completed a month-long double-blind randomized pharmacological intervention for parental ADHD. Effects of parental stimulant medication administered for an extended duration were assessed by parent ratings of parent-child functioning in the home setting and immediately following a laboratory parent-child interaction task conducted at an academic mental health center. Data were collected from September 2010 to June 2013.

Results: Stimulant medication versus placebo was associated with larger reductions in parental ADHD (d = 1.01-1.09), impairment (d = 0.67-0.82), and executive dysfunction (d = 0.74-0.94) in the home setting. No significant benefits of stimulant medication emerged in measures of parenting or child behavior at home. In the laboratory setting, parents treated with stimulant medication versus placebo reported fewer ADHD

symptoms ($d = 1.01-1.05$) and their interaction was more successful ($d = 0.83$) and pleasant ($d = 0.92$). Several additional trends emerged showing beneficial effects of stimulant medication on parent-child functioning.

Conclusion: Parents treated with stimulant medication evidenced some improvements in parent-child functioning, which support the use of pharmacological intervention to improve functioning in families with parent-child ADHD

J Child Adolesc Psychopharmacol. 2017;27:274-80.

OCULOMOTOR ABNORMALITIES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ARE IMPROVED BY METHYLPHENIDATE.

Bucci MP, Stordeur C, Septier M, et al.

Background: There are relatively few studies of saccadic eye movements in children with attention-deficit/hyperactivity disorder (ADHD). The aim of this study was to examine inhibitory abilities of eye movements in children with ADHD and to explore the effect of methylphenidate (MPH) on eye movement performance.

Methods: Thirty-one children with ADHD (mean age 9.9 \pm 0.4 years) and 31 sex-, age-, and IQ-matched children with normal development were examined. Saccades elicited not only by the gap, step, overlap, and antisaccade paradigms but also a simple fixation paradigm have been recorded using an eye tracker. The latency of each type of saccade, the error rate of antisaccades, and the number of saccades made during fixation have been measured.

Results: Children with ADHD and naive to treatment with respect to controls showed significantly shorter mean latency of voluntary saccades (overlap paradigm), more frequent errors during the antisaccade paradigm, and higher number of saccades made during fixation. After 1 month of MPH treatment, all these parameters changed significantly and reached control values.

Conclusion: Taken together, these results suggest that oculomotor abilities are poor in children with ADHD, which may correlate with deficits in inhibitory mechanisms. Treatment with MPH improves oculomotor performances through adaptive strategies, which may involve brain structures related to cognitive inhibition

J Consult Clin Psychol. 2017.

GIRLS WITH CHILDHOOD ADHD AS ADULTS: CROSS-DOMAIN OUTCOMES BY DIAGNOSTIC PERSISTENCE.

Owens EB, Zalecki C, Gillette P, et al.

Objective: To ascertain adult outcomes in 10 domains reflecting symptomatology (internalizing, externalizing, self-injury, substance use), attainment (education, employment), and impairment (health, social, driving, overall) as a function of both childhood diagnosis of attention-deficit/hyperactivity disorder (ADHD) and persistence of ADHD symptoms across time.

Method: We prospectively followed 140 grade-school-aged girls with rigorously diagnosed childhood ADHD and 88 age- and ethnicity-matched comparison girls for 16 years. Outcome measures were obtained via self- and parent-report questionnaires, interviews, and objective tests.

Results: Childhood ADHD, whether it remitted or persisted, was a pernicious risk factor for a limited number of poor outcomes, including low educational attainment, unplanned pregnancy, body mass index (BMI), and clinician-rated impairment. Childhood ADHD that persisted over time, whether completely or partially, was associated with a number of additional detrimental outcomes in the externalizing, internalizing, self-injury, occupational, social, and overall impairment domains. Finally, in this all-female sample, ADHD was not associated with objective measures of employment, substance use, or driving outcomes.

Conclusions: We discuss the considerable impairments accruing from both childhood-limited and adult-persisting ADHD, with major implications for the health and well-being of females with this neurodevelopmental disorder

Journal of Neuroimmune Pharmacology. 2017;1-13.

SYSTEMIC INFLAMMATION DURING THE FIRST POSTNATAL MONTH AND THE RISK OF ATTENTION DEFICIT HYPERACTIVITY DISORDER CHARACTERISTICS AMONG 10 YEAR-OLD CHILDREN BORN EXTREMELY PRETERM.

Allred EN, Dammann O, Fichorova RN, et al.

Although multiple sources link inflammation with attention difficulties, the only human study that evaluated the relationship between systemic inflammation and attention problems assessed attention at age 2 years. Parent and/or teacher completion of the Childhood Symptom Inventory-4 (CSI-4) provided information about characteristics that screen for attention deficit hyperactive disorder (ADHD) among 793 10-year-old children born before the 28th week of gestation who had an IQ ≥ 70 . The concentrations of 27 proteins in blood spots obtained during the first postnatal month were measured. 151 children with ADHD behaviors were identified by parent report, while 128 children were identified by teacher report. Top-quartile concentrations of IL-6R, TNF- α , IL-8, VEGF, VEGF-R1, and VEGF-R2 on multiple days were associated with increased risk of ADHD symptoms as assessed by a teacher. Some of this increased risk was modulated by top-quartile concentrations of IL-6R, RANTES, EPO, NT-4, BDNF, bFGF, IGF-1, PIGF, Ang-1, and Ang-2. Systemic inflammation during the first postnatal month among children born extremely preterm appears to increase the risk of teacher-identified ADHD characteristics, and high concentrations of proteins with neurotrophic properties appear capable of modulating this increased risk

J Am Acad Child Adolesc Psychiatry. 2017;56:336-43.

PSYCHOTIC SYMPTOMS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: AN ANALYSIS OF THE MTA DATABASE. Vitiello B, Perez AG, Arnold LE, et al.

Objective To assess the prevalence of psychotic symptoms among youths (14–25 years of age) with a childhood diagnosis of attention-deficit/hyperactivity disorder (ADHD) combined type.

Method Participants in the Multimodal Treatment Study of Children with ADHD (MTA) and a local normative comparison group (LNCG) were systematically assessed 6, 8, 10, 12, 14, and 16 years after the original enrollment at a mean age of 8.5 years. Trained research assistants administered a psychosis screener, and positive screens were referred to study clinicians to confirm or exclude psychosis. Possible associations between screening positive and alcohol or substance use were assessed.

Results Data were available from 509 MTA participants (88% of original MTA sample; mean age 25.1 years) and 276 LNCG participants (96% of original sample; mean age 24.6 years) at year 16. Twenty-six MTA participants (5%; 95% CI 3–7) and 11 LNCG participants (4%; 95% CI 2–6) screened positive for at least 1 psychotic symptom ($p = .60$). Most psychotic symptoms were transient. The prevalence of clinician-confirmed psychotic symptoms was 1.1% (95% CI 0.2–2.1) in the MTA group and 0.7% (0–1.7) in the LNCG ($p = .72$). Greater cannabis use was reported by those who screened positive ($p < .05$) and were confirmed positive ($p < .01$).

Conclusion There was no evidence that ADHD increased the risk for psychotic symptoms. In the ADHD and normative comparison groups, more frequent cannabis use was associated with a greater likelihood of experiencing psychotic symptoms, thus supporting the recommendation that youth should not use cannabis

Mental Health and Physical Activity. 2017;12:110-15.

DOSE-RESPONSE EFFECTS OF EXERCISE ON BEHAVIORAL HEALTH IN CHILDREN AND ADOLESCENTS.

Bowling A, Slavet J, Miller DP, et al.

Purpose Aerobic exercise may positively affect behavior in children but little research has been conducted among those with behavioral health disorders (BHD). This study is a secondary exploration of data originally collected from an RCT that tested effects of a cybercycling intervention on behavior in children with BHD. We examine dose-response relationships between duration and intensity of cybercycling and minutes of disciplinary time spent out of class (TOC) and self-regulation scores (SRS); additionally we examine potential effect modification by Attention-Deficit/Hyperactivity Disorder (ADHD) diagnosis.

Methods We extracted data from study days on which participants ($N = 103$, 83.5% male, age 11.8 ± 2.3) cybercycled during physical education classes. Minutes of riding and average heart rate for each session were collected via the bicycles. The Conners Abbreviated Teacher Rating Scale (SRS) and minutes of TOC were recorded daily. Ride duration and average heart rate were treated as continuous predictors of outcomes using mixed-effects linear regression.

Results For every 10 min of riding, children had an associated decline of 10.7 min of TOC ($p < 0.001$) and 1.2 points improvement in self-regulation score ($p = 0.001$). For each increase of 10 beats per minute average heart rate children had an associated decline of 1.3 min ($p = 0.05$) and 0.21 points ($p < 0.05$). Children with ADHD experienced 12.9 min less time out of class ($p < 0.05$) for each 10 additional minutes of riding.

Conclusion Duration in particular had significant, linear relationships with improved behavioral outcomes among children with a variety of BHD; children with ADHD may experience the greatest benefits

Molecular Autism. 2017;8.

SHARED GENETIC INFLUENCES BETWEEN DIMENSIONAL ASD AND ADHD SYMPTOMS DURING CHILD AND ADOLESCENT DEVELOPMENT.

Stergiakouli E, Davey SG, Martin J, et al.

BACKGROUND: Shared genetic influences between attention-deficit/hyperactivity disorder (ADHD) symptoms and autism spectrum disorder (ASD) symptoms have been reported. Cross-trait genetic relationships are, however, subject to dynamic changes during development. We investigated the continuity of genetic overlap between ASD and ADHD symptoms in a general population sample during childhood and adolescence. We also studied uni- and cross-dimensional trait-disorder links with respect to genetic ADHD and ASD risk.

METHODS: Social-communication difficulties ($N \leq 5551$, Social and Communication Disorders Checklist, SCDC) and combined hyperactive-impulsive/inattentive ADHD symptoms ($N \leq 5678$, Strengths and Difficulties Questionnaire, SDQ-ADHD) were repeatedly measured in a UK birth cohort (ALSPAC, age 7 to 17 years). Genome-wide summary statistics on clinical ASD (5305 cases; 5305 pseudo-controls) and ADHD (4163 cases; 12,040 controls/pseudo-controls) were available from the Psychiatric Genomics Consortium. Genetic trait variances and genetic overlap between phenotypes were estimated using genome-wide data.

RESULTS: In the general population, genetic influences for SCDC and SDQ-ADHD scores were shared throughout development. Genetic correlations across traits reached a similar strength and magnitude (cross-trait $r_g \leq 1$, $p_{min} = 3 \times 10^{-4}$) as those between repeated measures of the same trait (within-trait $r_g \leq 0.94$, $p_{min} = 7 \times 10^{-4}$). Shared genetic influences between traits, especially during later adolescence, may implicate variants in K-RAS signalling upregulated genes ($p_{meta} = 6.4 \times 10^{-4}$). Uni-dimensionally, each population-based trait mapped to the expected behavioural continuum: risk-increasing alleles for clinical ADHD were persistently associated with SDQ-ADHD scores throughout development (marginal regression $R^2 = 0.084\%$). An age-specific genetic overlap between clinical ASD and social-communication difficulties during childhood was also shown, as per previous reports. Cross-dimensionally, however, neither SCDC nor SDQ-ADHD scores were linked to genetic risk for disorder.

CONCLUSIONS: In the general population, genetic aetiologies between social-communication difficulties and ADHD symptoms are shared throughout child and adolescent development and may implicate similar biological pathways that co-vary during development. Within both the ASD and the ADHD dimension, population-based traits are also linked to clinical disorder, although much larger clinical discovery samples are required to reliably detect cross-dimensional trait-disorder relationships

Monatsschr Kinderheilkd. 2017;1-4.

DYSPRAXIA: SPECIFIC DEVELOPMENTAL DISORDER OF MOTOR FUNCTION.

Lammel P, Schulte-Markwort M.

Background: The specific developmental coordination disorder (DCD) is a chronic disorder with significant consequences for activities of daily living of affected children and adolescents.

Objectives: Epidemiology, clinical significance, diagnostic criteria and therapy recommendations.

Methods: Analysis and overview of the current literature about DCD.

Results: Most children show a moderate level of impairment in activities of daily living or at school. Despite the prevalence DCD is nevertheless not well known in many fields of the healthcare system and educational disciplines, it is not taken seriously enough or treated with ineffective methods over long periods of time.

Conclusion: In view of the frequency and negative consequences for those affected, further studies are urgently needed

Nervenarzt. 2017;1-8.

RETROSPECTIVE RECORDING OF CHILDHOOD ADHD SYMPTOMS: FOLLOW-UP OF ADULTS FORMERLY DIAGNOSED WITH CHILDHOOD ADHD AND/OR CHILDHOOD CONDUCT DISORDER.

Wolf F, Heinzel-Gutenbrunner M, Becker K.

Background: The Wender Utah Rating Scale (WURS) is recommended for retrospective recording of childhood attention deficit hyperactivity disorder (ADHD) symptoms. Hence the present study explored the validity of the WURS and its short forms (WURS-25, WURS-k, WURS-15-G, IDA items) by screening adult subjects who had been diagnosed with either ADHD or conduct disorder (CD) during childhood.

Material and methods: From 317 contacted former patients of the department for child and adolescent psychiatry, 20 adults previously diagnosed with ADHD (20 male, mean age 27.3 years) and 20 adults previously diagnosed with CD (and concurrent exclusion of childhood ADHD, 15 male, mean age 33.5 years) took part in the follow-up examination. Besides the WURS the socioeconomic status, current ADHD symptoms and further anamnestic details were obtained. Statistical analysis was performed with SPSS Statistics.

Results: The five IDA items showed a greater capacity for retrospective recording of childhood ADHD symptoms than the WURS or its short forms. Only the IDA items significantly ($p = 0.001$) separated subjects with a diagnosis of childhood ADHD from subjects with a diagnosis of childhood CD; however, the specificity was only 40% (cut-off = 10, concurrent sensitivity = 90%).

Conclusion: The validity of the WURS and its short forms is limited, especially if CD was present during childhood. As recommended in the guidelines, standardized instruments for retrospective recording of childhood ADHD symptoms should be supplemented with a history reported by third parties (e. g. parents) or with insight into school reports

Neurologia. 2017.

COGNITIVE PROFILE AND DISORDERS AFFECTING HIGHER BRAIN FUNCTIONS IN PAEDIATRIC PATIENTS WITH NEUROFIBROMATOSIS TYPE 1.

Vaucheret PE, Lopez BA, Puga C, et al.

Introduction: Neurofibromatosis type 1 (NF1) is a common neurocutaneous syndrome often associated with specific cognitive deficits that are rarely monitored during follow-up of these patients.

Objective: The purpose of our study is two-fold. First, we aimed to describe the cognitive profile of patients with NF1 and detect disorders in higher brain functions associated with the disease. Second, we identified the reasons for consultation associated with school performance in these patients.

Methods: We conducted a descriptive cross-sectional study of 24 paediatric patients (ages 5 to 16) with NF1 who underwent neuropsychological assessment.

Results: The most frequent reasons for consultation were attention deficits (58.33%), learning disorders (25%), poor motor coordination (25%), and language impairment (0.8%). Although 96% of the patients displayed impairments in at least one of the assessed areas, only 83.34% of the parents had reported such impairments. Attention-deficit/hyperactivity disorder was present in 58.33% of the patients, whereas 33.33% had nonverbal learning disabilities, 20.83% had expressive language disorder, 8.33% had borderline intellectual functioning, 4.16% had mental retardation, and only 4.16% showed no cognitive impairment.

Conclusion: Higher brain functions are frequently impaired in paediatric patients with NF1. Although many parents report such disorders, they can go undetected in some cases. Neuropsychological assessment is recommended for all paediatric patients with NF1 to detect cognitive impairment and provide early, effective rehabilitation treatment

Neuropediatrics. 2015;46.

EXECUTIVE DYSFUNCTION IN NEUROFIBROMATOSIS TYPE 1: COMPARISON TO IDIOPATHIC ADHD.

Heimgärtner M, Granström S, Mautner V, et al.

Aims: Neurofibromatosis type 1 (NF1) is a genetic disorder with various physical and cognitive symptoms. One of the core deficits in the neurocognitive profile of NF1 is executive dysfunction (ED). Consistently, deficits in impulse control, planning, and working memory have been found in patients with NF1. However, ED is also a hallmark of attention deficit hyperactivity disorder (ADHD) and approximately 50% of patients with NF1 fulfill the diagnostic criteria of ADHD, leaving a large number from the remaining population with subclinical attention problems. This suggests, ED in NF1 might simply be because of the comorbid ADHD, but the current research reveals that ED is present independently of an ADHD diagnosis. In an ongoing, large-scale, observatory study, we investigate whether patients with NF1 with and without ADHD differ from patients with idiopathic ADHD.

Methods: Up to now, we included 52 children with NF1+ADHD, NF1-only, or idiopathic ADHD, aged between 6 and 11 years. We provided the parent questionnaire for the Behavior Rating Inventory of Executive Function (BRIEF), and assessed intelligence (WISC-IV) and severity of ADHD symptoms (Conners-3, DISYPS-KJ). Socioeconomic status (SES) was measured with the Winkler Index.

Results: There were no significant differences between the patient groups in sex, age, and SES, but the NF1-only group had a significantly higher IQ (mean, 101.38; SD, 7.95) than the NF1+ADHD group (mean, 90.58; SD, 10.49). ADHD severity was significantly pronounced in the two ADHD groups, but did not differ between these two groups. Taking IQ into account, both the groups were significantly more impaired in impulse control ($p=0.032$), working memory ($p=0.001$), planning ($p=0.003$), and monitoring ($p=0.002$), when compared with the NF1-only group. The NF1-only group was neither affected in attention functions nor in executive functions.

Conclusion: Patients with NF1+ADHD show a similar pattern of ED as patients with idiopathic ADHD, whereas patients with "pure" NF1 do not seem to be impaired. In contrast to previous research, we found comorbid ADHD to be the decisive factor for ED in NF1

Neuropsychiatry. 2016;6:75-79.

INFLUENCE OF TEMPERAMENTS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS AMONG PRESCHOOL CHILDREN.

Yoo HJ, Ha JH, Yu J, et al.

The objective of this study was to evaluate the relationship between attention deficit hyperactive symptoms and temperament and character profiles among preschool-age children. Total 694 preschool age children (mean age=5.7-10.45) were recruited for the study. The preschool Temperament and Character Inventory (psTCI) and DuPaul ADHD rating scale (K-ARS) were applied to evaluate the children. Statistical analysis was done to explore the association between psTCI profiles and ADHD symptom domains. The total ARS score was positively correlated with novelty seeking and harm avoidance. Inattention symptom domain was positively correlated both with novelty seeking and harm avoidance, whereas hyperactive symptom domain was only correlated with novelty seeking. Novelty seeking might be a universal genetic background for ADHD, and the level of harm avoidance could potentially be used to classify subtypes of ADHD

Neuropsychology. 2017.

PERCEPTUAL AND RESPONSE-DEPENDENT PROFILES OF ATTENTION IN CHILDREN WITH ADHD.

Caspersen ID, Petersen A, Vangkilde S, et al.

Objective: Attention-deficit hyperactivity disorder (ADHD) is a complex developmental neuropsychiatric disorder, characterized by inattentiveness, impulsivity, and hyperactivity. Recent literature suggests a potential core deficit underlying these behaviors may involve inefficient processing when contextual stimulation is low. In order to specify this inefficiency, the aim of the present study was to disentangle perceptual and response-based deficits of attention by supplementing classic reaction time (RT) measures with an accuracy-only test. Moreover, it was explored whether ADHD symptom severity was systematically related to perceptual and response-based processes.

Method: We applied an RT-independent paradigm (Bundesen, 1990) and a sustained attention task (Dockree et al., 2006) to test visual attention in 24 recently diagnosed, medication-naïve children with ADHD, 14 clinical controls with pervasive developmental disorder, and 57 healthy controls. Outcome measures included perceptual processing speed, capacity of visual short-term memory, and errors of commission and omission.

Results: Children with ADHD processed information abnormally slow ($d = 0.92$), and performed poorly on RT variability and response stability (d 's ranging from 0.60 to 1.08). In the ADHD group only, slowed visual processing speed was significantly related to response lapses (omission errors). This correlation was not explained by behavioral ratings of ADHD severity.

Conclusions: Based on combined assessment of perceptual and response-dependent variables of attention, the present study demonstrates a specific cognitive profile in children with ADHD. This profile distinguishes the disorder at a basic level of attentional functioning, and may define subgroups of children with ADHD in a way that is more sensitive than clinical rating scales

Neuropsychology. 2017 Feb;31:200-08.

EVALUATION OF RELATIONAL REASONING BY A TRANSITIVE INFERENCE TASK IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Brunamonti E, Costanzo F, Mammi A, et al.

Objective: Here we explored whether children with ADHD have a deficit in relational reasoning, a skill subtending the acquisition of many cognitive abilities and social rules.

Method: We analyzed the performance of a group of children with ADHD during a transitive inference task, a task requiring first to learn the reciprocal relationship between adjacent items of a rank ordered series (e.g., $A > B$; $B > C$; $C > D$; $D > E$; $E > F$), and second, to deduct the relationship between novel pairs of items never matched during the learning (e.g., $B > D$; $C > E$).

Results: As a main result, we observed that children with ADHD were impaired in performing inferential reasoning problems. The deficit in relational reasoning was found to be related to the difficulty in managing a unified representation of ordered items.

Conclusion: The present finding documented a novel deficit in ADHD, contributing to improving the understanding of the disorder

Nord J Psychiatry. 2017;71:296-303.

PROCESSING SPEED CAN MONITOR STIMULANT-MEDICATION EFFECTS IN ADULTS WITH ATTENTION DEFICIT DISORDER WITH HYPERACTIVITY.

Nielsen NP, Wiig EH, Børnæs S, et al.

Background: Treatment responses to methylphenidate by adults with ADHD are generally monitored against DSM-IV/DSM-V symptomatology, rating scales or interviews during reviews.

Aims: To evaluate the use of single- and dual-dimension processing-speed and efficiency measures to monitor the effects of pharmacological treatment with methylphenidate after a short period off medication.

Methods: A Quick Test of Cognitive Speed (AQT) monitored the effects of immediate-release methylphenidate in 40 previously diagnosed and medicated adults with ADHD. Processing speed was evaluated with prior prescription medication, without medication after a 2-day period off ADHD medication, and with low-dose (10/20 mg) and high-dose (20/40 mg) methylphenidate hydrochloride (Medikinet IR).

Results: Thirty-three participants responded to the experimental treatments. One-way ANOVA with post-hoc analysis (Scheffe) indicated significant main effects for single dimension colour and form and dual-dimension colour–form naming. Post-hoc analysis indicated statistical differences between the no- and high-dose medication conditions for colour and form, measures of perceptual speed. For colour–form naming, a measure of cognitive speed, there was a significant difference between no- and low-dose medication and between no- and high-dose medications, but not between low- and high-dose medications.

Conclusions: Results indicated that the AQT tests effectively monitored incremental effects of the methylphenidate dose on processing speed after a 2-day period off medication. Thus, perceptual (colour and form) and cognitive speed (two-dimensional colour–form naming) and processing efficiency (lowered shift costs) increased measurably with high-dose medication. These preliminary findings warrant validation with added measures of associated behavioural and cognitive changes

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Nord J Psychiatry. 2017;1-9.

MULTIMODAL TREATMENT IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A 6-MONTH FOLLOW-UP.

Duric NS, Assmus J, Gundersen D, et al.

Background: Different treatment approaches aimed at reducing attention-deficit/hyperactivity disorder (ADHD) core symptoms are available. However, factors such as intolerance, side-effects, lack of efficacy, high new technology costs, and placebo effect have spurred on an increasing interest in alternative or complementary treatment.

Aim: The aim of this study is to explore efficacy of multimodal treatment consisting of standard stimulant medication (methylphenidate) and neurofeedback (NF) in combination, and to compare it with the single treatment in 6-month follow-up in ADHD children and adolescents.

Methods: This randomized controlled trial with 6-month follow-up comprised three treatment arms: multimodal treatment (NF + MED), MED alone, and NF alone. A total of 130 ADHD children/adolescents participated, and 62% completed the study. ADHD core symptoms were recorded pre-/post-treatment, using parents' and teachers' forms taken from Barkley's Defiant Children: A Clinician's Manual for Assessment and Parent Training, and a self-report questionnaire.

Results: Significant ADHD core symptom improvements were reported 6 months after treatment completion by parents, teachers, and participants in all three groups, with marked improvement in inattention in all groups. However, no significant improvements in hyperactivity or academic performance were reported by teachers or self-reported by children/adolescents, respectively, in the three groups. Changes obtained with multimodal treatment at 6-month follow-up were comparable to those with single medication treatment, as reported by all participants.

Conclusions: Multimodal treatment using combined stimulant medication and NF showed 6-month efficacy in ADHD treatment. More research is needed to explore whether multimodal treatment is suitable for ADHD children and adolescents who showed a poor response to single medication treatment, and for those who want to reduce the use of stimulant medication

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Pediatr Drugs. 2017;1-16.

SAFETY, TOLERABILITY AND EFFICACY OF DRUGS FOR TREATING BEHAVIOURAL INSOMNIA IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW WITH METHODOLOGICAL QUALITY ASSESSMENT.

Anand S, Tong H, Besag FMC, et al.

OBJECTIVE: A large proportion of paediatric patients with attention-deficit/hyperactivity disorder (ADHD) have associated sleep problems which not only affect the child's wellbeing but also impact family functioning. Management of sleep problems is consequently an important aspect of overall ADHD management in paediatric patients. Although some drugs are being used off-label for the management of paediatric insomnia, there is scant clinical evidence supporting their use. Our aim was to identify and assess the quality of published studies reporting the safety, tolerability and efficacy of drugs used for treating behavioural insomnia in children with ADHD.

METHODS: After an initial screen to determine which drugs were most commonly used, we conducted a systematic review of English-language publications from searches of PubMed, EMBASE, PsycINFO and two trial register databases to February 2017, using keywords 'clonidine', 'melatonin', 'zolpidem', 'eszopiclone', 'L-theanine', 'guanfacine', 'ADHD', 'sleep disorder' and 'children'. For quality assessment of included studies, we used the CONSORT checklist for randomised control trials (RCTs) and the Downs and Black checklist for non-RCTs.

RESULTS: Twelve studies were included. Two case series for clonidine, two RCTs and four observational studies for melatonin and one RCT each for zolpidem, eszopiclone, L-theanine and guanfacine. Of the 12 included studies, only one on eszopiclone scored excellent for quality. The quality of the rest of the studies varied from moderate to low. For clonidine, melatonin and L-theanine, improvements in sleep-onset latency and total sleep duration were reported; however, zolpidem, eszopiclone and guanfacine failed to show any improvement when compared with placebo. Clonidine, melatonin, L-theanine, eszopiclone and guanfacine were well tolerated with mild to moderate adverse events; zolpidem was associated with neuropsychiatric adverse effects.

CONCLUSION: There is generally poor evidence for prescribing drugs for behavioural insomnia in children with ADHD. Further controlled studies are warranted

Pediatr Res. 2017;81:434-42.

ASSOCIATION BETWEEN BREASTFEEDING DURATION AND COGNITIVE DEVELOPMENT, AUTISTIC TRAITS AND ADHD SYMPTOMS: A MULTICENTER STUDY IN SPAIN.

Boucher O, Julvez J, Guxens M, et al.

Background: Several studies have related longer breastfeeding duration to better intellectual performance in children. By contrast, few studies have investigated the potential protective effects of breastfeeding against behavioral problems such as attention deficit hyperactivity disorder (ADHD) symptoms, and even fewer on autism spectrum disorders (ASD) traits.

Methods: We examined the association between breastfeeding duration and cognitive development, attention, ADHD symptoms, and autistic traits using data from the INMA Project, a Spanish multicenter birth-cohort study, and taking into account the intensity of breastfeeding. Duration of any, predominant, and exclusive breastfeeding was documented during infancy through maternal questionnaires. Children (N = 1,346; mean age = 4.9 y) were assessed using the McCarthy Scales of Children's Abilities, Conners' Kiddie Continuous Performance Test, criteria of the DSM-ADHD symptoms form list, and the Childhood Autism Spectrum Test.

Results: After adjustment for several confounders, longer duration of breastfeeding was independently associated with better cognitive development and with fewer autistic traits.

Conclusion: This study provides further evidence of a positive association of breastfeeding with cognitive function apart from socio-environmental factors, and also suggests a protective role against autistic traits. Results are in agreement with recommendations for prolonged breastfeeding duration to promote child development

Pharmacoepidemiol Drug Saf. 2017;26:274-84.

ADHD MEDICATIONS AND CARDIOVASCULAR ADVERSE EVENTS IN CHILDREN AND ADOLESCENTS: CROSS-NATIONAL COMPARISON OF RISK COMMUNICATION IN DRUG LABELING.

Sieluk J, Palasik B, DosReis S, et al.

PURPOSE: Regulators approve written medical information for healthcare professionals and consumers, but the consistency of these sources has not been studied. We investigated the consistency of information regarding four cardiovascular risks of attention-deficit/hyperactivity disorder (ADHD) medications approved in four countries.

METHODS: Professional and consumer product labeling for five ADHD medications approved in Australia, Canada, the UK, and the USA were obtained in March/April 2016. Language describing the relationship between medication and elevated blood pressure and/or heart rate, myocardial infarction, stroke, and sudden death was extracted verbatim and classified into one of four categories based on the described relationship between medication and adverse event: "confirmed," "unconfirmed," "mixed," and "not mentioned." We judged the consistency of messages delivered to healthcare professionals and consumers as either "consistent" or "inconsistent."

RESULTS: We obtained 20 healthcare professional labels and 20 corresponding consumer labels for the five ADHD medications registered in all four countries. Not all professional and consumer labeling contained language regarding all four adverse events. Of the 80 theoretically evaluable drug-risk pairs, 38 (48%) were not evaluable because of absence of mention of the adverse event in the consumer label. For the remaining 42, the potential causal relationship was expressed consistently in professional and consumer labeling in 25 (60%) cases. The cardiovascular risk profile was not described consistently across all four countries for any of the five drugs.

CONCLUSIONS: Product labeling provides healthcare professionals and consumers with inconsistent messages regarding the potential causal relationship between stimulant use and specific cardiovascular risks in children and adolescents

PLoS ONE. 2017;12.

FAMILY-BASED ASSOCIATION STUDY OF DRD4 GENE IN METHYLPHENIDATE-RESPONDED ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Leung PWL, Chan JKY, Chen LH, et al.

The 48-basepair (48-bp) variable number tandem repeat (VNTR) polymorphism in exon 3 of the dopamine receptor D4 gene (DRD4) is implicated in the etiology of attention-deficit/ hyperactivity disorder (ADHD). In particular, ADHD in European-ancestry population is associated with an increased prevalence of the 7-repeat (7R) allele of the exon 3 VNTR. However, it is intriguing to note that the 7R allele has been found to be of very low prevalence in the Chinese general population. In a previous case-control study, our research team had found that the 7R allele was similarly absent in Chinese ADHD children in Hong Kong. Instead, there was an increased prevalence of the 2R allele in Chinese ADHD children. Interestingly, in Asian samples, the 2R allele had been found to be an evolutionary derivative of the 7R allele with equivalent biochemical functionality. So, the finding of an association between ADHD and 2R allele in Chinese population does not exactly contradict the original 7R allele finding in European-ancestry population. However, given the potential pitfall of population stratification in the previous case-control design, this current study tested the 2R allele and ADHD association using a methodologically more rigorous familybased approach on 33 Chinese ADHD probands who had favorable clinical responses to stimulant medication (methylphenidate). Haplotype Relative Risk (HRR) analysis and Transmission Disequilibrium Test (TDT) both showed a significant preferential transmission of the 2R allele from the biological parents to ADHD probands (pone-tailed = 0.038, OR = 2.04; pone-tailed = 0.048, OR = 2.29, respectively). A second hypothesis speculates that it is the deviation, including 7R and 2R alleles, from the conserved ancestral 4R allele which confers risk to ADHD. Thus, a preferential transmission of non-4R alleles, against the 4R allele, from biological parents to their ADHD probands is predicted. Both HRR analysis and TDT confirmed such prediction (pone-tailed = 0.029, OR = 2.07; pone-tailed = 0.032, OR = 2.43, respectively). This study re-confirmed the original finding of a previous study that in Chinese population, the 2R allele of the DRD4 exon 3 VNTR was related to ADHD. This endorses the general thesis that DRD4 exon 3 VNTR polymorphism is related to ADHD, despite that

the exact length or number of repeats of the associated alleles varies across ethnicity. This in turn supports the dopamine dysregulation theory of ADHD

PLoS ONE. 2017;12.

THE ASSOCIATION BETWEEN METHYLPHENIDATE TREATMENT AND THE RISK FOR FRACTURE AMONG YOUNG ADHD PATIENTS: A NATIONWIDE POPULATION-BASED STUDY IN TAIWAN.

Chen VCH, Yang Y-H, Liao Y-T, et al.

Attention-deficit hyperactivity disorder (ADHD) is associated with higher risk for fracture. Whether the medical treatment for ADHD would mitigate the risk remains unclear. In this study, we sought to investigate the effect of methylphenidate treatment on risk for fracture, as well the moderational role of treatment duration on the risk of fracture, in a large national sample. Cases less than 18 years old were identified from Taiwan's National Health Insurance Research Database with a new primary diagnosis of ADHD (ICD-9:314) between 1996 and 2013. A total of 6201 cases with ADHD were included as the study cohort. The cases were divided into 3 groups according to the duration of methylphenidate treatment (0, 1-180, and more than 180 days). All groups were followed until the end of 2013 for first diagnoses of fracture (ICD-9 codes 800 to 829). Cox proportional hazards models were applied. Compared to the group without methylphenidate treatment, the risk for fracture was lower among the group treated for more than 180 days. The adjusted hazard ratio was 0.77 (95% Confidence interval: 0.63-0.94). The groups treated for 180 days or fewer had no significant difference in the risk for fracture. In conclusion, methylphenidate treatment was associated with lower risk for fracture among ADHD patients. The association was evident only in the cohort treated for more than 180 days

Postgrad Med. 2017 Apr;129:375-81.

PARENT-BASED DIAGNOSIS OF ADHD IS AS ACCURATE AS A TEACHER-BASED DIAGNOSIS OF ADHD.

Bied A, Biederman J, Faraone S.

OBJECTIVE: To review the literature evaluating the psychometric properties of parent and teacher informants relative to a gold-standard ADHD diagnosis in pediatric populations.

METHOD: We included studies that included both a parent and teacher informant, a gold-standard diagnosis, and diagnostic accuracy metrics. Potential confounds were evaluated. We also assessed the 'OR' and the 'AND' rules for combining informant reports.

RESULTS: Eight articles met inclusion criteria. The diagnostic accuracy for predicting gold standard ADHD diagnoses did not differ between parents and teachers. Sample size, sample type, participant drop-out, participant age, participant gender, geographic area of the study, and date of study publication were assessed as potential confounds.

CONCLUSION: Parent and teachers both yielded moderate to good diagnostic accuracy for ADHD diagnoses. Parent reports were statistically indistinguishable from those of teachers. The predictive features of the 'OR' and 'AND' rules are useful in evaluating approaches to better integrating information from these informants

Preventive Med Reports. 2017;6:210-13.

PILOTING A MOBILE HEALTH INTERVENTION TO INCREASE PHYSICAL ACTIVITY FOR ADOLESCENTS WITH ADHD.

Schoenfelder E, Moreno M, Wilner M, et al.

Physical activity (PA) reduces symptoms of Attention Deficit Hyperactivity Disorder (ADHD); interventions to increase PA may improve functioning and health for adolescents with ADHD. Mobile health (mHealth) technology and social media constitute promising interactive modalities for engaging adolescents who are at highest risk for ADHD treatment drop-out in interventions to increase PA. The current pilot study evaluated feasibility and acceptability of an innovative intervention incorporating an mHealth-linked wearable

activity tracker (Fitbit Flex) and a Facebook group to increase PA among adolescents with ADHD. 11 adolescents diagnosed with ADHD (age 14–18, $m = 15.5$; 54% female) participated in a 4-week trial utilizing the Fitbit Flex in conjunction with (1) weekly personalized step count goals (2) social support through a Facebook group and (3) daily text messages about PA. The study took place in the greater Seattle, Washington area in the fall of 2015. Adolescents completed online surveys twice per week to rate their ADHD symptoms and positive and negative mood states, and parents rated adolescent ADHD symptoms weekly. Participants were adherent to the study protocol and acceptability of the intervention was high. Linear mixed models indicated that participants significantly increased their average weekly steps over the course of the study and demonstrated improvements in both adolescent and parent-reported ADHD Inattentive symptoms. Results indicate that this mHealth intervention is engaging and promising for increasing PA among adolescents with ADHD, and warrant further study. Implications for improving ADHD symptoms and overall functioning for this undertreated population are discussed

Psychiatr Psychol Klin. 2016;16:68-80.

THE DYNAMICS OF ATTENTIONAL AND INHIBITORY FUNCTIONS IN THE PRESENCE OF DISTRACTING STIMULI IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, HIGH-FUNCTIONING AUTISM AND OPPOSITIONAL DEFIANT DISORDER.

Borkowska AR.

The objective of this study is to elucidate the specific nature of attention and response inhibition deficits in three clinical groups: attention-deficit/hyperactivity disorder, oppositional defiant disorder, and high-functioning autism, as compared to children with a typical development. The analysis approached task performance dynamics as a function of time and the presence of distracting stimuli.

Material and method: 108 children aged 7-12 years participated in the study - 21 diagnosed with oppositional defiant disorder, 21 with high-functioning autism, 19 with attention-deficit/hyperactivity disorder; 47 made the control group. The study employed the MOXO-CPT to evaluate attention and inhibition functions.

Results: Pairwise comparisons of clinical groups with typically-developing children in their performance on the entire test indicated considerable differences between the control group and children with both oppositional defiant disorders and attention-deficit/hyperactivity disorder, but not between healthy subjects and children with autism. Performance profiles varied depending on the group, i.e. the type of disorder, and the level of the test, i.e. stimulus duration and intensity, but they were different for the particular studied aspects of attention and/or inhibition. High levels of similarity in functioning for all clinical groups were found in the measures of response accuracy, i.e. sustained attention and the speed of accurate response. The tendency to provide unnecessary responses and difficulties in complying with rules were found only in children with oppositional-defiant disorders. Impulsiveness rates increased over time in the attention-deficit/hyperactivity disorder group, fluctuated over time in autism, while in the oppositional defiant disorder group performance was stable over time, but worse than in the control group.

Conclusions: The dynamics of attentional and inhibitory control in clinical groups differs considerably in comparison to typically-developing children. The most substantial differences between clinical groups are observed in the inhibition indices

Psychiatrische Praxis. 2017.

NEW WAYS OF DIAGNOSING ADHD IN ADULTS: THE ESSEN-INTERVIEW-FOR-SCHOOL-DAYS-RELATED-BIOGRAPHY (EIS-B).

Grabemann M, Zimmermann M, Strunz L, et al.

Objective Diagnosing Attention-Deficit-Hyperactivity Disorder (ADHD) in adults requires that ADHD has already been present in childhood. However, recall of ADHD-symptoms in childhood is fallible, for example influenced by mood. Furthermore, diagnostics need a procedure to handle oblivion and judgment biases.

The Essen-Interview-for-school-days-related-biography (EIS-B) addresses these problems and offers a tool for retrospectively diagnosing childhood ADHD in adults.

Method 36 patients with ADHD, 27 patients with depression or adjustment disorders and 39 healthy controls were included in the pilot study. All participants were comparable regarding age and gender.

Results Internal consistency varied between $\alpha=0.58$ and $\alpha=0.97$, split-half-reliability was $r=0.98$, inter-rater-reliability yielded $\kappa=0.66$. Retest-reliability varied between $r=0.40$ and $r=0.88$. Sensitivity was 82%. Specificity yielded 100%.

Discussion The results indicate that EIS-B is a reliable and valid interview to retrospectively elucidate symptoms of childhood ADHD in adult patients. Further studies should aim for replication of our results using a larger sample size

Psychiatry Res. 2017.

Do ADHD SUBTYPES RELATED TO SPECIFIC IMPAIRMENT OF COGNITIVE FUNCTIONS IN BOYS WITH TS?

Mao S, Yang R.

Sleep Med. 2017;33:91-96.

EVALUATION OF SLEEP ORGANIZATION IN PATIENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AND ADHD AS A COMORBIDITY OF EPILEPSY.

Kalil NF, Nunes ML.

OBJECTIVE/BACKGROUND: Epilepsy or attention deficit hyperactivity disorder (ADHD) can influence sleep organization in different ways. The aim of this study was to evaluate sleep organization in children and adolescents with ADHD and epilepsy, and to analyze the influence of methylphenidate.

METHODS: This was an observational, cross-sectional study of children and adolescents with epilepsy, who were seizure free for at least three months, and were also diagnosed with ADHD. They were selected from the epilepsy and child neurology outpatient clinic of a university hospital in Brazil. After sample size calculation, patients were consecutively included into four different groups, with 21 patients each: epilepsy + ADHD using methylphenidate, epilepsy + ADHD not using methylphenidate, only ADHD, and a healthy control group. All participants were evaluated with the Sleep Disturbance Scale for Children (SDSC) and monitored with actigraphy for five nights/days.

RESULTS: Actigraphic analysis showed a higher number of night awakenings in the epilepsy + ADHD groups; they were most prominent in the group without methylphenidate ($p = 0.001$). Parental reports demonstrated a higher risk for sleep disturbances in the epilepsy + ADHD without methylphenidate and the ADHD groups ($p < 0.001$).

CONCLUSION: Primary ADHD as a comorbidity of epilepsy impairs sleep organization in children, and the use of short-acting methylphenidate seems to improve it. Both objective (actigraphic) and subjective (SDSC) measures showed significant sleep alterations between primary ADHD and ADHD as a comorbidity of epilepsy; this was most prominent in the group without methylphenidate

Stress. 2017;20:149-58.

MOTHERS' PARENTING STRESS IS ASSOCIATED WITH SALIVARY CORTISOL PROFILES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Korpa T, Pervanidou P, Angeli E, et al.

The aim of this study was to explore the relation between mothers' parenting stress and the functioning of the hypothalamic-pituitary-adrenal axis (HPAA), as expressed by daily salivary cortisol concentrations, in their children diagnosed with attention deficit hyperactivity disorder (ADHD). Seventy-five children aged 6-11 years diagnosed with ADHD predominant hyperactive-impulsive/combined (ADHD-HI/C, N = 49) and inattentive symptoms (ADHD-I, N = 26) and 45 healthy peers and their mothers participated in the study.

Mothers completed measures assessing their children's ADHD status, perceived parenting stress (Parenting Stress Index - Short Form, PSI-SF), mothers' symptoms of psychopathology, social support and socioeconomic status. Children's salivary cortisol samples were collected at six different time points on a single day. Mothers of children with ADHD-HI/C reported higher levels of parenting stress than mothers of children with ADHD-I and controls. All PSI-SF subscales showed significant associations with children's cortisol awakening response (CAR) in both ADHD groups, with the exception of the parental distress subscale in the ADHD-I group. In both ADHD groups, the parent-child dysfunctional interaction subscale, the difficult child subscale and the PSI total score were significantly associated with children's CAR. An interrelation is revealed between mothers' high levels of parenting stress and HPA axis functioning in children with ADHD. In this population, CAR has been identified as a sensitive peripheral measure of HPA axis functioning in children. Lay summary This study showed that in families of children diagnosed with ADHD, there is a complex relation between the mothers' high levels of parenting stress and children's atypical hypothalamic-pituitary-adrenal axis functioning

Trials. 2017;18.

EFFECT OF PYCNOGENOL-« ON ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): STUDY PROTOCOL FOR A RANDOMISED CONTROLLED TRIAL.

Verlaet AAJ, Ceulemans B, Verhelst H, et al.

BACKGROUND: Methylphenidate (MPH), the first choice medication for attention-deficit hyperactivity disorder (ADHD), is associated with serious adverse effects like arrhythmia. Evidence on the association of ADHD with immune and oxidant-antioxidant imbalances offers potential for antioxidant and/or immunomodulatory nutritional supplements as ADHD therapy. One small randomised trial in ADHD suggests, despite various limitations, therapeutic benefit from Pycnogenol®, a herbal, polyphenol-rich extract.

METHODS: This phase III trial is a 10-week, randomised, double-blind, placebo and active treatment controlled multicentre trial with three parallel treatment arms to compare the effect of Pycnogenol® to MPH and placebo on the behaviour of 144 paediatric ADHD and attention-deficit disorder (ADD) patients. Evaluations of behaviour (measured by the ADHD-Rating Scale (primary endpoint) and the Social-emotional Questionnaire (SEQ)), immunity (plasma cytokine and antibody levels, white blood cell counts and faecal microbial composition), oxidative stress (erythrocyte glutathione, plasma lipid-soluble vitamins and malondialdehyde and urinary 8-OHdG levels, as well as antioxidant enzyme activity and gene expression), serum zinc and neuropeptide Y level, urinary catecholamines and physical complaints (Physical Complaints Questionnaire) will be performed in week 10 and compared to baseline. Acceptability evaluations will be based on adherence, dropouts and reports of adverse events. Dietary habits will be taken into account.

DISCUSSION: This trial takes into account comorbid behavioural and physical symptoms, as well as a broad range of innovative immune and oxidative biomarkers, expected to provide fundamental knowledge on ADHD aetiology and therapy. Research on microbiota in ADHD is novel. Moreover, the active control arm is rather unseen in research on nutritional supplements, but of great importance, as patients and parents are often concerned with the side effects of MPH.

TRIAL REGISTRATION: Clinicaltrials.gov number: NCT02700685 . Registered on 18 January 2016. EudraCT 2016-000215-32 . Registered on 4 October 2016

Value Health. 2017.

CHALLENGES OF DEVELOPING AN OBSERVABLE PARENT-REPORTED MEASURE: A QUALITATIVE STUDY OF FUNCTIONAL IMPACT OF ADHD IN CHILDREN.

Matza LS, Margolis MK, Deal LS, et al.

Background: Informant-reported outcome measures, usually completed by parents, are often administered in pediatric clinical trials with the intention of collecting data to support claims in a medical product label. Recently, there has been an emphasis on limiting these measures to observable content, as recommended in the US Food and Drug Administration guidance on patient-reported outcomes. This qualitative study

explores the concept of observability using the example of childhood attention deficit/hyperactivity disorder (ADHD).

Methods: Concept elicitation interviews were conducted with children (aged 6-12 years) diagnosed with ADHD and parents of children with ADHD to identify concepts for a potential parent-reported measure of functional impact of childhood ADHD. The observability of each concept was considered.

Results: Of the 30 parents (90% females; mean age = 42.0 years), 24 had a child who was also interviewed (87.5% males; mean age = 9.6 years). Areas of functional impact reported by parents and/or children included the following: 1) functioning within the home/family, 2) academic performance, 3) school behavior, 4) social functioning, 5) emotional functioning, and 6) decreased self-efficacy. Parents cited many examples of direct observation at home, but opportunities for observation of some important areas of impact (e.g., school behavior and peer relationships) were limited.

Conclusions: Findings illustrate the substantial functional impairment associated with childhood ADHD while highlighting the challenges of developing informant-reported outcome measures limited to observable content. Because ADHD has an impact on children's functioning in a wide range of contexts, a parent-report measure that includes only observable content may fail to capture important aspects of functional impairment. Approaches for addressing this observability challenge are discussed

Value Health. 2017;20:602-09.

ECONOMIC BURDEN OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AMONG PEDIATRIC PATIENTS IN THE UNITED STATES.

Gupte-Singh K, Singh RR, Lawson KA.

Objectives To determine the adjusted incremental total costs (direct and indirect) for patients (aged 3–17 years) with attention-deficit/hyperactivity disorder (ADHD) and the differences in the adjusted incremental direct expenditures with respect to age groups (preschoolers, 0–5 years; children, 6–11 years; and adolescents, 12–17 years).

Methods The 2011 Medical Expenditure Panel Survey was used as the data source. The ADHD cohort consisted of patients aged 0 to 17 years with a diagnosis of ADHD, whereas the non-ADHD cohort consisted of subjects in the same age range without a diagnosis of ADHD. The annual incremental total cost of ADHD is composed of the incremental direct expenditures and indirect costs. A two-part model with a logistic regression (first part) and a generalized linear model (second part) was used to estimate the incremental costs of ADHD while controlling for patient characteristics and access-to-care variables.

Results The 2011 Medical Expenditure Panel Survey database included 9108 individuals aged 0 to 17 years, with 458 (5.0%) having an ADHD diagnosis. The ADHD cohort was 4.90 times more likely (95% confidence interval [CI] 2.97–8.08; $P < 0.001$) than the non-ADHD cohort to have an expenditure of at least \$1, and among those with positive expenditures, the ADHD cohort had 58.4% higher expenditures than the non-ADHD cohort ($P < 0.001$). The estimated adjusted annual total incremental cost of ADHD was \$949.24 (95% CI \$593.30–\$1305.18; $P < 0.001$). The adjusted annual incremental total direct expenditure for ADHD was higher among preschoolers (\$989.34; 95% CI \$402.70–\$1575.98; $P = 0.001$) than among adolescents (\$894.94; 95% CI \$428.16–\$1361.71; $P < 0.001$) or children (\$682.71; 95% CI \$347.94–\$1017.48; $P < 0.001$).

Conclusions Early diagnosis and use of evidence-based treatments may address the substantial burden of ADHD

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ASTHENIA IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND THEIR TREATMENT.

Chutko LS, Surushkina SY, Nikishena IS, et al.

Objective. To study asthenia in adolescents with attention deficit hyperactivity disorder (ADHD) and assess the efficacy of nooclerin.

Material and methods. We examined 60 patients, aged from 12 to 15 years, with ADHD. A comparative analysis of ADHD demonstrated the predominance of an inattentive type (ADHD-I) and a combined type (ADHD-C).

Results and conclusion. Symptoms of asthenia were found in 56% of adolescents with ADHD-C and in 96.7% with ADHD-I. The high efficacy and safety of nooclerin in the treatment of ADHD was demonstrated. The improvement of mental state was achieved in 76.7% of patients

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RESEARCH REPORT

Dysfunctional personality traits in adolescence: effects on alerting, orienting and executive control of attention

Maria Casagrande¹ · Andrea Marotta^{1,4} · Valeria Canepone¹ · Alfredo Spagna¹ · Caterina Rosa² · Giancarlo Dimaggio³ · Augusto Pasini²

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Abstract The present study examined attentional networks performance in 39 adolescents with dysfunctional personality traits, split into two group, Group < 10 and Group ≥ 10 , according to the number of criteria they met at the Structured Clinical Interview for DSM-IV Axis II Personality Disorders. The attentional performance has been tested by means of a modified version of the Attentional Network Test (ANTI-V) which allows testing both phasic and tonic components of the alerting system, the exogenous aspect of the orienting system, the executive network and their interactions. Results showed that the orienting costs of having an invalid spatial cue were reduced in the Group ≥ 10 criteria compared to the Group < 10 . Moreover, adolescents included in the Group ≥ 10 showed lower conflict when attention was cued to the target location (valid trials) but showed normal interference when there was no overpowering focus of attention (invalid trials). The results found with ANOVA after splitting the sample into two categorical groups were

also observed in a complementary correlation analysis keeping intact the continuous nature of such variables. These findings are consistent with the notion that dysfunctional features of personality disorders may represent the psychological manifestations of a neuropsychological abnormality in attention and executive functioning. Finally, we discuss the implications of this attentional anomaly for dysfunctional personality traits and behaviour.

Keywords Personality disorders · Attentional networks · Exogenous orienting · Cognitive control · Attention network test

Introduction

In the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV TR; American Psychiatric Association 2000), personality disorders (PD) are defined as an enduring pattern (inflexible and pervasive) of inner experience and behaviour that deviates markedly from what is normative within the individual's culture. Interestingly, as delineated in DSM-IV TR, personality disorders may not only express themselves by problems in the regulation of affectivity and interpersonal functioning but also through cognition. According to some studies (i.e. Coolidge et al. 2004), many of the dysfunctional features of PD may represent the psychological manifestations of a neuropsychological deficit in executive functioning and attention. Consistent with this view, some individuals with PD appear to have many of the characteristics of classic executive function deficits such as poor judgment, decision-making difficulties, selective attention problems, impulsivity, and inflexibility. However, it is not really understood which mechanism or component of the attentional system is mainly impaired in PD. According

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to the attention network approach, human attentional system encompasses three functionally and anatomically independent networks, which work together in everyday life and are dissociable from perception and action: alerting, orienting and executive control (Fan et al. 2002; Petersen and Posner 2012; Posner and Rothbart 2007). The orienting network is responsible for the movement of attention through space in order to select and focus on the to-be-attended stimulus; the executive network allows to the monitoring and resolution of conflict between expectation, stimulus and response; and the alerting network is involved in achieving (phasic alerting) and maintaining (tonic alerting) a general state of activation of the cognitive system. Abnormal executive cognitive functioning has been established in some specific PD such as schizotypy (Wan et al. 2006, 2008), borderline personality disorder (Gvirts et al. 2012; Posner et al. 2002) and psychopathy (e.g. Dolan and Park 2002; Morgan and Lilienfeld 2000; Ogilvie et al. 2011; Hiatt et al. 2004; Schiffer et al. 2014; Zeier et al. 2009). Other types of attentional deficits, such as alerting deficits, but not executive function deficits, have been also found to be associated with psychopathic symptoms in early adolescence (Racer et al. 2011). Orienting impairment has also been observed in borderline personality disorder (Fertuck et al. 2005), in schizotypal personality disorder (Raine et al. 1997; Schug et al. 2007) and in antisocial personality disorder APD (Schug et al. 2007).

The present study represents an initial examination of basic attention processes among adolescents with dysfunctional personality traits. This investigation is predicated on the following two assumptions: (1) the personality disorders can be measured dimensionally rather than categorically, and (2) the already proven adequacy of the use of non-clinical populations to study the personality disorders and their features (e.g. APA 2013; Jang et al. 1996; Livesley et al. 1993; Raine et al. 1992). Verheul et al. (2007) account that knowing how many criteria a patient meet for a PD can be more helpful for predicting the outcome than knowing whether the PD diagnosis is met: meeting five criteria suggests significant personality pathology and meeting 10 or more criteria is linked with greater psychological impairment. Individuals with more PD traits demonstrate more symptoms, poorer social functioning and higher levels of alexithymia than individuals with fewer PD traits (Dimaggio et al. 2013). Moreover, there are numerous studies supporting the diagnostic validity of PD in adolescence (for extensive reviews of this literature, see Bleiberg 2001; or Kernberg et al. 2000) and many of the deficits seen in adult personality disorders have been also observed in youth with elevated PD traits (Shiner 2009). Some deficits in basic attentional processes are present throughout development (e.g. Fair et al. 2012), and we can assume that these deficits may be more visible in younger populations because of their less developed

compensatory strategies. Early identification of these attentional deficits can be very useful in planning prevention programs and treatment of patients with personality disorders, given the difficulty of treating subjects with this psychopathology in adulthood.

To evaluate attentional mechanisms among youth with dysfunctional personality traits, a measure that can dissociate between specific domains of attention is needed. In the present study, we adopted a variant of the attention network task (ANT; Fan et al. 2002), the ANTI-Vigilance (ANTI-V;¹ Roca et al. 2011), a test enables to examine individual differences in efficiency of the brain networks of alerting (phasic and tonic), orienting and executive attention discussed above within the context of a quick and simple computerized task. Alerting is assessed by comparing reaction times (RTs) for targets preceded by alerting cues informing the temporal onset of the target with those not preceded by any cue (i.e. alerting effect). The orienting is assessed by comparing RTs for spatially cued targets with RTs for spatially uncued targets (i.e. orienting effect). Executive attention is assessed by comparing RTs for targets flanked by congruent distractors with those flanked by incongruent distractors (i.e. the conflict effect). The ANT has been successfully used to address the attentional performance in healthy adults (Callejas et al. 2004, 2005; Federico et al. 2013; Martella et al. 2011; Spagna et al. 2014, 2016), children (Federico et al. 2016), adolescents (Racer et al. 2011) and clinical patients (Casagrande et al. 2011; Marotta et al. 2015; Martella et al. 2014). Dysfunctional personality traits were assessed by the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II; First et al. 1997). We also administered the GAF (Hall 1995) as a measure of functioning, and the SCL-90-R (Derogatis 1983) as a measure of psychopathological symptoms and global distress.

We directly tested the following prediction: if personality disorders are manifestations of executive function deficits (i.e. Coolidge et al. 2004), adolescents with a higher number of dysfunctional personality traits will exhibit attentional deficits on the ANTI-V, specifically in executive control.

Materials and methods

Participants

We selected 39 drug-naïve adolescents (mean age: 15 ± 1.60 years; range 13.5–18 years; 21 males and 18

¹ The ANT has been developed to obtain an individual index of the three attentional networks (alerting, orienting, and executive control). However, alerting network measures have been usually inferred using only a phasic alertness task. The ANTI-V is useful to achieve also a direct measure of vigilance in addition to the usual ANT scores.

females) who were consecutive referrals and first admitted (no former psychiatric evaluation) to the Day Hospital of a Child Psychiatry Unit of the University of Rome “Tor Vergata” on the basis of one or more of the following symptoms: difficulties in interpersonal relationships, behavioural problems, poor school performance, anxiety and depression. The participants were selected as being right-handed and all of them reported normal or corrected to normal vision. The clinical sample of 39 subjects was divided into two groups, according to the number of dysfunctional PD traits met at the SCID-II. The SCID-II was administered by an expert and trained child and adolescent psychiatrist. One group ($n = 18$) met 10 or more criteria and received diagnosis of at least one PD, as 10 criteria are considered a cut-off which allows for the diagnosis of PD not otherwise specified. The second group ($n = 21$) included adolescents with a range of PD criteria from 0 to 9; none of them had a PD. The participants in the first group received the following PD diagnosis: borderline ($N = 5$), histrionic ($N = 1$), schizotypal ($N = 1$), avoidant ($N = 2$) and not otherwise specified ($N = 9$). The inclusion criteria to participate in the study were no history of mental retardation, brain trauma, neurological diseases or physical impairments. The main participants’ characteristics are reported in Table 1.

Measure

The Italian version of the Structured Clinical Interview for DSM-IV Personality Disorders (SCID-II; Mazzi et al. 2003) was administered to all patients enrolled in the research. By means of the SCID-II (First et al. 1997), the full range of PD traits found in DSM-IV TR was assessed (with the exception of the antisocial personality disorder which cannot be diagnosed before the age of 18 years). Although the SCID-II is primarily designed for measuring personality disorders in adults, previous studies including adolescent samples have shown that the SCID-II is a useful instrument in adolescence (Feenstra et al. 2011; Tromp and Koot 2010).

Symptom Checklist-90-R (SCL-90-R; Derogatis 1977). The SCL-90-R is a 90-items self-report inventory that was primarily designed to reflect the psychological symptom patterns of psychiatric and medical patients. The SCL-90-R measures nine primary symptom dimensions: somatization (SOM), obsessive–compulsive (O–C), interpersonal sensitivity (I–S), depression (DEP), anxiety (ANX), hostility (HOS), phobic anxiety (PHOB), paranoid ideation (PAR), psychoticism (PSY) and it allows computation of three global indexes: the global severity index (GSI), that detects the extent or depth of the individual’s psychiatric disturbance; the Positive Symptom Total (PST), that counts the

total number of symptoms; and the Positive Symptom Distress Index (PSDI), representing the intensity of symptoms.

The global assessment of functioning (GAF; Hall 1995) evaluates global functioning on a scale ranging from 1 to 100; scores higher than 70 indicate satisfactory mental health, good overall functioning and no more than minimal or transient distress or impairment. Scores between 61 and 70 signify mild impairment or distress; scores between 51 and 60 reveal moderate impairment; and scores below 51 indicate severe impairment. In adult outpatients, GAFS scores have high rates of inter-rater reliability (intra-class correlation 0.86) and are significantly related to responses on SCL 90-R, as indexed by the global severity index (Skodol et al. 2007).

Attention Network Task The ANTI-V (Roca et al. 2011, 2012) is a computerized task designed to assess alerting, orienting and executive attention (see Fig. 1). The following stimuli were presented: a black fixation cross, a warning tone, a black asterisk and a row of five cars pointing either left or right. The distance of the central target car was manipulated, being either centred or significantly displaced (i.e. appearing closer to one of the immediate flanker cars). Also, the vertical and horizontal location of each car was slightly changed in each trial, adding a random variability (± 4 pixels) to make it more difficult to distinguish between the centred and the displaced target car. The background was grey, and a two-lane road with two parking lanes was represented in the centre of the screen. The target (central car) and its flankers appeared on one of the two parking lanes, above or below the fixation cross. The instructions presented the task to the participants as a game, in which they were working in a Centre for Traffic Management and studying the drivers’ parking habits. The participants were presented for 200 ms with a row of five cars, above or below the fixation point. They had to indicate the direction of the central car, by pressing “c” (for left) or “m” (for right) on the keyboard. A period of 2000 ms was allowed for responses. The background road and the fixation point remained present until the end of the experiment. In every trial, the duration of the initial empty scene was randomly determined (400–1600 ms), and the duration of an identical final scene was adjusted so that the total trial time was 4100 ms. In half the trials, the flanker cars were pointing in the same direction as the central target car (congruent condition) and in the other half, in the opposite direction (incongruent condition). Also, 100 ms before the row of cars appeared, an asterisk was briefly presented (50 ms), either in the same location as the forthcoming target central car (valid visual cue condition), in the opposite location (invalid visual cue condition), or was preceded by no asterisk (no

Table 1 Means, standard errors (SE) and ANOVA results of: (a) age and IQ, (b) variables (SCID criteria number, scores in the cluster A, cluster B and cluster C) employed to distinguish the two groups of participants and (c) all the dependent variables considered in order to assess different psychological symptoms and characteristics in the two groups of participants

Variables	Group ≥ 10		Group < 10		ANOVA results		
	Mean	SE	Mean	SE	$F_{(1,40)}$	p	Partial η^2
Age	15.61	0.40	14.86	0.30	2.37	0.13	0.06
IQ	100.67	1.91	105.30	2.33	2.23	0.14	0.06
SCID criteria number	17.22	1.86	4.67	0.61	46.50	0.001	0.56
Cluster A	2.83	0.82	0.76	0.29	6.40	0.02	0.15
Cluster B	5.72	0.97	1.19	0.33	21.99	0.001	0.37
Cluster C	4.44	0.60	1.52	0.38	18.03	0.001	0.33
GAF	56.39	1.14	61.52	1.30	8.49	0.01	0.19
SOM	0.73	0.13	0.39	0.07	6.05	0.02	0.14
O–C	1.10	0.19	0.48	0.10	9.42	0.004	0.20
I–S	1.04	0.17	0.45	0.12	8.75	0.006	0.19
DEP	1.21	0.17	0.56	0.15	8.71	0.006	0.19
ANX	0.91	0.15	0.43	0.10	7.18	0.01	0.16
HOS	0.92	0.21	0.51	0.10	3.23	0.08	0.08
PHOB	0.48	0.12	0.14	0.05	7.98	0.008	0.18
PAR	0.96	0.17	0.41	0.09	8.56	0.006	0.19
PSI	0.63	0.14	0.13	0.05	12.90	0.001	0.26
GSI	0.91	0.12	0.41	0.07	12.81	0.001	0.26
PSDI	1.82	0.08	1.51	0.09	7.06	0.02	0.16
PST	43.33	4.56	24.67	3.23	11.62	0.002	0.24

IQ intelligence quotient, *GAF* global assessment of functioning, *SOM* somatization, *O–C* obsessive-compulsive, *I–S* interpersonal sensitivity, *DEP* depression, *ANX* anxiety, *HOS* hostility, *PHOB* phobic anxiety, *PAR* paranoid ideation, *PSY* psychoticism, *GSI* global severity index, *PSDI* positive symptom distress index, *PST* positive symptom total

visual cue condition). These three visual cue conditions were equally probable. In addition, either a 50-ms auditory warning signal (2000 Hz) was presented 500 ms before the target car was shown (warning tone condition) or it was not presented (no-warning tone condition). Finally, in 25% of the trials, the target (central car) was significantly displaced to the right or to the left. The participants were encouraged to identify these infrequent stimuli by pressing an alternative response key (spacebar) and ignoring the direction of the central car in these trials. The task was composed of 5 blocks of 64 trials each (48 trials for the usual ANTI conditions and 16 vigilance trials with the displaced central target condition). In the first (practice) block, visual feedback on accuracy was provided. This first block was followed by a pause, and there were no more rest periods until the end of the task.

General procedure

The adolescents were first submitted to psychiatric evaluation, then psychological questionnaires and the ANTI-V (Roca et al. 2011) were administered. The study was performed in accordance with the ethical standards of Declaration of Helsinki. The Child Psychiatry and Neurology Institute Ethical Committee approved the study. All parents

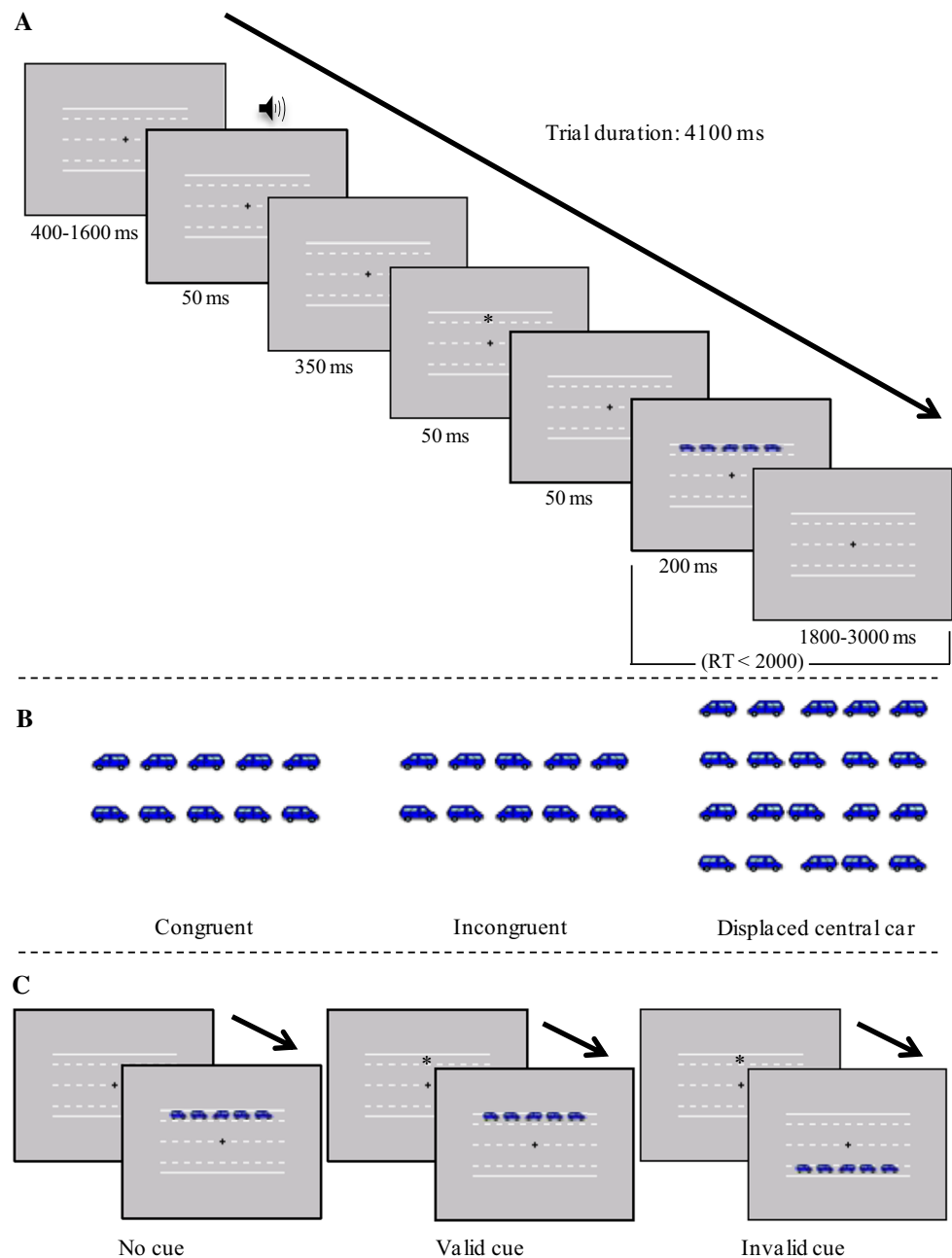
or legal guardians of adolescents gave written informed consent before testing.

Data analysis

Data were analysed using Statistica (Statsoft, Inc Tulsa, OK) v. 6.1. To analyse sociodemographic participants' characteristics, one-way analysis of variance (ANOVA) considering the group (Group ≥ 10 and Group < 10) as independent variable was performed on both age and IQ. To analyse the psychopathological profile of the two groups (Group ≥ 10 and Group < 10), one-way ANOVAs were performed on the GAF; the SCL-90-R scales (SOM; O–C; I–S; DEP; ANX; HOS; Phobic PHOB; PAR; PSY) and the three global indices: GSI; PSDI and PST. One-way ANOVAs were also performed on the variables (SCID criteria number, scores in the clusters A, B and C) employed to distinguish the two groups of participants.

To analyse the attentional networks on the two groups of adolescents, a *Group* (Group ≥ 10 and Group < 10) \times *Warning* (warning and no-warning) \times *Cue* (invalid and valid) \times *Flanker* (congruent and incongruent) ANOVA was performed on both mean RTs of corrected trials and percentage of errors. Furthermore one-way ANOVAs considering the group as independent variable were

Fig. 1 Procedure and stimuli used in the attention network test for interactions and vigilance (ANTI-V). **a** Schematic representation of the procedure. **b** The target stimuli. **c** The visual cue conditions



performed on: alerting effect (RTs no-warning–RTs warning), orienting effect (RTs invalid–RTs valid), conflict effect (RTs incongruent flanker–RTs congruent flanker), attentional costs (RTs invalid–RTs no-cue) and attentional benefits (RTs no-cue–RTs valid). Higher costs reflect the price due to disengaging attention from an invalid position, while higher benefits represent the orienting advantage of having a valid spatial cue.

To assess vigilance, the signal detection theory (SDT; Green and Swets 1966; see Stanislaw and Todorov 1999 for a review) indexes of sensitivity (d') and response bias

(β) were computed from hits (proportion of correct spacebar responses to infrequent targets) and false alarms (proportion of incorrect spacebar responses to frequent targets). When the proportion of hits or false alarms was 0 or 1, those values were substituted by 0.01 and 0.99, respectively, to obtain an appropriate approximation of the SDT indexes. One-way ANOVAs considering the group as independent variable were performed on number of hits, false alarms, d' , β and the mean RTs of the vigilance task.

To further analyse the interactions, planned comparison were used.

Finally, Pearson's correlation coefficient was used to analyse relationship between the number of PD traits and the attentional scores.

Results

Psychopathological profile

Both age and IQ were not different in the two groups of adolescents, while the GAF, the individual scales and the global indices of the SCL-90-R were higher in the Group ≥ 10 than in the Group < 10 . Mean (\pm SE) and ANOVA results are reported in Table 1.

Reaction times

Mean reaction times, standard error and mean numbers of errors are shown in Table 2. The effect of *Group* was not significant [$F_{(1,37)} = 1.57$, $p = 0.22$; Group $\geq 10 = 780$ vs. Group $< 10 = 838$ ms]; all the other main effects were significant: *Warning* [$F_{(1,37)} = 11.47$, $p < 0.002$, $\eta_p^2 = 0.24$], *Cue* [$F_{(1,37)} = 79.03$, $p < 0.001$, $\eta_p^2 = 0.68$] and *Flanker* [$F_{(1,37)} = 79.70$, $p < 0.001$, $\eta_p^2 = 0.68$]. Participants were faster when a warning tone was presented than when it was absent (warning = 799 ms vs. no-warning = 819 ms), when the visual cue was valid than invalid (valid = 780 ms vs. invalid = 838 ms) and when the flanker was congruent than incongruent (772 vs. 846 ms).

The *Cue* \times *Flanker* [$F_{(1,37)} = 7.90$, $p < 0.01$, $\eta_p^2 = 0.18$] and the *Group* \times *Cue* \times *Flanker* [$F_{(1,37)} = 4.86$, $p < 0.04$, $\eta_p^2 = 0.18$; see Fig. 2] interactions were significant. No other interactions were significant. To further examine the *Group* \times *Cue* \times *Flanker* interaction, a *Group* \times *Cue* ANOVA was performed on conflict effect (RTs incongruent–

RTs congruent). This analysis revealed a significant effect of *Group* with a lower conflict effect in the Group ≥ 10 compared to the Group < 10 (36 vs. 65 ms, respectively; $F_{(1,37)} = 4.80$, $p < 0.04$, $\eta_p^2 = 0.11$). No differences were found between valid and invalid trials [$F_{(1,37)} = 1.24$, $p = 0.27$]. Importantly, the *Group* \times *Cue* interaction was significant [$F_{(1,37)} = 4.94$, $p < 0.04$, $\eta_p^2 = 0.12$]: planned comparisons revealed that the conflict effect was the same in the two groups of participants when the cue was invalid ($F < 1$), while it was lower in the Group ≥ 10 compared to the Group < 10 when the cue was valid [$F_{(1,37)} = 5.99$, $p < 0.02$, $\eta_p^2 = 0.14$].

Percentage of errors

The ANOVA on mean percentage of errors confirm a significant effect for *Warning* [$F_{(1,37)} = 11.11$, $p < 0.01$, $\eta_p^2 = 0.23$], *Cue* [$F_{(1,37)} = 4.17$, $p < 0.05$, $\eta_p^2 = 0.10$] and *Flanker* [$F_{(1,37)} = 7.69$, $p < 0.01$, $\eta_p^2 = 0.17$]. Participants were more accurate when a warning tone was presented than when it was absent (no-warning = 4.16 vs. warning = 2.31), when the visual cue was valid than invalid (valid = 2.71 vs. invalid = 3.76) and when the flanker was congruent than incongruent (2.28 vs. 4.19). The *Group* [$F_{(1,37)} = 1.28$, $p = 0.27$], the *Cue* \times *Flanker* [$F_{(1,37)} = 3.65$, $p = 0.07$] and all the other interactions were not significant ($F < 1.7$).

Attentional effect

Alerting, orienting and conflict effects were not significant (see Table 3).

Costs The Group ≥ 10 had lower costs than Group < 10 [Group $\geq 10 = 9.68$ vs. Group $< 10 = 55.30$; $F_{(1,37)} = 6.06$, $p < 0.02$, $\eta_p^2 = 0.14$; Fig. 3].

Table 2 Means RTs (\pm SD) and percentage of errors in each experimental condition of the ANTI-V, separately in the two groups of adolescents

Warning	Cue	Flanker	Group ≥ 10			Group < 10		
			RTs	SD	% Errors	RTs	SD	% Errors
No-warning	Invalid	Congruent	765.11	149.20	3.92	826.46	176.84	2.14
		Incongruent	868.38	123.56	6.02	909.23	153.96	7.60
	Valid	Congruent	752.72	169.62	3.54	782.82	154.94	2.68
		Incongruent	774.55	158.13	5.60	875.17	165.77	1.81
	No-cue	Congruent	779.46	165.38	5.72	831.40	134.55	2.51
		Incongruent	852.92	156.84	7.33	913.47	143.97	7.00
Warning	Invalid	Congruent	759.75	139.49	1.44	816.85	147.69	1.19
		Incongruent	842.30	162.91	4.63	913.87	153.54	3.10
	Valid	Congruent	720.19	161.29	1.79	752.38	137.65	1.53
		Incongruent	758.47	134.49	3.19	824.60	141.67	1.57
	No-cue	Congruent	766.32	170.95	3.17	769.34	117.95	1.79
		Incongruent	816.36	168.41	4.79	850.80	159.72	4.77

Fig. 2 Conflict effect in the invalid and valid trials in the two groups of adolescents. The Group ≥ 10 had a lower conflict than the Group < 10 when the cue was valid ($p < 0.02$); in the Group ≥ 10 the conflict effect was higher in the invalid than valid trials ($p < 0.02$). * $p < 0.02$

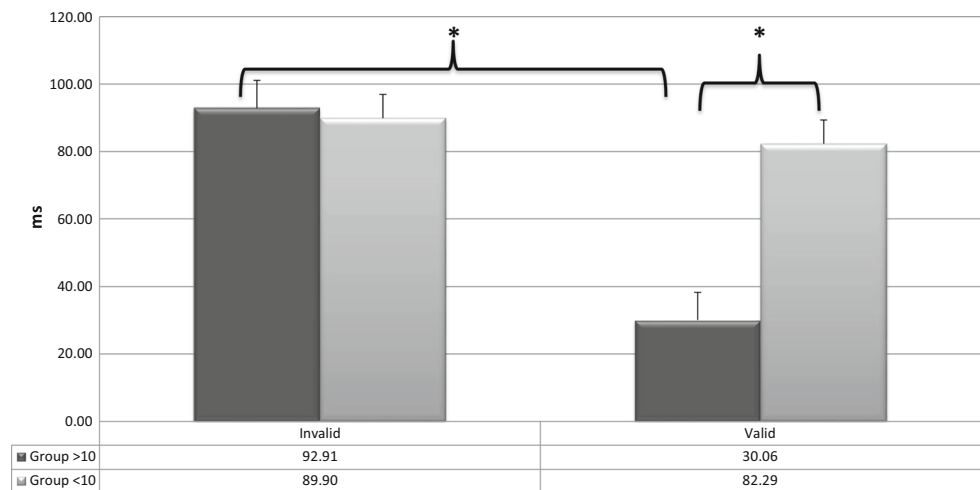


Table 3 Means, standard error (SE) and ANOVA results of attentional effects (orienting, alerting, conflict, costs and benefits), vigilance indices (proportion of hits and false alarms, d' , β and RTs of vigilance trials) in the two groups of participants

Variables	Group ≥ 10		Group < 10		ANOVA results		
	Mean	SE	Mean	SE	$F_{1,37}$	p	Partial η^2
Alerting	24.85	19.50	62.37	11.29	2.97	0.09	0.07
Orienting	57.40	11.07	57.86	7.37	<1	–	–
Conflict	61.57	8.58	84.65	9.83	3.03	0.09	0.08
Costs	9.68	16.15	55.30	10.15	6.06	0.02	0.14
Benefits	52.01	13.35	21.57	9.66	3.55	0.07	0.09
Hits	0.55	0.05	0.59	0.04	<1	–	–
False alarms	0.03	0.01	0.03	0.01	<1	–	–
d'	2.04	0.13	2.20	0.13	<1	–	–
β	8.04	1.89	7.65	1.09	<1	–	–
Vigilance	958.87	26.08	986.69	26.07	<1	–	–

Benefits The Group ≥ 10 had higher benefits than Group < 10 , but this difference was only marginally significant [Group $\geq 10 = 52.01$ vs. Group $< 10 = 21.57$; $F_{(1,37)} = 3.55$, $p = 0.07$, $\eta_p^2 = 0.09$; see Fig. 3].

Vigilance

The global RTs of vigilance trials as well as the vigilance indices (hits, false alarms, d' and β) did not differ in the two groups of adolescents (all $F < 1$; see Table 3).

Correlations

Pearson's correlations between the number of PD traits and the attentional scores (alerting, orienting, conflict, costs, benefits and vigilance scores) showed a significant correlation only for the costs. However, since the ANOVA showed significant Group \times Cue \times Flanker interaction, the Pearson's correlations were also performed by considering the conflict effect separately for the valid and the invalid trials. Results have shown a significant correlation only for the valid trials. The results are reported in Table 4.

Discussion

The adolescents were divided into two groups (Group ≥ 10 and Group < 10), on the basis of the severity of their disease, measured as a number of SCID-II traits they met (Tyrer and Johnson 1996; Verheul et al. 2007; Wilberg et al. 2008; Dimaggio et al. 2013). The cut-off 10 was chosen according to findings showing that meet 10 criteria indicate a significant impairment in the personality functioning (Verheul et al. 2007). The analysis of individual traits confirm the validity of the criteria chosen to divide the sample; in fact the number and the severity of psychopathological symptoms were greater in the adolescents with a greater number of dysfunctional personality traits. Accordingly, the Group ≥ 10 meets a greater number of SCID-II criteria in each cluster (cluster A; B; C) than the Group < 10 . Moreover, in line with other studies (Carcione et al. 2011; Dimaggio et al. 2013; Nicolò et al. 2011; Verheul et al. 2007), the global functioning was more compromised and psychopathological symptoms were higher in the Group ≥ 10 than in the Group < 10 .

Fig. 3 Attentional costs and benefits in the two groups of adolescents. * $p < 0.02$; ° $p = 0.09$

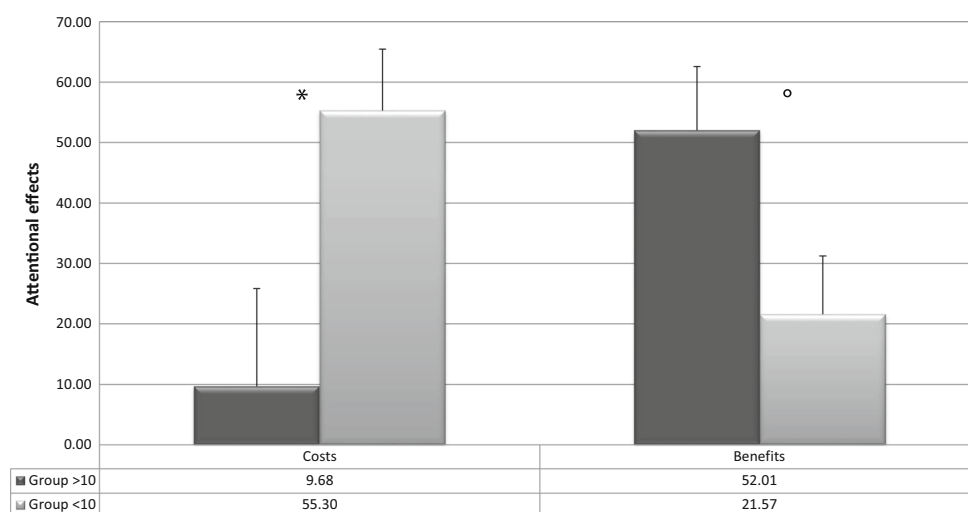


Table 4 Correlations between the number of personality disordered traits and the attentional scores considering all participants ($N = 39$)

	PD traits
Orienting	−0.093
Alerting	−0.293
Conflict	−0.208
Conflict valid	−0.384*
Conflict invalid	0.018
Costs	−0.369*
Benefits	0.087
Hits	−0.133
False alarms	0.024
d'	−0.082
β	0.170

The conflict effect (RTs incongruent flanker–RTs congruent flanker) was also separately computed by considering the valid trials (conflict valid) and the invalid trials (conflict invalid)

* $p < 0.05$

The ANTI-V allows clearly distinguishing the functioning of the three attentional networks and their interactions. Indeed, the principal Roca's et al. (2011, 2012) findings have been replicated: significant main effects for the warning signal, the visual cue and the flanker conditions, as well as main expected interactions were obtained.

Relevant to this study, we also observed that the Group ≥ 10 , compared to the Group < 10 , displayed a reduction in attentional costs (invalid minus no-cue conditions), whereas the benefits of presenting a valid spatial cue (valid minus no-cue conditions) tended to be slightly higher (although this difference was only marginally significant). These findings suggest that the number of the dysfunctional personality traits modulate the ability to

orient the attention in the space. In particular, the group with more dysfunctional personality traits was more able to rapidly disengage attention from an invalid cue to a target. This effect cannot be merely attributed to the fact that they ignored the spatial cues, given that valid cues facilitated performance for both groups of adolescents. These data suggest a less disruptive effect on performance of the invalid cues in the Group ≥ 10 group than in the Group < 10 group, that could be due to a greater ability of adolescents with more dysfunctional personality to ignore information that is detrimental to their current aims. Consistently with this view, it is important to note that adolescents included in the Group ≥ 10 present a better executive control (e.g. lower conflict effect) than adolescents included in the Group < 10 and this effect was particularly evident when their attention was cued to the target location (valid trials), whereas they showed normal conflict effects in invalid trials. The results found with ANOVA after splitting the sample into two categorical groups were also observed in a complementary correlation analysis keeping intact the continuous nature of such variables.

In the ANT task, conflict is a robust effect that is readily observed in healthy populations. However, unusually large conflict effects are indicative of poor executive control, as they reflect excessive processing of the task-irrelevant information. Generally, increased conflict effects have been associated with many forms of psychopathology, including attention-deficit/hyperactivity disorder (Casagrande et al. 2011; Johnson et al. 2008), bipolar disorder (Marotta et al. 2015) and schizophrenia (Breton et al. 2011). The increased conflict effect exhibited in these disorders has been usually associated with difficulty in maintaining an attentional focus and excessive distraction from irrelevant information. However, in the present study the performance of adolescents with more dysfunctional personality traits suggests that their attention, once

correctly oriented (valid trials), is actually less permeable to distracting contextual information than that of the adolescents with less dysfunctional personality traits. This result, apparently paradoxical, had not been predicted. Therefore, we have tried to explain it. The adolescents with a greater number of dysfunctional personality traits showed a minor conflict when the attention was selectively focused in the spatial position in which the target and the flankers (valid cue condition) were presented. In this condition, everything falls within the spotlight of attention (both target and flankers) it is perceived better and therefore a greater conflict it is observed (e.g. Callejas et al. 2005; Spagna et al. 2014). The fact that in the group ≥ 10 a very low conflict is observed in the valid trials condition leads us to the assumption that they do not sufficiently process the contextual information. A similar pattern of results has been reported in individuals with antisocial personality disorder and psychopathy (Hiatt et al. 2004; Schiffer et al. 2014; Zeier et al. 2009). In these cases, it has been proposed that if the demands of the task focus attention on target stimuli, it is easier to set an early selection filter that facilitates focusing on the target and ignoring incongruent stimuli (e.g. Zeier et al. 2009). Therefore, similarly to the individuals with antisocial personality disorder and psychopathy, adolescents with more dysfunctional personality traits may be especially prone to employ such attention filters that allow them to reduce the conflict due to incongruent contextual information. Although it is somewhat counterintuitive that superior executive control would be associated with dysfunctional personality traits, it is consistent with the importance of contextual information processing for regulating behaviour (Newman and Lorenz 2003). According to the response modulation hypothesis (Patterson and Newman 1993), deficits in adapting to changing circumstances result from an inability to process contextual information signalling the need to change behaviour in the midst of a dominant response. Our findings suggest that the so-called response modulation is considerably flatter in the more dysfunctional group of adolescents than in the less dysfunctional group. These results are of considerable clinical interest, suggesting that many of the destructive and antisocial behaviours exhibited by people with personality disorders might be in part due to a single-minded pursuit behaviour insensible to the internal and external contextual information that should constrain or interrupt their inadequate behaviour. Surely this behaviour can be functional to their psychopathological profile, but it can be suggested that a psychological improvement in their personality traits could also change this attentional behaviour. If other studies would confirm this finding, the minor conflict effect in a valid condition might be considered a marker of pathological dysfunction, while the absence of this effect, following a psychotherapeutic

treatment, could be considered a behavioural marker of mental health improvement. Consequently, implementing interventions to improve the ability to process contextual information and adapt the behaviour accordingly could be quite important for the treatments of adolescents with dysfunctional personality traits.

Interpretation of our findings should be tempered by the limitations of our study. First of all, our sample of adolescents was too small to directly compare the dimensional approach proposed in this study with the classical PD distinction based on the three different clusters (i.e. cluster A, B, C). Despite differences in attentional performances were observed as a function of the number of the dysfunctional personality traits, it is difficult to argue that these differences can be generalized to all different specific subtypes of PD. Finally, all the patients were Caucasian, limiting the generalization of results to other ethnic groups.

To conclude, the use of Roca et al.'s version of ANT (2011) gave us striking results showing the benefit of having clear measures for attentional networks and their interaction. In particular, the results of this study provide evidence of a significant association between dysfunctional personality traits and abnormal attentional performances in adolescents: participants with more dysfunctional personality traits were more able to rapidly disengage attention from an invalid spatial cue and display significantly lower conflict to response incongruent information (e.g. better cognitive control) when attention was cued to the target location. While the attentional behaviour exhibited by adolescents with more dysfunctional personality traits seems to be adaptive within the parameters of the ANTI-V methodology, we propose that their insensitivity to important contextual information may reflect a response modulation deficit and underlie failures to inhibit behaviour in social interactions with detrimental effects in their interpersonal relationships. Accordingly, understanding the nature of this response modulation deficit, and further uncovering its specific association with the behavioural problems of personality disorders, represents an essential next step towards knowing and treating adolescents with dysfunctional personality traits.

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Psychotic Symptoms in Attention-Deficit/Hyperactivity Disorder: An Analysis of the MTA Database

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Objective: To assess the prevalence of psychotic symptoms among youths (14–25 years of age) with a childhood diagnosis of attention-deficit/hyperactivity disorder (ADHD) combined type.

Method: Participants in the Multimodal Treatment Study of Children with ADHD (MTA) and a local normative comparison group (LNCG) were systematically assessed 6, 8, 10, 12, 14, and 16 years after the original enrollment at a mean age of 8.5 years. Trained research assistants administered a psychosis screener, and positive screens were referred to study clinicians to confirm or exclude psychosis. Possible associations between screening positive and alcohol or substance use were assessed.

Results: Data were available from 509 MTA participants (88% of original MTA sample; mean age 25.1 years) and 276 LNCG participants (96% of original sample; mean age 24.6 years) at year 16. Twenty-six MTA participants (5%; 95% CI 3–7) and 11 LNCG participants (4%; 95% CI 2–6)

screened positive for at least 1 psychotic symptom ($p = .60$). Most psychotic symptoms were transient. The prevalence of clinician-confirmed psychotic symptoms was 1.1% (95% CI 0.2–2.1) in the MTA group and 0.7% (0–1.7) in the LNCG ($p = .72$). Greater cannabis use was reported by those who screened positive ($p < .05$) and were confirmed positive ($p < .01$).

Conclusion: There was no evidence that ADHD increased the risk for psychotic symptoms. In the ADHD and normative comparison groups, more frequent cannabis use was associated with a greater likelihood of experiencing psychotic symptoms, thus supporting the recommendation that youth should not use cannabis.

Key words: attention-deficit/hyperactivity disorder, psychosis, cannabis, screening

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Attention-deficit/hyperactivity disorder (ADHD) is a common disorder of childhood that tends to persist into adolescence and adulthood. Psychotic disorders are rare before puberty, but their incidence increases in adolescence and peaks in early adult life. Schizophrenia, which has a population lifetime morbidity risk of 0.7%, has onset in the second or third decade of life, and early-onset schizophrenia, defined as onset before 18 years of age, accounts for approximately one-fourth of cases.¹ Schizophrenia is typically preceded by functional impairments and developmental delays,² and ADHD symptoms are often part of the prodrome of psychosis.^{3,4}

Although the prevalence of psychotic disorders is low, isolated psychotic experiences are relatively common during development. A 3.7% prevalence of hallucinations and/or delusions was recently reported in a community sample of 7,054 youths 11 to 21 years old.⁵ A 7% prevalence of psychotic experiences was found in an epidemiologic sample of 1,112 adolescents 13 to 16 years old.⁶ Subthreshold symptoms, such as unusual thoughts and auditory

misperceptions (illusions), are even more common, with rates as high as 12% in youth.⁵

Psychotic symptoms are diagnostically nonspecific and can be found in the context of conditions other than schizophrenia, such as major depression, mania, substance abuse, seizure disorders, and other neurologic disturbances.⁷ Population-based epidemiologic surveys have indicated that the mean lifetime prevalence of psychotic experiences in the non-clinically referred general population is approximately 6%.⁸ These psychotic symptoms have little psychopathologic meaning unless they are severe or persistent.^{9,10}

The association between ADHD symptoms and psychosis has been mainly studied by retrospective assessments of adults diagnosed with a psychotic disorder. A study of 122 adult patients with first-episode schizophrenia spectrum disorders reported an ADHD prevalence of 17%.¹¹ Few data are available on the rate of psychosis in ADHD samples. A 10-year prospective case-control study of 140 children with ADHD and 120 matched controls did not find a difference in the rate of psychosis.¹² One case of psychotic disorder was found in a systematic follow-up of 135 men (mean age 41 years) who were diagnosed with ADHD in childhood.¹³ However, another study, which followed 208 children with ADHD up to a mean age of 31.1 years, found a 3.8% incidence of schizophrenia, representing a significant increase over the general population rate of 0.7%.¹⁴ An increased risk



Supplemental material cited in this article is available online.

for schizophrenia and bipolar in relatives of people with ADHD also was reported.¹⁵

We report on the results of a 10-year prospective screening for psychotic symptoms conducted on a large cohort of individuals first diagnosed as children with ADHD combined type and a normative comparison group.^{16,17} As part of systematic follow-up assessments of participants in the Multimodal Treatment Study of Children with ADHD (MTA), a screener for possible psychotic symptoms was periodically administered over a 10-year period (year 6 to year 16 after baseline) up to a mean age of 25 years. In parallel, a local normative comparison group (LNCG) received the same assessments. These data were analyzed to examine whether psychotic symptoms occurred more frequently in the MTA sample than in the LNCG. In addition, possible associations of positive psychosis screening with substance abuse, IQ, and parental mental illness, which have been found to be risk factors for psychotic experience in the general population,^{18,19} were assessed.

METHOD

Design

This was a systematic follow-up of those who participated in the MTA, whose design and results have been extensively reported.^{16,20} At the end of the 14-month clinical trial, participants were naturalistically treated in the community and eligible for periodic follow-up assessments to evaluate mental health and other domains of functioning.

Sample

The MTA sample has been described in detail in previous publications.¹⁶ Briefly, it consisted of 579 children 7.0 to 9.9 years of age (mean \pm standard deviation 8.5 ± 0.8 years; 80% boys; 61% white, 20% African American, and 8% Hispanic) meeting *DSM-IV* criteria for ADHD combined type who were randomized to receive pharmacotherapy with stimulant medication, behavior therapy, their combination, or community care for 14 months and then treated naturalistically and periodically reassessed for the following 15 years.^{17,21,22} Among the exclusion criteria for MTA participation (as assessed at 7–9 years of age) were IQ below 80; *DSM-IV* diagnosis of bipolar disorder, psychosis, impairing obsessive-compulsive disorder, or Tourette's syndrome; use of neuroleptic medication in the previous 6 months; suicidal or homicidal behavior; and major neurologic or medical illness. An LNCG was added to the follow-up study, consisting of 289 participants randomly selected from the same schools and grades, with the same sex proportion as the MTA patients and with the same inclusion and exclusion criteria except for ADHD diagnosis. At baseline, the LNCG received a comprehensive assessment battery, which also included the Diagnostic Interview Schedule for Children–Version IV and teacher-reported ratings of ADHD.²² LNCG children were not excluded for having symptoms of ADHD. However, sensitivity analyses were conducted after excluding 27 LNCG children who met diagnostic criteria for ADHD.

Assessments

Psychotic symptoms were assessed at 6, 8, 10, 12, 14, and 16 years after the original MTA study entry. At each assessment point, trained research assistants interviewed and rated the participants for

possible psychotic symptoms using the Psychosis Screener and Follow-Up Diagnostic Impression (Supplement 1, available online). Raters were not blinded to participant status (i.e., MTA or LNCG). Participants were asked about having experienced perceptions suggestive of auditory, visual, or somatic/tactile hallucinations and assessed for possible unusual ideas or thoughts suggestive of delusional thinking. The screening for somatic/tactile hallucinations started with the year 12 assessment. As part of the interview, participants were assessed for disorganized speech and unusual or bizarre behavior and for possible negative symptoms of psychosis, including flat affect, social withdrawal, and poverty of thoughts. The raters were trained to be broadly inclusive. Experiences and signs that could not be explained otherwise were considered possibly psychotic.

Each positive psychotic symptom (i.e., auditory, visual, and somatic/tactile hallucinations and delusions) was scored by the rater as 1 (absent), 2 (possibly present but not psychotic), 3 (probably present and psychotic), or 4 (definitively present and psychotic). Negative psychotic symptoms (i.e., disorganized speech or appearance, inappropriate and flat affect, and social withdrawal) were rated as 1 (absent), 2 (mild, e.g., minimal emotional expression), 3 (moderate, e.g., monotone speech, poor eye contact), or 4 (severe, e.g., no emotional expression, no connection with interviewer). Participants with a screening rating score of at least 3 on any of the positive symptoms or of 4 on any of the negative symptoms were considered positive at the screening and referred to the study clinician (a child psychiatrist or psychologist) who rated the symptoms as spurious and not pathologic, pathologic but not psychotic, or possibly psychotic.

The Substance Use Questionnaire^{22,23} was administered at all assessments, beginning with the 2-year follow-up. It asked the participants about frequency of use of alcohol and other substances (e.g., marijuana, inhalants) within the past 6 months (at 2- to 10-year follow-up) and within the past 12 months (at 12- to 16-year follow-up). Responses were recoded to estimate the number of times alcohol, marijuana, or another substance, respectively, was used within 12 months, and, for each participant, the average times of use across all the assessment points were computed and used for the analyses. For nicotine, participants were asked to indicate the use of cigarettes or other forms of tobacco in the past month at the 2- to 10-year follow-up assessments and in the past 12 months at the 12- to 16-year follow-up assessments. For each assessment point, use was scored as 0 (did not use at all), 1 (used less than daily), or 2 (used daily), and for each participant, the average score across all assessments was computed and analyzed.

In parallel, starting with year 12, participants self-reported health issues in the previous 2 years, including having received a psychiatric diagnosis, such as schizophrenia, schizoaffective disorder, major depression, or bipolar disorder.

The data were collected from 2002 through 2012 at the following clinical sites: University of California–Berkley; Duke University Medical Center; University of California–Irvine; Long Island Jewish Medical Center and New York University; McGill University and Montreal Children's Hospital; University of Pittsburgh; and Columbia University and New York State Psychiatric Institute and Mount Sinai Medical Center, New York.

Data Analyses

Standard descriptive statistics were applied to the data. Group differences were tested with nonparametric or parametric tests as appropriate and specified in the Results section, with statistical significance accepted at a 2-tailed *p* value less than .05 without correction for multiple tests in these secondary analyses.

RESULTS

Psychotic Symptom Screening in Participants With ADHD Versus Normative Group

Data were available from 509 MTA participants (87.5% of originally enrolled MTA sample) and 276 LNCG participants (95.5% of original sample). The participants who were retained were compared with those lost to follow-up. In the MTA, the non-retained group ($n = 70$) had a statistically significant larger proportion of men, lower IQ, and lower family income than the retained group, but there were no differences in race or history of parental mental illness. In the LNCG, the non-retained group ($n = 13$) had lower family income than the retained group but did not differ for sex, race, IQ, or history of parental mental illness. Among retained participants, the MTA differed from the LNCG by younger age, lower IQ, and history of parental mental illness (Table 1).

The number of participants at each assessment point ranged from 290 to 436 in the MTA group and from 191 to 252 in the LNCG (Table S1, available online). The mean number of follow-up assessments per participant during the 10-year period was 4.7 ± 1.5 (median 5) in the MTA and 5.2 ± 1.2 (median 6) in the LNCG ($t = 4.79$, $df = 786$, $p < .0001$). During the 10-year period of observation, 26 MTA participants (5%; 95% CI 3–7) and 11 LNCG participants (4%; 95% CI 2–6) screened positive for at least 1 psychotic symptom (Fisher exact test, $p = .60$; Table 2).

The rates of positive screens did not significantly differ between the MTA and the LNCG when the subgroups with the same number of visits were compared. Among participants who had at least 4 assessments, the rate of positive screening was 5.5% in the MTA ($n = 405$) and 4.4% in the LNCG ($n = 251$; Fisher exact test, $p = .59$). The results of no statistically significant difference between the MTA and the

LNCG did not change when sensitivity analyses were conducted excluding the 27 LNCG participants with diagnosable ADHD (4.0%; 95% CI 1.5–6.4; Table S2, available online).

Of the 26 MTA participants who screened positive, 8 had originally been randomized to combined treatment, 7 to medication management only, 4 to behavior therapy, and 7 to community comparison. The difference in the rate of positive screening by the original treatment group was not statistically significant.

Of the 37 participants who screened positive, 36 had more than 1 biennial assessment. Among these 36, a positive screen occurred in more than 1 assessment for 8 participants (21.6% of cases), and the remaining 29 (78.4% of cases) screened positive only once.

Delusions, alone or accompanied by another psychotic symptom, accounted for positive screening for 54% ($n = 20$) of positive screens. Auditory hallucinations, alone or with other symptoms, accounted for 46% ($n = 17$) of positive screens (Table S3, available online). Negative symptoms of psychosis (social isolation and withdrawal) accounted for only 1 positive screening.

Screening positive was not associated with sex, ethnicity (Caucasian versus other), or lower IQ. Positive-screened participants were more likely to have a mother with history of mental health problems than those with negative screens (Table 3).

The 37 participants who screened positive were referred to the study clinician for further evaluation. However, this evaluation was missing for 7 participants (4 in MTA group and 3 in LNCG). Among the 26 MTA positive screens, psychosis was confirmed in 6 cases and ruled out in 16, and 4 had missing clinical evaluation. Of the 11 LNCG positive screens, psychosis was confirmed in 2 cases and excluded in 6, and 3 had missing clinical evaluation. The rate of confirmed psychosis (while considering the missing cases “not confirmed”) did not differ significantly between the MTA group (1.1%; 95% CI 0.2–2.1) and the LNCG (0.7%; 95% CI 0.3–1.7; Fisher exact test, $p = .5$, not significant). If the cases with missing evaluation are considered as “psychosis not excluded,” then the rate of psychosis confirmed or not excluded was 1.9% (95% CI 0.6, 2.9) in the MTA group and 1.8% (95% CI 0.2–3.4) in the LNCG (Fisher exact test, $p = 1.0$, not significant; Table 2).

The original MTA treatment assignment of the 9 participants with confirmed or not excluded psychosis was combined treatment for 3, medication management for 2, and community control for the remaining 4.

Upon administration of the health survey at assessment years 12, 14, and 16, a community diagnosis of schizophrenia or schizoaffective disorder was reported by 3 MTA participants (0.4%; 95% CI 0.2–0.95) and 2 LNCG participants (0.7%; 95% CI 0.3–1.7). These 5 participants also were positive at the psychosis screening (2 had clinician’s review and were confirmed psychotic, and the other 3 had missing clinician review). No diagnosis of schizophrenia or schizoaffective disorder was reported by participants who were negative at the psychosis screening.

TABLE 1 Study Sample

	MTA (n = 509)	LNCG (n = 276)	p
Age at year 16 assessment (y), mean (SD)	25.12 (1.07)	24.58 (1.15)	<.0001
Men, n (%)	402 (80)	222 (79)	.63
Caucasian, n (%)	283 (56)	138 (50)	.13
IQ, mean (SD)	101.5 (14.7)	108.7 (19.1)	<.0001
Mother’s mental illness history, n (%) ^a	101 (22)	37 (14)	.01
Father’s mental illness history, n (%) ^b	69 (18)	25 (11)	.02

Note: LNCG = local normative comparison group; MTA = Multimodal Treatment Study of Children with ADHD (attention-deficit/hyperactivity disorder); SD = standard deviation.

^aMTA $n = 454$ and LNCG $n = 261$.

^bMTA $n = 394$ and LNCG $n = 234$.

TABLE 2 Psychotic Symptom Screening Outcome

	MTA (n = 509)		LNCG (n = 276)		<i>p</i> ^c
	n	% (95% CI)	n	% (95% CI)	
Screened positive at any of the assessment points	26	5.1 (3.1–7.0)	11	3.9 (1.6–6.2)	.60
Psychosis was confirmed by further clinical review ^a	6	1.1 (0.2–2.1)	2	0.7 (0–1.7)	.72
Psychosis was confirmed or not ruled out ^b	10	1.9 (0.7–3.1)	5	1.8 (0.2–3.3)	1.00

Note: LNCG = local normative comparison group; MTA = Multimodal Treatment Study of Children with ADHD (attention-deficit/hyperactivity disorder).

^aClinical review was missing for 4 MTA and 3 LNCG participants.

^bIncluding those with confirmed psychosis and those with missing clinician review.

^cFisher exact test.

Psychotic Symptoms and Substances of Abuse

Screening positive for psychotic symptoms was associated with greater use of cannabis, but not of alcohol, nicotine, or other substances, in the MTA group and the LNCG (Table 4 and Figure 1). Participants whose psychotic symptoms were confirmed positive reported statistically significant greater use of cannabis and nicotine, but not of alcohol or other drugs, than the rest of the sample (Table 5). These results did not change when these analyses were repeated after excluding the 27 LNCG participants who were found to have diagnosable ADHD at the baseline assessment battery (Tables S4 and S5, available online). Nicotine and cannabis use were statistically significantly correlated in the MTA group (Spearman correlation coefficient $\rho = 0.47$, $p < .0001$) and the LNCG ($\rho = 0.59$, $p < .0001$).

DISCUSSION

This was a prospective study of youths diagnosed with ADHD combined type in childhood and periodically reassessed up to a mean age of approximately 25 years. During a 10-year follow-up period (6–16 years after baseline), 5.1% of participants with ADHD screened positive at least once for a self-reported psychotic experience. This rate was not statistically different from that found in a concurrently assessed local normative community sample and is consistent with that reported in community samples of youths and adults.^{5,19} These data indicate that a diagnosis of ADHD does not increase the risk of psychotic experiences or of a psychotic disorder, a finding that is consistent with other follow-up studies of children with ADHD into adulthood.^{13,24}

The major strength of this study is the consistent and repeated prospective assessments of psychosis over 10 years for a large and well-defined cohort of children with ADHD combined type 15 to 25 years of age, a period that is known to be the time of highest risk for developing psychotic disorders. The MTA sample was well characterized at entry, with exclusion of intellectual disability, autism, or other major psychopathology. Other strengths are the good sample retention (>85%) over the years and the concurrent assessment of an LNCG.

Several important limitations must be considered. First, a diagnosis of bipolar or psychotic disorder or treatment with neuroleptic medication in the previous 6 months was reason for exclusion from the MTA at study screening when participants were 7 to 9 years of age. Although none of the children who underwent formal screening for possible participation were excluded because they met any of these criteria, we cannot exclude the possibility that referral sources, being aware of the entry criteria, might not have referred children with psychosis. However, the LNCG was selected using the same criteria, thus attenuating the impact of possible biases. Second, the screening instrument used for this study antedates the development of detailed and probably more sensitive and specific instruments, such as the Structured Interview for Prodromal Syndromes, Comprehensive Assessment of At-Risk Mental States, or Prodromal Questionnaire, which are now used to assess psychosis in youth.^{25,26} Third, although they were trained to collect data without bias, the raters who interviewed the MTA and LNCG participants were not blinded to their group status. Fourth, data for some clinical reviews after positive screening were missing from the database. As a way of

TABLE 3 Psychosis Symptom Screening and Sex, Ethnicity, IQ, and Family Psychiatric History

	Screened Positive		Screened Negative		<i>p</i>
	Total n	n (%) ^a	Total n	n (%) ^a	
Men	37	26 (70)	831	674 (81)	.10
Caucasian	35	15 (57)	824	450 (45)	.17
IQ, mean (SD)	37	99.2 (15.7)	822	103.6 (16.7)	.11
Biological mother with mental health problems, yes	29	18 (36)	763	114 (19)	.03
Biological father with mental health problems, yes	23	5 (22)	669	93 (14)	.28

Note: *p* value by χ^2 or *t* test. SD = standard deviation.

^aExcept where noted.

TABLE 4 Psychotic Symptom Screening and Alcohol, Cannabis, Nicotine, and Other Drugs of Abuse in the Multimodal Treatment Study of Children With ADHD (Attention-Deficit/Hyperactivity Disorder; MTA) and Local Normative Comparison Group (LNCG)

	MTA ⁺ (n = 26)	MTA ⁻ (n = 483)	LNCG ⁺ (n = 11)	LNCG ⁻ (n = 265)	p ^b
Alcohol					.93
Median (IQR) ^a	17 (43)	19 (43)	9 (34)	21 (36)	
Mean (SD)	64.4 (147.8)	37.3 (56)	56.6 (121.6)	31.4 (36.1)	
Range	0–730	0–677	0–415	0–230	
Marijuana					.03 ^c
Median (IQR)	14 (179)	3 (122)	46 (147)	1 (40)	
Mean (SD)	108.7 (155.5)	84.1 (156.1)	103.9 (148.4) ^d	46.3 (95.2)	
Range	0–437	0–1,095	0–489	0–489	
Nicotine					<.001 ^d
Median (IQR)	0.5 (1.4)	0.5 (1.1)	0.5 (1.0)	0.25 (0.8)	
Mean (SD)	0.9 (0.9)	0.6 (0.6)	0.5 (0.5)	0.4 (0.5)	
Range	0–3	0–3	0–1.3	0–2.1	
Other drugs					.79
Median (IQR)	0 (2)	0 (1)	0 (1)	0 (1)	
Mean (SD)	23.3 (74.1)	10.7 (50.4)	10.4 (32.2)	3.8 (15.3)	
Range	0–366	0–547	0–107	0–156	

Note: IQR = interquartile range; SD = standard deviation.
^aDifference of upper and lower quartiles.
^bKruskal-Wallis test.
^cStatistically significant difference between positive and negative screens.
^dStatistically significant differences between LNCG-negative and the MTA subgroups.

addressing this deficiency, separate analyses considering these cases non-confirmed or not excluded were conducted, without significant changes in the results. Fifth, possible family history of psychosis was not part of the database. In support of the sensitivity of the methods used in this study,

of those who were diagnosed with psychotic disorder in the community and reported it as adults, all were tured in our screening procedures, and none of those who screened negative reported a community diagnosis of psychotic disorder.

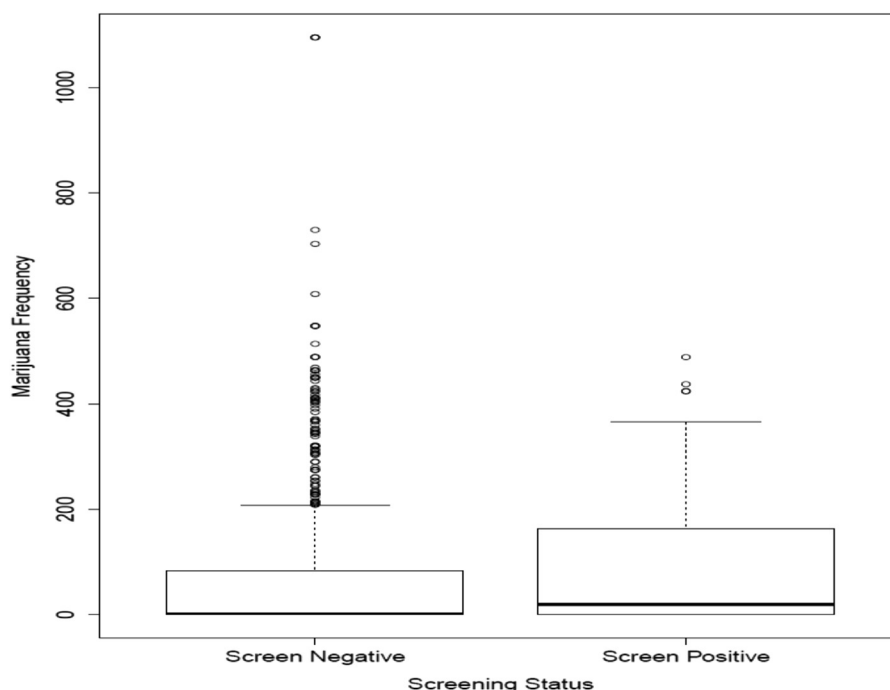
FIGURE 1 Frequency of cannabis use among the positive (n = 37) and negative (n = 748) screens for psychotic experiences. Note: Frequency is expressed as the reported number of times that cannabis was used in the past 12 months.

TABLE 5 Psychotic Symptom Screening and Alcohol, Cannabis, and Other Drug of Abuse

	Screened Positive (n = 37)	Screened Negative (n = 748)	<i>p</i> ^a	Confirmed Positive (n = 8)	All Others (n = 777)	<i>p</i> ^a
Alcohol			NS			.28
Median (IQR)	17 (47)	20 (40)		32 (99)	20 (40)	
Mean (SD)	62.1 (138.9)	35.2 (49.9)		136 (248.2)	35.4 (51.6)	
Range	0–730	0–677		4–730	0–677	
Marijuana			<.05			<.001
Median (IQR)	20 (162)	3 (83)		175 (291)	2 (82)	
Mean (SD)	107.3 (151.4)	70.7 (138.8)		222 (181.4)	70.9 (138.3)	
Range	0–487	0–1,095		6–489	0–1,095	
Nicotine			.12			<.0001
Median (IQR)	0.5 (1.3)	0.4 (1.0)		1.6 (0.6)	0.4 (1.0)	
Mean (SD)	0.8 (0.8)	0.5 (0.6)		1.7 (0.4)	0.5 (0.6)	
Range	0–3	0–3		1.1–2.3	0–3	
Other drugs			NS			.42
Median (IQR)	0 (.2)	0 (1)		0 (5)	0 (1)	
Mean (SD)	19.5 (64.3)	8.2 (41.6)		47.9 (128.5)	8.4 (41.2)	
Range	0–366	0–547		0–366	0–547	

Note: IQR = interquartile range (difference between upper and lower quartiles); NS = not significant.

^aWilcoxon-Mann-Whitney test.

Delusions and auditory hallucinations were the most common type of psychotic symptom reported. The repeated, prospective, within-subject assessments showed that most psychotic experiences were transient. These findings are consistent with reports that psychotic experiences in the general population are usually transient and that only a small proportion of the 8% to 10% who experience them develop psychotic disorders.¹⁰ Unlike studies in community samples,⁵ we did not find that lower IQ or non-European ethnicity were risk factors for psychotic experiences. However, the MTA excluded at entry children with IQ below 80.

The analyses associated more frequent use of cannabis, but not of alcohol or other drugs of abuse, with a greater risk for screening positive and being confirmed positive for psychotic symptoms in the MTA and the LNCG. This finding is consistent with other previous reports that cannabis increases the risk for psychosis.^{27–32} Specifically, it is the sustained, rather than sporadic, use of cannabis by adolescents that has been associated with increased risk of subclinical psychotic symptoms and especially paranoia.^{28,29} The data from this study show that ADHD per se does not increase the risk for cannabis-associated psychotic symptoms.

Consistent with the well-known association between tobacco use and psychosis,³³ the analyses also found that the participants who screened and were confirmed positive had used nicotine more frequently than the other participants. However, merely screening positive was not linked to nicotine use. Although the role of nicotine in psychosis is still a matter of debate,³⁴ the association of nicotine with psychosis is generally considered to reflect common risk factors rather than to be a causal effect.

In conclusion, in this sample of youths with childhood diagnosis of ADHD combined type, the rate of psychotic symptoms through a mean age of 25 years was not higher than that found in a normative comparison group and was

consistent with the epidemiologically expected rate of psychosis. Psychotic symptoms were transient phenomena in approximately three-fourths of cases. The results confirm that sustained cannabis use is associated with an increased risk of psychotic experiences, thus supporting the recommendation that cannabis should not be used during development. These data also confirm that a diagnosis of ADHD does not increase the risk of psychotic experiences or of a psychotic disorder. &

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Evaluation of Relational Reasoning by a Transitive Inference Task in Attention-Deficit/Hyperactivity Disorder

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Objective: Here we explored whether children with ADHD have a deficit in relational reasoning, a skill subtending the acquisition of many cognitive abilities and social rules. **Method:** We analyzed the performance of a group of children with ADHD during a transitive inference task, a task requiring first to learn the reciprocal relationship between adjacent items of a rank ordered series (e.g., $A > B$; $B > C$; $C > D$; $D > E$; $E > F$), and second, to deduct the relationship between novel pairs of items never matched during the learning (e.g., $B > D$; $C > E$). **Results:** As a main result, we observed that children with ADHD were impaired in performing inferential reasoning problems. The deficit in relational reasoning was found to be related to the difficulty in managing a unified representation of ordered items. **Conclusion:** The present finding documented a novel deficit in ADHD, contributing to improving the understanding of the disorder.

Keywords: ADHD, inferential reasoning, problem solving

Inferential reasoning is the ability to conclude the relationship among ideas or items by using logical processes and information or facts previously learned (Preston & Eichenbaum, 2013; Ryan,

Moses, & Villate, 2009; Vasconcelos, 2008; Zeithamova, Schlichting, & Preston, 2012). With regard to an instance, it could be possible to conclude that Tom is taller than John after experiencing the following high-hierarchy; Paul > Tom > Marc > John > Luc. This ability is involved in several aspects of our daily life. For example, it subtends the mathematical abilities or the comprehension of the reciprocal relationships between the roles of the individuals of a social context.

The efficient use of inferential reasoning, requires the correct learning and storage of different memories and the ability to make flexible relational links between them, for instance, by encoding items with common elements (Moses, Villate, Binns, Davidson, & Ryan, 2008; Ryan et al., 2009; Schlichting & Preston, 2015).

To study the cognitive abilities involved in inferential reasoning controlled versions of the Transitive Inference (TI) tasks have been developed experimentally (Acuna, Eliassen, Donoghue, & Sanes, 2002; Brunamonti, Genovesio, Carbè, & Ferraina, 2011; Bryant & Trabasso, 1971; Vasconcelos, 2008; Zeithamova, Dominick, & Preston, 2012; Zeithamova et al., 2012). A typical TI task is divided in a *learning* and in a *test* phase. During the learning phase, it is required to learn the reciprocal relationships between pairs of stimuli of a rank ordered set, for example, $A > B$; $B > C$; $C > D$; $D > E$; $E > F$. In the test phase, it is required to deduct the relationship between items never paired during the learning as:

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A>C, A>D, A>E, A>F, B>D, B>E, B>F, C>E, C>F, D>F. The TI task has been employed to evaluate inferential reasoning abilities in humans and in several animal species to verify whether they are able to solve inferential reasoning problems (for review see Vasconcelos, 2008), in children (Bryant & Trabasso, 1971; Wright & Smailes, 2015), as well as in patients with brain injuries (Koscik & Tranel, 2012; Waechter, Goel, Raymont, Kruger, & Grafman, 2013). The picture which has emerged from these studies is that TI is a complex task which solution relies on different cognitive abilities (Libben & Titone, 2008; Moses, Ostreicher, & Ryan, 2010; Ryan et al., 2009; Solomon, Frank, Smith, Ly, & Carter, 2011) involving different brain systems (Brunamonti et al., 2014; Moses et al., 2008; Preston & Eichenbaum, 2013). The main mechanisms raised to account for TI task performance are a *relational flexibility* higher-level mechanism and lower level *associative strategies* (Libben & Titone, 2008; Moses et al., 2008). The *relational flexibility* mechanism counts on the encoding of the reciprocal relationship between the items within a unified mental representation, which is then explored in order to make comparisons in the case of inexperienced pairs. Strategies based on this cognitive mechanism require the temporary activation of a spatially organized mental schema of the ranked items, and the comparison between their relative positions (Acuna et al., 2002; Brunamonti et al., 2014; Libben & Titone, 2008; Zeithamova et al., 2012). In fact, both spatial and nonspatial ordered information were often found to be cognitively represented as a spatially organized “mental line” (Brunamonti, Falcone, Genovesio, Costa, & Ferraina, 2012; Holmes & Lourenco, 2011; Prado, Noveck, & Van Der Henst, 2010; Previtali, de Hevia, & Girelli, 2010; Schwarz & Keus, 2004; Shaki & Fischer, 2008). In a TI task, the mental line is represented with item A on one end (e.g., right), item F on the other end (e.g., left), and items B, C, D, and E located linearly between (Brunamonti et al., 2011; Chen, Swartz, & Terrace, 1997; D’Amato & Colombo, 1990; Prado et al., 2010; Roberts & Phelps, 1994). To properly solve TI tasks, it is required to maintain the linear representation of the ordered items active by efficient working and long-term memory abilities and to extract reciprocal representation of the mental line (Brunamonti et al., 2011, 2014; Libben & Titone, 2008).

Conversely, the *associative strategies* count on the reinforcement history of each item during the learning phase. A way to account for the reinforcement history is to consider that during the learning phase the two extreme items A (always the winner) and F (always the looser) acquire opposite strength in driving the choice. The intermediate items, with a probability to be chosen close to 50%, acquire intermediate value strengths, proportional to their proximity to the two extreme items (Frank, Rudy, & O’Reilly, 2003). Therefore, a strategy relying on the *relational flexibility* could be favored in comparing two middle items in which their value is balanced. On the contrary, if one of the extreme items occurs during a pair comparison, the choice is likely driven by its strength to attract the response, and a decision relying on the associative mechanism is more likely adopted.

Furthermore, if during the test phase, pairs of items used during learning are presented, a retrieval process mediated by long-term memory is thought to intervene (Frank et al., 2003; Heckers, Zalesak, Weiss, Ditman, & Titone, 2004; Ryan et al., 2009).

The complexity of TI tasks is believed to be a valuable tool to estimate the efficiency of the cognitive functions involved in the

task and the integrity of the underlying neural circuits in population of patients with psychiatric diseases (Titone, Ditman, Holzman, Eichenbaum, & Levy, 2004), in older age populations (Moses et al., 2010; Ryan et al., 2009) or in neurodevelopmental disorders (Solomon et al., 2011). For example, it has been observed that adults suffering from autism spectrum disorders failed to solve TI tasks relying on the associative learning strategy whereas they were good as controls in solving problems through the relational reasoning mechanism (Solomon et al., 2011).

In Attention-Deficit/Hyperactivity Disorder (ADHD), deficits in attention, working memory, and executive control, but also in learning, have been regularly observed in both children and adult populations (Di Trani et al., 2011; Pani et al., 2013; Rhodes, Park, Seth, & Coghill, 2012; Skodzik, Holling, & Pedersen, 2013). Even if the neuropsychological deficits found in ADHD are strictly entailed in inferential reasoning, this ability is not yet explored in this population of children.

We were interested in understanding whether children with ADHD proficiently solve a six-item TI task and to find out which strategy they adopt, whether they rely their performance more on a relational flexibility mechanism or on an associative strategy. To better clarify the cognitive processes involved in inferential reasoning, we also explored the relationship between working memory, long-term memory, linear spatial organization measures obtained from neuropsychological tasks and the results in TI task.

Method

Participants

Thirty-seven (33 males) with diagnosis of ADHD and 33 typically developing (TD) children (29 males) were included in the study. Children with ADHD were recruited from the Child Neuropsychiatry Unit at the Bambino Gesù Children’s Hospital, and TD children from local primary and secondary schools. For both groups, exclusion criteria were: IQ below 85, as assessed by the Colored Progressive Matrices (CPM; Raven, 2008); evidence of neurological disorders, pervasive developmental disorders, and receptive language disorders. The two groups did not differ for Chronological Age (CA; ADHD: 10.2 ± 1.1 ; TD: 9.9 ± 1.1 ; $t_{68} = 1.0$; $p = 0.31$) and for IQ (ADHD: 108.3 ± 13.0 ; TD: 111.5 ± 12.5 ; $t_{68} = 1.0$; $p = 0.3$).

Children with ADHD underwent a child psychiatric examination conducted by experienced developmental psychiatrists and neuropsychologists. ADHD diagnosis was based on developmental history, extensive clinical examination and the semistructured interview K-SADS-PL (Kaufman et al., 1997; Kaufman, Brent, Rao, & Ryan, 2004) conducted to parent and child separately. Following the *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5; American Psychiatric Association, 2013), children with ADHD were characterized as: 28 fulfilled diagnostic criteria for ADHD Combined presentation, 2 for ADHD Hyperactive-Impulsive and none for the ADHD Inattentive presentation. Patients with ADHD NOS (Not Otherwise Specified) were not included in the study.

All participants and their parents gave written informed consent after receiving a comprehensive description of the study. The study was approved by the local Ethics Committee (reference number: 1111_OPBG_2016).

Measures: Transitive Inference Task

All participants were submitted to a computerized TI task adapted for children. The task was composed by the learning phase and the test phase.

During the learning phase the participants were required to learn the relationship between 6 items (black and white bitmaps – 30 × 30 mm – abstract images, each with the same proportion of white area over a black background) that were ranked arbitrarily by one of the authors (Figure 1, Panel A; $A > B > C > D > E > F$). To allow the children to figure out the relationship between the six items, they were instructed to select the higher between adjacent items in the sequence (AB, BC, CD, DE, EF) by using a trial and error strategy. This learning phase was composed by two steps: a *study phase* and a *recall phase*. During the study phase, each pair of the same adjacently ranked items (for instance AB) were presented in blocks of 15. Each block was repeated until the percentage of correct responses was at least 80% for each pair. Then, the next pair (for instance BC) was presented with the same rule. Once the participant reached the learning criterion for all pairs, they moved to the recall phase. In this phase, adjacent studied pairs were presented randomly in a block of 100 trials (20 presentations of each pair, 10 times with the target item in the upper position and 10 times in the lower position). At the end of each block an automated procedure provided to the participant a feedback on his or her performance by displaying on the screen a number of smiley faces proportional to the proportion of correct responses ($\odot < 20\%$; $\odot\odot = > 20 < 40\%$; $\odot\odot\odot = > 40 < 60\%$; $\odot\odot\odot\odot > 60 < 80\%$; $\odot\odot\odot\odot\odot = > 80\%$). Children were told that they could move to the test phase once they achieved at least four smiley faces. One or more blocks of 100 trials were presented until the percentage of correct responses reached the criterion.

In the test phase, the participants were required to infer the relationship between pairs of items never presented together during the learning (AC, AD, AE, AF, BD, BE, BF, CE, CF, DF). These 10 novel pairs of items were randomly intermixed with the 5 learned pairs (AB, BC, CD, DE, EF). In the test phase, for each Participant 150 trials (10 presentations of each pair, 5 times with the target item in the upper position and 5 times in the lower position) were collected.

In the study phase, recall phase and test phase, the trial began with a fixation point appearing at the middle of a screen (Figure 1, Panel B). After 1 sec, a pair of items, located one above and one below the fixation point, appeared on the display. The participants had to indicate the higher item in rank between the two, by typing the upper or the lower pointing arrow on a computer keyboard. If no response was provided within 2 sec from the items onset, the trial was aborted and a new trial was presented. Two different acoustic feedbacks informed the participants whether they have responded correctly or not.

During the experimental sessions, the participants were seated on a chair, facing a 15" computer screen in a dimly illuminated room. The presentation of the stimuli and the responses were controlled by a custom made routine running in the Matlab (www.mathworks.com; see also Brunamonti, Ferraina & Parè, 2012 for similar methods in other experimental paradigms) and based on the Psychophysical toolbox (Brainard, 1997).

Neuropsychological Evaluation

Spatial working memory task. The *N*-back task required the participants to respond when the current stimulus's location matched the location of the previously presented item. Participants were administered the *n*-back task by a computerized program (<http://brainworkshop.sourceforge.net/>) that registered the corrected responses. Participants were told to press the 'I' key on the keyboard denoting target with their right index finger. In the 1-back condition, the target was any location identical to the location immediately preceding it (i.e., the location presented one trial back). In the 2-back condition, the target was any location that was identical to the one presented two trials back. In the 3-back condition, the target was any location that was identical to the one presented three trials back. Stimuli were presented at a rate of one location every 3 seconds. Participants completed 35 trials per condition. The number of corrected detected targets and the errors were considered to calculate a percentage accuracy value. Only when the accuracy was $\geq 80\%$, the next *N*-back level was submitted. An efficiency index was calculated and considered in the analysis, based on the last *n*-back span achieved (i.e., percentage accuracy value $\geq 80\%$) and the percentage of accuracy obtained in the next not achieved *n*-back (i.e., percentage accuracy value $< 80\%$). For example, if the last *N*-back reached was 2 and the percentage of accuracy of the next not achieved *N*-back was 30%, the score obtained was 2.30.

Pairing long-term memory task. The study phase of the task consisted in the presentation of nine pairs of photos vertically arranged, including a butterfly and a flower (for details see Costanzo, Vicari, & Carlesimo, 2013). The test phase was given immediately after the study phase. For each test item, the studied butterfly photos was presented at the center of the PC screen; a horizontal array of three flowers appeared simultaneously in the

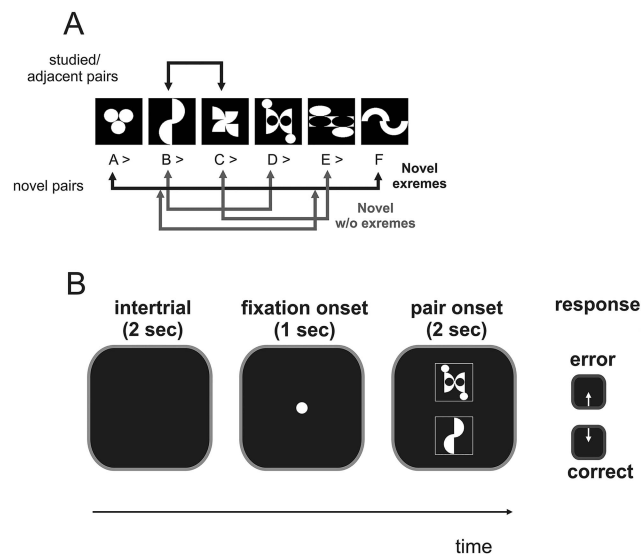


Figure 1. Transitive Inference (TI) task. (A) Rank-ordered items. Different categories of problems are illustrated. (B) Sequence of the task events. One second after the presentation of a fixation point (white spot) at the middle of a screen, a pair of items (30 × 30 mm each) were presented on the display, centered 20 mm above and below the fixation spot. The participants had to indicate the higher item in rank between the two, by typing the upper or the lower pointing arrow on a computer keyboard.

lower part of the screen. Each flower triplet was composed by the flower that had been presented together with the probe butterfly during the study phase and two others that had been presented together with two different butterflies during the study phase. The participants were requested to indicate the flower that had been presented with the butterfly during the study phase (maximum score: 9). Study and test phases were presented for three consecutive times and the number of elements correctly recognized in the three trials was considered in the analysis.

Visual Attentional Shifting Task

Visual Attention was measured by a spatial cuing paradigm in which covert attention (without eye movements) is engaged across two locations of a forthcoming target stimulus by a peripheral, informative spatial cue (i.e., cue location predicts target location) at two variable cue-target intervals (50 and 300 ms). A modified version of the Visual Spatial Attention Task (Ruffino et al., 2014) was used. Two circles (2.5°) were displayed peripherally (8° eccentricity, one to the left and one to the right of the fixation point) and 500 ms later the visual cue was shown, consisting of a narrow (1.5° visual angle) displayed for 50 ms above one of the circles. In the response trials of the present version, a target (dot, 0.5° ; duration 50 ms) was presented after one of two cue-target stimulus onset asynchronies (SOA, 50 or 300 ms) in one of the two possible locations. The probability that the cue was presented in the target location was 50% (i.e., the cue location was predictive of target location). In contrast, in catch trials the target was not presented and participants did not have to respond. Catch trials were intermixed with response trials. Participants were instructed to react as quickly as possible to the onset of the visual targets by pressing the spacebar on the computer keyboard (detection task). Simple RTs and error rates were recorded by the computer. The maximum time allowed to respond was 1500 ms. The intertrial interval was 1000 ms; after that time the trial started automatically. The experimental session consisted of 144 trials.

Number Insertion Task

The subtest is derived from the *Battery for evaluating Math abilities* (Biancardi & Nicoletti, 2004) that explores several aspects of math with 10 different tasks. The Number Insertion subtest required to place a number (one to five digits) in one of four possible positions among three other numbers. Both accuracy (maximum score: 12) and speed were measured and considered in the analysis.

Data Analysis

Transitive inference task. Responses on novel pairs of items (i.e., not adjacent pairs, not experienced during the study phase) and studied pairs (i.e., pairs of adjacent items) were separately analyzed.

Performance on novel pairs in the test phase. Novel pairs were grouped into two categories: (a) novel pairs not including extreme items (*Novel w/o extremes*), which were novel pairs not including the item A or the item F (i.e., BD, CE, BE); and (b) novel pairs involving only the extreme items (*Novel extremes*), formed by the always winner item A and the always loser item F (i.e., AF).

Performances on the novel pairs were analyzed on the proportion of correct responses.

Learning curves and performance on studied pairs in the test phase. Learning curves were calculated to evaluate, within each group, the process of acquisition of the relationship between the adjacent pairs during the study phase and the recall phase. For each participant the trials obtained during the study phase (each pair presented in blocks of trials) and the recall phase (all the pairs randomly presented) were grouped according to their sequence of presentation, and the sequence of successfully performed trials was evaluated by computing a learning curve based on a nonrandom walk hypothesis (Papazachariadis et al., 2012). Starting from zero, a learning curve of the sequence of trials was built by adding or subtracting the value 0.5 (the probability to respond successfully at each given trial) to the previous value, if a given trial was correct or incorrect, respectively.

Statistical Analyses

The performances of the two groups were compared by using the Mann–Whitney *U*, because the assumption of homogeneity of the variance, monitored with Levene's test, was violated for some variables (i.e., Pairs: AF, AB, CE, DE; Number insertion accuracy).

Neuropsychological measures were analyzed after converting raw scores to *z* scores based on the mean and the standard deviation of normative data of the task (for the Number Insertion accuracy and speed) or, when normative data were not available, on the mean and standard deviation of TD children (for the *N*-back efficiency index, Pairing Long-term Memory Task, Visual Attention SOA50 score and Visual Attention SOA300 score). Spearman's Rank Correlation Coefficient was used to test correlation between measures.

Each learning curve was modeled with a linear trend-line and the slope of the line was considered as an estimate of the efficiency of the learning process. A 2×5 mixed ANOVA with Group (ADHD vs. TD) as between-subjects factors and the Estimate of the Learning Process Efficiency for each studied pairs (AB vs. BC vs. CD vs. DE vs. EF) as within-subject factors. The assumption of homogeneity of the variance was monitored with Levene's test. Tukey's HSD post hoc test was used to qualify significant effects.

Results

Transitive Inference Task

Performance in novel pairs. The two groups were compared on the mean performance on *Novel w/o extremes* (the mean of BD, CE and BE) and on the mean performance on *Novel extremes* (AF; see Figure 2). The mean performance on *Novel w/o extremes* was significantly lower in children with ADHD than in TD children ($U = 406$; $p = 0.01$, $n_{ADHD} = 37$; $n_{TD} = 33$; $\eta_p^2 = 0.09$). However, groups did not differ on *Novel extremes* ($U = 492.5$; $p = 0.16$, $n_{ADHD} = 37$; $n_{TD} = 33$; $\eta_p^2 = 0.05$).

By considering the two groups together, the mean of the correct responses in novel pairs without extremes (*Novel w/o extremes*) was found correlated with the Number Insertion task speed ($r = 0.24$, $p = 0.04$; CI: 0.00; 0.25: better performance in novel w/o extremes corresponding to faster execution in Number Insertion

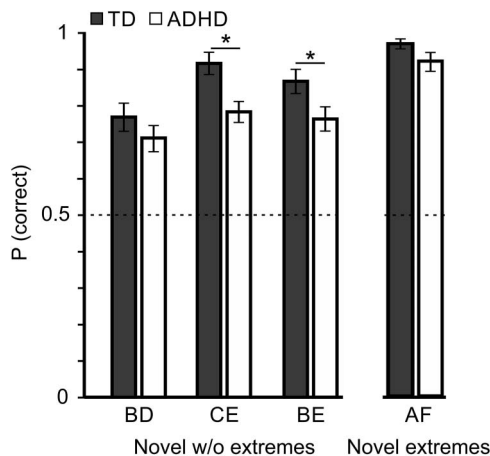


Figure 2. Proportion of correct responses, $p(\text{correct})$ of Typically Developing (TD) children and of children with ADHD in trials including the novel pairs without extremes (*w/o extremes*: BD, CE and BE) and the novel pairs with only extremes (*Novel extremes*: AF). In the novel pairs without extremes, children with ADHD showed a lower performance than TD children, due to lower scores obtained in CE and BE (CE: $U = 389.5$; $p < 0.01$, $n\text{ADHD} = 37$; $n\text{TD} = 33$; $\eta_p^2 = 0.13$; BE: $U = 433.0$; $p = 0.04$, $n\text{ADHD} = 37$; $n\text{TD} = 33$; $\eta_p^2 = 0.07$). Vertical bars indicate *SEM*. * indicates statistically significant p value.

task) and with the Pairing Long-term Memory task score ($r = 0.24$, $p = 0.04$; CI: 0.01; 0.45: better performance in novel w/o extremes corresponding to higher scores in the Pairing Long-term Memory task). Moreover, also the mean of the correct responses in novel pairs with extremes (*Novel extremes*) was significantly correlated with the Pairing Long-term Memory task score ($r = 0.27$, $p = 0.02$; CI: 0.04; 0.48: better performance in novel extremes

corresponding to higher scores in the Pairing Long-term Memory task) and with the N-back efficiency index ($r = 0.38$, $p = 0.001$; CI: 0.16; 0.57: better performance in novel w/o extremes corresponding to higher scores in the N-back task).

Performance in studied pairs. The performance of the studied pairs was evaluated during learning and during the test phase (see Figure 3).

The learning curves of a TD participant during the acquisition of each adjacent pair of the ordered set was displayed as an example (Figure 3A).

The mixed ANOVA on the estimate of learning process efficiency for each studied pairs (AB vs. BC vs. CD vs. DE vs. EF) documented that the slope of the regression line differed between studied pairs ($F_{4,272} = 22.78$, $p < 0.001$; $\eta_p^2 = 0.25$) because the estimate of learning process efficiency was higher for extreme items (p always < 0.001) than for the middle items (AB vs. BC, AB vs. CD, EF vs. BC, EF vs. CD) compared. However, no effect for Group ($F_{1,68} = 0.04$; $p = 0.84$; $\eta_p^2 = 0.006$) nor for the interaction Groups \times Studied Pairs ($F_{1,68} = 1.39$; $p = 0.24$; $\eta_p^2 = 0.02$) was found.

The two groups were compared in the same pairs of items (mean of BC, CD, and DE) of the test phase, after the learning had occurred (Figure 3C). Children with ADHD showed significant lower scores than TD children ($U = 307$; $p = .003$, $n\text{ADHD} = 37$; $n\text{TD} = 33$; $\eta_p^2 = 0.0115$).

By considering the two groups together, the mean performance in the middle items (mean of BC, CD, and DE) was correlated to neuropsychological measures to better understand which cognitive process could be related to the performance in the studied pairs. A positive correlation of the mean performance in the middle items was found with the Number Insertion task speed ($r = 0.26$; $p = 0.03$; CI: 0.02; 0.46: better performance in the middle items corresponding to higher speed in Number Insertion task), the

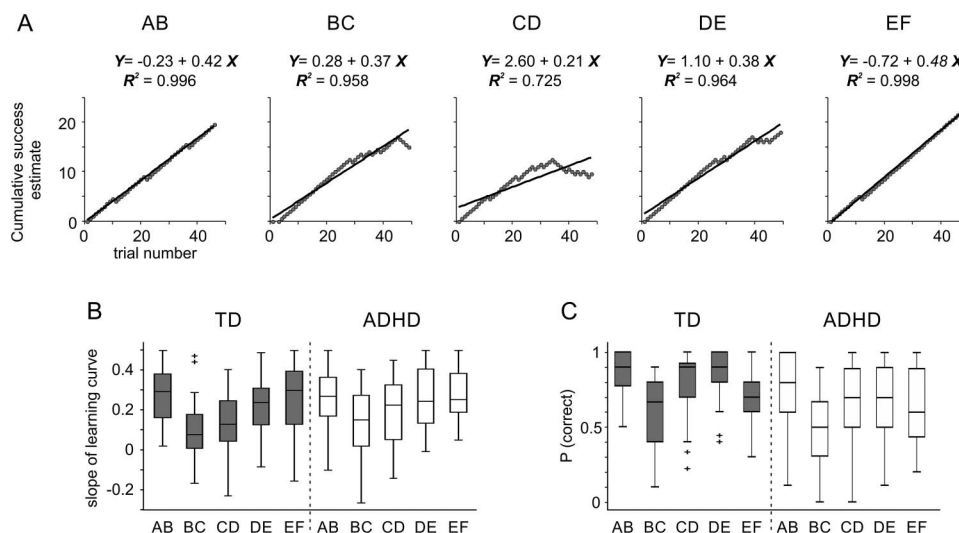


Figure 3. Learning curves and performance in the studied pairs during test (A). Learning curves for each pair comparison across the learning and the recall phase for a representative TD child. The parameters of the linear fitting on the observed performance and the goodness of fit are reported (B). Box plot of the distribution of the slopes of the trend-line of the learning curve for each pair across all the TD children (gray boxes) and children with ADHD (white boxes). (C) Performance in studied pairs during the test phase in both groups of children (color group code as in B).

Pairing Long-term Memory task score ($r = 0.28$; $p = 0.02$; CI: 0.05; 0.48: better performance in the middle items corresponding to higher scores in Pairing Long-term Memory), and the *N*-back efficiency index ($r = 0.25$, $p = 0.04$; CI: 0.02; 0.46: better performance in the middle items corresponding to higher scores in the *N*-back task).

Neuropsychological Evaluation

The analysis on neuropsychological measures (see Figure 4) documented that children with ADHD had lower scores than TD children in the Pairing Long-term Memory task ($U = 277$; $p < 0.001$, $n_{ADHD} = 37$; $n_{TD} = 33$; $\eta_p^2 = 0.12$), were slower than TD children in solving the Number Insertion task ($U = 289$; $p < 0.01$, $n_{ADHD} = 37$; $n_{TD} = 33$; $\eta_p^2 = 0.17$), and showed lower efficiency index than TD children in the *N*-back ($U = 339$; $p = .001$, $n_{ADHD} = 37$; $n_{TD} = 33$; $\eta_p^2 = 0.14$).

Discussion

The present study was aimed at evaluating whether TI problems were efficiently solved by children with ADHD and which was the cognitive strategy adopted to solve the task.

Our results documented that children with ADHD had difficulties in solving TI trials including novel pairs without the extremes A and F (i.e., *Novel w/o extremes*). Conversely, their performance did not differ from that of TD children in solving AF trials (i.e., *Novel extremes*). According to the associative learning theory (Frank et al., 2003; Wynne, 1997; Wynne, von Fersen, & Staddon, 1992), to solve TI trials including extremes a reinforcement learning mechanism could mainly drive the choice, because of the presence in a pair of the extreme item A and F (A is always reinforced and F never reinforced) and making the discrimination of the pairs AB and EF less ambiguous than the other pairs. On the other hand, to solve TI trials without extremes a unified mental schema to represent reciprocal relationship between the items and to make comparisons between pairs is needed. Indeed, the recruitment of a *relational flexibility* mechanism has been observed to be related to the capability to extract the relation between items and organize them as a unified representation on a “mental line”

(Brunamonti et al., 2011; Gazes, Chee, & Hampton, 2012; Jacobs, 2006; Libben & Titone, 2008; Moses et al., 2010; Ryan et al., 2009).

Notably, to maintain active the linear representation of the ordered items by memory could help compare items, identify their relation and organize them as a mental line. By considering the two groups together, our correlation analysis documented that the proportion of correct response of *Novel w/o extremes* pairs correlated with the Number Insertion task speed and with the Pairing Long-term Memory task score. The ability to correctly solve pairs without extremes is then associated with the ability to represent a mental line for correctly indicating the position of a given number on a physical line but also requires to memorize the ordered items.

The lower proportion of correct response obtained by children with ADHD in novel pairs *w/o extremes* could be related to their difficulty in manipulating ordered items as numbers on a mental number line and/or to their difficulty in maintaining in memory ordered items to create a unified representation of them (Moses et al., 2010; Prado et al., 2010; Ryan et al., 2009). In elders, for example, the lower performance on *Novel w/o extremes* has been related to their reduced ability to extract relations between items, and to their preference to rely on a bottom up strategy to solve TI problems, driven by the value of the items acquired by the reinforcement during the learning (Moses et al., 2010).

Both the top down relational flexibility and the bottom up value associative mechanisms have been studied in several pathological populations (Koscik & Tranel, 2012; Solomon et al., 2011; Titone et al., 2004; Waechter et al., 2013). For example, Solomon et al. (2011) have verified the efficiency of the value transfer strategy and the relational flexibility mechanism in a group of adults suffering of autism spectrum disorders using a five-items TI task. In these patients results documented difficulties in comparisons strongly driven by the value of the extreme pair AE. On the contrary, patients performed as well as controls with the pair BD, in which the integrity of the relational flexibility mechanism is mainly involved. Notably this pattern is opposite to that seen in our children with ADHD. We interpreted the deficit found in our children with ADHD in using relational flexibility mechanism required for TI as a consequence of their frontal lobe dysfunctions (Ma et al., 2012). However, the performance in TI trials involving novel pairs with extreme items A and F was found related to both long-term memory and working memory processes (with Pairing Long-term Memory task score and with *N*-back task efficiency index), confirming the role of the retrieval process in solving novel pairs with extreme items (Heckers et al., 2004; Ryan et al., 2009). Because our results showed that children with ADHD had lower scores than TD children in working memory, long-term memory, and number insertion task, their preserved abilities in evaluating novel pairs with extremes could be attributable more to their attempts to solve the task based on compensatory strategies using associative mechanisms than memory abilities or the mental representation of the relation between items.

To verify the efficiency of learning abilities, we compared the performance of the children with ADHD to that TD children during the acquisition of the relationship between the studied pairs. Our results documented that the estimate of learning process efficiency of the two groups did not differ. Indeed, the analysis of the slope of the regression line documented that the two groups of children did not differ on their performance in the studied pairs,

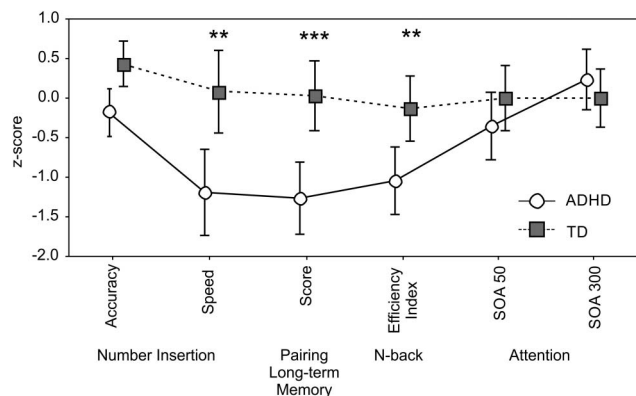


Figure 4. Normalized scores of neuropsychological evaluation scales. Significant between groups post hoc comparisons are reported. *** $p < 0.001$; ** $p < 0.01$. Vertical bars indicate 95% C.I.

both showing more difficulties in learning middle items than extreme items. In other words, the lack of difference in training history between the two groups (the proportion of positive feedback received by each item during the acquisition of the relationship between the studied pairs did not differ in the two groups), the different performance between TD children and children with ADHD found in the subsequent test phase cannot rely on different efficiency of associative mechanisms.

However, groups differed on the scores of the studied pairs (mean of BC, CD, and DE) of the test phase, after the learning had occurred. The proportion of correct responses of children with ADHD was lower than that of TD children. Looking at the correlational analysis, this performance on the studied pairs was linked to long-term memory abilities (the Pairing Long-term Memory task), working memory abilities (the *N*-back task), and the ability to locate numbers in a number line (Number Insertion task). The lower performance in children with ADHD than in TD children could be interpreted, again, as the consequence of the deficits found in children with ADHD in these cognitive domains, as documented by the neuropsychological evaluation.

TI ability is supported by multiple, interacting brain systems. Studies demonstrated important contributions from the frontal regions (Brunamonti et al., 2016; Kosciak & Tranel, 2012; Libben & Titone, 2008), parietal regions, medial temporal areas, in particular the hippocampus (Greene, Gross, Elsinger, & Rao, 2006; Heckers et al., 2004; Knauff, Fangmeier, Ruff, & Johnson-Laird, 2003; Nagode & Pardo, 2002), and the basal ganglia (Frank et al., 2006, 2004; Moses et al., 2010). In children with ADHD, neuroimaging studies have reported abnormalities in brain areas crucial for the control of attention and cognition (Bush, 2011; Seidman et al., 2005) as the frontal cortex, the parietal cortex, the cerebellum, but also in brain regions essential for associative learning as thalamus and hippocampus, and in the connectivity between the temporal lobe and the prefrontal cortex (Posner et al., 2014; Xia et al., 2012). Although it is speculative, the impaired performance on TI tasks in children with ADHD may be then interpreted as a consequence of both frontal and temporal lobe dysfunctions.

In sum, our results indicate that the preferential strategy used by children with ADHD to solve the TI task could rely more on associative mechanisms rather than on memory abilities or the mental representation of the relation between items. However, TI ability seemed to be not fully preserved in children with ADHD, because they were less efficient than TD children in making inference between novel items, probably because of their difficulties in controlling and in maintaining in memory a unified representation of related items. Further studies, including direct measures of the awareness of the reciprocal relationship between the items (Libben & Titone, 2008; Moses et al., 2010) are needed to better understand this issue.

The approach used in the present work as well as in previous researches aimed at studying the cognitive mechanisms involved in TI (Libben & Titone, 2008; Moses et al., 2010) had the limitation to fully control the learning processes taking place during the test phase. Indeed, in the test phase, only the first comparison between nonadjacent pairs should be believed as the result of the transitive inference process. Starting from the second comparison between nonadjacent items, this comparison is not novel anymore. The repeated exposure to the same pair of nonadjacent items and the reinforce history of each item are variables that could affect the

entire performance of the test phase. To our knowledge this issue was only partially treated in a very few previous studies with monkeys (Brunamonti et al., 2016; Jensen et al., 2013) and should be taken into account in future studies on TI.

Mathematical skills, text-processing skills as well as understanding the social rules, trusting other people or building friendships with a person rather than one other person and many other cognitive and social processes are all influenced by relational reasoning abilities (Carpenter Rich, Loo, Yang, Dang, & Smalley, 2009; Coleman et al., 2010; Favrel & Barrouillet, 2000; Kim & Song, 2011; Markovits, & Dumas, 1999; Ragni & Knauff, 2013; Sedek, Piber-Dabrowska, Maio, & Von Hecker, 2011; Winstanley, Eagle, & Robbins, 2006). Understanding the nature of the deficit reported in these abilities of children with ADHD may improve their cognitive and social development.

In conclusion, our study documents a deficit in relation reasoning in children with ADHD. To the best of our knowledge this is the first report documenting this finding and, because of the implication of relation reasoning in the cognitive and the affective development, it may contribute to some clinical manifestation of the disorders. Moreover, describing which strategy ADHD children use to solve a relation reasoning task offers significant information to the better understanding of the disorder and to guide possible therapeutic approaches.

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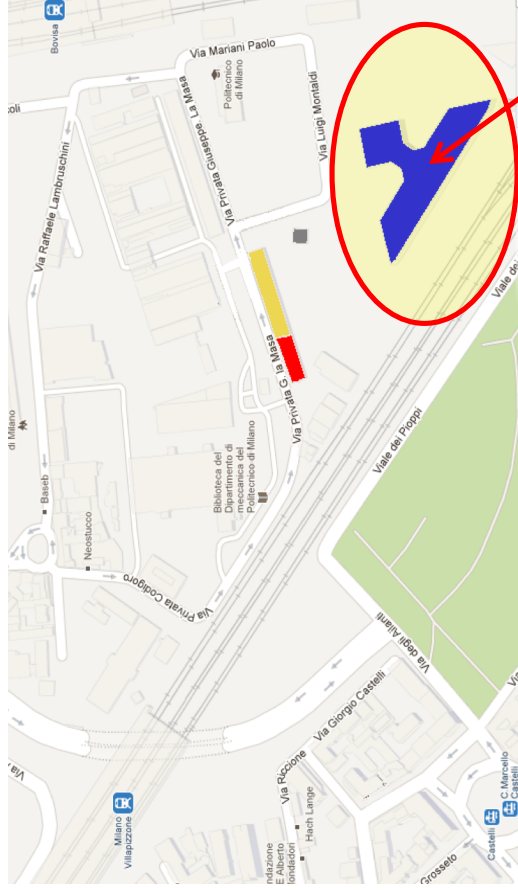
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L'IRCCS – Istituto di Ricerche Farmacologiche Mario Negri si trova a Milano in zona Bovisa nelle vicinanze del Campus Politecnico (Ingegneria) e della Triennale Bovisa.

E' facilmente raggiungibile con il passante ferroviario, scendendo alle fermate di Bovisa (FNM) o Villapizzone (FS).

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Con il patrocinio della:



Segreteria scientifica:

M. Antonella Costantino – Direttore UONPIA*

Segreteria organizzativa:

Jessica Babboni – Centro ADHD – UONPIA*

* Fondazione IRCCS Ca' Granda – Osp. Maggiore Policlinico, via Fanti, 6 – Milano

La partecipazione è gratuita ed è stato richiesto l'accreditamento ECM (Regione Lombardia) per le seguenti figure professionali: medici, psicologi, educatori professionali, terapisti della neuro e psicomotricità dell'età evolutiva, assistenti sanitari, infermieri ed infermieri pediatrici, tecnici della riabilitazione pediatrica, farmacisti, fisioterapisti, logopedisti.

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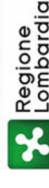
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FONDAZIONE IRCCS CA' GRANDA
OSPEDALE MAGGIORE POLICLINICO



Sistema Socio Sanitario



ASST Santi Paolo e Carlo

ADHD: Audit Clinico sull'appropriatezza della terapia farmacologica



Milano, 10 maggio, 2017

Ore 8.30-17.00 - AULA GUASTI

IRCCS

Istituto di Ricerche Farmacologiche Mario Negri

Via G. La Masa 19 - 20156 Milano



SPEDALI CIVILI BRESCIA

PRESENTAZIONE

L'Audit Clinico è l'iniziativa condotta da clinici, che si pone l'obiettivo di migliorare la qualità e gli outcomes dell'assistenza attraverso una revisione strutturata fra pari, per mezzo della quale i clinici esaminano la propria attività e i propri risultati in confronto a standard espliciti e la modificano se necessario, sottoponendo i risultati di tali modifiche a nuove verifiche.

Il nuovo Progetto *Percorsi diagnostico-terapeutici in rete per l'ADHD* si è posto un nuovo importante obiettivo per rafforzare il lavoro e l'impegno degli ultimi anni: consolidare la struttura della rete curante per l'ADHD in Lombardia, ampliarla alla partecipazione di nuovi servizi e garantire risposte terapeutiche e interventi formativi e informativi omogenei ed appropriati in tutto il territorio regionale.

Nello specifico si prefigge di implementare l'adesione dei Centri al monitoraggio strutturato e programmato dei percorsi di cura e diffondere modalità di audit clinico. I Centri ADHD nell'ambito del Progetto dovranno assumere un ruolo attivo all'interno della rete UONPIA per implementare e diffondere e coordinare gli obiettivi previsti a livello regionale e garantire un percorso di audit ad essi relativi.

Questo primo Audit clinico cercherà pertanto di andare a verificare, per poi migliorare, l'appropriatezza del trattamento farmacologico nei pazienti con ADHD.

RELATORI

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PROGRAMMA

08:30 – 09:00 Registrazione

09:00 – 9:20

La metodologia dell'audit clinico nell'ambito del progetto

Laura Reale

09:20 – 11:30

Audit sull'appropriatezza dell'indicazione al trattamento farmacologico dei bambini e adolescenti con ADHD nel Registro Lombardo

Monica Saccani e i referenti dei Centri ADHD

11:30 – 13:00

ESERCITAZIONE IN GRUPPO ALLARGATO: L'ANALISI DEGLI SCOSTAMENTI E IL MIGLIORAMENTO DEI PERCORSI

Coordinano:

Antonella Costantino, Massimo Molteni, Ottaviano Martinelli

13:00 – 14:00 Pausa Pranzo

14:00 – 15:45

TAVOLA ROTONDA:

PRESENTAZIONE DI CASI CLINICI: DOSAGGIO, MONITORAGGIO, SOSPENSIONE DELLA TERAPIA FARMACOLOGICA NELL'ADHD

Coordina: Monica Saccani

Presentano: referenti dei centri ADHD

15:45 – 16:45

ESERCITAZIONE IN GRUPPO ALLARGATO

Monica Saccani

16:45 – 17:00

DISCUSSIONE E CONCLUSIONI

Monica Saccani, Laura Salvoni, Maurizio Bonati



Il Progetto: "Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia" è stato finanziato dalla Regione Lombardia con Decreto della Dg Welfare N. 1077 del 02 febbraio 2017. Il progetto coinvolge 18 Centri di Riferimento per l'ADHD e il Laboratorio per la Salute Materno Infantile dell'IRCCS - Istituto di Ricerche Farmacologiche Mario Negri. Coordinatore del Progetto è la UONPIA dell'ASST di Brescia.



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DIAGNOSI DIFFERENZIALE E COMORBILITA' IN ADOLESCENZA

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<http://www.centroetaevolutiva.it/formazione/giornate-studio/diagnosi-differenziale-comorbilita-adolescenza>

PROGRAMMA

8.15 - Registrazione dei partecipanti

9.20 – Dati Epidemiologici della Psicopatologia in adolescenza.

Gian Marco Marzocchi – *Università di Milano Bicocca & Centro per l'Età Evolutiva di Bergamo.*

9.40 – La psicopatologia e i disturbi del neurosviluppo. Quali linee per il futuro dei servizi?

Massimo Molteni – *Dipartimento Psicopatologia dello Sviluppo, Associazione La Nostra Famiglia - IRCCS E. Medea Bosisio Parini (LC).*

10.30 – Disregolazione emotiva come predittore per i disturbi dell'umore in adolescenza ed età adulta.

Gabriele Masi – *IRCCS Stella Maris Calambrone (PI).*

11.30 – Disturbi dirompenti del comportamento: approccio evolutivo, dimensionale, fattori di rischio e prognosi.

Dino Maschietto – *UOC NPI San Donà di Piave (VE).*

12.30 - 14.00 Pranzo

14.00 - Conoscere e Ri-conoscere i disturbi d'ansia e depressivi attraverso l'adolescenza.

Maria Nobile - *Associazione La Nostra Famiglia - IRCCS E. Medea Bosisio Parini (LC).*

15.00 – La valutazione diagnostica dei DSA nell'adolescente e nel giovane adulto.

Enrico Ghidoni – *Fondazione Italiana Dislessia, Centro di Neuroscienze Anemos (RE).*

16.00 - Diagnosticare e comprendere la Sindrome di Asperger durante l'Adolescenza.

Davide Moscone – *Psicologo e Psicoterapeuta, Direttore clinico di CuoreMenteLab (RM), presidente dell'Associazione Spazio Asperger ONLUS.*

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

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