NEWSLETTER

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Acad Pediatr. 2015;15:289-96.

A PLANNED CARE APPROACH AND PATIENT REGISTRY TO IMPROVE ADHERENCE TO CLINICAL GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Geltman PL, Fried LE, Arsenault LN, et al.

Background Attention-deficit/hyperactivity disorder (ADHD) affects almost 2.4 million US children. Because American Academy of Pediatrics guidelines for ADHD recommend use of standardized diagnostic instruments, regular follow-up and the chronic care model, this pilot project sought to implement and assess an electronic registry of patients with ADHD combined with care coordination by a planned care team.

Methods This quality improvement project was structured with 2 intervention and 2 control clinics to facilitate evaluation of the use of a planned care system for management of ADHD. Care teams included a pediatrician, nurse, medical assistant, and care coordinator and tracked patients using an electronic registry with data drawn from the EMR. Clinical work flows were pilot tested to facilitate use of the Vanderbilt scales and their incorporation into the EMR at intervention sites. Outcome measures included 2 recommended clinical follow-ups based on HEDIS measures as well as use of the Vanderbilt rating scales. Initiation phase measure was for follow-up after initiating medication, while the continuation phase measure was for subsequent follow-up during the first year of treatment. Measures were monitored during the project year and then also in the ensuing period of spread of the intervention to other sites.

Results Although the modified HEDIS initiation phase measure for patients newly on medication remained static at approximately 50% throughout the project period, the continuation phase measure showed improvement from 35% at baseline to 45% at the end of the project assessment year, a 29% increase. Follow-up for patients stable on medications also remained unchanged during the project period, but during subsequent spreading of the intervention to nonproject sites, follow-up of these patients improved to over 90%. In adjusted analyses, patients with ADHD at intervention sites were over 2 times more likely than patients at control sites to have had a Vanderbilt score documented in their records.

Conclusions The project achieved modest improvements in the diagnostic and treatment process for patients with ADHD. The use of a planned care system and electronic patient registry shows promise for improving the diagnosis and treatment process for patients with ADHD.

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

Acta Paediatr Int J Paediatr. 2015. [Epub ahead of print]

RISKY SEXUAL BEHAVIOUR AMONG ADOLESCENTS MAY BE RELATED TO ADHD.

Nylander C, Tindberg Y, Fernell E.

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ADHD Atten Deficit Hyperact Disord. 2014;6:303-12.

THE RELATIONSHIP BETWEEN ADHD SYMPTOMATOLOGY AND SELF-HARM, SUICIDAL IDEATION, AND SUICIDAL BEHAVIOURS IN ADULTS: A PILOT STUDY.

Taylor MR, Boden JM, Rucklidge JJ.

The aim of this study was to explore whether individuals with attention-deficit/hyperactivity disorder (ADHD) are at risk of harm over the lifespan due to increased rates of self-harm, suicidal ideation and suicidal behaviour, and whether this association is mediated by psychosocial factors. Sixty-six adults (43 men, 23 women; 18null65 years) participated in this study involving clinical interview and retrospective self-report measures of ADHD symptoms, self-harm/suicidal behaviour, mental health disorders, and coping style measures. Significant associations were found between ADHD symptom severity and self-reported histories of self-harm behaviour, suicidal ideation, and suicide attempts (all p values <.05). These relationships between self-destructive behaviours and ADHD symptom severity were found to be significantly and differentially mediated by psychosocial variables (all p values <.05) including comorbidity (mood, anxiety, drug, and alcohol abuse disorders) and emotion-focussed coping style. This study suggests that linkages between self-injurious behaviour and ADHD symptomatology may be due primarily to comorbid mental health disorders and emotion-focussed coping. The identification of these mediating factors and processes may potential pathways for intervention in reducing suicide and self-harm risk amongst those with ADHD symptoms.

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ADHD Atten Deficit Hyperact Disord. 2015. [Epub ahead of print]

THE CLINICAL PROFILE OF CHILDREN WITH ADHD THAT REQUIRE OROS-METHYLPHENIDATE COMBINED WITH SHORTER-ACTING FORMULATIONS.

Zelnik N, Terkel-Dawer R.

Long-acting methylphenidate (MPH) formulations, including OROS-MPH, were found to be effective in alleviating ADHD symptoms throughout the day. However, sustained stimulant activity may lead to prolonged suppression of appetite and insomnia. In this study, we characterized the clinical profile of children and adolescents for whom a once-daily lower dose of OROS-MPH combined with a shorter-acting agent was more tolerable than single higher OROS-MPH dose. In our cohort of 128 children treated with OROS-MPH, 47 (36.7 %) better tolerated a lower dose of OROS-MPH combined with short-acting MPH formulations (Group I). Nevertheless, for the majority (81 patientsnull63.3 %), a standard single moderate dose of OROS-MPH was sufficient (Group II). The mean daily doses of MPH were: 0.83 (plus or minus) 0.21 mg/kg for Group I and 1.06 (plus or minus) 0.29 mg/kg for Group II. There were no significant differences in the prevalence of learning disorders, tic disorders, epilepsy and conduct disorders between these two groups. However, anxiety and marginally depression were more prevalent in Group I (46.8 and 9.7 %) than in Group II (27.2 and 1.2 %). Patients in Group I were also more tending to receive psychotherapy than patients in Group II.

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Altern Ther Health Med. 2015;21 Suppl 1:52-62.

IMMUNE REACTIVITY TO FOOD COLORING.

Vojdani A, Vojdani C.

Artificial food dyes are made from petroleum and have been approved by the US Food and Drug Administration (FDA) for the enhancement of the color of processed foods. They are widely used in the food and pharmaceutical industries to increase the appeal and acceptability of their products. Synthetic

food colorants can achieve hues not possible for natural colorants and are cheaper, more easily available, and last longer. However, since the use of artificial food coloring has become widespread, many allergic and other immune reactive disorders have increasingly been reported. During the past 50 y, the amount of synthetic dye used in foods has increased by 500%. Simultaneously, an alarming rise has occurred in behavioral problems in children, such as aggression, attention deficit disorder (ADD), and attention-deficit/hyperactivity disorder (ADHD). The ingestion of food delivers the greatest foreign antigenic load that challenges the immune system. Artificial colors can also be absorbed via the skin through cosmetic and pharmaceutical products. The molecules of synthetic colorants are small, and the immune system finds it difficult to defend the body against them. They can also bond to food or body proteins and, thus, are able to act in stealth mode to circumvent and disrupt the immune system. The consumption of synthetic food colors, and their ability to bind with body proteins, can have significant immunological consequences. This consumption can activate the inflammatory cascade, can result in the induction of intestinal permeability to large antigenic molecules, and could lead to cross-reactivities, autoimmunities, and even neurobehavioral disorders. The Centers for Disease Control (CDC) recently found a 41% increase in diagnoses of ADHD in boys of high-school age during the past decade. More shocking is the legal amount of artificial colorants allowed by the FDA in the foods, drugs, and cosmetics that we consume and use every day. The consuming public is largely unaware of the perilous truth behind the deceptive allure of artificial color.

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Am J Public Health. 2015 Mar;105:524-29.

PSYCHOTROPIC DRUG USE AMONG PRESCHOOL CHILDREN IN THE MEDICAID PROGRAM FROM 36 STATES.

Garfield LD, Brown DS, Allaire BT, et al.

OBJECTIVES: We determined the prevalence of and indications for psychotropic medication among preschool children in Medicaid.

METHODS: We obtained 2000 to 2003 Medicaid Analytic Extract data from 36 states. We followed children in 2 cohorts, born in 1999 and 2000, up to age 4 years. We used logistic regression to model odds of receiving medications for (1) attention-deficit disorder/attention-deficit hyperactivity disorder, (2) depression or anxiety, and (3) psychotic illness or bipolar.

RESULTS: Overall, 1.19% of children received at least 1 psychotropic drug. Medications for attention-deficit disorder/attention-deficit hyperactivity disorder treatment were most common (0.61% of all children), followed by depression or anxiety (0.59%) and psychotic illness or bipolar (0.24%). Among children, boys, those of other or unknown race compared with White, and those with other insurance compared with fee for service-only had higher odds of receiving a prescription (odds ratio [OR]=1.80 [95% confidence interval (CI)=1.74, 1.86], 1.87 [1.66, 1.85], and 1.14 [1.01, 1.28], respectively), whereas Black and Hispanic children had lower odds (OR=0.51 [95% CI=0.48, 0.53] and 0.37 [0.34, 0.39], respectively).

CONCLUSIONS: Preschoolers are receiving psychotropic medications despite limited evidence supporting safety or efficacy. Future research should focus on implementing medication use practice parameters in infant and toddler clinics, and expanding psychosocial interventions for young children with behavioral problems.

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Am J Med Genet Part B Neuropsychiatr Genet. 2015;168:162-69.

CADHERIN-13 GENE IS ASSOCIATED WITH HYPERACTIVE/IMPULSIVE SYMPTOMS IN ATTENTION/DEFICIT HYPERACTIVITY DISORDER.

Salatino-Oliveira A, Genro JP, Polanczyk G, et al.

Several efforts have been made to find new genetic risk variants which explain the high heritability of ADHD. At the genome level, genes involved in neurodevelopmental pathways were pointed as candidates. CDH13 and CTNNA2 genes are within GWAS top hits in ADHD and there are emerging notions about their contribution to ADHD pathophysiology. The main goal of this study is to test the association between SNPs in CDH13 and CTNNA2 genes and ADHD across the life cycle in subjects with ADHD. This study included 1,136 unrelated ADHD cases and 946 individuals without ADHD. No significant association between

CDH13 and CTNNA2 was observed between cases and controls across different samples (P(greater-than or equal to)0.096 for all comparisons). No allele was significantly more transmitted than expected from parents to ADHD probands. The CDH13 rs11150556 CC genotype was associated with more hyperactive/impulsive symptoms in youths with ADHD (children/adolescents clinical sample: F=7.666, P=0.006, FDR P-value=0.032; Pelotas Birth Cohort sample: F=6.711, P=0.011, FDR P-value=0.032). Although there are many open questions regarding the role of neurodevelopmental genes in ADHD symptoms, the present study suggests that CDH13 is associated with hyperactive/impulsive symptoms in youths with ADHD.

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Am J Med Genet Part B Neuropsychiatr Genet. 2015. [Epub ahead of print]

CAUSAL DISCOVERY IN AN ADULT ADHD DATA SET SUGGESTS INDIRECT LINK BETWEEN DAT1 GENETIC VARIANTS AND STRIATAL BRAIN ACTIVATION DURING REWARD PROCESSING.

Sokolova E, Hoogman M, Groot P, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common and highly heritable disorder affecting both children and adults. One of the candidate genes for ADHD is DAT1, encoding the dopamine transporter. In an attempt to clarify its mode of action, we assessed brain activity during the reward anticipation phase of the Monetary Incentive Delay (MID) task in a functional MRI paradigm in 87 adult participants with ADHD and 77 controls (average age 36.5 years). The MID task activates the ventral striatum, where DAT1 is most highly expressed. A previous analysis based on standard statistical techniques did not show any significant dependencies between a variant in the DAT1 gene and brain activation [Hoogman et al. (2013); Neuropsychopharm 23:469-478]. Here, we used an alternative method for analyzing the data, that is, causal modeling. The Bayesian Constraint-based Causal Discovery (BCCD) algorithm [Claassen and Heskes (2012); Proceedings of the 28th Conference on Uncertainty in Artificial Intelligence] is able to find direct and indirect dependencies between variables, determines the strength of the dependencies, and provides a graphical visualization to interpret the results. Through BCCD one gets an opportunity to consider several variables together and to infer causal relations between them. Application of the BCCD algorithm confirmed that there is no evidence of a direct link between DAT1 genetic variability and brain activation, but suggested an indirect link mediated through inattention symptoms and diagnostic status of ADHD. Our finding of an indirect link of DAT1 with striatal activity during reward anticipation might explain existing discrepancies in the current literature. Further experiments should confirm this hypothesis.

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Am J Med Genet Part B Neuropsychiatr Genet. 2015. [Epub ahead of print]

NEUROPSYCHOLOGICAL AND DIMENSIONAL BEHAVIORAL TRAIT PROFILES IN COSTA RICAN ADHD SIB PAIRS: POTENTIAL INTERMEDIATE PHENOTYPES FOR GENETIC STUDIES.

Peskin VA, Ordonez A, Mackin RS, et al.

Attention deficit hyperactivity disorder (ADHD) is associated with substantial functional impairment in children and in adults. Many individuals with ADHD have clear neurocognitive deficits, including problems with visual attention, processing speed, and set shifting. ADHD is etiologically complex, and although genetic factors play a role in its development, much of the genetic contribution to ADHD remains unidentified. We conducted clinical and neuropsychological assessments of 294 individuals (269 with ADHD) from 163 families (48 multigenerational families created using genealogical reconstruction, 78 affected sib pair families, and 37 trios) from the Central Valley of Costa Rica (CVCR). We used principal components analysis (PCA) to group neurocognitive and behavioral variables using the subscales of the Child Behavior Checklist (CBCL) and 15 neuropsychological measures, and created quantitative traits for heritability analyses. We identified seven cognitive and two behavioral domains. Individuals with ADHD were significantly more impaired than their unaffected siblings on most behavioral and cognitive domains. The verbal IQ domain had the highest heritability (92%), followed by auditory attention (87%), visual processing speed and problem solving (85%), and externalizing symptoms (81%). The quantitative traits identified here have high heritabilities, similar to the reported heritability of ADHD (70-90%), and may

represent appropriate alternative phenotypes for genetic studies. The use of multigenerational families from a genetically isolated population may facilitate the identification of ADHD risk genes in the face of phenotypic and genetic heterogeneity.

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Am J Med Genet Part C Semin Med Genet. 2015;169:117-22.

PHENOTYPIC VARIABILITY IN DEVELOPMENTAL COORDINATION DISORDER: CLUSTERING OF GENERALIZED JOINT HYPERMOBILITY WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER, ATYPICAL SWALLOWING AND NARRATIVE DIFFICULTIES.

Celletti C, Mari G, Ghibellini G, et al.

Developmental coordination disorder (DCD) is a recognized childhood disorder mostly characterized by motor coordination difficulties. Joint hypermobility syndrome, alternatively termed Ehlers-Danlos syndrome, hypermobility type (JHS/EDS-HT), is a hereditary connective tissue disorder mainly featuring generalized joint hypermobility (gJHM), musculoskeletal pain, and minor skin features. Although these two conditions seem apparently unrelated, recent evidence highlights a high rate of motor and coordination findings in children with gJHM or JHS/EDS-HT. Here, we investigated the prevalence of gJHM in 41 Italian children with DCD in order to check for the existence of recognizable phenotypic subgroups of DCD in relation to the presence/absence of gJHM. All patients were screened for Beighton score and a set of neuropsychological tests for motor competences (Movement Assessment Battery for Children and Visual-Motor Integration tests), and language and learning difficulties (Linguistic Comprehension Test, Peabody Picture Vocabulary Test, Boston Naming Test, Bus Story Test, and Memoria-Training tests). All patients were also screening for selected JHS/EDS-HT-associated features and swallowing problems. Nineteen (46%) children showed gJHM and 22 (54%) did not. Children with DCD and gJHM showed a significant excess of frequent falls (95 vs. 18%), easy bruising (74 vs. 0%), motor impersistence (89 vs. 23%), sore hands for writing (53 vs. 9%), attention deficit/hyperactivity disorder (89 vs. 36%), constipation (53 vs. 0%), arthralgias/myalgias (58 vs. 4%), narrative difficulties (74 vs. 32%), and atypical swallowing (74 vs. 18%). This study confirms the non-causal association between DCD and gJHM, which, in turn, seems to increase the risk for non-random additional features. The excess of language, learning, and swallowing difficulties in patients with DCD and gJHM suggests a wider effect of lax tissues in the development of the nervous system.

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Anadolu Psikiyatr Derg. 2015 Mar;16:69-73.

DIKKAT EKSIKLIGI HIPERAKTIVITE BOZUKLUGU TANILI ÇOCUKLARDA DOGUM SIRASI. = BIRTH ORDER IN CHILDREN DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Evrensel A, Alparslan S, Yorbik Ö.

Objective: Etiopathogenesis of attention deficit hyperactivity disorder (ADHD) has not been elucidated. It has been thought that environmental and genetic factors played a role in it. Perinatal fetal traumas might cause minimal brain damage. Being a first born child is a risk factor in term of exposure to birth traumas. There are few studies which focus on the effect of birth order in ADHD. The present study aims to analyze the birth order characteristics of children with ADHD.

Methods: The birth orders of children, 16 females and 49 boys with ADHD were determined with Slater's Index. Data were compared with the control group.

Results: The birth order index of children with ADHD was statistically lower compared to the control group. This results indicate that the firstborn children are more likely to have ADHD.

Discussion: The results of this research show first or one of the first born children are more under exposure to perinatal traumas and for those reason minimal brain damages play an important role in etiopathogenesis of ADHD.

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Assessment. 2015 Apr;22:198-207.

ADAPTING THE POSTERIOR PROBABILITY OF DIAGNOSIS INDEX TO ENHANCE EVIDENCE-BASED SCREENING: AN APPLICATION TO ADHD IN PRIMARY CARE.

Lindhiem O, Yu L, Grasso DJ, et al.

This study adapts the Posterior Probability of Diagnosis (PPOD) Index for use with screening data. The original PPOD Index, designed for use in the context of comprehensive diagnostic assessments, is overconfident when applied to screening data. To correct for this overconfidence, we describe a simple method for adjusting the PPOD Index to improve its calibration when used for screening. Specifically, we compare the adjusted PPOD Index to the original index and naïve Bayes probability estimates on two dimensions of accuracy, discrimination and calibration, using a clinical sample of children and adolescents (N = 321) whose caregivers completed the Vanderbilt Assessment Scale to screen for attention-deficit/hyperactivity disorder and who subsequently completed a comprehensive diagnostic assessment. Results indicated that the adjusted PPOD Index, original PPOD Index, and naïve Bayes probability estimates are comparable using traditional measures of accuracy (sensitivity, specificity, and area under the curve), but the adjusted PPOD Index showed superior calibration. We discuss the importance of calibration for screening and diagnostic support tools when applied to individual patients.

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Behav Brain Funct. 2015;11.

PARENT RATINGS OF EXECUTIVE FUNCTION IN YOUNG PRESCHOOL CHILDREN WITH SYMPTOMS OF ATTENTION-DEFICIT/-HYPERACTIVITY DISORDER.

Skogan AH, Zeiner P, Egeland J, et al.

Background: Recent research has demonstrated that deficits in basic, self-regulatory processes, or executive function (EF), may be related to symptoms of attention-deficit/hyperactivity disorder (ADHD) already during the preschool period. As the majority of studies investigating these relations in young children have been based primarily on clinically administered tests, it is not clear how early symptoms of ADHD may be related to observations of EF in an everyday context. The preschool version of the Behavior Rating Inventory of Executive Function (BRIEF-P) was developed to provide information about EF through observable, behavioral manifestations of self-regulation, and is the most commonly used rating scale for EF assessment in children.

Methods: Relations between symptoms of ADHD reported in the Preschool Age Psychiatric Assessment interview (PAPA), and EF as measured by the BRIEF-P (parent form), were investigated in a large, nonreferred sample of preschool children (37-47 months, n = 1134) recruited from the Norwegian Mother and Child Cohort Study (MoBa) at the Norwegian Institute of Public Health. The inventory's discriminative ability was examined in a subsample consisting of children who met the diagnostic criteria for either ADHD, oppositional defiant disorder (ODD) or anxiety disorder, and typically developing controls (n = 308). The four groups were also compared with regard to patterns of EF difficulties reported in the BRIEF-P.

Results: Of the five BRIEF-P subscales, Inhibit and Working Memory were the two most closely related to ADHD symptoms, together explaining 38.5% of the variance in PAPA symptom ratings. Based on their scores on the Inhibit and Working Memory subscales (combined), 86.4% of the children in the ADHD and TD groups were correctly classified. ADHD symptoms were associated with more severe difficulties across EF domains, and a different EF profile in comparison to children with other symptoms (anxiety, ODD) and to typically developing controls.

Conclusions: Early symptoms of ADHD were linked to parent-reported difficulties primarily within inhibition and working memory, suggesting that deficiencies within these two EF domains characterize early forms of ADHD. Our findings support the clinical utility of the BRIEF-P as a measure of EF in young preschool children with symptoms of ADHD.

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Biol Psychiatry. 2015;77:214S.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) SYMPTOMS AND PROBLEMATIC INTERNET USE IN CHILDREN AND ADOLESCENTS.

Jolin EM, Weller RA.

Background: Depression, anxiety disorders, and excessive alcohol use are associated with problematic Internet use (PIU) in youth. As ADHD is the most common psychiatric illness in children, its relationship with PIU is of interest. This study examines the relationship between ADHD symptoms and PIU in children and adolescents.

Methods: A PubMed search utilizing the key words Internet, Internet addiction, heavy Internet use, and PIU combined with the terms ADHD, hyperactivity, impulsivity, and attention deficits was conducted. The search spanned from inception through June, 2014. To be included, studies had to be in English, have at least 100 subjects, and have a subject mean age of 18 years or less. Effect sizes were calculated from published data.

Results: 9 cross-sectional studies and 1 longitudinal study with 13,409 unique subjects met inclusion criteria. 7 studies were conducted in Asia and 3 in Europe. ADHD symptoms and PIU scores were assessed by self-report. ADHD symptoms were measured by 5 different instruments. PIU was assessed by 5 different measures across 10 studies. All of the cross-sectional studies found a significant association between ADHD symptoms and PIU. Effect sizes were small (n=2), moderate (n=3), and large (n=4). The longitudinal study found baseline ADHD predicted PIU at 2 year follow-up, but effect size was small.

Conclusions: Although methodology varied considerably among studies, these preliminary studies suggested a positive association between ADHD symptoms and PIU in youth. Longitudinal studies with improved methodologies are needed to determine whether youth with ADHD are at increased risk for PIU.

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Biol Psychiatry. 2015;77:43S.

BRAIN CORRELATES OF THE INTERACTION BETWEEN 5-HTTLPR AND PSYCHOSOCIAL STRESS MEDIATING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SEVERITY.

Van Der Meer D.

Background: Serotonin transporter 5-HTTLPR genotype has been found to moderate the effect of stress on severity of attention-deficit/ hyperactivity disorder (ADHD), with stronger effects of stress in carriers of the short allele than in individuals homozygous for the long allele. The underlying neurobiological mechanism of this gene-environment interaction in ADHD is unknown. This study aimed to determine whether 5-HTTLPR moderates the effect of stress on brain grey matter volume and, if so, which brain regions mediate the effect of this gene-environment interaction on ADHD severity.

Methods: Structural magnetic resonance imaging, 5-HTTLPR genotype, and stress exposure questionnaire data were available for 701 adolescents and young adults participating in the multicenter ADHD cohort study NeuroIMAGE (from 385 families; 291 with ADHD, 78 with subthreshold ADHD, 332 healthy controls; 55.8% males; average age 17.0 years). ADHD symptom count was determined through multi-informant questionnaires. For the analysis, we combined a whole-brain voxel-based morphometry approach with mediation analysis.

Results: Stress exposure was associated with significantly less grey matter volume in the precentral gyrus, middle and superior frontal gyrus, frontal pole, and cingulate gyrus for S-allele carriers than for participants homozygous for the L-allele. The association of this gene-environment interaction with ADHD symptom count was mediated by grey matter volume in the frontal pole and anterior cingulate gyrus.

Conclusions: 5-HTTLPR genotype moderates the effect of stress on brain regions involved in social cognitive processing and cognitive control. Specifically regions important for cognitive control link this gene-environment interaction to ADHD severity.

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Biol Psychiatry. 2015;77:344S.

THE NEURAL CORRELATES OF RESPONSE INHIBITION IN ADOLESCENTS WITH ADHD, OCD AND ASD .

Bhaijiwala M, Schachar RJ.

Background: The cancellation of a motor response or reactive inhibition and withholding a prepotent response or prospective inhibition are two aspects of the response inhibition process. Atypical response inhibition has been observed in ADHD, OCD and ASD. However, it remains unclear if the alterations are either in the same or different aspects of response inhibition or even if the functional neural architecture is similar or unique in each disorder. The aim of this study is to investigate and compare the neural impairments in prospective and reactive inhibition in ADHD, OCD and ASD.

Methods: Twenty-nine adolescents with ADHD, OCD and ASD (age range 9-18) were imaged while performing the stop-signal task (SST).

Results: All three groups showed distinct patterns of activity and indicated that the response inhibition deficit is disorder specific. The ADHD and OCD groups showed impairments in prospective but not reactive inhibition while the ASD showed no deficit when compared to the other two neurodevelopmental disorders.

Conclusions: This study has increased our understanding of response inhibition deficits in three disorders and validates the need to approach neurodevelopmental disorders as distinct and heterogeneous entities.

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Biol Psychiatry. 2015;77:199S.

PHARMACOLOGICAL MEDIATION OF COGNITION IN CHILDREN AND ADOLESCENTS PRESENTING WITH CROSS-DISORDER SYMPTOMS OF ADHD AND ANXIETY.

Kohn MR, Griffiths KR, Clarke S, et al.

Background: Attention Deficit Hyperactivity Disorder (ADHD) and comorbid anxiety may be classified by performance on objective tests of cognition, independent of traditional diagnosis. Atomoxetine (ATX) is a selective norepinephrine reuptake inhibitor that produces a widespread increase in brain norepinephrine and a secondary and selective increase in prefrontal dopamine. It remains unclear whether atomoxetine provides pharmacological mediation of cognitive improvements in children and adolescents presenting with cross-disorder symptoms of ADHD and anxiety via primary action or through reduction in anxiety.

Methods: 136 children and adolescents with ADHD (43 with comorbid anxiety disorders) were enrolled in a randomized crossover trial of 6 weeks treatment each with atomoxetine and placebo. The primary endpoint was performance on tests of cognitive function (IntegNeuroTM), and secondary endpoints were ADHD and anxiety symptoms on the ADHD-Rating Scale and Conner's Parent Rating Scale Anxious-Shy subscale. Data were analyzed using mixed models in which treatment arm was an independent factor and dependent measures were change in each endpoint.

Results: Relative to placebo, atomoxetine was related to improvements in sustained attention (EF (Cohen's d):0.28, p=.014) and in distinct aspects of cognitive control; executive function on a maze task (EF:0.18, p=.019) and response inhibition on Go-NoGo task (EF:0.43, p=.003). Symptoms of anxiety improved (EF:0.20, p=.042). This change was independent of changes in cognition.

Conclusions: The effects of atomoxetine on cognition and anxiety occur independently, suggesting a dual mechanism for the pharmacological mediation of atomoxetine in ADHD. Cognition is a clinically applicable metric for quantifying pharmacologically mediated improvements in cross-disorders of ADHD and anxiety.

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Biol Psychiatry. 2015;77:88S.

A GENOME WIDE ASSOCIATION STUDY OF QUANTITATIVE ADHD DIMENSIONS IN A COMMUNITY-BASED SAMPLE OF CHILDREN AND ADOLESCENTS.

Crosbie J, Burton CL, Erdman L, et al.

Background: ADHD is a heritable childhood-onset disorder characterized by inattention (IA) and hyperactivity/impulsivity (HI). Genome-wide association studies (GWAS) to date have failed to pinpoint the genetic risk variants underlying ADHD; however, using dimensional quantitative traits in large community

samples may help boost power for GWAS studies of ADHD. To this end, we conducted a genome-wide association study (GWAS) of IA/HI traits in a large community sample of children and adolescents.
Methods: DNA and ratings of ADHD traits based on the Strengths and Weaknesses of Attention-Deficit/Hyperactivity Disorder Symptoms and Normal Behavior Scale (SWAN) were collected on 17263 youth visiting a Science Museum. From salivary DNA, we genotyped 5366 unrelated Caucasians using the Illumina HumanCoreExome and OMNI1 beadchips. 9,598,793 imputed and genotyped SNPs that passed standard quality control (QC) metrics were included in the analysis. Association was tested using linear regressions for the quantitative IA and HI z-scores separately using principal components to control for population-structure.
Results: 89% percent of the sample passed QC (N = 5066). Phenotypically, IA and HI were positively correlated (R = 0.66, p < 0.01) and as a result shared the same top SNP: rs1087989 (IA: p = 1.8x10-6 & HI: p = 7.7x10-7; (lambda) = 0.99) on chromosome 12 near KCNC2 (MAF = 0.3) which is involved in synaptic transmission.
Conclusions: Both IA and HI traits may be associated with a similar genetic risk variant involved in neuronal communication. These analyses are the first step in an analysis pipeline which will examine rare variants, gene-set approaches.

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Biol Psychiatry. 2015;77:314S-5S.

TOWARDS AN UNDERSTANDING OF THE NEURAL PROCESSES UNDERPINNING PERSISTENCE AND REMISSION IN ADHD.

Shaw P.

Background: Defining the neural mechanisms underpinning the variable course of ADHD into adulthood would facilitate the prediction of outcome and stimulate novel treatment approaches. Here, we link brain structure and function with course of ADHD in a cohort followed from childhood to adulthood.
Methods: From neuroanatomic magnetic resonance images we defined cerebral cortical trajectories on 276 children followed into adulthood (92 with DSM-IVR ADHD; 184 controls; mean age at study entry of 10yrs, SD 4). At last observation (mean age 24yrs, SD 3), we obtained diffusion tensor imaging and delineated brain activation during response inhibition, using functional MR (fMRI) and magnetoencephalography (MEG). Clinical assessments were made throughout.
Results: (1) Remission of ADHD (N=55; 60%) was linked with a convergence during adolescence towards typical cortical dimensions, rectifying early anomalies. This was prominent in the default mode and cognitive control networks. Conversely, cortical anomalies persisted into adulthood in those who symptoms also persisted. (2) Atypical white matter microstructure (reflected by decreased fractional anisotropy) was found in persistent but not remitting ADHD in tracts of the brain systems mediating cognitive control (superior longitudinal) and emotion regulation (uncinate) (3) The degree of anomalous brain activation as assayed by fMRI and MEG during response inhibition also reflected the degree to which ADHD persisted into adulthood
Conclusions: Remission from ADHD is linked with a convergence towards more typical structure and function in the brain systems mediating cognitive control and emotion regulation. A future goal is to devise novel treatments which emulate these neural processes of recovery.

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Biol Psychiatry. 2015;77:108S.

EVIDENCE OF ALTERED NEUROPIL DEVELOPMENT IN ADHD CHILDREN: A LONGITUDINAL IN VIVO 31P MRS STUDY AT 3 TESLA.

Stanley JA, Wu H, Goradia DD, et al.

Background: In vivo 31P MRS is sensitive in detecting changes during development in the molecular biochemistry of cortex that reflects neuropil expansion/contraction by measuring precursors of membrane phospholipids (MPLs) [phosphocholine (PC); phoshoethanolamine (PE)]. In a cross-sectional study, we have reported subcortical/cortical deficits in MPL precursor levels of ADHD children that are suggestive of

altered neuropil development (Stanley et al. 2008). In this study, the purpose was to investigate whether longitudinal changes in precursor levels differed between ADHD and controls.
Methods: A 3D multi-voxel 31P MRS at 3T was collected in 31 ADHD males (10.7(plus or minus)2.4yrs) and 31 controls (10.2(plus or minus)2.32yrs) at baseline, and at 1- and 2-year follow-up. Metabolite levels from the DLPFC, ACC, striatum and thalamus were quantified, and group differences at baseline and group-by-time-point interactions were statistically analyzed.
Results: At baseline, PC levels were reduced in the right DLPFC (p=0.020) and right ACC (p=0.042) of ADHD children compared to controls. The longitudinal data showed decreasing PE levels with age in the right DLPFC (p=0.021), decreasing PC levels with age in the left striatum (p=0.0049), and increasing PE levels with age in the right thalamus (p=0.032) all in ADHD children compared to controls.
Conclusions: These results show, for the first time distinct altered developmental trajectories of MPL precursor levels in the DLPFC, striatum and thalamus of ADHD children. Active MPL synthesis is critical in providing cell membrane structure to dendritic and synaptic connections and astrocytes (i.e., neuropil expansion) and these deficits continue to support a greater rate of neuropil contraction over time in the DLPFC and striatum of ADHD children. (Figure Presented).

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Biol Psychiatry. 2015;77:12S.

METHYLPHENIDATE TREATMENT OF CHRONIC IRRITABILITY: SYMPTOM IMPROVEMENT AND UNDERLYING NEURAL MECHANISMS.

Hulvershorn L.

Background: Some children with ADHD display chronic irritability with temper outbursts. Despite high rates of medication use, little is known about effective pharmacotherapies for the mood regulation component of their symptoms. Methylphenidate (MPH) is a dopamine and norepinephrine acting agent with known benefit for multiple symptoms of ADHD, including emotion regulation. Neural mechanisms underlying MPH's effects on emotion aren't well characterized.
Methods: Medication-free, right-handed 10-15 year olds (n=23) with ADHD and disruptive mood dysregulation disorder were treated open-label with MPH (Concerta TM). Functional MRI scans using a facial emotion-matching task were acquired before and after 4 weeks of MPH treatment. A whole brain voxel-wise analysis ($p<0.05$) compared face - shape activation from pre- to post-medication scan.
Results: All participants tolerated dose escalation with few side effects. A significant improvement on parent ratings of the Emotion Regulation Checklist was noted from baseline to week 4 of treatment (p=0.01). On the task, participants demonstrated similarly high rates of accuracy when matching shapes (>90%) and faces (>70%). There were no differences between pre- or postscans for face or shape matching accuracy. Significant pre- vs. post-medication BOLD signal activation increases in the right inferior frontal gyrus (k=62 voxels) and right cerebellum (k=105) were found.
Conclusions: In this unpublished, open-label fMRI study, MPH was well tolerated at therapeutic doses and resulted in parent-rated improvements in emotion regulation. MPH appears to have increased BOLD activation in the inferior frontal gyrus, a region associated with inhibitory control, suggesting influences of cognitive control regions on emotion regulation.

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Biol Psychiatry. 2015;77:285S-6S.

HEART RATE VARIABILITY DURING COGNITIVE LOAD IN ADHD: A PHYSIOLOGICAL MARKER OF SUBTYPE?

Griffiths KR, Hermens DF, Tsang TW, et al.

Background: Autonomic dysregulation in attention deficit hyperactivity disorder (ADHD) may underlie the common cognitive deficits in sustained attention and response inhibition. While numerous studies have reported reduced skin conductance and heart rate variability during restingstate, few have investigated how these physiological measures are affected during cognitive load. This study aimed to investigate autonomic reactivity to cognitive load and the relationship with cognitive ability in un-medicated children with ADHD.

Methods: Electro-dermal activity and electrocardiogram and were recorded during resting state and cognitive load (continuous performance and GoNoGo tasks) in 56 children and adolescents with ADHD and 56 matched typically developing controls (TDC). Skin conductance level (SCL) and frequency domain HRV data were extracted.
Results: During resting state, ADHD exhibited reduced SCL (p=.01) and increased low to highfrequency ratio (LFHF) HRV (p=.005) relative to TDC. LFHF ratio remained high relative to TDC during cognitive challenge, driven by increased low frequency power. ADHD participants with reduced LFHF HRV during sustained attention had greater inattention subscale scores on the ADHD-RS and Conner's Parent Rating Scale (p<.001 & p=.016), but showed no difference to those with high LFHF in cognitive performance.
Conclusions: Reduced sympathetic relative to parasympathetic tone (indicated by low LFHF ratio) during activation may represent a mechanism underlying the inattentive ADHD subtype. Future research could investigate the validity of this measure in predicting likelihood of treatment response to noradrenergic agents.

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Biol Psychiatry. 2015;77:105S.

BRAIN STRUCTURE AND ADHD ACROSS THE LIFE SPAN: AN ENIGMA COLLABORATION.

Hoogman M, Hibar D, Van HK, et al.

Background: Neuroimaging studies show structural alterations of various brain regions in children and adults diagnosed with ADHD. In part due to inconsistencies in published results, it remains unclear, however, how these differences develop across the lifespan, and whether effects are brain-wide or localized to particular neurological structures and pathways. To clarify brain changes across the lifespan in a large worldwide sample, an ADHD Working Group was formed within the ENIGMA consortium (http:// enigma.ini.usc.edu/).
Methods: Within the ENIGMA-ADHD Working Group cohorts from around the world analyzed MRI scans using fully automated and validated neuroimaging segmentation software (FSL FIRST or FreeSurfer), for which protocols are available on our website. Volumetric summaries of subcortical regions were pooled together and shared across the consortium. Meta- and Mega-analysis for the case-control volume differences of hippocampus, nucleus accumbens, amygdala, caudate nucleus, putamen, pallidum, and thalamus were carried out.
Results: The working group comprises 23 international sites including 1544 cases and 1729 controls. This pooled sample has an age-range of 4-63 years and includes 66% males. Our preliminary case-control meta-analysis showed subtle but significantly smaller volumes for the nucleus accumbens (Cohen's d: 0.13), amygdala (d: 0.15), caudate nucleus (d: 0.11), and putamen (d: 0.11) for cases compared to controls. The results of the mega- analysis showed similar effect sizes, with greater significance (lower p-value). Several structures had age-dependent effects.
Conclusions: Brain structure differences related to ADHD across the lifespan remain largely unexplored. As large, well-powered longitudinal studies are still scarce, the ENIGMA-ADHD Working Group, with a large cross-sectional sample across six decades of the lifespan, is beginning to address this gap.

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Biol Psychiatry. 2015;77:200S.

EYE MOVEMENTS: GOOD MARKER OF METHYLPHENIDATE EFFICIENCY IN ADHD.

Seassau M, Duval F, Erb E, et al.

Background: Attention-Deficit/hyperactivity disorder (ADHD) is characterized by behavioral symptoms of inattention and may include hyperactivity and impulsivity. The impulsivity and inattention suggest deficits in the voluntary control of behavior. Eye movements depend on structures implicated in attention and in motor control, both criteria areas of dysfunction in ADHD. In the present study, objective was to evaluate the effect of methylphenidate (MPH) using eye movements in ADHD patients, naive to treatment.
Methods: Fifty nine ADHD patients (44 adults and 15 children) participated to this study. Saccade and antisaccade tasks were proposed to drug naive patients during a first examination (V1) early in the morning

(T1) and at midday (T2). Same tasks were then proposed during a second examination (V2), just after the first dose of MPH (10 mg per os). MPH efficiency was measured by the comparison of V1 and V2. Test-retest effect was measured between T1 and T2. Latencies, velocities, precision, accuracy and percentage of anticipatory errors were analyzed.
Results: We found a positive effect of MPH on percentage of anticipatory ($p<0.009$); on accuracy ($p<0.0002$); on latencies ($p<0.0008$); and on precision ($p<0.01$). Performances were significantly better On-MPH than Off-MPH, particularly on antisaccades tasks. Standard deviations were also shorter On-MPH compared to Off-MPH ($p<0.0001$). Same pattern of performances was observed on adults and on children. Importantly, no test-retest effect was observed between T1 and T2.
Conclusions: MPH modified motor planning and response inhibition in ADHD patients. Benefits could be observed using reflexive saccades and antisaccades just after the first dose of MPH. These results suggest that eye movements could be a good marker of MPH efficiency in ADHD.

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Biol Psychiatry. 2015;77:15S.

PRENATAL ANXIETY AND CHILD EMOTIONAL, BEHAVIOURAL AND COGNITIVE OUTCOMES; GENE ENVIRONMENT INTERACTIONS.

Glover V.

Background: If a mother is anxious or depressed during pregnancy her child is more likely to have emotional, behavioural or cognitive problems, even after allowing for a range of confounders. However most children are not affected, and those that are can be affected in different ways. Here we have tested the hypotheses that the effects of prenatal anxiety on child internalizing symptoms are moderated by genetic variation in the child's brain-derived neurotrophic factor (BDNF), and ADHD and cognitive symptoms by catechol-O-methyl transferase (COMT) genes
Methods: We used data from the Avon Longitudinal Study of Parents and Children (ALPSPAC) population cohort (n=8584). Maternal anxiety was assessed by the Crown Crisp questionnaire at 32 weeks. Internalizing symptoms, and ADHD symptoms were assessed from 4 to 13 years of age using the Strengths and Difficulties Questionnaire, and ADHD diagnosis by the Development and Wellbeing Assessment (DAWBA) at 15 years. Working memory was assessed at age 8 by the backward digit span test. Obstetric and psychosocial risk and postnatal maternal symptoms were included as covariates.
Results: There was genetic moderation of the prenatal anxiety effect on internalizing symptoms by the BDNF polymorphisms (rs11030121 and rs7124442) up to age 13 ($p=0.018$ and $p=0.029$ respectively). COMT (val158met (rs4680)) genotype moderated the association between maternal prenatal anxiety and child ADHD in both childhood and adolescence ($p<0.05$), as well as working memory ($p<0.01$).
Conclusions: These new findings suggest a role for both BDNF and COMT gene/environment interactions in specific individual vulnerabilities to the effects of prenatal anxiety.

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Biol Psychiatry. 2015;77:105S.

DOPAMINE TRANSPORTER GENE VARIATION MODULATES INTRINSIC BRAIN ACTIVITY IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Shang C-Y, Gau SSF.

Background: The dopamine transporter gene (DAT1) has been consistently reported to be associated with attention-deficit hyperactivity disorder (ADHD). However, studies have not characterized the resting brain alterations in children with ADHD and their correlations with the severity of ADHD symptoms. This study aimed to examine the relationship between DAT1 genotype and resting state functional connectivity in children with ADHD.
Methods: Using resting state functional MRI (RS-fMRI) and genetic analysis of the DAT1 gene, we investigated how intrinsic brain activity contributed to ADHD depending on DAT1 genotype in 37 drug-naive children with ADHD, including 17 subjects with a haplotype of rs27048 (C)/rs429699 (T) and 20 subjects

without this C/T haplotype. We analyzed intrinsic functional brain architecture with the fractional amplitude of low-frequency fluctuations (fALFFs).
Results: We found an association of ADHD with distinct intrinsic brain activity pattern depending on DAT1 haplotype. A haplotype of rs27048 (C)/rs429699 (T) was associated with fALFF decrease in the left superior temporal gyrus, left cingulate gyrus, and left precentral/postcentral gyri. The severity of ADHD symptom was negatively correlated with fALFF in bilateral middle and inferior occipital gyri. These results remained statistically significant after corrections for multiple comparisons.
Conclusions: A novel gene-brain-behavior association was identified in which intrinsic activity alternations in distinct brain regions measured by fALFF was related to DAT1 haplotype and ADHD symptoms in children with ADHD. Our findings could be a key to better understanding the pathway from genotype to phenotype in ADHD.

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Biol Psychiatry. 2015;77:69S.

PREDICTING FUNCTIONAL ACTIVATION OF READING SUBNETWORKS WITH A NOVEL READING TENDENCY INDEX.

Mohl B, Goradia DD, Jones LL, et al.

Background: Reading Disability (RD) is prevalent in children with ADHD. Proficiency in reading fluency requires good decoding skills and ability to recognize words, which may be affected by ADHD impairments. We introduce a novel index that quantifies imbalances between reading strategies [e.g., sight reading vs. decoding] and hypothesize that this index will predict functional activation of specific reading subnetworks during an fMRI reading task.
Methods: 41 boys (14 control, 15 ADHD, 11 ADHD/+RD) completed two fMRI paradigms, weighted toward decoding or word recognition. Drift rates for each skill were calculated using the Drift Diffusion Model. The difference between the inverse drift rates generated the novel Reading Tendency Index, which classified three reading groups (Decoders, Fluent/Balanced, and Sight Readers). Functional activation patterns during a word recognition fMRI task were evaluated between groups.
Results: Contrasts based on diagnostic criteria (i.e., ADHD and ADHD/+RD) did not reveal significant functional activation differences related to reading subnetworks. However, when grouping based on the novel index, Decoders evidenced hyperactivation of the left iPL (BA 39/40) and IFG (BA 44) relative to Fluent/Balanced readers and hypoactivation of left middle temporal gyrus (BA 22) compared to either group.
Conclusions: The novel Reading Tendency Index effectively delineated subjects such that clusters of impairments and functional activation differences in reading subnetworks corresponded with theoretical predictions. While larger studies are needed to validate the index, the current study demonstrates a powerful classification of readers based on individual tendencies, rather than disabilities, which has implications for remediation.

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Biol Psychiatry. 2015;77:33S.

EEG-BASED ASSESSMENT OF BRAIN-AROUSAL REGULATION (RESEARCH DOMAIN CRITERION): RELEVANCE FOR AFFECTIVE DISORDERS AND ADHD.

Hegerl U.

Background: According to a recently presented concept the hyperactivity and sensation seeking observed in overtired children, ADHD and mania have to be interpreted as autoregulatory attempts of the organism to stabilize vigilance (nullBrain-arousalnull) by increasing external stimulation. Correspondingly the withdrawal and sensation avoidance in major depression (MD) is interpreted as a reaction to a state of tonically high vigilance. Vigilance regulation is a converging biomarker which can be objectively assessed with a recently developed EEG-based algorithm (Vigilance Algorithm Leipzig, VIGALL).Studies on its physiological, diagnostic and predictive validity will presented.
Methods: Physiological validity: GWAS + candidate gene analyses concerning vigilance regulation (n = 820). Changes of vigilance regulation during therapeutic sleep deprivation in MD (n=18) and healthy

controls (n=18). Diagnostic validity: vigilance regulation in unmedicated (n=40) and medicated (n=61) patients with MD compared to healthy controls, to patients with bipolar disorder studied both during mania (n = 17) and depression (n=19), and to adult ADHD (n=80). Predictive validity: vigilance regulation in responders and nonresponders to treatment with antidepressants (n = 71).
Results: Vigilance regulation is hyperstable in MD compared to healthy controls and normalizes with improvement of depression. In bipolar patients an unstable vigilance regulation with rapid declines to drowsiness or sleep states is observed during mania and the opposite during depression.
Conclusions: Vigilance regulation as assessed with the VIGALL is a state modulated trait and a valid biomarker for assessing brain-arousal regulation. This biomarker has also diagnostic and predictive validity making it promising for clinical and research purposes.

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Brain Sciences. 2015 Mar;5:32-57.

MULTISENSORY INTEGRATION AND CHILD NEURODEVELOPMENT.

Dionne-Dostie E, Paquette N, Lassonde M, et al.

A considerable number of cognitive processes depend on the integration of multisensory information. The brain integrates this information, providing a complete representation of our surrounding world and giving us the ability to react optimally to the environment. Infancy is a period of great changes in brain structure and function that are reflected by the increase of processing capacities of the developing child. However, it is unclear if the optimal use of multisensory information is present early in childhood or develops only later, with experience. The first part of this review has focused on the typical development of multisensory integration (MSI). We have described the two hypotheses on the developmental process of MSI in neurotypical infants and children, and have introduced MSI and its neuroanatomic correlates. The second section has discussed the neurodevelopmental trajectory of MSI in cognitively-challenged infants and children. A few studies have brought to light various difficulties to integrate sensory information in children with a neurodevelopmental disorder. Consequently, we have exposed certain possible neurophysiological relationships between MSI deficits and neurodevelopmental disorders, especially dyslexia and attention deficit disorder with/without hyperactivity.

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Child Abuse Negl. 2015. [Epub ahead of print]

THE RELATIONSHIP BETWEEN EARLY ADVERSITIES AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Fuller-Thomson E, Lewis DA.

This study examined whether retrospectively reported childhood physical abuse, childhood sexual abuse and/or exposure to parental domestic violence were associated with self-report of a health-professional diagnosis of attention-deficit/hyperactivity disorder (ADHD) among adults. We analyzed nationally representative data from the 2012 Canadian Community Health Survey-Mental Health using gender-specific bivariate and logistic regression analyses (n = 10,496 men; n = 12,877 women). For both men and women, childhood physical abuse was associated with significantly higher odds of reporting ADHD (men odds ratio [OR] = 1.66, p <. .001; women OR = 1.95, p <. .001). For both genders, childhood sexual abuse was also significantly related to higher odds of ADHD (men OR = 2.57, p <. .001; women OR = 2.55, p <. .001); however, exposure to parental domestic violence was only associated with elevated odds of ADHD among women (men OR = 0.89, p = .60; women OR = 1.54, p = .03). The results demonstrate a link between childhood physical and sexual abuse and ADHD for both men and women. Future prospective studies are required to further understand this interesting relationship.

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Clin Pediatr. 2015;54:376-81.

DISPARITIES IN IDENTIFICATION OF COMORBID DIAGNOSES IN CHILDREN WITH ADHD.

Gipson TT, Lance EI, Albury RA, et al.

Aims. This study explores disparities in identification of educationally relevant comorbidities and medication prescribing practices for children with attention-deficit hyperactivity disorder (ADHD) and either comprehensive neurodevelopmental evaluations or evaluations limited by insurance to behavior management with medication.

Methods. This study was a retrospective chart review of 5- to 10-year-old children with ADHD diagnosed at the initial evaluation. Data collected included demographics, rates of comorbid conditions, medication management, and educational interventions.

Results. The 2 groups were similar in age, educational supports, and medication management. The group with insurance permitting comprehensive evaluations was more likely to be Caucasian, have higher parental education levels, and have more comorbid conditions identified with academic impact.

Conclusions. School-aged children with ADHD are likely to receive similar educational and medication management despite differences in evaluations. However, our data suggest that children who received comprehensive evaluations had greater identification of comorbid conditions that may influence academic, behavioral, and social outcomes.

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Clin Pract Epidemiol Ment Health. 2013;9:96-102.

SELF-ESTEEM EVALUATION IN CHILDREN AND ADOLESCENTS SUFFERING FROM ADHD.

Mazzone L, Postorino V, Reale L, et al .

Background: Several recent studies investigated the relationship between self-esteem and ADHD, however, the results are still controversial. In the present study we analyze the characteristics of self-esteem in a sample of children and adolescents suffering from ADHD, with a particular focus on the relationship between ADHD symptoms severity and treatment strategies.

Methods: A total of 85 patients with ADHD (44 drug-free and 41 drug-treated, 23 of which atomoxetine-treated and 18 Methylphenidate-treated) and 26 healthy controls were enrolled in the study in order to evaluate self-esteem using the Self-esteem Multidimensional Test (TMA).

Results: ADHD subjects revealed lower scores on all self-esteem domains compared to controls. Both ADHD drug-free (47.1%) and ADHD drug-treated (44.1%) groups showed significantly higher rates of subjects in the pathological range as compared to normal control group (8.8%) (p .001) with a higher percentage of subjects in the pathological range. Among ADHD drug-treated subjects, the methylphenidate group showed higher self-esteem scores as compared to the atomoxetine group.

Conclusion: A lower self-esteem profile is more common in subjects suffering from ADHD than in healthy controls, suggesting the importance of an early detection of psychological well-being in these children in order to reduce the ADHD symptoms long-term impacts.

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Cogn Behav Pract. 2015;22:141-51.

A COGNITIVE-BEHAVIOR THERAPY AND MENTORING PROGRAM FOR COLLEGE STUDENTS WITH ADHD.

Anastopoulos AD, King KA.

College students with ADHD are at increased risk for a number of functional impairments, the severity of which is of sufficient clinical significance to warrant intervention (DuPaul & Weyandt, 2009). Very little treatment research of this type has been conducted to date (Green & Rabiner, 2012). The need for such research is critical, given the increasing numbers of students with ADHD attending college (Pryor, Hurtado, DeAngelo, Blake, & Tran, 2010), their increased risk for dropping out of college, and the known negative life outcomes for which they may be at increased risk later as adults (Barkley, Murphy, & Fischer, 2008). To address this situation we recently developed and began testing Accessing Campus Connections and Empowering Student Success (ACCESS). The active phase of ACCESS provides group cognitive behavior therapy (CBT), accompanied by individual mentoring. Booster group CBT and mentoring sessions are

provided during a maintenance phase. Preliminary findings have revealed significant increases in ADHD knowledge, use of organizational skills, and reductions in maladaptive thinking, all of which are presumed mechanisms of clinical change. Such changes have been accompanied by reductions in ADHD symptoms, improvements in executive functioning, educational benefits, improved emotional well-being, and increased use of disability services and other campus resources. Although promising, such findings are limited by the fact that ACCESS has thus far been tested in an open clinical trial. Thus, additional research is needed to determine its efficacy and effectiveness.

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Community Mental Health Journal. 2015 Apr;51:347-53.

CHILD ATTENTION DEFICIT HYPERACTIVE DISORDER CO MORBIDITIES ON FAMILY STRESS: EFFECT OF MEDICATION.

Silva D, Houghton S, Hagemann E, et al.

We examined the degree of parental and child mental health in a community sample of children diagnosed with Attention Deficit Hyperactive Disorder and the effect on family stress prior to and during treatment using a community retrospective questionnaire study. In total 358 questionnaires were returned for analysis where 92 % of children had at least one co-morbid condition and mental health conditions in parents was common. Overall, the Family Strain Index was significantly reduced after commencement of medication ($p < 0.0001$), but remained higher in families where the children had either externalizing disorders or autism spectrum disorder.

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Current Psychology: A Journal for Diverse Perspectives on Diverse Psychological Issues. 2015 Mar;34:97-111.

THE MEDIATING ROLE OF AGGRESSIVE BEHAVIOUR, EMOTIONAL AND BEHAVIOURAL INSTABILITY ON THE ASSOCIATION BETWEEN ADHD SYMPTOMS AND BEST FRIEND CONFLICTS.

Zucchetti G, Ortega E, Scholte RHJ, et al.

This study examined the direct association between Attention Deficit Hyperactivity Disorder (ADHD) symptoms (i.e. inattention and hyperactivity symptoms) and children's experience of best friend conflicts, and the mediating role of aggression, emotional and behavioural instability, exploring possible gender differences. The sample consisted of 334 children (52 % female; Mage = 9.38, SD = 0.89) attending primary schools in northwest Italy. ADHD symptoms were measured with a questionnaire completed by teachers whereas others variables were assessed a self-report questionnaire completed by the children. Analyses revealed that inattention and hyperactivity symptoms were differently associated with best friend conflicts according to gender. Among boys, only hyperactivity symptoms were associated with best friend conflicts whereas among girls only inattention symptoms contributed to best friend conflicts. Aggression and emotional and behavioural instability were found to mediate these associations for both genders. These findings suggest that to understand fully the association between ADHD symptoms and best friend conflicts it might be helpful to consider the different manifestations of that association by gender, whilst also considering behavioural and emotional dimensions of children's psychosocial adjustment.

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Environ Res. 2015 Feb;137:373-81.

MANGANESE AND SELENIUM CONCENTRATIONS IN UMBILICAL CORD SERUM AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDHOOD.

Ode A, Rylander L, Gustafsson P, et al.

Existing evidence on the effects of manganese and selenium during fetal life on neurodevelopmental disorders is inadequate. This study aims to investigate the hypothesized relationship between fetal exposure to manganese and selenium and attention deficit hyperactivity disorder (ADHD) diagnosis in childhood. Children born between 1978 and 2000 with ADHD (n=166) were identified at the Department of Child and Adolescent Psychiatry in Malmo, Sweden. Controls from the same region (n=166) were selected

from the Medical Birth Register and were matched for year of birth and maternal country of birth. Manganese and selenium were measured in umbilical cord serum. The median cord serum concentrations of manganese were 4.3mug/L in the cases and 4.1mug/L in the controls. The corresponding concentrations of selenium were 47 and 48mug/L. When the exposures were analyzed as continuous variables no associations between cord manganese or selenium concentration and ADHD were observed. However, children with selenium concentrations above the 90th percentile had 2.5 times higher odds (95% confidence interval 1.3-5.1) of having ADHD compared to those with concentrations between the 10th and 90th percentiles. There was no significant interaction between manganese and selenium exposure (p=0.08). This study showed no association between manganese concentrations in umbilical cord serum and ADHD. The association between ADHD diagnoses in children with relatively high cord selenium was unexpected and should be interpreted with caution.

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Epilepsy Behav. 2015 Apr;45:234-41

ALTERED ATTENTION NETWORKS IN BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES (BECTS): A RESTING-STATE FMRI STUDY.

Xiao F, Li L, An D, et al.

It is noteworthy that some children with benign childhood epilepsy with centrotemporal spikes (BECTS) show attention problems despite their favorable seizure outcome. Resting-state functional magnetic resonance imaging (fMRI) is a method widely used to detect brain network alterations in neuropsychiatric diseases. We used resting-state functional magnetic resonance imaging (fMRI) to investigate specific brain networks related to attention deficit in children with BECTS. Resting-state fMRI was performed in patients with BECTS with ADHD (n = 15) and those with BECTS without ADHD (n = 15) and in healthy controls (n = 15). Unbiased seed-based whole-brain functional connectivity analysis was used to study the connectivity pattern of three resting-state networks, including the ventral attention network (VAN) and the dorsal attention network (DAN) and the default mode network (DMN). Patients with BECTS with ADHD displayed decreased functional connectivity in the DAN compared with other two groups, while patients with BECTS without ADHD showed increased functional connectivity in the DAN. Moreover, we found increased functional connectivity in the VAN and in the DMN in patients with BECTS with or without ADHD when comparing with controls. These results showed that the newly-diagnosed children with BECTS displayed brain activity alterations in the ventral and dorsal attention networks. The difference in the extent of impairment in the dorsal attention network of patients with BECTS with ADHD and patients with BECTS without ADHD may lead to improved understanding of the underlying neuropathophysiology and treatment of BECTS with ADHD and BECTS without ADHD.

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Epilepsy Curr. 2015;15:190.

GENDER DIFFERENCES AND ADHD AMONG CHILDREN WITH EPILEPSY.

Trobliger R, Lancman ME, Lancman M.

Rationale: Media attention has been given to the question of overdiagnosis of ADHD among children and with such overmedication or significant side effects. This is concerning given reports of 69% of children with ADHD taking medication. Prior research on gender differences among the general population has suggested different prevalence rates among boys and girls. Prior research has also suggested different presentations, with girls having lower ratings on inattention, hyperactivity, and impulsivity measures. Some credence has been given that boys are overdiagnosed, given that certain aspects of ADHD (including high energy levels) are more associated with boys. This raises concerns that some boys may be medicated unnecessarily. This study examined gender differences among children with epilepsy on a screening of ADHD symptoms, with an eye towards the question of overdiagnosis and impact on treatment.

Methods: Parental observations of levels of ADHD symptoms were assessed using the Conners 3 Parent. A total of 218 cases of children with diagnoses of epilepsy were included, with 110 males and 108 females. All subjects had a history of epileptogenic activity on EEG studies. The mean age was 11.27 years, with a

range of 6 to 18. Gender differences in percentages rated to have significant ADHD symptomology were computed using Chi Square analysis with SPSS.
Results: Significant findings were noted between genders. A significant difference was seen between boys and girls among those meeting criteria for ADHD. Boys were 13.1% more likely to be rated by their parents as meeting criteria, with nearly a half of boys versus nearly a third of girls rated at significant levels. A significant difference was also noted between boys and girls among those with significant criteria of hyperactivity/impulsivity symptoms. Boys were 18.9% more likely to be rated by their parents as meeting criteria, with nearly a third of boys versus approximately 1/10th of girls rated with significant symptomology. No significant gender difference was noted between boys and girls on parent ratings of inattention symptomology.
Conclusions: Given the significant gender differences noted on measures of hyperactivity/impulsivity, this research raises questions however regarding the possibility of pathologization of behaviors normally associated with boys. This in turn raises concerns regarding overmedication. An increase in prevalence rates over the years, combined with increase in medication of children with ADHD raises concerns regarding the effects of such. These concerns are particularly salient for boys. Some studies have suggested that a combination of medication and therapy is the best approach for treatment. Others have suggested that behavior therapy - by itself or with a small dosage of medication - is more effective than medication therapy alone. Still other work has suggested that medication is less effective over time. More research needs to be focused on behavior therapy and the message communicated to the public - that therapy can be effective, which can address concerns regarding the effects of taking medications.

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Epilepsy Curr. 2015;15:132.

THE IMPACTS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER ON EPILEPSY CHILDREN.

Park S.

Rationale: We would like to investigate the prevalence of attention-deficit hyperactivity disorder(ADHD) among children being treated for epilepsy, and determine the different characteristics of epilepsy patients with ADHD as opposed to the patients without ADHD, which will help in treating patients with two overlapped diseases.
Methods: We retrospectively reviewed 184 patients diagnosed as epilepsy and treated with antiepileptic drug in pediatric neurology department of Seoul St. Mary's hospital from March, 2009 to May, 2012. The patients were between ages of 6 and 18 years. Only the patients who had regular checkups at least 1 year were included in the study.
Results: 1) Out of 184 patients, 69 patients(37.5%) had both ADHD and epilepsy. 2) In epilepsy children with ADHD, male outnumbered female by almost two fold (male 67: female 33) (P=0.022). 3) In epilepsy children with ADHD, major focus of epileptiform discharges was identified as central part by 39% in EEG(electroencephalogram) (P=0.014). 4) 56% of patients who did not have ADHD could control epilepsy with single anticonvulsant, as opposed to 36% of patients with both ADHD and epilepsy (P=0.001). Therefore, the presence of ADHD in patients with epilepsy had a connection with the therapeutic response to anticonvulsants, and this can be one of a useful predictive factor of response to early treatment.
Conclusions: Patients with ADHD and epilepsy showed noticeable difference and poor response to epilepsy treatment, as opposed to patients with just epilepsy. Therefore, early detection and establishment of countermeasures for ADHD is necessary. (Table presented)

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Epilepsy Curr. 2015;15:222.

EFFECTS OF EPILEPSY IN ADHD AND QUALITY OF LIFE.

Salam M, Works K.

Rationale: Seizures are common neurologic disorder in childhood. ADHD is also a common neuropsychological disorder. Both conditions require prolonged pharmacological therapies and have significant comorbidites such as depression and mood changes, resulting in poor quality of life. Children

with seizures and ADHD may have significant impairment of sense of well being that should be recognized promptly.
Methods: This is a prospective study of children in a neurology clinic with controls from a general pediatric clinic of a teaching hospital. Total of 20 children each of epilepsy, ADHD and controls, ages 8-18, using scales: The Mood and Feelings Questionnaire, Kutcher Adolescent Depression Scale, The Satisfaction of Life Scale and NICHQ Children Vanderbilt Assessment Scale.
Results: 89% of children with epilepsy were on anti-epilepsy drugs, 76% of ADHD children were on psycho stimulants, half of these children had grades of B average. 15% of children with seizure, 19% with ADHD, 10% of control showed possible depression by The Mood and Feeling Scales. The Satisfaction with Life Scales showed 9.5% of ADHD, 11% of seizure and 0% control felt their lives were below average or dissatisfied.
Conclusions: This showed great resilience, however family interaction, counseling, education, self-empowerment and medication can improve life. (Figure Presented).

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Epilepsy Curr. 2015;15:308.
ADHD IN CHILDHOOD EPILEPSY: CLINICAL DETERMINANTS OF SEVERITY AND OF RESPONSE TO METHYLPHENIDATE.
Rheims S, Herbillon V, Milh M, et al .
Rationale: Attention deficit hyperactivity disorder (ADHD) is commonly observed in children with epilepsy. However, factors associated with development of ADHD and which might help to guide its therapeutic management remain to be determined.
Methods: We conducted a multicenter prospective observational study which included children, aged 6-16 years, suffering from both epilepsy and ADHD according to DSM IV criteria. Children with significant intellectual disability (IQ < 70) were excluded. After inclusion, patients entered a 12-16 weeks follow-up period during which they were either treated with methylphenidate or they did not receive specific ADHD-treatment, at the discretion of the treating physician. Severity of ADHD was evaluated with the ADHD-rating scale IV. The level of significant clinical response was defined at 25% reduction in the total score.
Results: 149 patients were included (mean age 9.6(plus or minus)2.3 years). 47 children had non-idiopathic focal epilepsy, 42 idiopathic focal epilepsy, 26 childhood absence epilepsy, 20 other forms of idiopathic generalized epilepsy and 14 unclassified epilepsy. 79 patients were seizure free at inclusion, including 31 for whom AED treatment was not considered necessary. In the remaining patients, the mean seizure frequency during the four weeks preceding study inclusion was 11.6(plus or minus)39.5. Fifty-three patients had school difficulties. At inclusion, the ADHD Rating Scale-IV total score was 30.2(plus or minus)9.5, the inattentive subscore was 17.1(plus or minus)4.8 and the hyperactive subscore was 12.9(plus or minus)6.9. We did not detect differences of ADHD Rating Scale-IV total score or subscores across patients' age or gender, age at epilepsy onset, epilepsy syndrome, seizure frequency or number of ongoing antiepileptic drugs. No correlation between school difficulties and ADHD severity was observed. Methylphenidate was introduced in 50 patients (34%), including 40 in whom follow-up evaluation is currently available. These latter had higher ADHD Rating Scale-IV total score than patients in whom no specific ADHD-treatment was introduced (32.5(plus or minus)10.2 vs 28.7(plus or minus)8.8, p=0.019). After a follow-up of three months, patients treated with methylphenidate demonstrated a mean decrease of ADHD Rating Scale-IV total score of 11.1(plus or minus)11.5 points. 25 patients (63%) demonstrated (greater-than or equal to)25% decrease of ADHD Rating Scale-IV total score and 13 (32%) (greater-than or equal to)50% decrease. Mean decrease of ADHD Rating Scale-IV scores did not significantly vary across patients' age or gender, age at epilepsy onset, epilepsy syndrome, seizure frequency or number of ongoing antiepileptic drugs.
Conclusions: We did not detect any epilepsy-related factor associated with severity of ADHD. A third of patients did not respond to methylphenidate. A better understanding of the pathological process which underlies ADHD development in childhood epilepsy is required to develop alternative and/or complementary therapeutic strategies.

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European Child & Adolescent Psychiatry. 2015 Mar;24:309-18.

THE ROLE OF DCDC2 GENETIC VARIANTS AND LOW SOCIOECONOMIC STATUS IN VULNERABILITY TO ATTENTION PROBLEMS.

Riva V, Marino C, Giorda R, et al.

Both genetic and socio-demographic factors influence the risk for behavioral problems in the developmental age. Genetic studies indicate that shared genetic factors partially contribute to behavioral and learning problems, in particular reading disabilities (RD). For the first time, we explore the conjoint role of DCDC2 gene, an identified RD candidate gene, and socioeconomic status (SES) upon behavioral phenotypes in a general population of Italian children. Two of the most replicated DCDC2 markers [i.e., regulatory element associated with dyslexia 1 (READ1), rs793862] were genotyped in 631 children (boys = 314; girls = 317) aged 11–14 years belonging to a community-based sample. Main and interactive effects were tested by MANOVA for each combination of DCDC2 genotypes and socioeconomic status upon emotional and behavioral phenotypes, assessed by Child Behavior Check-List/6–18. The two-way MANOVA (Bonferroni corrected p value = 0.01) revealed a trend toward significance of READ1(4) effect (F = 2.39; p = 0.016), a significant main effect of SES (F = 3.01; p = 0.003) and interactive effect of READ1(4) × SES (F = 2.65; p = 0.007) upon behavioral measures, showing higher attention problems scores among subjects 'READ1(4 +) and low SES' compared to all other groups (p values range 0.00003–0.0004). ANOVAs stratified by gender confirmed main and interactive effects among girls, but not boys. Among children exposed to low socioeconomic level, READ1 genetic variant targets the worst outcome in children's attention.

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European Child & Adolescent Psychiatry. 2015 Mar;24:265-81.

THE NEUROIMAGE STUDY: A PROSPECTIVE PHENOTYPIC, COGNITIVE, GENETIC AND MRI STUDY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER. DESIGN AND DESCRIPTIVES.

von Rhein D, Mennes M, van Ewijk H, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a persistent neuropsychiatric disorder which is associated with impairments on a variety of cognitive measures and abnormalities in structural and functional brain measures. Genetic factors are thought to play an important role in the etiology of ADHD. The NeuroIMAGE study is a follow-up of the Dutch part of the International Multicenter ADHD Genetics (IMAGE) project. It is a multi-site prospective cohort study designed to investigate the course of ADHD, its genetic and environmental determinants, its cognitive and neurobiological underpinnings, and its consequences in adolescence and adulthood. From the original 365 ADHD families and 148 control (CON) IMAGE families, consisting of 506 participants with an ADHD diagnosis, 350 unaffected siblings, and 283 healthy controls, 79 % participated in the NeuroIMAGE follow-up study. Combined with newly recruited participants the NeuroIMAGE study comprehends an assessment of 1,069 children (751 from ADHD families; 318 from CON families) and 848 parents (582 from ADHD families; 266 from CON families). For most families, data for more than one child (82 %) and both parents (82 %) were available. Collected data include a diagnostic interview, behavioural questionnaires, cognitive measures, structural and functional neuroimaging, and genome-wide genetic information. The NeuroIMAGE dataset allows examining the course of ADHD over adolescence into young adulthood, identifying phenotypic, cognitive, and neural mechanisms associated with the persistence versus remission of ADHD, and studying their genetic and environmental underpinnings. The inclusion of siblings of ADHD probands and controls allows modelling of shared familial influences on the ADHD phenotype.

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Eur Child Adolesc Psychiatry. 2015. [Epub ahead of print]

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER DIMENSIONALITY: THE RELIABLE NULLGNULL AND THE ELUSIVE NULLSNULL DIMENSIONS.

Wagner F, Martel MM, Cogo-Moreira H, et al.

The best structural model for attention-deficit/hyperactivity disorder (ADHD) symptoms remains a matter of debate. The objective of this study is to test the fit and factor reliability of competing models of the dimensional structure of ADHD symptoms in a sample of randomly selected and high-risk children and pre-adolescents from Brazil. Our sample comprised 2512 children aged 6null12 years from 57 schools in Brazil. The ADHD symptoms were assessed using parent report on the development and well-being assessment (DAWBA). Fit indexes from confirmatory factor analysis were used to test unidimensional, correlated, and bifactor models of ADHD, the latter including nullgnull ADHD and nullsnull symptom domain factors. Reliability of all models was measured with omega coefficients. A bifactor model with one general factor and three specific factors (inattention, hyperactivity, impulsivity) exhibited the best fit to the data, according to fit indices, as well as the most consistent factor loadings. However, based on omega reliability statistics, the specific inattention, hyperactivity, and impulsivity dimensions provided very little reliable information after accounting for the reliable general ADHD factor. Our study presents some psychometric evidence that ADHD specific (nullsnull) factors might be unreliable after taking common (nullgnull factor) variance into account. These results are in accordance with the lack of longitudinal stability among subtypes, the absence of dimension-specific molecular genetic findings and non-specific effects of treatment strategies. Therefore, researchers and clinicians might most effectively rely on the nullgnull ADHD to characterize ADHD dimensional phenotype, based on currently available symptom items.

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Eur Child Adolesc Psychiatry. 2015;24:463-70.

MINOR NEURODEVELOPMENTAL IMPAIRMENTS ARE ASSOCIATED WITH INCREASED OCCURRENCE OF ADHD SYMPTOMS IN CHILDREN BORN EXTREMELY PRETERM.

Elgen SK, Sommerfelt K, Leversen KT, et al.

ADHD is more common in children born preterm than at term. The purpose of the study was to examine if, and to what extent, ADHD symptoms are associated with minor neurodevelopmental impairments (NDI) in extremely preterm children. In a national population-based cohort with gestational age 22null27 weeks or birth weight <1,000 g assessed at 5 years of age, scores on Yale Childrennulls Inventory (YCI) scales (seven scales) were related to normal functions vs. NDI defined as mild impairments in cognitive function (IQ 70null84), motor function (Movement Assessment Battery for children score > the 95th percentile or freely ambulatory cerebral palsy), vision (correctable), and hearing (no hearing aid). YCI was completed for 213 of 258 eligible children (83 %). Children with minor NDIs (n = 98) had significantly higher scores (more ADHD symptoms) than those without NDI (n = 115) on the YCI scales of Attention, Tractability, Adaptability and Total score. Increasing numbers of minor NDIs were associated with higher mean YCI scores. In multivariate analysis only decreased hearing, IQ, and male gender were significantly associated with scores on the Attention scale. Thirty-three children (16 %) had scores >3 on the Attention scale (probably ADHD), and the proportion was significantly higher for those with mild NDIs compared to those without (Odds ratio = 2.7, 95 % CI 1.3null6.0). Children born extremely preterm with minor NDIs were more likely to have ADHD symptoms than those with no NDI, and increasing number of minor NDIs were associated with more ADHD symptoms.

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Eur J Paediatr Neurol. 2015;19:383-85.

ATTENTION PROBLEMS IN CHILDREN WITH EPILEPSY. HOW IS THE LONG-TERM OUTCOME?

Bechtel N, Weber P.

Introduction Attention deficit/hyperactivity disorder (ADHD) is one of the most common childhood disorders and frequently seen in other conditions like epilepsy as well. The prevalence of ADHD in the general paediatric population is estimated at 3-6% persisting into adulthood in up to one third of persons affected.

The prevalence of ADHD in epilepsy is understood to be significantly higher. Approximately one third of children with epilepsy do also have a diagnosis of ADHD. How these attention problems develop over the years is however not clear. We therefore evaluated the severity of attention problems in children with epilepsy at late childhood and assessed it again in adolescence. Data was being compared with attention problems of children with developmental ADHD. Method 16 boys with diagnosed combined idiopathic epilepsy/ADHD and 14 boys with developmental ADHD were investigated twice; at a mean age of 10.94 (SD = 1.63) and then again at a mean age of 15.82 (SD = 2.0). At the baseline examination all patients completed Raven's Progressive Matrices to assess intelligence. To measure symptom severity of ADHD, parents were asked to complete the short version of the Conner's Rating Scale for Parents at both times. Parents of children with combined epilepsy/ADHD furthermore gave information about seizure frequency and intake of anticonvulsants. Results Patient groups did not significantly differ in age and IQ. Results of the baseline examination revealed elevated scores in both patient groups for the Conner's Rating Scales; ADHD group: M = 16.86 (SD = 5.35); Epilepsy/ADHD group: M = 14.77 (SD = 4.76) but no differences between the groups (p =.29; z =.39). Qualitatively, patients with developmental ADHD showed more abnormalities in the area of hyperactivity/impulsivity while patients with epilepsy/ADHD had more problems with inattention. Results of the follow-up examination showed a significant reduction of symptoms in the ADHD group of minus 4.23 points; M = 12.63 (SD = 3.89) (p =.02); The reduction in the epilepsy/ADHD group was even bigger with minus 6.77 points; M = 8.00 (SD = 6.46) (p =.03). However, difference between the two groups reached no significance (p =.079; z = 1.19). None of the patients with epilepsy has had seizures in the meantime. Conclusion We found a significant reduction of ADHD symptoms in our patients from the time of late childhood to adolescence. That symptoms of ADHD, especially hyperactivity, lessen with age is known from the literature (Biedermann et al., 2010). We found the same data for patients with idiopathic epilepsy and ADHD. Over the same period of time problems of attention improved substantially. We conclude that development and brain maturation may have a similar positive effect on attention problems in children with epilepsy than in developmental ADHD.

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Eur J Pediatr. 2015. [Epub ahead of print]

CHRONIC CONDITIONS AND COEXISTING ADHDNULLA COMPLICATED COMBINATION IN ADOLESCENTS.

Nylander C, Fernell E, Tindberg Y.

Adolescents with chronic conditions (CCs) take more health risks than peers. However, coexisting ADHD has not sufficiently been considered. The aim of the present study was to investigate the impact of different CCs on protective factors and health-risk behaviors, taking coexisting ADHD into account. A school-based study among 6895 15- and 17-year-old students was performed in the county of Sormland, Sweden in 2011 (response rate 80 %). The questionnaire explored background factors, CCs, protective factors, and health-risk behaviors. CCs were reported by 11 %, while 55 % were healthy. Students with CCs more often reported coexisting ADHD than healthy students. In adolescents with neurological conditions, the odds ratio for having ADHD was 7.34 (95 % CI 3.00null17.99) as compared to healthy peers. Few protective factors (<4) and clustered health-risk behaviors ((greater-than or equal to)4) were more common among students with CCs, especially if ADHD or a combination including ADHD was reported. Conclusion: CCs and coexisting ADHD are associated with few protective factors and clustered-health risk behaviors. Adolescents with ADHDnullin addition to a chronic conditionnullshould be specially acknowledged by health care professionals in order to prevent health risk behaviors. ADHD should be considered when studying these outcomes in adolescents.(Table presented.).

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Eur Psychiatry. 2015. [Epub ahead of print]

MATERNAL TOBACCO SMOKING IN PREGNANCY AND CHILDREN'S SOCIO-EMOTIONAL DEVELOPMENT AT AGE 5: THE EDEN MOTHER-CHILD BIRTH COHORT STUDY.

Melchior M, Hersi R, van der Waerden J, et al.

Background: There is debate as to whether maternal tobacco use in pregnancy is related to offspring behaviour later on. We tested this association examining multiple aspects of children's behaviour at age 5 and accounting for parental smoking outside of pregnancy, as well as child and family characteristics.

Methods: Data come from a prospective community based birth cohort study (EDEN; n = 1113 families in France followed since pregnancy in 2003-2005 until the child's 5th birthday). Maternal tobacco use in pregnancy was self-reported. Children's socio-emotional development (emotional symptoms, conduct problems, symptoms of hyperactivity/inattention, peer relationship problems, prosocial behaviour) was assessed by mothers using the Strengths and Difficulties Questionnaire (SDQ) at age 5 years. Logistic regression analyses controlled for Inverse Probability Weights (IPW) of maternal tobacco use calculated based on study center, children's characteristics (sex, premature birth, low birth weight, breastfeeding), maternal characteristics (age at the child's birth, psychological difficulties and alcohol use in pregnancy, post-pregnancy depression, and smoking), paternal smoking in and post-pregnancy, parental educational attainment, family income, parental separation, and maternal negative life events.

Results: Maternal smoking in pregnancy only predicted children's high symptoms of hyperactivity/inattention (sex and study center-adjusted ORs: maternal smoking in the 1st trimester: 1.95, 95%CI: 1.13-3.38; maternal smoking throughout pregnancy: OR = 2.11, 95%CI: 1.36-3.27). In IPW-controlled regression models, only children of mothers who smoked throughout pregnancy had significantly elevated levels of hyperactivity/inattention (OR = 2.20, 95%CI: 1.21-4.00).

Conclusions: Maternal tobacco smoking in pregnancy may contribute directly or through epigenetic mechanisms to children's symptoms of hyperactivity/inattention.

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Front Psychiatry. 2015;6.

INTRA-INDIVIDUAL RESPONSE VARIABILITY ASSESSED BY EX-GAUSSIAN ANALYSIS MAY BE A NEW ENDOPHENOTYPE FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Henriquez-Henriquez MP, Billeke P, Henriquez H, et al.

Intra-individual variability of response times (RTisv) is considered as potential endophenotype for attentional deficit/hyperactivity disorder (ADHD). Traditional methods for estimating RTisv lose information regarding response times (RTs) distribution along the task, with eventual effects on statistical power. Ex-Gaussian analysis captures the dynamic nature of RTisv, estimating normal and exponential components for RT distribution, with specific phenomenological correlates. Here, we applied ex-Gaussian analysis to explore whether intra-individual variability of RTs agrees with criteria proposed by Gottesman and Gould for endophenotypes. Specifically, we evaluated if normal and/or exponential components of RTs may (a) present the stair-like distribution expected for endophenotypes (ADHD > siblings > typically developing children (TD) without familiar history of ADHD) and (b) represent a phenotypic correlate for previously described genetic risk variants. This is a pilot study including 55 subjects (20 ADHD-discordant sibling-pairs and 15 TD children), all aged between 8 and 13 years. Participants resolved a visual Go/Nogo with 10% Nogo probability. Ex-Gaussian distributions were fitted to individual RT data and compared among the three samples. In order to test whether intra-individual variability may represent a correlate for previously described genetic risk variants, VNTRs at DRD4 and SLC6A3 were identified in all sibling-pairs following standard protocols. Groups were compared adjusting independent general linear models for the exponential and normal components from the ex-Gaussian analysis. Identified trends were confirmed by the non-parametric Jonckheere-Terpstra test. Stair-like distributions were observed for (mu) ($p = 0.036$) and s ($p = 0.009$). An additional "DRD4-genotype" null "clinical status" interaction was present for t ($p = 0.014$) reflecting a possible severity factor. Thus, normal and exponential RTisv components are suitable as ADHD endophenotypes.

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Front Psychiatry. 2015;6.

ATTENTION- DEFICIT/HYPERACTIVITY DISORDER IN RELATION TO ADDICTIVE BEHAVIORS: A MODERATED-MEDIATION ANALYSIS OF PERSONALITY RISK FACTORS AND SEX.

Davis C, Cohen A, Davids M, et al.

Introduction: Research has shown that those with ADHD have an increased risk for addiction disorders like alcoholism and substance abuse. What is less clear is the mechanism(s) whereby ADHD gives rise to increased engagement in addictive behaviors, and whether there are sex differences in the ADHD-addiction propensity. Both ADHD and addictions have also been associated with personality traits such as impulsivity, reward seeking, anxiousness, and negative affect. In this study, we tested a moderator-mediation model which predicted that both sex and ADHD-symptom status would make independent contributions to the variance in personality risk and in addictive behaviors, with males, and those with diagnosed ADHD, scoring higher on both dependent variables. Our model also predicted that the effect of sex and ADHD-symptom status on addictive behaviors would be via the mediating or intervening influence of personality risk factors.

Methods: A community-based sample of young men and women took part in the study. Among these individuals, 46 had received a life-time diagnosis of ADHD. The non-diagnosed participants were dichotomized into a high-ADHD symptom group (n=83) and a low-symptom group (n=84).

Results: We found that a high-risk personality profile may, in part, account for the relationship between ADHD symptomatology and the use/abuse of a broad range of addictive behaviors. However, we found no sex differences in personality risk for addiction or in the use of addictive behaviors; nor did sex moderate the relationships we assessed.

Conclusions: While ADHD Status showed a strong relationship with both dependent variables in the model, we found no difference between those who had been diagnosed with ADHD and treated with stimulants, and their high-symptom non-diagnosed/non-treated counterparts. These results add support to claims that the treatment of ADHD with stimulant medication neither protects nor fosters the risk for substance abuse disorders.

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Gene. 2015. [Epub ahead of print]

ASSOCIATION OF LPHN3 RS6551665 A/G POLYMORPHISM WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER IN KOREAN CHILDREN.

Hwang IW, Lim MH, Kwon HJ, et al .

Attention deficit hyperactivity disorder (ADHD) is a common and highly heritable disorder of school-age children. Its heritability was estimated at 80-90% but the genetic component underpinning this disorder remains to be disclosed. Recently, a highly consistent association between latrophilin3 (LPHN3) gene and ADHD was reported. In the present study, we examined the association between the LPHN3 rs6551665 A/G polymorphism and ADHD in Korea. The samples used in the study consisted of 150 ADHD children and 322 controls. The ADHD children were diagnosed according to DSM-IV. ADHD symptoms were evaluated with Dupaul Parent ADHD Rating Scales. LPHN3 rs6551665 SNP was determined by PCR-RFLP. Hardy-Weinberg equilibrium, genotype and allele frequency differences between the case and the control, and odds ratio were examined using the chi-square and exact tests. The LPHN3 gene locus was found to have no deviation from the Hardy-Weinberg expectation. We observed a significant association between the ADHD children and control group in genotype frequency ($p = 0.01$) and allele frequency ($p = 0.02$). The ADHD children appeared to have a surplus of GG genotype (OR 2.959, 95% CI 1.416-6.184, $p = 0.003$) and G allele (OR 1.44, 95% CI 1.062-1.945, $p = 0.02$). The association was more distinctive when analysis was confined to male samples ($p = 0.005$), the OR of male controls and cases was 4.029 (95% CI 1.597-10.164, $p = 0.002$) and the OR having G allele vs. A allele was 1.46 (95% CI 1.002-2.127, $p = 0.048$). Thus our results imply that the LPHN3 rs6551665 GG genotype and G allele may provide a significant effect on the ADHD, although larger sample sizes and functional studies are necessary to further elucidate these findings.

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Gesundh okon Qual manage. 2015. [Epub ahead of print]

NULLEXPENSIVENULL LONG-TERM PSYCHOTHERAPY VS. NULLCOST-EFFECTIVENULL COMBINED BEHAVIORAL THERAPY/MEDICATION TREATMENT: COMPARISON OF TOTAL TREATMENT COSTS OF CHILDREN WITH ADHD AND ODD.

Laezer KL, Tischer I, Gaertner B, et al.

Aim: A follow-up study to a controlled trial on the effectiveness of long-term psychoanalytical psychotherapy versus a combination of behavioral therapy and medication treatment for children diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD) was conducted to compare total treatment costs.

Method: Treatment costs of all symptom-related interventions were investigated for a sub-sample of 18 children from both treatment groups (matched pairs with respect to age, sex, diagnosis and IQ) and evaluated for an average time period of 41 months. Data was collected through interviews with parents, and from patient files and other relevant documents.

Results: On its own, the psychoanalytical therapy showed to be more than twice as expensive than the combination of behavioral therapy and medication treatment. However, once, additional treatments related to the diagnosis of ADHD and ODD and their costs (for inpatient and outpatient care, further psychotherapy, speech correction, community services in terms of family and teacher assistances among others) were included for both groups, the costs for the combined behavioral therapy/medication treatment group were 23 times higher than for the long-term psychoanalytical psychotherapy treatment group.

Conclusion: The frequently mentioned prejudice that long-term psychoanalytical therapy is too expensive and cost-ineffective requires revision when considering the costs of additional treatment measures linked to the combined behavioral therapy/medication treatment.

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Hum Brain Mapp. 2014;35:5179-89.

BRAINSTEM ABNORMALITIES IN ATTENTION DEFICIT HYPERACTIVITY DISORDER SUPPORT HIGH ACCURACY INDIVIDUAL DIAGNOSTIC CLASSIFICATION.

Johnston BA, Mwangi B, Matthews K, et al.

Despite extensive research, psychiatry remains an essentially clinical and, therefore, subjective clinical discipline, with no objective biomarkers to guide clinical practice and research. Development of psychiatric biomarkers is consequently important. A promising approach involves the use of machine learning with neuroimaging, to make predictions of diagnosis and treatment response for individual patients. Herein, we describe predictions of attention deficit hyperactivity disorder (ADHD) diagnosis using structural T<inf>1</inf> weighted brain scans obtained from 34 young males with ADHD and 34 controls and a support vector machine. We report 93% accuracy of individual subject diagnostic prediction. Importantly, automated selection of brain regions supporting prediction was used. High accuracy prediction was supported by a region of reduced white matter in the brainstem, associated with a pons volumetric reduction in ADHD, adjacent to the noradrenergic locus coeruleus and dopaminergic ventral tegmental area nuclei. Medications used to treat ADHD modify dopaminergic and noradrenergic function. The white matter brainstem finding raises the possibility of "catecholamine disconnection or dysregulation" contributing to the ADHD syndrome, ameliorated by medication.

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Hum Brain Mapp. 2014;35:5262-78.

ATOMIC DYNAMIC FUNCTIONAL INTERACTION PATTERNS FOR CHARACTERIZATION OF ADHD.

Ou J, Lian Z, Xie L, et al.

Modeling abnormal temporal dynamics of functional interactions in psychiatric disorders has been of great interest in the neuroimaging field, and thus a variety of methods have been proposed so far. However, the temporal dynamics and disease-related abnormalities of functional interactions within specific data-driven discovered subnetworks have been rarely explored yet. In this work, we propose a novel computational framework composed of an effective Bayesian connectivity change point model for modeling functional

brain interactions and their dynamics simultaneously and an effective variant of nonnegative matrix factorization for assessing the functional interaction abnormalities within subnetworks. This framework has been applied on the resting state fmagnetic resonance imaging (fMRI) datasets of 23 children with attention-deficit/hyperactivity disorder (ADHD) and 45 normal control (NC) children, and has revealed two atomic functional interaction patterns (AFIPs) discovered for ADHD and another two AFIPs derived for NC. Together, these four AFIPs could be grouped into two pairs, one common pair representing the common AFIPs in ADHD and NC, and the other abnormal pair representing the abnormal AFIPs in ADHD. Interestingly, by comparing the abnormal AFIP pair, two data-driven abnormal functional subnetworks are derived. Strikingly, by evaluating the approximation based on the four AFIPs, all of the ADHD children were successfully differentiated from NCs without any false positive.

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International Journal for the Advancement of Counselling. 2015 Mar;37:17-27.

THE USE OF TRAUMA COUNSELING FOR CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Pottinger AM.

Children with Attention-Deficit Hyperactivity Disorder (ADHD) are at risk for behavioral problems and so are frequently brought to the attention of counselors. The literature is limited, however, in examining specific counseling techniques for this population, and particularly in discussing counseling in a developing country where children do not readily access mental health services. Based on parallels in symptoms between children with ADHD and those with violence exposure, the author has adapted the components of a trauma intervention model and applied it to counseling children with ADHD in Jamaica. This article examines a structured counseling approach based on the trauma model, and concludes with a discussion on the usefulness and limitations of this approach in regard to children with ADHD.

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Int J Dev Neurosci. 2010;28:707.

BRAIN ACTIVATION IN CHILDREN PLACED IN SITUATION OF SELF-REGULATION.

Poissant H, Mendrek A, Senhadji N, et al.

Self-regulation refers to the active evaluation of the cognitive processes implicated in goal-directed behavior. A dysfunction of the ventromedial prefrontal and anterior cingulate cortices, which affects executive function, could partly account for the problems observed in the ADHD. These regions are implicated in inhibition, attention, planning and regulation. Determine (1) brain activations and (2) behavioral data in children placed in a situation of self-regulation. Forty right-handed children (16 ADHD and 24 CONT) performed the task consisting of identifying the incoherent (INC) items among 56 pictorial stories presented in a block-design manner during two runs of fMRI. Behavioral data showed a significant interaction group X task for RT measurement but no significant effect for error rate measurement. Time-per-target showed a significant interaction (ADHD are slower vs. CONT and faster in INC vs. CO). There is also a marginal significant effect of interaction between time x task for RT measurement. The fMRI analysis of the INC-COH contrast revealed activations in the dorsolateral prefrontal (DLPF) cortex in the ADHD group and orbitofrontal and anterior cingulate cortex (AAC) in the controls. There were additional activations in the temporal and parietal cortices in the ADHD children. The results imply that children with ADHD recruit different neural circuitry to arrive at a performance similar to healthy children on the self-regulation task.

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Int J Eating Disord. 2015 Apr;48:345-48.

THE IMPACT OF DISCONTINUING METHYLPHENIDATE ON WEIGHT AND EATING BEHAVIOR.

Benard V, Cottencin O, Guardia D, et al.

Chronic administration of the amphetamine-derivative methylphenidate (MPH) may induce appetite reduction and weight loss. By contrast, the effects that stopping chronic MPH may exert on eating behavior

and body weight are poorly known. We report the case of a male patient with childhood attention deficit/hyperactivity disorder (ADHD), who discontinued MPH treatment at the age of 11 years and was lost to follow-up until the age of 16. The patient's body mass index increased by five points within 1 year of MPH cessation while the symptoms of ADHD were re-emerging. The patient secondarily developed DSM-5 criteria for eating disorders. Discontinuing chronic MPH can significantly affect weight and eating behavior. Such risks should warrant further studies, as they could be particularly increased in patients with ADHD, who share common vulnerability factors with both obesity and eating disorders.

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Journal of Attention Disorders. 2015 Apr;19:284-92.

PSYCHOSTIMULANT PRESCRIPTION FOR ADHD IN NEW SOUTH WALES: A LONGITUDINAL PERSPECTIVE.

Prosser B, Lambert MC, Reid R.

Objective: There is a need for Australian studies of ADHD that utilize the individual child as the unit of analysis because they provide a more accurate picture of national patterns (in new prescriptions, start age, and duration). The aim of this study was to build toward a national picture of patterns in psychostimulant use for ADHD by undertaking a retrospective analysis of archival data on prescriptions within New South Wales (NSW), Australia's most populated state.

Method: A person-based data set was used to assess (a) rate of new prescriptions by age group, (b) demographic characteristics (age of start, male:female ratio), (c) duration of use, and (d) comparisons across the two decades.

Results: Five findings were observed: (a) The prevalence of psychostimulant use was 1.24% in 2010, (b) there was significant variability in the rate of new prescriptions by age group after 2003, (c) start age declined over the 1990 to 2000 period, but began to increase from 2000 to 2010, (d) the male:female ratio declined, and (e) the duration of psychostimulant use declined consistently.

Conclusion: Results suggest disconnect between persistence across the life span and actual treatment patterns. A decline in medication treatment for more than 1 year and the growing proportion of discontinuous treatment suggests a need for strategies to assist families with the transition onto and off medications.

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Journal of Attention Disorders. 2015 Apr;19:275-83.

NONMEDICAL USE OF PRESCRIPTION ADHD STIMULANT MEDICATIONS AMONG ADULTS IN A SUBSTANCE ABUSE TREATMENT POPULATION: EARLY FINDINGS FROM THE NAVIPPRO SURVEILLANCE SYSTEM.

Cassidy TA, McNaughton EC, Varughese S, et al.

Objective: To examine nonmedical use (NMU) of prescription ADHD stimulants among adults evaluated for substance abuse treatment.

Method: 147,816 assessments from the National Addictions Vigilance Intervention and Prevention Program (NAVIPPRO) system (10/01/2009 through 03/31/2012) examined NMU prevalence, routes of administration (ROA), and diversion sources.

Results: Past 30-day NMU for prescription stimulants (1.29%) was significantly lower than that of prescription opioids (19.79%) or sedatives (10.62%). For stimulant products, NMU for Adderall was 0.62, followed by Adderall XR (0.42), Ritalin (0.16), Vyvanse (0.12), and Concerta (0.08); product differences likely have limited clinical relevance given the low estimates (< 1%). Higher NMU per prescriptions was for Adderall (4.92), Ritalin (4.68), and Adderall XR (3.18) compared with newer formulations (Vyvanse 1.26, Concerta 0.89). Diversion source was mainly family/friends with no differences between products; swallowing whole was the most frequent ROA.

Conclusion: Prescription stimulant NMU was low compared with other prescription medications among individuals assessed for substance abuse problems, with little difference among specific products.

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Journal of Child and Adolescent Psychiatric Nursing. 2015 Feb;28:43-49.

MINDFULNESS-BASED PSYCHOEDUCATION FOR PARENTS OF CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER: AN APPLIED CLINICAL PROJECT.

Anderson SB, Guthery AM.

Topic: Attention-deficit/hyperactivity disorder (ADHD) affects more than 5 million American children; the likelihood of their parents experiencing stress is high, which may lead to negative outcomes. Mindful parenting is a parent training modality that teaches compassion, listening, and creative engagement with one's child, and has been shown to be effective in decreasing levels of parental stress.

Purpose: An 8-week evidence-based applied clinical project (N = 7) was designed to answer the question: In parents of children with the diagnosis of ADHD, or exhibiting ADHD traits, what is the effect of providing mindful parenting psychoeducation in addition to standard of care treatment on levels of parental stress post intervention?

Sources Used: An exhaustive literature search was performed using the Cumulative Index to Nursing and Allied Health Literature, the Cochrane Library, Psyc-INFO, and PubMed.

Conclusions: Outcomes were measured using the Parenting Stress Index, Fourth Edition Short Form (PSI-4-SF). Scores on the Total Stress scale decreased significantly after 8 weeks (p = .018); a significant decrease also occurred across two of the three PSI-4-SF subscales (Parental Distress and Parent-Child Dysfunctional Interaction). Recommendations for practice change, suggestions for future clinical inquiry, and project limitations are discussed.

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Journal of Child Psychology and Psychiatry. 2015 Apr;56:477-87.

ATYPICAL NEURAL RESPONSES TO VOCAL ANGER IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Chronaki G, Benikos N, Fairchild G, et al.

Background Deficits in facial emotion processing, reported in attention-deficit/hyperactivity disorder (ADHD), have been linked to both early perceptual and later attentional components of event-related potentials (ERPs). However, the neural underpinnings of vocal emotion processing deficits in ADHD have yet to be characterised. Here, we report the first ERP study of vocal affective prosody processing in ADHD.

Methods Event-related potentials of 6–11-year-old children with ADHD (n = 25) and typically developing controls (n = 25) were recorded as they completed a task measuring recognition of vocal prosodic stimuli (angry, happy and neutral). Audiometric assessments were conducted to screen for hearing impairments.

Results Children with ADHD were less accurate than controls at recognising vocal anger. Relative to controls, they displayed enhanced N100 and attenuated P300 components to vocal anger. The P300 effect was reduced, but remained significant, after controlling for N100 effects by rebaselining. Only the N100 effect was significant when children with ADHD and comorbid conduct disorder (n = 10) were excluded.

Conclusion This study provides the first evidence linking ADHD to atypical neural activity during the early perceptual stages of vocal anger processing. These effects may reflect preattentive hyper-vigilance to vocal anger in ADHD.

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Journal of Child Psychology and Psychiatry. 2015 Apr;56:453-59.

BIRTH WEIGHT AS AN INDEPENDENT PREDICTOR OF ADHD SYMPTOMS: A WITHIN-TWIN PAIR ANALYSIS.

Pettersson E, Sjölander A, Almqvist C, et al.

Background: Studies have found an association between low birth weight and ADHD, but the nature of this relation is unclear. First, it is uncertain whether birth weight is associated with both of the ADHD dimensions, inattentiveness and hyperactivity-impulsivity. Second, it remains uncertain whether the association between birth weight and ADHD symptom severity is confounded by familial factors.

Method: Parents of all Swedish 9- and 12-year-old twins born between 1992 and 2000 were interviewed for DSM-IV inattentive and hyperactive-impulsive ADHD symptoms by the Autism—Tics, AD/HD and other Comorbidities (A-TAC) inventory (N = 21,775 twins). Birth weight was collected prospectively through the

Medical Birth Registry. We used a within-twin pair design to control for genetic and shared environmental factors.
Results: Reduced birth weight was significantly associated with a mean increase in total ADHD (ß = -.42; 95% CI: -.53, -.30), inattentive (ß = -.26; 95% CI: -.33, -.19), and hyperactive-impulsive (ß = -.16; 95% CI: -.22, -.10) symptom severity. These results imply that a change of one kilogram of birth weight corresponded to parents rating their child nearly one unit higher (going from "no" to "yes, to some extent" on a given symptom) on the total ADHD scale. These associations remained within pairs of MZ and DZ twins, and were also present when restricting the analyses to full term births.
Conclusions: There is an independent association between low birth weight and all forms of ADHD symptoms, even after controlling for all environmental and genetic confounds shared within twin pairs. These results indicate that fetal growth restriction (as reflected in birth weight differences within twin pairs) and/or the environmental factors which influence it is in the casual pathway leading to ADHD.

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Journal of Child Psychology and Psychiatry. 2015 Apr;56:460-67.

NEONATAL JAUNDICE AND INCREASED RISK OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A POPULATION-BASED COHORT STUDY.

Wei CC, Chang CH, Lin CL, et al.

Background: Previous studies have posited conflicting results regarding the relationship between neonatal jaundice and the subsequent risk of attention-deficit hyperactivity disorder (ADHD). We therefore performed a large population study with a defined neonatal jaundice cohort to investigate the incidence and risk of physician-diagnosed ADHD in Taiwan.
Methods: From 2000 to 2004, 24,950 neonatal jaundice cases and 69,964 matched nonjaundice controls were identified. At the end of 2008, the incidence rate and hazard ratios (HRs) of physician-diagnosed ADHD were calculated.
Results: The incidence of ADHD was 2.48-fold greater in the jaundice cohort than in the nonjaundice cohort (3.84 vs. 1.51 per 100,000 person-years) in the study period. The HR of ADHD was substantially greater for male, preterm, and low-birth-weight infants with neonatal jaundice. The risk of developing ADHD in the jaundice cohort was greater after a diagnosis of neonatal jaundice for more than 6 years (HR: 2.64; 95% confidence interval: 2.13–3.28). The risk of ADHD increased for neonates with higher serum bilirubin levels requiring phototherapy and with longer admission days.
Conclusion: Neonates with jaundice are at high risk for developing physician-diagnosed ADHD during their growth period. A risk alert regarding neurologic consequences is urgently required after a neonatal jaundice diagnosis. Additional studies should be conducted to clarify the pathogenesis of these relationships.

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Journal of Child Psychology and Psychiatry. 2015 Apr;56:423-31.

AETIOLOGICAL OVERLAP BETWEEN ANXIETY AND ATTENTION DEFICIT HYPERACTIVITY SYMPTOM DIMENSIONS IN ADOLESCENCE.

Michelini G, Eley TC, Gregory AM, et al.

Background: Anxiety and attention-deficit/hyperactivity (ADH) problems are common in adolescence, often co-occur, and are characterised by high heterogeneity in their phenotypic expressions. Although it is known that anxiety and ADH problems correlate, the relationships between subtypes of anxiety and ADH problems have been scarcely investigated.
Methods: Using a large population sample of adolescent twins and siblings we explored the phenotypic and aetiological association between anxiety subtypes (panic/agoraphobia, separation anxiety, social anxiety, physical injury fears, obsessive-compulsive symptoms and generalised anxiety) and the two ADH dimensions (attention problems and hyperactivity/impulsivity). Both phenotypes were assessed using self-report questionnaires.

Results: The association between ADH problems and anxiety could be entirely attributed to attention problems, not hyperactivity/impulsivity. Most of the correlations between anxiety subtypes and attention problems showed an approximately equal role of genetic and nonshared environmental factors.
Conclusions: The high heterogeneity within anxiety and ADH problems should be taken into account in order to better understand comorbidity between them.

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J Consult Clin Psychol. 2015;82:1115-27.

A TWO-SITE RANDOMIZED CLINICAL TRIAL OF INTEGRATED PSYCHOSOCIAL TREATMENT FOR ADHD-INATTENTIVE TYPE.

Pfiffner LJ, Hinshaw SP, Owens E, et al.

Objective: This study evaluated the efficacy of the Child Life and Attention Skills (CLAS) program, a behavioral psychosocial treatment integrated across home and school, for youth with attention-deficit/ hyperactivity disorder-inattentive type (ADHD-I).
Method: In a 2-site randomized controlled trial, 199 children (ages 7-11 years) were randomized to CLAS (N = 74), parent-focused treatment (PFT, N = 74), or treatment as usual (TAU, N = 51). We compared groups on parent and teacher ratings of inattention symptoms, organizational skills, social skills, and global improvement at posttreatment and also at follow-up during the subsequent school year.
Results: CLAS resulted in greater improvements in teacher-reported inattention, organizational skills, social skills, and global functioning relative to both PFT and TAU at posttreatment. Parents of children in CLAS reported greater improvement in organizational skills than PFT and greater improvements on all outcomes relative to TAU at posttreatment. Differences between CLAS and TAU were maintained at follow-up for most parent-reported measures but were not significant for teacherreported outcomes.
Conclusions: These findings extend support for CLAS across 2 study sites, revealing that integrating parent, teacher, and child treatment components, specifically adapted for ADHD-I, is superior to parent training alone and to usual care. Direct involvement of teachers and children in CLAS appears to amplify effects at school and home and underscores the importance of coordinating parent, teacher, and child treatment components for cross-setting effects on symptoms and impairment associated with ADHD-I.

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J Neurosci Methods. 2015. [Epub ahead of print]

LOCOMOTOR ACTIVITY MEASURES IN THE DIAGNOSIS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: META-ANALYSES AND NEW FINDINGS.

Garcia ML, Cortese S, Anderson D, et al.

Introduction: Our aim was to assess differences in movement measures in attention-deficit/hyperactivity disorder (ADHD) vs. typically developing (TD) controls.
Methods: We performed meta-analyses of published studies on motion measures contrasting ADHD with controls. We also conducted a case-control study with children/adolescents (n = 61 TD, n = 62 ADHD) and adults (n = 30 TD, n = 19 ADHD) using the McLean motion activity test, semi-structured diagnostic interviews and the behavior rating inventory of executive function and Conners (parent, teacher; self) rating scales.
Results: Meta-analyses revealed medium-to-large effect sizes for actigraph (standardized mean difference [SMD]: 0.64, 95% confidence interval (CI): 0.43, 0.85) and motion tracking systems (SDM: 0.92, 95% CI: 0.65, 1.20) measures in differentiating individuals with ADHD from controls. Effects sizes were similar in studies of children/adolescents ([SMD]: 0.75, 95% CI: 0.50, 1.01) and of adults ([SMD]: 0.73, 95% CI: 0.46, 1.00). In our sample, ADHD groups differed significantly in number of head movements (p = 0.02 in children; p = 0.002 in adults), displacement (p = 0.009/. p <. 0.001), head area (p = 0.03/. p <. 0.001), spatial complexity (p = 0.06/. p = 0.02) and temporal scaling (p = 0.05/. p = 0.04). Mean effect sizes were non-significantly larger (d = 0.83, 95% CI: 0.20, 1.45) in adults vs. children/adolescents with ADHD (d = 0.45, 95% CI: 0.08, 0.82). In the concurrent go/no-go task, reaction time variability was significantly greater in ADHD (p <. 0.05 in both age groups) than controls.

Conclusions: Locomotor hyperactivity remains core to the construct of ADHD even in adults. Our results suggest that objective locomotion measures may be particularly useful in evaluating adults with possible ADHD.

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Journal of Research in Reading. 2015 Feb;38:73-90.

READING DIFFICULTIES AND ATTENTION-DEFICIT/HYPERACTIVITY BEHAVIOURS: EVIDENCE OF AN EARLY ASSOCIATION IN A NONCLINICAL SAMPLE.

Luoni C, Balottin U, Zaccagnino M, et al.

Attention-deficit/hyperactivity disorder (ADHD) often co-occurs with reading disability. A cross-sectional study in an Italian-speaking, nonclinical sample was conducted in an attempt to document the existence of an early association between reading difficulties (RD) and ADHD behaviours. We recruited a sample of 369 children in their first year at primary school. Of the sample, 8.4% displayed RD; 7.0% had ADHD; 3.5% presented both RD and ADHD behaviours; 50% of the children with ADHD displayed RD; 41.9% of those with RD displayed ADHD behaviours. Low socioeconomic status was associated with a fourfold increased probability of displaying RD (odds ratio = 3.98), but not ADHD behaviours. In this nonclinical sample, we detected an early association between ADHD behaviours and RD. A key role in this association may be played by inattention symptoms, which occurred with significantly increased frequency also in the group presenting only RD.

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J Voice. 2015. [Epub ahead of print]

HYPERFUNCTIONAL VOICE DISORDER IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD). APHENOTYPIC CHARACTERISTIC?

Barona-Lleo L, Fernandez S.

Objective: The purpose of this study was to detect specific vocal aerodynamic patterns in attention deficit hyperactivity disorder (ADHD) patients and to define a possible new phenotypic feature of this disorder that must be diagnosed and treated.

Study Design: This is a prospective study.

Methods: Seventy-nine children aged 5-13years were recruited: 44 children with ADHD diagnosis and 35 children, as a control group, matched according to age and gender. All children were evaluated in the voice laboratory. Each subject repeated sustained vowels, syllables, words, and sentences several times. Intraoral pressure, transglottal airflow, microphone, and electroglottograph results were recorded and analyzed. Children affected by ADHD, with adequate tolerance, were evaluated endoscopically and by the speech therapist.

Results: The aerodynamic analysis shows that the subglottal pressure is higher and transglottal airflow is lower in ADHD children compared with the children of the control group. Those differences are statistically significant. The endoscopic physical examination showed vocal nodules in 25 children (78.125%) and hyperfunctional vocal behavior in all ADHD children studied.

Conclusions: We proposed that every child with ADHD disorder must be evaluated from a laryngeal point of view (otolaryngologist and speech therapist) as an important part of the diagnosis and global treatment. It could be considered as a new phenotypic characteristic of this disorder.

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Kidney Int. 2015;87:800-06.

DURATION OF CHRONIC KIDNEY DISEASE REDUCES ATTENTION AND EXECUTIVE FUNCTION IN PEDIATRIC PATIENTS.

Mendley SR, Matheson MB, Shinnar S, et al.

Chronic kidney disease (CKD) in childhood is associated with neurocognitive deficits. Affected children show worse performance on tests of intelligence than their unaffected siblings and skew toward the lower end of the normal range. Here we further assessed this association in 340 pediatric patients (ages 6-21)

with mild-moderate CKD in the Chronic Kidney Disease in Childhood cohort from 48 pediatric centers in North America. Participants underwent a battery of age-appropriate tests including Conners' Continuous Performance Test-II (CPT-II), Delis-Kaplan Executive Function System Tower task, and the Digit Span Backward task from the age-appropriate Wechsler Intelligence Scale. Test performance was compared across the range of estimated glomerular filtration rate and duration of CKD with relevant covariates including maternal education, household income, IQ, blood pressure, and preterm birth. Among the 340 patients, 35% had poor performance (below the mean by 1.5 or more standard deviations) on at least one test of executive function. By univariate nonparametric comparison and multiple logistic regression, longer duration of CKD was associated with increased odds ratio for poor performance on the CPT-II Errors of Commission, a test of attention regulation and inhibitory control. Thus, in a population with mild-to-moderate CKD, the duration of disease rather than estimated glomerular filtration rate was associated with impaired attention regulation and inhibitory control.

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Klin Psikofarmakol Bul. 2014;24:S225.

EFFECTS OF ATOMOXETINE ON DEPRESSION AND ANXIETY SYMPTOMS IN CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER: PRELIMINARY FINDINGS OF A PROSPECTIVE, OPEN-LABEL STUDY.

Kutuk F, Kultur SE, Tuna-Cak H .

Objective: Attention deficit-hyperactivity disorder (ADHD) is a common socially impairing neuropsychiatric disorder with onset in childhood. Anxiety and depression symptoms may accompany the core symptoms of ADHD in nearly one third of the children. The aim of the study is to evaluate the effects of atomoxetine HCl on self-reported anxiety symptoms, self and parent reported depression symptoms as well as parent and teacher reported core ADHD symptoms in children diagnosed with ADHD.

Method: Twenty-five children aged between 7-12 years and diagnosed as having ADHD based on DSM-IV-TR criteria were enrolled in an open label trial for atomoxetine HCL treatment. None of the patients had a DSM-IV-TR criteria based neither major depression nor any kind of an anxiety disorder. Anxiety symptoms were recorded using the State-Trait Anxiety Inventory, depression symptoms using self and parent reported the Children's Depression Inventory and the core symptoms of ADHD using the Conners Parents/Teachers Rating Scales at baseline and after 6 weeks of atomoxetine HCl treatment.

Results: As reported by both parents and teachers on each subscale of the Conners Parents/Teachers Rating Scales (all p values ranged between 0.001-0.031),a six weeks of atomoxetine HCL treatment at an average dose of 1.10 mg/kg/day was associated with significant improvements in the core ADHD symptoms. Moreover parent reported depression and self-reported state anxiety scores decreased significantly (p: 0.004, p: 0.027). However, self-reported depression and trait anxiety scores did not show significant differences at the end of the six-week trial. Fourteen patients complaint about mild side effects mostly decreased appetite and irritability but none of the patients withdrew from the study.

Conclusion: The findings from this study demonstrate that even short-term atomoxetine treatment significantly improves core ADHD symptoms. In addition, atomoxetine treatment is associated with a significant decrease in anxiety and depression symptoms in ADHD even when these are not comorbid diagnosis.

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Klin Psikofarmakol Bul. 2014;24:S223.

EXECUTIVE FUNCTIONS AND SOCIAL RESPONSIVENESS IN CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER.

Kurt-Ayyildiz D, Orengul AC, Bikmazer A, et al.

Objective: Attention Deficit - Hyperactivity Disorder (ADHD), consisting of attention problems, hyperactivity and impulsivity as core symptoms together with social difficulties, is one of the most common neurodevelopmental disorders of childhood. Children with ADHD have been suggested to have problems with executive functions (EF) and social functioning. The difficulties in EF have many everyday implications

such as insuence on academic achievement, and social competence. Social dysfunctioning may be of crucial importance for the prognosis of children with ADHD.
Methods: In this study, we examined the EF and social responsiveness of the children with ADHD and compared them with those of control group. Forty three children with the diagnosis of ADHD and age matched 33 controls were assessed by a detailed form for sociodemographic characteristics and Kiddie Schedule for Affective Disorders and Schizophrenia Present and Lifetime Version for clinical psychiatric diagnoses. Parents of the participants completed Behavioral Rating Inventory of Executive Functions (BRIEF), Social Responsiveness Scale (SRS).
Results: Inhibition, set-shifting, emotional control, initiation, working memory, planning and organization, organization of materials and monitoring subscores of BRIEF, BRIEF total score and SRS total score were significantly higher in the ADHD group ($p<0.05$). In the ADHD group, BRIEF total score were moderately correlated with SRS total score ($r=0.58$; $p<0.05$).
Conclusion: It was found that the children with ADHD demonstrated much more impairment in executive functions and social responsiveness. These problems necessitate clinical attention.

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Klin Psikofarmakol Bul. 2014;24:S226.

TREATMENT CHOICE IN ASSOCIATION OF ATTENTION DEFICIT-HYPERACTIVITY DISORDER WITH WILLIAMS AND MOEBIUS SYNDROMES: CASE REPORTS.

Irmak A, Ince-Tasdelen B, Ozmen S, et al.

Williams syndrome is a neurodevelopmental disorder caused by micro-deletion at chromosome 7q11.23. It is associated with ADHD by 65-84% Moebius syndrome is a rarely seen congenital syndrome with non-progressive nature, which is characterized by facial and ocular paralysis. It may be associated with mental retardation and ADHD. Our aim is to present our experience regarding difficulties in the medical treatment of ADHD cases associated with syndromes and therapeutic effectiveness. Case 1: A six-year old girl referred to our clinic with hyperactivity, inattention. She had been attending to special education; that she had been hyperactive and walked in the class during lesson. In the interview dysmorphic facial appearance was striking, she was diagnosed as Williams Syndrome. With initial diagnosis of ADHD, short-acting methylphenidate was prescribed, which was then gradually titrated up to 1 mg/kg. In the control visit, methylphenidate treatment was withdrawn due to ongoing complaints of inattention, hyperactivity and difficulty in adaptation to school in the patient who had newly onset nervousness, irritability and obsessions. Thus; atomoxetine therapy was prescribed and dose was escalated to 1.5 mg/kg. In control visits, there was improvement in hyperactivity and parents of the patient reported she had better attention and improved nervousness. The patient is still attending control visits. Case 2: A nine-year old boy referred to our clinic with inattention, disinterest to lessons and hyperactivity. He had low academic success since first grade. In the interview, facial asymmetry and expressionless facial appearance were striking. He was diagnosed as Moebius syndrome. Methylphenidate was prescribed with initial diagnosis of ADHD, which was gradually titrated up to 1 mg/kg. However, it was withdrawn due to onset of phobias and visual hallucinations as well as lack of improvement in attention problems. Atomoxetine was then prescribed which was gradually titrated up to 1.2 mg/kg. In control visits, there was improvement in hyperactivity and academic success while he had no problem in adaptation to classmates. The patient is still attending to control visits. Early diagnosis allows early introduction of treatment in ADHD and providing appropriate management can allow better prognosis in syndromic children. Dramatic occurrence of adverse effects in our patients suggests that there is an increased vulnerability to adverse effects of methylphenidate in syndromes when compared to other ADHD entities and that one should give attention regarding adverse effects, with close monitoring. These patients have great similarity to findings in the literature regarding adverse effects. No clinical improvement was achieved by methylphenidate; however, atomoxetine treatment provided marked benefit in our cases. These findings are inconsistent to studies proposing high success rates for methylphenidate in the literature. Although these cases suggest that atomoxetine treatment can be primarily preferred in patients with syndromes and ADHD regarding effectiveness and adverse effect profile, further studies are needed about atomoxetine treatment in association of syndromes with ADHD.

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Klin Psikofarmakol Bul. 2014;24:S341-S342.

RESTING METABOLIC RATE AND BODY COMPOSITION IN CHILDREN WITH ADHD.

Alpaslan AH, Ucok K, Coskun KS, et al.

Objectives: Attention deficit hyperactivity disorder (ADHD) is among the most common neurobehavioral problems afsicting children between 6 and 17 years of age; its prevalence in the United States is believed to range from 2% to 18% in this age group. ADHD is considered to be a heritable, chronic, neurobehavioral disorder that is characterized by hyperactivity, inattention, and impulsivity. In children with ADHD appear some differences in physique, growth and development. There is not enough evidence in the scientific literature to establish clear conclusions on pulmonary functions, resting metabolic rate and body composition in children with ADHD. The aim of this study was to compare pulmonary functions, resting metabolic rate (RMR), and body composition parameters in patients with ADHD and healthy controls.
Methods: The study involved eighty (n=80) children between the ages of 8 and 12 (mean age 9.6 years). The ADHD group included respectively 30 boys and 10 girls, while the control group comprised 40 age and gender-matched children without any other physical or chronic mental diseases. In this cross-sectional study, RMR was measured by indirect calorimeter. Anthropomorphic measurements including BMI, neck, shoulder, chest, waist, hip and abdomen circumferences were measured for all of the participants. Parents completed Conners' Parent Rating Scale and The Pediatric Quality of Life Inventory (PedsQL) for their children; teachers completed Conners' Teacher Rating Scale and all of the participants were administered to PedsQL for themselves. Differences were considered significant if the p values were less than 0.05.
Results: There were no significant differences between groups for socio-demographical features (age, BMI, age and education level of parents, number of sibling; $p>0.05$). ADHD group has higher scores on Conners' Rating Scales compared with Control group ($p<0.05$). Additionally it was found that quality of life of ADHD group is worse than control group ($p<0.05$). When the ADHD and Control groups were compared with respect to resting metabolic rate, and body composition parameters there were no significant differences abdomen circumference, waist/hip ratio and resting metabolic rate between the groups ($p>0.05$).
Conclusions: Functional neuroimaging and electro-physiologic studies revealed biological differences between children with and without ADHD, and together with the heritable nature and the strong genetic background. To our knowledge, this is the first study in our country, which has investigated a possible association between ADHD, RMR and body composition. The comparison of ADHD (newly diagnosed) and healthy control groups included in the current study show similar RMR and body composition parameters. Furthermore, we suggest long-term studies, which are needed to test how the investigated parameters change over the span of life in subjects with ADHD.

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Klin Psikofarmakol Bul. 2014;24:S359.

A CASE COMORBID WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND ANXIETY DISORDER.

Gokce S.

Attention Deficit Hyperactivity disorder (ADHD), is one of the most frequent psychiatric disorders in childhood. It has been reported that among children at school age, the prevalence of ADHD varies between 2% and 20% and prevalence of comorbidity is high. In children diagnosed with ADHD, the most common comorbid diagnosis after oppositional-defiant disease is anxiety disorder. Although ADHD is a frequently comorbid with anxiety disorders, factors associated with anxiety disorders in ADHD has not been addressed adequately. According to the results of clinical and epidemiological studies, there is a consistent and reciprocal relation between ADHD and anxiety disorders, and the rate of ADHD increases in the presence of anxiety disorders compared to community samples, and vice versa. It has also been suggested that there is an independent association between these two disorders. Case: We will discuss diagnosis, treatment and prognosis of a 11 year old boy came to Erenkoy psychiatric and neurologic research and training hospital child and adolescent psychiatry clinic with academic problems, attention deficit, hyperactivity symptoms, free soating anxiety, obsessions and compulsions. Discussion: It is surprising that although ADHD and anxiety disorders are frequently comorbid, there are a few studies on this issue of their coexistence. When the adverse effects of the coexistence of these two disorders on

clinical practice, treatment options, course and prognosis are taken into consideration, it becomes evident that more structured and long terms studies are required on this issue.

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Klin Psikofarmakol Bul. 2014;24:S158-S159.

HENOCH-SCHONLEIN PURPURA WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER .

Yusufoglu C, Sonkaya AR, Taymur I.

Henoch-Schonlein purpura (HSP) is one of the most common vasculitis of childhood and frequently associated with the gastrointestinal tract involvement, manifesting as abdominal pain, vomiting and GI bleeding. The etiology is unclear. Interaction of several environmental factors, including infections and multiple genes has been proposed to play a role in pathogenesis. Neurological symptoms are rare although non-specific headache followed by subtle encephalopathy with minimal changes in mental status, such as labile mood, apathy and hyperactivity may be more common than previously thought. In a prospective study 46% of 26 patients had abnormal EEGs. It represents a diffuse vasculitis that is secondary to hypersensitivity. Neuropsychiatric conditions can also be seen in the latter, including attention deficit hyperactivity disorder (ADHD), being more frequent in the chronic forms of the disease. We report a case of a 11-year-old male HSP patient with ADHD. He is a 6th grader. When he was in primary school, he learned reading at 1st class. He had a high academic achievement but he has been getting bored quickly of lessons since the 1st class and he has got attention problems. The case had no resume medical histories. ECG is within the normal values. From when our case was 2-3 years of age, was referred Behcet Uz Hospital in September 2001 with the purpuric rashes, swollen legs. He had taken antibiotic. The case had no history of infection or animal/insect bites at least until the onset of rashes. The case was diagnosed as having HSP. ADHD is one of the most common childhood brain disorders and can continue through adolescence and adulthood. Symptoms include difficulty staying focused and paying attention, difficulty controlling behavior, and hyperactivity (over-activity). These symptoms can make it difficult for a child with ADHD to succeed in school, get along with other children or adults, or finish tasks at home. ADHD is a common disorder of complex pathology with several possible treatment options. The first-line treatment of ADHD is the prescription of stimulant drugs such as methylphenidate. In this case we point out that methylphenidate with behavioral management was associated with benefit in the management of ADHD with HSP and additional cognitive impairments. Methylphenidate appears to be a safe and effective treatment for ADHD in the majority of children with HSP. In our case a 12-year-old child with a diagnosis of ADHD had an academic success; methylphenidate treatment was carried out and our patient has got benefits. If Children diagnosed with ADHD have a history of vasculitis, the treatment of methylphenidate may be the first option. During the early years of children, as the neurodevelopment is in progress, HSP should be followed up in advanced stages for ADHD, if diagnosed.

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Klin Psikofarmakol Bul. 2014;24:S356.

SERUM VITAMIN D LEVELS IN ADHD PATIENTS.

Altun-Varmis D, Metin O, Yolga-Tahiroglu A, et al.

Objective: ADHD is a common neuropsychiatric disorder in children and adolescents. Experimental data of Vitamin D demonstrate that vitamin D has a remarkable role in proliferation, differentiation, neurotrophism, neuroprotection, neurotransmission, and neuroplasticity. Low levels of vitamin D were associated with depression, seasonal affective disorder, and schizophrenia in adults, but little is known about vitamin D effect on mental health in the pediatric population. In this study, we aimed to investigate serum vitamin D levels in pediatric ADHD patients.

Methods: The study population included 20 females and 32 males aged 6 to 17 years were admitted to the outpatient clinic of the Child and Adolescent Psychiatry Department, between March 2013 and February 2014. Serum 25-OH vitamin D levels of participants were collected on routine admission laboratory testing. Vitamin D levels were classified as low and normal; depends on seasonal norms basis Vitamin D levels (lower limit; 20 ng/ml for the summer, in winter 10 ng/ml). Patients, who met the criteria of the Diagnostic

and Statistical Manual of Mental Disorders for ADHD, were recruited. Conners Parent Rating Scale (CPRS) and Conners Teacher Rating Scale (CTRS) scores, which were kept in the files of ADHD patients were calculated. Socio-demographic information as well as environmental risk factors that may play a role in the etiology, which may be related physical illness, comorbid diagnoses, ADHD subtypes were examined and the obtained data investigated the correlation between with vitamin D levels. Stroop Color-Word Test (ST) was used to evaluate the attentional functions. Average performance on the Stroop test was calculated based on total test time (ST-T), total error rate (ST-E), and correct response (ST-C) incorrectness.
Results: This study was conducted on 52 children with ADHD (32 (61.5%) boys, and 20 (38.5%) girls), aged between 6 and 17 years (mean(plus or minus)SD: 11.4(plus or minus)3.0 years). The mean serum 25-OH-vitamin D level was 17.4(plus or minus)9.8 ng/ml (for boys: 19.4(plus or minus)11.3, for girls: 14.4(plus or minus)5.5 ng/ml; p=0.08). Subjects with a history of frequent infections were more likely to have low levels of 25-(OH) vitamin-D in comparison to those without this history (p=0.011). The ST-C scores of ADHD patients having low serum vitamin D levels were significantly higher than those, who had normal Vitamin D levels (respectively, 2.9(plus or minus)2.7, 5.2(plus or minus)2.8 ng/ml, p=0.025).
Conclusion: Vitamin D deficiency could be associated with a number of psychiatric and neurological conditions. Multiple studies demonstrated that reduced DA and/or NE function hypothesis in ADHD. Abnormal dopamine regulation in certain areas of the central nervous system might have a role in the etiology of ADHD. In our study, results from Stroop Test and frequency of infection history in patients having low vitamin D levels refers to possible relationship between immune dysfunction and 25-(OH) vitamin-D deficiency. It should be investigated further prospective and controlled studies.

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Klin Psikofarmakol Bul. 2014;24:S290.

CO-EXISTENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER AND RATHKE CLEFT CYST: A CASE REPORT.

Guler G, Yildirim V, Ekinci O, et al.

Rathke Cleft Cyst (RCC) is remnant of Rathke pouch, which is formed by invaginations stomodaeum in 3rd or 4th week of gestational life. It is a benign tumor of the pituitary gland. Generally, asymptomatic, symptomatic cysts are quite rare. Although defined as a developmental cyst, it is more common in adults than children, and two times more common in females. To our research, this is the first case of coexistence of Attention deficit hyperactivity disorder (ADHD) and RCC. On the other hand, this case is the second youngest male patient who is diagnosed with RCC in the literature; first one is 4.5 year-old. A 7-year-old-boy was brought to the Child and Adolescent Psychiatry Clinic with forgetfulness and hyperactivity. His development was delayed in reference to his peers (Delayed speech and walking). In the family history; his sister has Panic Disorder, and his uncle has mental retardation. Although he has attended to first grade class for nearly seven months, he could not learn to read and many complaints such as excessive speech at lessons, distractibility in homework, came from the teachers in this period. He is going to go to the repeat first class next year. He was diagnosed with ADHD and Mental Retardation. Magnetic resonance imaging (MRI) has been asked because of the child's atypical facial appearance, mental retardation and growth retardation. Rathke cyst (1.2x1.8x1.7 cm) was incidentally detected on brain MRI in the process of treatment and follow-up. Performed on blood tests FSH: 0.71 mIU/ml (0.95-11.95) LH: 0.03 mIU/ml (1.14-8.75) testosterone: 0.04 ng/ml (1.42-9.23), results of thyroid function tests, prolactin and cortisol levels were in the normal range. The patient was consulted to endocrinology and neurosurgery departments. We learned that transfenoidal surgery is planned. This is the first case presented in the literature about the coexistence of ADHD and RCC. RCC is rare in pediatric population. Headache, endocrine abnormality and visual loss are the major features of RCC. Our patient was asymptomatic; the cyst was recognized by chance. If there is no other condition with hypogonadotropic hypogonadism, people usually do not consult with a doctor in prepubertal period. Unless treatments are properly managed in adolescents and teenagers, some permanent health problems may be seen in following years. Thus, early diagnosis is important for children. In our clinic, we investigate thyroid hormones, hemogram, iron parameters etc. to diagnose diseases such as ADHD symptoms hyperthyroidism, hypothyroidism and iron deficiency anemia. If we had

wanted endocrinological blood tests, we could have had a chance to capture pituitary lesions. If not in all cases, sometimes it may be useful to make MRI and detailed blood test patients who is with mental retardation, growth retardation, atypical facial appearance, considered a syndrome.

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EVALUATION OF EMOTION RECOGNITION AND SOCIAL COGNITION ABILITIES IN ATTENTION DEFICIT AND HYPERACTIVITY DISORDER PATIENTS.

Kose S, Ozbaran B, Guney-Uzunkopru SS, et al.

Objective: Previous studies often show Attention deficit hyperactivity disorder (ADHD) comorbidity in children with Autism Spectrum Disorders (ASD), however, current studies state that there could be undefined autistic features in children with ADHD. Deficits in social functioning, emotion recognition and social cognitive abilities are the core symptoms of ASD. In ADHD, there happens to be difficulties in social functioning areas, besides deficits in number of daily life activities such as cognitive, academic, familial and vocational functions. In this study, we aimed to compare emotion recognition and social cognition abilities between ADHD patients and normal controls.

Method: 20 patients diagnosed with ADHD that were regularly examined at Ege University Faculty of Medicine, Child and Adolescent Psychiatry Outpatient Clinic and 20 controls were included in the study. Comprehension Test, Faux Pau Test, Eyes Test and Faces Tests were performed. The statistical analyses were performed using SPSS 16.0 program.

Results: 80% (n=16) of the ADHD group were male and the 20% (n=4) were female. 5% (n=1) of the control group were male and the 95% (n=19) were female. Mean age of the ADHD patients was 11.95(plus or minus)1.50 and the controls was 13.75(plus or minus)1.37. The differences in Faces Test, Eyes Test, Faux Pau and Comprehension Test between the two groups were significant. It was statistically shown that the age and gender differences between the two groups did not affect test performances. There was also no significant difference on test performances between the 10 patients that were on medication and another 10 that were not. Both the group that was on medication and the other group that was not, performed worse than normal controls.

Conclusion: The findings indicate that the ADHD group has inability in emotion recognition and social cognition. We think that it is also important to pay attention to the deficits in social functioning and social cognition of ADHD patients through the treatment process. Studies with larger samples are suggested for investigating the factors related with the social cognitive deficits in ADHD and whether there is a social deficit or ASD- related ADHD subgroup or not.

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Klin Psikofarmakol Bul. 2014;24:S148.

EVALUATION OF THE PLASMA LEPTIN, ADIPONECTIN, NEUROPEPTIDE Y LEVEL IN PEDIATRIC PATIENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Ozel-Ozcan O, Arslan M, Gungor S, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is the most common psychiatric disorder in children. Relationship of the disorder with obesity is well known, but the mechanism has not been understood yet. Recent studies found out 1,5-2 fold increase in risk for overweight/obesity in patients with ADHD compared to normal population. The aim of the present study was to evaluate plasma leptin, adiponectin, neuropeptide Y (NPY) levels and to investigate the mechanism and etiology of weight gain in patients with ADHD.

Methods: The study was conducted in Department of Child and Adolescent Psychiatry, Medical Faculty of Inonu University from February 2013 to April 2013. 36 patients with a diagnosis of ADHD according to the DSM-IV- TR criteria (drug naive) and 40 healthy children were enrolled in this study. Plasma leptin, adiponectin and NPY levels were measured; age, height, weight were recorded and body mass index (BMI), BMI percentile, weight to height values were calculated for all patients enrolled in the study.

Results: This study included 29 (80.6 %) males and 7 (19.4%) females in the ADHD group and 29 (72.5%) males and 11 (27,5%)females in the control group. The mean age in the ADHD group was 9.3 years and

8.8 years in the control group. In the control group, 35 (87,5%) patients had normal, 1 (2.5%) had increased and 4 (10%) patients had decreased BMI percentile. 35 (75%) patients had normal, 5 (13.9%) patients had increased and 4 (11.1%) patients had decreased BMI percentile in the ADHD group. No significant difference was found between two groups in terms of age, gender, height, weight, BMI, BMI percentile, weight to height value and NPY plasma levels. Adiponectin plasma levels (p=0,003) and leptin / adiponectin ratio (p=0,009) were significantly higher in ADHD group.
Conclusion: These results suggest that weight gain in patients with ADHD may be related to the decrease in plasma adiponectin levels and increase in leptin / adiponectin ratio.

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PLASMA DOPAMINE AND NORADRENALINE LEVELS IN CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Pekcanlar-Akay A, Resml H, Ozek-Erkuran H, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is an important psychiatric disorder due to its prominent effects on the patients' and their families' quality of life, with a 5% prevalence worldwide. Although the pathogenesis of ADHD is still largely unknown, evidences derived as results from many studies focus primarily on dopaminergic and noradrenergic systems. The aim of this study is to determine plasma dopamine (DA) and noradrenaline (NA) levels of the cases diagnosed with ADHD at the pre-treatment process and to compare these levels with DA and NA levels of the healthy control group.
Method: Fifty children with ADHD and 50 healthy children between ages 6-12 were included in the study. Psychiatric diagnoses were determined by using Kiddie Schedule for Affective Disorders and Schizophrenia for School Aged Children- Present and Lifetime Version (K-SADS- PL) as semi-structured clinical interview and plasma DA and NA levels were measured before the initiation of treatment. Cases' parents were asked to fill in Child Behavior Checklist for ages 4-18 (CBCL) and Dupaul ADHD scale while their teachers were asked to fill in Conners Teacher Rating Scale- short form. ADHD symptom severity was measured by Clinical Global Impression scale (CGI).
Results: No statistically significant difference was found for NA levels between case and control group while there was a borderline statistically significant difference for plasma DA levels (p=0.990 and p=0.05, respectively). No statistically significant difference was found, when plasma DA and NA levels were compared for ADHD subtypes in the case group (p=0.390 and p=0.213, respectively).
Conclusion: Evidences regarding neurobiological causes that may affect the emergence of ADHD support the possible roles of catecholaminergic pathways over cognition and movement. Getting a better understanding of the possible roles of catecholaminergic and non-catecholaminergic systems in ADHD might help in both getting a better grip of the disorder and determining better treatment regimen that shall target the disorder.

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THERAPEUTIC APPROACHES TO ATTENTION DEFICIT HYPERACTIVITY DISORDER COMORBID WITH AUTISM SPECTRUM DISORDERS.

Kilincaslan A.

Many individuals with Autism Spectrum Disorders (ADS) exhibit behaviors and symptoms associated with Attention Deficit Hyperactivity Disorder (ADHD). Comorbidity of ADHD symptoms in individuals with ASD have generally been reported to be between 30 and 50% although even higher rates (e.g., as high as 78%) have been reported in clinical samples. Individuals with co-occurring ASD and ADHD are more severely impaired than those with no ADHD. They exhibit significant deficits in social processing, adaptive functioning, executive control and motor problems, which cause major challenges with educational achievement, socialization and behavioral management in these children. ADHD symptoms are similar whether occurring alone or comorbid with autism, so children with ASD may benefit from the same systematically tested, evidence-based treatments that have been proven successful in typically developing

children with ADHD. Studies have demonstrated the efficacy of methylphenidate treatment of ADHD symptoms in children with ASD, however, the response rates were lower and discontinuation due to adverse effects were higher compared with the non-ASD ADHD population. Two additional medications (i.e., clonidine and atomoxetine) have also reported to be effective in randomized placebo-controlled trials. Atypical antipsychotic agents have been demonstrated to reduce ADHD symptoms in children with ASD, who have co-occurring irritability and agitation. Compared with typically developing children with ADHD, children who have ASD, as in other developmental disabilities seem to have lower effect sizes with these medications and are more sensitive to side effects, including emotionality and agitation. In this presentation, recent studies on treatment of children with ASD comorbid with ADHD will be presented together with our clinical and research experience.

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Klin Psikofarmakol Bul. 2014;24:S47.

COMORBIDITY BETWEEN OBESITY AND DIAGNOSED ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS: CASE REPORT.

Onal A.

Obesity is now reaching epidemic proportions in the pediatric population worldwide. Previous studies have reported associations between child overweight and some features of psychopathology as depressive symptoms, Attention deficit hyperactivity disorder, and low self-esteem. Attention deficit hyperactivity disorder is one of the most common psychiatric disorder which affects 5-10% of school age children worldwide. Although somewhat overlooked in the past, in recent years studies have focused on the relationship between ADHD and obesity. A 12-year-old male patient was referred to a child endocrinology outpatient clinic with his parents because of obesity complaint. The patient, who was diagnosed as having probable ADHD after the evaluation of the questionnaire filled out by his parents, was invited to the child and adolescent psychiatry outpatient clinic for further evaluation. ADHD was determined according to DSM-IV diagnostic criteria, information obtained from his parents and teacher. Additionally, sociodemographic form, the Conners Parents Rating Scale and Strengths and Difficulties Questionnaire (SDQ) were administered. Understanding the underlying pathological mechanisms would highlight the relation between ADHD and obesity could be beneficial about treatment and managing outcomes.

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EFFECTIVENESS AND ADVERSE EFFECTS OF METHYLPHENIDATE TREATMENT IN CHILDREN DIAGNOSED WITH DMDD AND ADHD: A RETROSPECTIVE STUDY.

Ozyurt G, Inal-Emiroglu N, Baykara B, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is a commonly diagnosed psychiatric disorder in children. Since there is a debate about the over-diagnosis of bipolar disorder (BP) in childhood and facilitating research on pediatric BD, Leibenluft et al(2003) described a clinical syndrome called severe mood dysregulation (SMD). The hallmark of SMD is extreme, impairing, and chronic irritability, accompanied by hyperarousal symptoms. In DSM-5, this disorder is renamed as Disruptive Mood Dysregulation Disorders (DMDD) and hyperarousal symptoms are removed from the criteria for avoiding over-diagnoses among children and adolescents with ADHD. Comorbidity with ADHD and DMDD is very common in children and adolescents and reported as 86.9%. DMDD diagnosis refers to children with persistent irritability, hyperarousal, and emotional reactivity and temper tantrums that lack other cardinal manic symptoms such as elevation. There has been increasing debate surrounding the diagnostic relevancy of DMDD and other manic-like symptoms in children with ADHD. However, there has been little investigation into the impact of these symptoms on the efficacy of ADHD treatments or into the development of treatments specifically for DMDD. In this study, we aimed to present a case series in terms of the effectiveness and safety of methylphenidate in children, who are diagnosed as having DMDD and ADHD.

Method: In collaboration with J.Kaufman, Ph.D., Leibenluftetal, developed modifications to the Schedule for Affective Disorders and Schizophrenia (K-SADS-PL) to ensure that DMDD could be diagnosed reliably. Cases who applied to Child and Adolescent Psychiatry Department of Dokuz Eylul University School of Medicine with the symptoms of ADHD and DMDD, and whose diagnostic confirmation according to KSADS-PL was provided as ADHD and DMDD and currently under follow up in our clinic were recruited to study. Their sociodemographic data, treatments, the using time, doses and adverse effects of methylphenidate were evaluated retrospectively by child psychiatrists.
Results: There were nine cases, who were diagnosed as ADHD and DMDD, they were all male. The average of their ages was 13.55, the average age with these diagnoses first evaluated was 8.44. The mean follow-up period was 45.11(plus or minus)26.84 months and the range was 2 and 86 months. Eight of nine cases had reported adverse effects with methylphenidate. Increasing irritability had been seen in all cases and increasing tantrums had been observed in five cases. Methylphenidate(MPH) treatment was tried once in eight of nine cases but only one of them used MPH twice and irritability was seen for two times during the period of usage of MPH.
Conclusion: Research on the pathophysiology and treatment of children with DMDD and ADHD is very important for cases and their families. The evidence-based knowledge is insufficient for clinicians on whether children with DMDD and ADHD should first receive stimulants and behavior therapy for ADHD or mood stabilizers for mood dysregulation. In the present study, MPH was not tolerable for children, who were diagnosed as ADHD and DMDD and MPH usage increased the irritability clearly but in Waxmonsky's study MPH and behavior therapy were both found tolerable and effective treatments for children with ADHD and DMDD; and in addition, they determined that additional treatments might be needed to optimize their functioning.

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ASSESSMENT OF LIFE QUALITY IN THE CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER BY COMPARISON WITH TYPE-1 DIABETES MELLITUS AND HEALTHY CONTROL GROUPS.

Yurteri-Cetin N, Akay A, Elldokuz H.

Objective: Attention deficit hyperactivity disorder (ADHD), which is characterized by developmentally inappropriate levels of hyperactivity, impulsivity, and inattentiveness, has been identified as an important psychiatric condition in terms of its prevalence (around 5% worldwide) and its impact on quality of life for patients and their families. Type 1 Diabetes Mellitus (DM) is one of the most common chronic diseases of childhood. In the present study, the life quality of children and adolescents with ADHD was compared both with the life quality of children and adolescents with Type 1 DM and with healthy control groups.
Method: 60 ADHD cases, 60 Type 1 DM patients and 60 healthy controls, in total 180 children and adolescents, aged between 8-16 years were enrolled in this prospective, case-control study. The diagnostic assessments of psychiatric disorders in all subjects were made according to the DSM-IV criteria, the Kiddie-Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and the Lifetime (K-SADS PL). Sociodemographic scale, Pediatric Quality of Life Scale for Children (PedsQL 4.0 TM) were applied to all of the children - adolescents and their parents. The results were assessed with appropriate statistical analysis.
Results: In our study, the mean age was found 130.25(plus or minus)16.31 months (10.8(plus or minus)1.4 years) in the case and the control groups. The majority of ADHD subjects (68.3%) were male. Children and adolescents in the control groups were matched to subjects in the ADHD group according to age and sex. As a result, no significant difference between the groups were found in terms of age and sex (p=0.995, p=0.633).Compared with healthy controls, children and adolescents with diagnosed ADHD reported lower self-concept in all subscales and total scores of PedsQL except nullPhysical Health Summarynull (nullEmotional Functioningnull, nullSocial Functioningnull, nullAcademic Functioningnull, nullPsychosocial Health Summarynull and nullScale Summarynull) (p<0.01). No significant difference was found in nullPhysical Health Summarynull score (p:0.216). Similarly, children and adolescents with diagnosed ADHD reported lower self-concept in terms of nullEmotional Functioningnull and nullPsychosocial Health Summarynull scores than reported by children and adolescents with Type 1 DM (p<0.05).

Conclusions: Life quality in terms of nullEmotional Functioningnull, nullSocial Functioningnull, nullAcademic Functioningnull and nullPsychosocial Healthnull were found to be impaired in ADHD subjects.

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Klin Psikofarmakol Bul. 2014;24:S95-S96.

SERUM LEVELS OF BRAIN-DERIVED NEUROTROPIC FACTOR CHANGES IN CHILDREN DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: AFTER 2 MONTHS OROS-METHYLPHENIDATE TREATMENT.

Pekcanlar-Akay A, Resml H, Alsen S, et al.

Objective: Attention deficit hyperactivity disorder (ADHD), characterized by core symptoms like hyperactivity, attention deficit and impulsivity far beyond the developmental levels is an important psychiatric illness with a prevalence of 5% worldwide and the effects on the patients' and their families' quality of life. Even though the pathogenesis of ADHD is still greatly unknown, evidences from different researches point out primarily the dopaminergic system. As a member of the neurotrophin family, brain-derived neurotrophic factor (BDNF) is a widely expressed neurotrophin in the brain. BDNF has an important role in the survival, differentiation and synaptic plasticity of a series of neuronal systems including dopaminergic neurons. For this reason, it is proposed that BDNF might play a role in the ADHD pathophysiology. In this study, a comparison was aimed to be made between serum BDNF levels in children with diagnosed ADHD for pretreatment and posttreatment with methylphenidate.

Method: Fifty children with diagnosis of ADHD within an age range of 6-12 years were recruited in the study. The psychiatric diagnoses were determined by applying a semi-structured interview with Kiddies Schedule for Affective Disorders and Schizophrenia for School Aged Children- Present and Lifetime Version (K-SADS-PL). The symptom severity of ADHD was measured by Clinical Global Impression (CGI) ADHD severity scale. Clinicians filled up Du Paul ADHD scale. The levels of serum BDNF were assessed before and after eight weeks treatment with effective dosages of methylphenidate.

Results: In present study mean plasma BDNF levels in the baseline were 2626.3 pg/ml and 3255.8 pg/ml in the end point, thus showing significantly higher mean serum BDNF levels at post-treatment than pretreatment (t=-2.147, df=49, p=0.037). There was statistical significant difference between three subtypes of ADHD (p=0.004). After Bonferroni correlation it was found that there were significant differences between both mixed subtype and predominantly attention deficit subtype (p=0.03) and between predominantly attention deficit subtype and predominantly hyperactivity-impulsivity subtype (p=0.14). Significant difference was not found in BDNF levels with or without comorbidity (p=0.671) and there was no correlation between BDNF and Du Paul or CGI scores.

Conclusion: The results showed a significant increase in serum BDNF in children with ADHD after 8 weeks treatment with methylphenidate. Also we observed an improvement in attention deficit symptoms with increasing baseline serum BDNF levels. Serum BDNF can be an indicator for prediction of treatment response, prognosis.

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PLASMA DOPAMINE AND NORADRENALINE LEVELS IN CHILDREN DIAGNOSED WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER: A PROSPECTIVE TREATMENT STUDY.

Pekcanlar-Akay A, Resml H, Ozek-Erkuran H, et al.

Objective: Attention deficit-hyperactivity disorder (ADHD) is an important psychiatric illness with a prevalence of 5% worldwide, which is characterized by core symptoms like hyperactivity, attention deficit and impulsivity and it effects on the patients' and their families' quality of life. Even though the pathogenesis of ADHD is still greatly unknown, evidences from different researches point out primarily the dopaminergic and noradrenergic (NA) system. In this study, it was aimed to be compared plasma dopamine (DA) and NA levels in children diagnosed with ADHD in baseline and after two months methylphenidate OROS treatment.

Method: 50 children with the diagnosis of ADHD within the age range of 6-12 years were recruited in the study. The psychiatric diagnoses were determined by applying a semi-structured interview with Kiddies Schedule for Affective Disorders and Schizophrenia for School Aged Children- Present and Lifetime Version (K-SADS-PL). The symptom severity of ADHD was measured by Clinical Global Impression (CGI) ADHD severity scale. Clinicians filled up Du Paul ADHD scale. Plasma DA and NA levels were measured before methylphenidate treatment and two months after beginning methylphenidate OROS.
Results: According to a paired samples T-test, mean plasma DA levels in the baseline were 169.27 and 180.82 in the end point, (t=-1.339, df=49, p=0.187) and baseline NA level was 232.03 and after methylphenidate OROS treatment it was 232.03 (t=1470, df=49, p=0.148). There were no significant changes for both DA and NA levels between pretreatment and post-treatment significant difference was not found between three subtypes of ADHD. The difference between DA and NA levels and comorbidity did not reach statistical significance and there was no correlation between DA and NA and Dupaul or CGI scores.
Conclusion: To our knowledge, this is the first study in which plasma DA and NA levels were measured pretreatment and two months after methylphenidate OROS treatment Catecholaminergic pathways have been implicated in the neurobiological causes responsible for the emergence of ADHD. A better understanding of the possible roles of catecholaminergic and non-catecholaminergic systems in ADHD could advance our understanding of the disorder and help determine better treatment regimens.

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T102C AND 1438 G/A POLYMORPHISMS OF THE SEROTONIN 2A RECEPTOR GENE IN ETIOLOGY AND COURSE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Guney E, Iseri E, Guntekin-Ergun S, et al.

Objective: The aim of this study was to investigate -1438A>G and T102C polymorphisms of serotonin 2A (5-HT2A) receptor gene frequencies in patients with Attention deficit hyperactivity disorder (ADHD) in comparison with a healthy control group and to determine the effects of these polymorphisms on the course and outcome of ADHD.
Methods: Fifty adolescent and young adults who were diagnosed with ADHD in childhood (between the years 1994 and 2001) were included in this study. Patients were followed in the Child and Adolescent Psychiatry Department of Gazi University Medical Faculty for 7-14 years, and they completed this follow-up period. The control group consisted of 50 adolescent and young adults, who were healthy physically and mentally. In adolescence and adulthood, the diagnosis was reached after semi-structured interview based on DSM-IV criteria. Ten milliliters of blood was taken from each participant. Genetic evaluation was performed with Polymerase Chain Reaction method. SPSS 11.5 was used for the statistical analysis. Categorical variables were analyzed with chi-square and Fisher-exact tests, while the independent t-test was used for continuous variables for two-category variables. Statistical significance was accepted as a p value of <0.05.
Results: a. Socio-demographic Features: In this study, 50 adolescents and young adults (39 male, 11 female; age range 16-25 years), who were diagnosed as having ADHD while childhood (age range at the time of diagnosis 6-10 years) and 50 healthy adolescents and young adults (33 male, 17 female; age range 16-25 years) were evaluated. In adolescence and young adulthood, the diagnosis of ADHD remained in 44 (88%) cases, whereas six (12%) had remission after the 7-14-year follow-up. b. Relationship of the 5HT2A receptor gene T102C and -1438 A>G Polymorphisms with ADHD: A significant difference in the frequency of CC, CT and TT genotypes of T102C polymorphism ((chi)2:1.629, p: 0.44) and AA, AG and GG genotypes of -1438A>G polymorphism ((chi)2: 0.065, p: 0.96) was not found between the ADHD and control groups. A significant difference was not found between patients with ADHD with CC, CT or TT genotypes in terms of the outcome of illness ((chi)2:0.114, p: 0.94). Similarly, there was no difference between patients with ADHD having AA, AG and GG genotypes in outcome terms ((chi)2:0.530, p: 0.76).
Conclusion: A significant association between -1438A>G and T102C polymorphisms of 5-HT2A receptor gene and ADHD was not found in the present study. A significant effect of these two polymorphisms on the outcome of ADHD in adolescence was not detected. The results of this study do not support a role for the serotonergic system in the development and course of ADHD. As this study including children diagnosed

as having ADHD in their pre-school and primary school periods evaluated in adolescence and adulthood periods, and was a follow-up investigation, the sample size was limited.

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Klin Psikofarmakol Bul. 2014;24:S187.

ADHD AND DISRUPTIVE MOOD DYSREGULATION DISORDER TREATMENT WITH OLANZAPINE AND METHYLPHENIDATE: A CASE REPORT.

Vatansever Z, Unver H, Karagoz D, et al.

Attention deficit hyperactivity disorder (ADHD) is one of the most common disorders in childhood which deficits of inattention, hyperactivity and impulsive behavior. Disruptive Mood Dysregulation Disorder is characterized by severe recurrent temper outbursts that are inconsistent with developmental level and manifest verbally or behaviorally. The disorder can co-exist with ADHD and conduct disorder. In treatment of ADHD most commonly used pharmacological agent is methylphenidate. Atypical antipsychotics (e.g. risperidone, aripiprazole, olanzapine...) can be added on the treatment in some cases because of unsatisfactory clinical response and comorbidities such as conduct disorder, pervasive developmental disorders, disruptive mood dysregulation disorder, mental retardation. Olanzapine is one of the FDA-approved atypical antipsychotic, which antagonize the dopaminergic (D1, D2, D4), serotoninergic (5-HT2A, 5-HT2C, 5-HT6), histaminergic (H1), alpha1- adrenergic and muscarinic (especially M1) receptors. It is used increasingly for the treatment of mood disorders, schizophrenia, conduct disorder and pervasive developmental disorders at child and adolescent psychiatry clinics. Studies pointed out that it caused mostly dry mouth, weigh gain, increase appetite, sedation and hyperlipidemia. In this article, we report a 8-years-old male patient, who have ADHD, disruptive mood dysregulation disorder and conduct disorder, treated with olanzapine and OROS methylphenidate. This issue deserves to get attention that these two psychopharmacologic agents were usable concominantly for ADHD and its comorbidities.

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Klin Psikofarmakol Bul. 2014;24:S157.

SOCIO-DEMOGRAPHIC AND BEHAVIORAL FACTORS RELATED TO UNINTENTIONAL INJURIES IN PRESCHOOL CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Ayaz M, Ayaz AB, Soylu N.

Objectives: Unintentional injuries are a significant cause of morbidity and mortality in preschool children. Unintentional injuries may result in mental and physical effects on children, which may last for a lifetime. The purpose of this study was to investigate the factors related to unintentional injuries in preschool children diagnosed as having Attention deficit hyperactivity disorder (ADHD).

Methods: This study included 237 preschool children diagnosed with ADHD, aged 4-5 years, from a child psychiatry outpatient clinic. Children with a pervasive developmental disorder diagnosis were not included in the study. Fractures, soft tissue traumas leaving scar tissue, burning, poisoning, and all traumas that required hospitalization, were defined as unintentional injuries. Diagnoses of ADHD in the children were determined by child psychiatrists according to DSM-IV criteria. Behavioral problems of children were assessed using the Child Behavior Checklist/4-18 (CBCL).

Results: Of the preschool children with ADHD examined in this study, 19.8% (n=47) had unintentional injuries. Additionally, 17% (n=8) of the children, who experienced unintentional injuries had multiple unintentional injuries. While 68.1% of accidents occurred at home, 32.9% occurred outside of the home. The regression analysis conducted in this research revealed that male gender, higher CBCL externalizing scores, and separation of parents were associated with unintentional injuries in preschool children with ADHD.

Conclusions: The results of the present study emphasize the fact that in preschool children with ADHD, there may be signs heralding severe injuries, which may lead to morbidity.

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Klin Psikofarmakol Bul. 2014;24:S11.

EXECUTIVE FUNCTIONS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Yulaf Y.

ADHD is now increasingly recognized as developmental impairment of executive functions (EFs), the brain's cognitive management system. Executive function (EF) is a set of self-regulatory mechanisms for planning, organizing, directing, and managing cognitive processes and emotional responses. Children with ADHD have serious difficulties with EF in so many areas that some psychiatrists and psychologists have proposed renaming this disorder as EF disorder or EF deficit disorder. Many of the executive dysfunctions described earlier are found in children with ADHD including difficulties with priority and time management, planning and organization, initiating and completing tasks in a timely manner, difficulty shifting cognitive set, a high level of procrastination, forgetfulness and poor working memory. Barkley proposed the hypothesis that attention-deficit/ hyperactivity disorder (ADHD) symptoms may be due to EF deficits. In a meta-analysis of 83 studies, children and adolescents with ADHD exhibited significant deficits compared to those without ADHD in neuropsychological measures of EF; the EF domains that showed impairments included planning, spatial and verbal working memory, response inhibition, and vigilance. The ES is mediated by various networks in the frontal, parietal and occipital cortices, the thalamus and the cerebellum. It is linked through a series of circuits connecting every region of the central nervous system. The circuits originate in the dorsolateral prefrontal cortex (PFC) / orbitofrontal cortex (OFC), project through the striatum, synapse at the level of the globus pallidus, substantia nigra and the thalamus and finally return to the PFC forming closed loops. Each circuit regulates specific functions. The circuit that is most responsible for coordinating EF is located primarily in the frontal lobe. Functional imaging studies have implicated the PFC as the primary site of cortical activation during tasks involving EF. There is not yet full agreement regarding exactly which functions should be classified as EFs. But there is a general agreement that there were three core EFs: 1) inhibition [inhibitory control, including self-control (behavioral inhibition) and interference control (selective attention and cognitive inhibition)], 2) working memory (WM), and 3) cognitive sexibility (also called set shifting, mental sexibility, or mental set shifting and closely linked to creativity). From these, higher order EFs are built such as reasoning, problem solving, and planning. The therapeutic effect of the stimulants in ADHD is associated with their effects on the catecholamine system. Impaired neurotransmission causing executive dysfunction occurs because of abnormalities of the dopamine transporter. All currently approved pharmacotherapies for ADHD, both stimulants and non-stimulants, work by potentiating neurotransmission in the PFC. In ADHD subjects, single doses of the non-stimulant atomoxetine produced selective effects on response inhibition in the absence of effects on attention and memory. Although a norepinephrine reuptake inhibitor, atomoxetine acts primarily via presynaptic norepinephrine transporter blockade and elevates dopamine in selective cerebral regions.

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DEPRESSION AND ANXIETY LEVELS OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Karaman D, Durukan I, Kara K.

Objective: The aim of this study is to compare the depression and anxiety levels of children with attention deficit hyperactivity disorder (ADHD) with healthy controls.

Method: 47 children and adolescents with ADHD, aged between 7-12, who were evaluated according to DSM-IV criteria and 44 healthy children and adolescents, who matched to patients in terms of age and education levels were included in this study. Sociodemographic data form, parent-report of Children's Depression Inventory (PR-CDI), child-report Children's Depression Inventory (CR-CDI), Spence Children's Anxiety Scale (SCAS) were applied to the participants.

Results: It was revealed that depression and anxiety levels of children with ADHD were significantly higher than healthy controls. Both CDI Parents and CDI Self Depressive symptom levels were positively correlated with age and anxiety symptom levels. The panic/agoraphobia, separation anxiety, social phobia, generalized anxiety subscales' scores of SCAS in ADHD were significantly higher than healthy controls ($p<0.05$).

Conclusions: The comorbidity of depression and anxiety disorders was found to be frequent in ADHD samples. Clinicians should be careful about comorbid depression and anxiety disorder when they treat children and adolescents with ADHD.

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Klin Psikofarmakol Bul. 2014;24:S321.

ATOMOXETINE USE IN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND COMORBID TIC DISORDER IN PANDAS: TWO CASE REPORTS.

Karakoc-Demirkaya S, Demirkaya M, Akin E, et al.

The acronym PANDAS is for pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections, has 5 criteria: presence of OCD and/or tic disorder, prepubertal symptom onset, sudden onset or episodic course of symptoms, temporal association between streptococcal infections and neuropsychiatric symptom exacerbations, and associated neurological abnormalities. Atomoxetine is a type of non-stimulant medicine with a selective noradrenaline re-uptake inhibitor activity. Here we report two cases with diagnosis of Attention deficit hyperactivity disorder and PANDAS. Both of them have tics therefore; we preferred atomoxetine for ADHD instead of stimulant agents. Sydenham's chorea (SC) was excluded by neurological examination. Their clinical global impression (CGI) severity (S) and improvement (I) scores were obtained. Case 1 is a 10-year-old girl. She was hospitalized two months ago for streptococcal pneumonia and high fever for 5 days, motor tics started in the 2nd day of hospitalization. She was admitted to clinic with complaint of involuntary movements of head, mouth, eye blinking and irritability She was diagnosed as tic disorder as PANDAS phenomena and ADHD mixed type. Her laboratory findings were normal except ASO. Her ASO level was higher (777.7 U/L). Atomoxetine (starting dose 10 mg, final dose 35 mg/day) was administered. Her CGI-S was 6, CGI-I was 2 for both ADHD and tic disorder. Decreased appetite was seen as side effect, but she lost only 1 kg in 3 months. She was also on penicillin prophylaxis, her final ASO level is still high with level of 216 U/L. Case 2 is a 13 1/2 year old boy. He has been followed for acute rheumatic fever (ARF) since 5 years old. He has involuntary movements for 3 years. He is on depot penicillin prophylaxis. EEG, cranial MR and CT assessments, laboratory findings were normal. Neurologic examination ruled out SC. His cardiac examination showed minimal mitral valve regurgitation. He was diagnosed with both PANDAS and ARF. Before admission to our clinic, he was treated with haloperidol and risperidone unsuccessfully. His mother and teachers complained about ADHD symptoms. Atomoxetine was administered (starting from 10 to 60 mg/day), his CGI-S was 5 and CGI-I for ADHD is 2 and for tics 3. Therefore aripiprazole (5 mg/day) was added to his treatment. Now his CGI-I is 2 for tics. Nausea, dizziness were seen as side effects. Here we present two cases with diagnosis of ADHD and tic disorder following by PANDAS. Instead of stimulants, atomoxetine is preferred for ADHD comorbid with tic disease. Our first case is successfully treated with atomoxetine whereas the other showed little improvement. Tic disorder was of acute type in the first case but chronic in the second case. Drug metabolisms may differ according to age and gender, leading to different effects on subjects.

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Klin Psikofarmakol Bul. 2014;24:S232-S233.

WHAT IS THE EFFECT OF ATOMOXETINE ON EPILEPSY IN A BOY WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER?

Yucel N, Yucel A.

Attention deficit-hyperactivity disorder (ADHD) is a prevalent neuropsychiatric disorder that occurs in childhood and ongoing in adulthood. Atomoxetine is a potent, specific, norepinephrine reuptake inhibitor that has no other affinity on any other neuronal reuptake pumps used in the treatment of ADHD, alternatively. High risks in terms of epileptic seizures have been observed in patients with ADHD. Here, we present the effect of atomoxetine on epilepsy in a boy with ADHD. A 10-year-old boy was admitted to our outpatient clinic with complaints of negligence, short temper, inattention and academic failure in the school. In his psychiatric examination, he was conscious, oriented and cooperated with a suent speech. He had concentration problems, hyperactivity and impulsivity. There was no hallucination and delusion. His IQ testing, physical examination and laboratory results were in normal range. His condition was compatible

with ADHD combined type according to DSM-V. He also had history of epilepsy for 4 years. The valproic acid 750 mg/day has been used for 3 years. His last seizure had been 2 month ago thus levetiracetam 600 mg/day was added his treatment. There was no history of psychiatric treatment. Atomoxetine, 25 mg/day, was initiated; and the dose was titrated up to 40 mg/day. The patient was invited to medical examination monthly. In the first month of follow-up period, the symptoms of attention deficiency decreased and school achievement improved. Furthermore, seizure was not observed in the subsequent year after the treatment of Atomoxetine. Follow up of patient is ongoing and he tolerated the medication well. Comorbidity of epilepsy is a condition that requires attention in terms of treatment. The threshold of seizures should be paid attention by the physicians. In the previous studies, the coexistence of ADHD and epilepsy was emphasized. In another study, evidence that increased risk of seizures is related with stimulants was demonstrated. Although there are the limited information about the treatment of atomoxetine in ADHD accompanied with epilepsy, based on our case, atomoxetine may be a safe treatment option in ADHD accompanied with epileptic comorbidity. However, this treatment option should be supported with further and well-attended multicenter studies.

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Klin Psikofarmakol Bul. 2014;24:S121-S122.

ATTACHMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER TO PEERS.

Dogan H, Oztop D, Olguner-Eker O, et al.

Objectives: Attention deficit hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity and impulsivity, which is observed in 3-7% of the children at school age. It is associated to significant disruption in developmental, cognitive, and academic domains. It manifests as reduced self-confidence, unhappiness, failure, impaired interpersonal relationships as a result of deficits in almost every domain of children's life and adversely affects mental wellbeing of children. Attachment is a condition that affects both individual's inner self and affiliations. There are studies reporting that there was insecure attachment in patients with ADHD rather than secure attachment. In this study we are going to see the effects of ADHD on peer attachment.

Method: Among patients presented to Child and Adolescent Psychiatry Department of Erciyes University, Medicine School, 50 patients aged 11-17 years, who were diagnosed as ADHD and had no concurrent psychiatric diagnosis or chronic disease were included to the study. Age- and sex-matched 50 healthy children and adolescent were employed as control group. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) interview and Wechsler Intelligence Scale for Children-Revised (WISC-R) was applied to all cases included. Parents were asked to complete sociodemographic data sheet about their children and Turgay DSM-IV-based child and adolescent behavior disorders screening and rating scale. Relationship Scale Questionnaire and Parental and Peer Attachment Scale were applied to patient and control groups.

Results: The mean age of groups was 12.78(plus or minus)1.67. There were 15 girls and 35 boys in the groups. 37 children were in secondary school and 13 children were in high school in ADHD group. In control group 38 of them were in secondary school and 12 of them were in high school. The mean score for dismissing attachment is 4.41(plus or minus)1.19, secure attachment is 3.99(plus or minus)1.06, fearful attachment is 3.68(plus or minus)1.45, and preoccupied attachment is 3.55(plus or minus)0.93 in ADHD group. In control group the mean score for secure attachment is 4.31(plus or minus)1.18, dismissing attachment is 3.99(plus or minus)1.09, fearful attachment is 3.69(plus or minus)1.34, and preoccupied attachment is 3.41(plus or minus)1.37.

Conclusion: In our study, insecure attachment to peers was found to be significantly higher in ADHD group. The highest rate was found in dismissing attachment to peers in both girls and boys. In some researches it has reported that patients with ADHD had insecure attachment whereas healthy adolescents had secure attachment. In conclusion, although ADHD is defined by disorders in cognitive and executive functioning, it is thought that social limitations were observed in children and adolescents with ADHD; that this difficulty in regulation is resected in relations to both peers and parents; and, thus it shares common

etiological factors with insecure attachment; and that they predispose to development of each other. Further studies with larger sample size are needed in this topic.

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Klin Psikofarmakol Bul. 2014;24:S123.

ATTACHMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER TO MOTHER.

Dogan H, Oztop D, Olguner-Eker O, et al.

Objectives: Attention deficit hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity and impulsivity, which is observed in 3-7% of the children at school age. It is associated to significant disruption in developmental, cognitive, and academic domains. It manifests as reduced self-confidence, unhappiness, failure, impaired interpersonal relationships as a result of deficits in almost every domain of children's life and adversely affects mental wellbeing of children. Attachment is a condition that affects both individual's inner self and affiliations. There are studies reporting that there is insecure attachment in patients with ADHD rather than secure attachment. In this study we are going to see the effects of ADHD on mother attachment.

Method: Among patients presented to Child and Adolescent Psychiatry Department of Erciyes University, Medicine School, 50 patients aged 11-17 years, who were diagnosed as having ADHD and had no concurrent psychiatric diagnosis or chronic disease were included in the study. Age- and sex-matched 50 healthy children and adolescent were employed as control group. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) interview and Wechsler Intelligence Scale for Children-Revised (WISC-R) was applied to all cases included. Parents were asked to complete sociodemographic data sheet about their children and Turgay DSM-IV-based child and adolescent behavior disorders screening and rating scale. Parental and Peer Attachment Scale was applied to patient and control groups.

Results: The mean age of groups was 12.78(plus or minus)1.67. There were 15 girls and 35 boys in the groups. The education level of control group mothers is better than ADHD group and ADHD group mothers had more psychiatric disorders than control group. The mean score of attachment to mother in ADHD group was 69, and 71 in control group. The mean score of girls in ADHD group was 69 and boys' was 66. In control group the mean score of girls is 70, and 72 for the boys.

Conclusion: When compared to controls, it was found that cases in ADHD group attached to mothers less safely. It was found that mothers of patients with ADHD had more negative reactive behavior control and had less motherhood pattern in a study. Therefore these negative behaviors affect child's attachment and quality of attachment to mother. Girls attached more safely to their mothers than boys in ADHD group. In a research it was found that boys with ADHD or conduct disorder had insecure attachment. In the control group, boys attached more safely than girls. In conclusion, although ADHD is defined by disorders in cognitive and executive functioning, it is thought that social limitations were observed in children and adolescents with ADHD; that this difficulty in regulation was resected in relations to both peers and parents; and, thus it shares common etiological factors with insecure attachment; and that they predispose to development of each other. Further studies with larger sample size are needed in this topic.

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Klin Psikofarmakol Bul. 2014;24:S268-S269.

RISPERIDONE-INDUCED PENILE ERECTION IN A PREPUBERTAL CHILD: A CASE REPORT.

Uygur B.

Attention deficit hyperactivity disorder (ADHD) is a heterogeneous behavioral syndrome resulting with significant functional impairment and characterized by the core symptoms of hyperactivity, impulsivity and inattention. Conduct disorder (CD) consists of a repetitive and persistent pattern of behaviors in which the basic rights of others and major age-appropriate societal norms or rules are violated. Risperidone, a benzisoxazole derivative, binds with high affinity to 5-HT2, dopamine D2, and (alpha)1-adrenergic receptors. This treatment has been shown to be safe and effective for both conduct disorder and comorbid ADHD in children. In this case report, a 4-year-old male who developed penile erections after using

risperidone is discussed. A 4-year-old male patient was diagnosed as CD and ADHD in another clinic and risperidone was started with an initial dose of 0.5 mg/day, with increments of 0.5 mg every seven days until 3 mg/daily (mean maximum dosage of 0.2 mg/kg/day), when a therapeutic response was reached. After five months, the daily dose was lowered to 1.5 mg/daily because of satisfactory clinical response. Two weeks after the dosage change, the patient started to suffer from penile erection episodes. These episodes were 5-6 erection episodes frequently in the daytime, lasting about five minutes and were not painful. The patient was not taking another medical agent other than risperidone. No other related medical condition, which will cause penile erection, was detected. After detailed examination, penile erections were thought to be related with risperidone. With the discontinuation of the drug, symptoms of penile erections disappeared and the child fully recovered from the adverse effect. DSM-V defines ADHD with three subtypes: a combined subtype in which all three-core signs are present in the last six months; a predominantly inattentive subtype in which only inattention is present in the last six months and a predominantly hyperactive-impulsive subtype in which only hyperactivity and impulsiveness are present in the last six months. In the DSM-5, CD is defined based on the presence of three of 15 criteria that should have been present in the last 12 months, and of which one must have been present in the past 6 months. Risperidone has been shown to be safe and effective for both conduct disorder and comorbid ADHD in children. Risperidone is associated with hyperprolactinemia, sexual dysfunction and priapism. The mechanism of the prolonged erection is thought to be with alpha-1 adrenergic blockage. Most of the literature about this adverse effect is from adult population and the data from pediatric population is very limited. The pediatric cases are frequently on poly-pharmacy. In our case, he was on mono-pharmacy and interestingly in the improvement stage of the treatment. To our knowledge, this is the smallest pediatric patient in literature with penile erection due to risperidone treatment, especially while the daily dosage was lowered. Therefore, although risperidone is reported to be safe and effective in the pediatric group, clinicians should be careful about this undesirable adverse effect in every stage of the treatment.

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EVALUATION OF MIR18A-5P, MIR22-3P, MIR24-3P, MIR106B-5P, MIR107, MIR125B-5P AND MIR155A-5P LEVELS IN CHILD AND ADOLESCENT PATIENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Kandemir H, Erdal ME, Selek S, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is one of the most prevalent childhood disorders. Although disorders etiology and pathogenesis have remained unknown, several theories about ADHD development have been proposed and many researchers believe that it might be caused by both genetic and environmental factors. In this study we evaluated miR18a-5p, miR22-3p, miR24-3p, miR106b-5p, miR107, miR125b-5p and miR155a-5p levels in child and adolescent ADHD patients.

Method: The research sample consisted of a group of 52 ADHD patients, and 52 healthy volunteer controls. Total RNA was extracted from Peripheral Whole Blood using Tri-Reagent. The hsa-miR-26b-5p was used as endogenous control microRNA. The mixed RNAs generated from the control group were used as a Reference RNA sample.

Results: There was no significant difference in age and sex between the two groups ($p>0.05$). Mirna 18a-5p, 22-3p, 24-3p, 106b-5p and 107 levels were statistically significantly decreased in ADHD patients ($p<0.05$). Mirna 155a-5p levels were increased in patients group ($p<0.05$). In the ROC curve Mir 107 levels under 0.4480 were highly predictive (PPV: 70.6) for the disease state and negative predictive value was 86,5%.

Conclusion: We found decreased mir 18a-5p,mir 22-3p, mir 24-3p, mir 106b-5p and mir 107 levels in patients. Previous studies examined relationship between miR-18a and reported this can be an important susceptibility mechanism for stress- related disorders. Dysregulation of mir22, mir 106b, mir107and mir24 in schizophrenia, bipolar disorders and autism has been reported. MiR-107 also has been studied in traumatic brain injury and neurodegenerative disease and fronto temporal dementia. We found increased mir 155a-5p in ADHD patients. mir155 dysregulation in depression patients and also Increased mir155 levels during lithium treatment has been reported. There could be a close relationship between levels of circulating miRNAs and ADHD. If we could understand how the signaling pathways were arranged by

miRNAs, impact on CNS development, function and pathology, this could improve our knowledge about ADHD etiology and treatment.

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Klin Psikofarmakol Bul. 2014;24:S200.

USAGE OF ATOMOXETINE FOR ENCOPRESIS AND ATTENTION DEFICIT-HYPERACTIVITY DISORDER.

Yucel N, Yucel A.

Atomoxetine, an effective treatment alternative of attention deficit-hyperactivity disorder (ADHD), is a selective presynaptic norepinephrine reuptake inhibitor. Also atomoxetine is shown as one of the options in the treatment of nocturnal enuresis and encopresis . A case with encopresis and ADHD will be presented in terms of atomoxetine treatment. A 7-year-old boy was admitted to our outpatient clinic with complaints of restlessness, forgetfulness, getting bored quickly, academic failure in the school and soiling his underwear. In his psychiatric examination; he was conscious, oriented, his cooperation was suent and understandable. He had concentration problems, hyperactivity and impulsivity. There was no hallucination and delusion. He also had encopresis occurring 5 to 6 times a week for 1 year. His intelligence level was within normal limits according to psychiatric examination and IQ testing. The diagnosis was compatible with ADHD combined type and encopresis with constipation and oversow incontinence according to DSM-V. There was no history of psychiatric treatment. First of all, for the treatment of encopresis, behavioral intervention was suggested, but he and his parents did not adapt the recommendations. Atomoxetine, 18 mg/day, was initiated; and the dose was titrated up to 40 mg/day. The patient was invited to medical examination monthly. In the first month of follow-up period, the symptoms of attention deficiency, impulsivity decreased and school achievement improved. Furthermore, encopresis was observed only three times in a month. At the end of fifth month, he tolerated the medication well, and there was no encopresis. Encopresis is described as the repeated passage of feces into inappropriate places. The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition describes two subtypes as nullwith constipation and oversow incontinencenull and nullwithout constipation and oversow incontinence.null The relationship between encopresis and attention difficulties, disruptive behavior, academic failure was declared. Coexistence of encopresis and ADHD symptoms are observed frequently. In the previous study, the efficacy of imipramine was demonstrated on encopresis. In addition, uses of atomoxetine and methylphenidate treatments were shown in two children with encopresis and ADHD. In our case, we observed the effects of atomoxetine on encopresis and ADHD however in terms of this observation needs to be studied with further studies.

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Klin Psikofarmakol Bul. 2014;24:S319.

COMBINED METHYLPHENIDATE AND ATOMOXETINE THERAPY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER; A RETROSPECTIVE STUDY.

Yuzuguldu O, Atar B, Ozbaran B, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder, which is characterized by hyperactivity, impulsivity and lower sustained attention. Most of the symptoms of ADHD resolved with pharmacotherapy. ADHD treatment consists stimulants (methylphenidate) and non-stimulants (atomoxetine). Combined therapy administrated in patients which symptoms doesn't resolve with monotherapy or couldn't use effective treatment dose because of adverse effects. Our purpose in this study is investigated efficiency, safety and tolerability of combined therapy.

Method: We included 12 patients, which apply to Ege University Child and Adolescent Psychiatry Department Disruptive Behavior Disorders Clinic and diagnosed with ADHD and using combined therapy. These patients' files searched retrospectively. We use Turgay ADHD scale, child behavior checklist (CBCL) for ADHD diagnosis, clinic global impression scales (CGI-S and CGI-I) for clinic evaluation. To evaluate patients mental capacity we use Wechsler Intelligence Scale for Children (WISC-R).

Results: We evaluate 12 patient with ADHD diagnosis and using combined therapy. Mentally retarded patients don't included. Age group is between 7 and 17. Current axis I disorders among participants were ADHD only (n=7, 58.3%), ADHD with conduct disorder (n=2, 16.7%), ADHD with other psychiatric

conditions (n=3, 25%). Commonest side effects in our patients are irritability (n=5, 41.6%), anorexia (n=3, 25%), palpitations (n=2, 16.7%), headache (n=1, 8.3%), no side effect (n=2, 16.7%). We found significant improvement in ADHD symptoms in 9 out of 12 patients (CGI-I point=2), minimal improvement in 2 patients (CGI-I point= 3), no change in 1 patient (CGI-I point=4).
Conclusion: Commonest side effects in our patients are irritability, headache, anorexia and palpitations. These side effects and their frequencies found similar with monotherapy. 9 out of this 12 patients show significant improvement in their symptoms, we found this improvement statistically important which means combined therapy enhance the effectiveness of monotherapy. These results about efficiency and safety are consistent with findings in recent literature.

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Klin Psikofarmakol Bul. 2014;24:S46.

IMPAIRMENTS IN SOCIAL SKILLS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CASE REPORT.

Ayaz AB.

In Attention deficit hyperactivity disorder (ADHD), the symptoms of attention deficit, hyperactivity and impulsivity occur and it is thought that this disorder insuences the school age children at the rate of 3-5% throughout the world. ADHS leads to loss of functioning in cognitive, academic, family and professional areas. Another area impaired in ADHS is social functioning. Impairment in social functionality mostly emerges in the form of refusal by peers and having consicts with other children and adults. In addition, impairment in social functioning is important for short and long-term unfavorable prognosis of ADHD. 5 year old boy were referred to a child and adolescent psychiatry clinic in 2009 with the symptoms of hyperactivity, temper tantrums, acting as the opposite sex, and impairments in social skills. He was assessed by a semi-structured interview based on DSM-IV criteria, and diagnosed as ADHD-combined subtype. The impairments in social functioning and the treatment modalities between 2009 and 2014 will be discussed in this section. The implementation of interventional programs in the involved areas such as early social skill training for preventing impairment in social functioning may help to alleviate the effect of disorder in adulthood. The efficiency of family training, judicious drug treatment and intervention programs should be increased. In interventions, comorbid disorders as well as ADHD should be taken into account and if necessary, supplementary treatment directed to these disorders should be added to the program.

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Klin Psikofarmakol Bul. 2014;24:S76.

INTERACTION OF BIOLOGICAL RHYTHM VARIABLES AND INTERNET ADDICTION IN PATIENTS WITH ADHD.

Soyata AZ, Gunduz Y, Kinay D, et al.

Objectives: Internet addiction is an ever-increasing problem among adolescents and young adults and it impairs life quality and functionality. Although a relationship between inattention/ hyperactivity symptoms and internet addiction has been reported, there is no previous study that assessed the contribution of biological rhythm variables to ADHD and internet addiction comorbidity. In this study, we hypothesized that internet and social media addictions are frequent in adult ADHD patients and this comorbidity is associated with impairment in biological rhythm variables. We also hypothesized that eveningness chronotype is frequent among adult ADHD patients and this trait is associated with Internet addiction.
Method: Sixty adult subjects, who were being followed at the Adult ADHD outpatient unit, were included in this study. They were administered a sociodemographic form, Adult ADHD Self Report Scale (ASRS), Biological Rhythm Interview of Assessment In Neuropsychiatry (BRIAN), Internet Addiction Test (IAT), Bergen Facebook Addiction Scale and Motives For Using Facebook Scale. Internet-addicted group consisted of patients, who had 50 or more score in IAT. Eveningness group consisted of patients whose sum of nineteenth and twenty first items in BRIAN were five or more. Comparisons were made between internet addicted/non-addicted, eveningness/morningness chronotype groups with Chi square and Mann Whitney U tests. Correlations were calculated with Spearman test.
Results: Mean age of the whole sample was 22.9 (75% male). 20.9% of the sample was grouped as internet-addicted. 47.7% of the sample had eveningness chronotype. Total ASRS score was correlated

with total BRIAN score (r=0.70, p=0.001) and its subscales, internet (r=0.50, p=0.001) and Facebook (r=0.40, p=0.009) addiction scores. Inattention (p=0.038), hyperactivity (p=0.021) and total ASRS (p=0.005) scores were higher in internet addicted group. Facebook addiction scores were also higher in internet-addicted group (p=0.02). Internet addiction score was correlated with eating, activity and social subscales of BRIAN. Internet addiction scores were correlated with inattention (r=0.43, p=0.004), hyperactivity (r=0.42, p=0.004) and Facebook addiction (r=0.48, p=0.001). Total BRIAN score (p=0.003) and subscales were higher in eveningness chronotype group. No differences were found in motives for using Facebook between groups.
Conclusion: To our knowledge, this is the first study assessing the relationship between ADHD, internet addiction, Facebook addiction and biological rhythm variables. We found 20.9% prevalence of internet addiction in adult ADHD patients. Impairment in biological rhythm variables was associated with both ADHD and internet addiction. Assessing and targeting internet and social media addiction may improve treatment response and functionality in adult ADHD patients.

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Klin Psikofarmakol Bul. 2014;24:S249.

PARENTING STYLES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Cop E, Cengel-Kultur E, Senses-Dinc G.

Objective: The aim of this study was to investigate mothering in a sample of 58 children with ADHD, and 30 without ADHD and relation between ADHD symptoms, child's characteristics, ADHD subtype, comorbidity and parenting styles.
Methods: All ADHD and comorbid psychiatric diagnoses were assessed by semi-structured standardized interviews. Children reported on the Parenting Style Inventory and their mothers reported on The Parental Attitude Research Instrument about mother's parenting style. Conners' Teacher and Parent Rating Scales were used to assess ADHD symptom severity.
Results: The results showed that ADHD group obtained less affection/care and more control from the mothers than those without ADHD. Child's hyperactivity and oppositional defiant behavior symptoms were significantly correlated with decreased maternal affection/care and increased maternal controls; child's conduct problems were significantly correlated with maternal overprotection.
Conclusion: Our findings suggested that childhood ADHD diagnosis was associated with impaired maternal process.

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Klin Psikofarmakol Bul. 2014;24:S121.

ATTACHMENT OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER TO FATHER.

Dogan H, Oztop D, Ozmen S, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is characterized by inattention, hyperactivity and impulsivity, which is observed in 3-7% of the children at school age. It is associated to significant disruption in developmental, cognitive, and academic domains. It manifests as reduced self-confidence, unhappiness, failure, and impaired interpersonal relationships as a result of deficits in almost every domain of children's life and adversely affects mental wellbeing of children. Attachment is a condition that affects both individual's inner self and affiliations. There are studies reporting that there was insecure attachment in patients with ADHD rather than secure attachment. In this study we are going to see the effects of ADHD on father attachment.
Method: Among patients presented to Child and Adolescent Psychiatry Department of Erciyes University, Medicine School, 50 patients aged 11-17 years, who were diagnosed as ADHD and had no concurrent psychiatric diagnosis or chronic disease were included in the study. Age- and sex-matched 50 healthy children and adolescent were employed as control group. Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version (K-SADS-PL) interview and Wechsler Intelligence Scale for Children-Revised (WISC-R) were applied to all cases included. Parents were asked to complete sociodemographic data sheet about their children and Turgay DSM-IV-based child and

adolescent behavior disorders screening and rating scale. Parental and Peer Attachment Scale was applied to patient and control groups.
Results: The mean age of groups is 12.78(plus or minus)1.67. There were 15 girls and 35 boys in the groups. There was no differences in sociodemographic data sheet between two groups' fathers (for example education, job, psychiatric disorder..). The mean score of attachment to father in ADHD group is 66, and 69 in control group. The mean score of both the girls and the boys in ADHD group is was 66. In control group the mean score of girls was 68 and 70 for the boys.
Conclusion: When compared to controls, it was found that cases in ADHD group attached to fathers less safely. In ADHD group, girls and boys attached equally safely to their fathers. In a research it was found that fathers of patients with ADHD had more negative reactive behavior control and less fatherhood pattern. In the control group, boys attached more safely to their fathers than girls. In conclusion, although ADHD is defined by disorders in cognitive and executive functioning, it is thought that social limitations were observed in children and adolescents with ADHD; that this difficulty in regulation was resected in relations to both peers and parents; and, thus it shares common etiological factors with insecure attachment; and that they predispose to development of each other. Further studies with larger sample size are needed in this topic.

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MOOD DYSREGULATION IN CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER: ITS EFFECTS ON THE RESPONSE TO METHYLPHENIDATE TREATMENT AND FUNCTIONALITY .

Usta BM, Karabekiroglu K, Yuce M.

Objective: Attention deficit hyperactivity disorder (ADHD) is one of the most frequent psychiatric disorders of childhood. ADHD, which is a multifactorial and clinically heterogeneous disease, leads to socioeconomic burden and undesirable academic and occupational results. Other psychiatric disorders and mood problems are likely to accompany a substantial proportion of children admitted to a clinic with a diagnosis of ADHD, and this enhances the severity of the clinical picture. It is a current debate whether ADHD and non-cyclical severe irritability is a variant of a development bipolar disorder or not. However, epidemiological and phenomenological data are needed about clinical risks, prognosis markers, protective factors and treatment options. In this study, we aimed to investigate the differences between ADHD with and without mood symptoms in terms of functionality and treatment outcome.
Methods: This study is a follow-up study with a naturalistic design. Patients who were diagnosed ADHD and were started methylphenidate treatment (n=44, mean age: 10.8) were included in the study. The irritable/dysphoric group (group with mood dysregulation) is defined as children who got 8 points and more from nulloppositional defiantnull portion of DSM-IV-Based Screening and Rating Scale for Child and Adolescent Behavior Disorders (CABD-S) and got points between 12 -18 in Child Depression Inventory (CDI). Functionality is measured by three Likert-type items (1-5 for each) including academic, social and behavioral functionality. Clinical Global Impression (CGI) were used to determine the clinical severity of ADHD. Follow-up measurements included the CGI-Severity, Functionality in the 6-12 weeks of treatment.
Results: ADHD + irritable/dysphoric group consisted of 11 children (9 boys, 2 girls, mean age: 10.9) and 33 children (18 boys, 15 girls, mean age: 10.8) in ADHD group. Functionality scores were significantly lower in the ADHD + irritable/dysphoric group compared to the control group (social: 2.5 vs. 3.0; behavioral: 2.7 vs. 3.3; academic 2.1 vs. 2.6) in the first clinical application ($p<0,05$). However, CGI-S scores were not significantly different (irritable/dysphoric group: 5.7 vs. control: 5.6). Methylphenidate was used at a dose of 24.7 mg/day on average. In the follow-up CGI-S scores were found to be significantly different (irritable/dysphoric group: 4.4 vs. control: 3.9) ($p<0.05$).
Conclusion: Comorbidity is a major problem in the clinical practice with ADHD patients. Especially irritability, defiance and depressive symptoms even without significant mood disorder diagnosis may interfere with treatment efficacy and have another burden for functionality of the patient. In this clinical sample with children, who were diagnosed with ADHD, we demonstrated that the irritability/dysphoria symptoms might decrease the level of social, behavioral and academic functionality and the response to

methylphenidate treatment. More comprehensive assessments in terms of mood dysregulation in ADHD patients are needed in further studies.

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Klin Psikofarmakol Bul. 2015;25:93-94.

THE ROLE OF ATOMOXETINE AND SYMPATHETIC PATHWAYS IN ENCOPRESIS WITH ADHD.

Yucel A, Yucel N, Oral E.

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Kobe J Med Sci. 2015;61:E19-E26.

ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD): AGE RELATED CHANGE OF COMPLETION TIME AND ERROR RATES OF STROOP TEST.

Thursina C, Rochmah MA, Kesumapramudya ND, et al.

BACKGROUND: Attention Deficit/Hyperactivity Disorder (ADHD) is a common neurobehavioral problem in children throughout the world. The Stroop test has been widely used for the evaluation of ADHD symptoms. However, the age-related change of the Stroop test results has not been fully clarified until now.
METHODS: Sixty-five ADHD and 70 age-matched control children aged 6-13 years were enrolled in this study. ADHD was diagnosed based on DSM-IV criteria. We examined the completion time and error rates of the Congruent Stroop test (CST) and Incongruent Stroop test (IST) in ADHD and control children.
RESULTS: No significant difference was observed in the completion time for CST or IST between the ADHD and control children at 6-9 years old. However, ADHD children at 10-13 years old showed significantly delayed completion time for the CST and IST compared with controls of the same age. As for the error rates of the CST and IST, ADHD and control children at 6-9 years old showed no difference. However, error rates of CST and IST in the ADHD children at 10-13 years were significantly higher than those of control of the same age.
CONCLUSIONS: Age may influence the results of Stroop test in ADHD children. For the ages of 10-13 years old, the Stroop test clearly separates ADHD children from control children, suggesting that it may be a useful screening tool for ADHD among preadolescent children.

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L'Encéphale: Revue de psychiatrie clinique biologique et thérapeutique. 2015 Feb;41:56-61.

COMORBIDITÉ PSYCHIATRIQUE AU TROUBLE DÉFICIT DE L'ATTENTION/HYPERACTIVITÉ EN POPULATION SCOLAIRE DANS LA RÉGION DE SFAX. TUNISIE : ÉTUDE TRANSVERSALE. = PSYCHIATRIC COMORBIDITY RELATED TO CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AT SCHOOLS IN SFAX, TUNISIA.

Khemakhem K, Ayedi H, Moalla Y, et al.

Introduction: Attention deficit hyperactivity disorder (ADHD) is a prevalent behavioral disorder particularly noticed among school children. It is often associated with other psychological troubles at the origin of an additional difficulty that has to be overcome.
Objective: Our research's aim was to study the comorbidity of school-aged children diagnosed with ADHD in Sfax, Tunisia.
Subjects and methods: A cross-sectional descriptive study was carried out from 1st April 2008 to 1st October 2008. Five hundred and thirteen pupils aged between 6 and 12, from primary arbitrarily chosen schools from Sfax were subjected to this study.
Measurements were carried out in two steps: parents and teachers of each child filled in separately Conners questionnaire, then children with a score in subscales inattention, hyperactivity impulsivity higher than 70 were selected for psychiatric interview that was intended to confirm or to invalidate the ADHD diagnosis and the possible comorbid diagnosis. The diagnoses were made according to DSM-IV-TR.
Results: We have noticed that 109 pupils exhibited at least one pathological score on the Conners questionnaire. After interviewing these 109 pupils, the results have shown that 51 among them fulfilled criteria of ADHD. Prevalence of ADHD was found to be 9.94 %. About 72.54 % of children with ADHD had

one or more comorbid disorder: learning disabilities (23.52 % of cases), anxiety disorder (31.37 % of cases), oppositional defiant disorder in (15.68 % of cases), mood disorder (3.92 % of cases), enuresis (13.72 % of cases) and slight mental retardation (1.95 % of cases).
Conclusion: We can say that this study has shown that ADHD school children's psychiatric comorbidity is similar to any other previous study.

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Med Eng Phys. 2015;37:416-23.
MEG ANALYSIS OF NEURAL DYNAMICS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH FUZZY ENTROPY.
Monge J, Gomez C, Poza J, et al.
The aim of this study was to analyze the neural dynamics in attention-deficit/hyperactivity disorder (ADHD). For this purpose, magnetoencephalographic (MEG) background activity was analyzed using fuzzy entropy (FuzzyEn), an entropy measure that quantifies signal irregularity, in 13 ADHD patients and 14 control children. Additionally, relative power (RP) was computed in conventional frequency bands (delta, theta, alpha, beta and gamma). FuzzyEn results showed that MEG activity was more regular in ADHD patients than in controls. Moreover, we found an increase of power in delta band and a decrease in the remaining frequency bands. Statistically significant differences (p-values <0.05; nonparametric permutation test for multiple comparisons) were detected for FuzzyEn in the posterior and left temporal regions, and for RP in the posterior, anterior and left temporal regions. Our results support the hypothesis that ADHD involves widespread functional brain abnormalities, affecting more areas than fronto-striatal circuits, such as the left temporal and posterior regions.

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Neurol Res Int. 2015;2015.
METHYLPHENIDATE EFFICACY: IMMEDIATE VERSUS EXTENDED RELEASE AT SHORT TERM IN MEXICAN CHILDREN WITH ADHD ASSESSED BY CONNERS SCALE AND EEG.
Durand-Rivera A, Alatorre-Miguel E, Zambrano-Sanchez E, et al.
Attention deficit hyperactivity disorder (ADHD) affects 5-6% of school aged children worldwide. Pharmacological therapy is considered the first-line treatment and methylphenidate (MPH) is considered the first-choice medication. There are two formulations: immediate release (IR) MPH and long-acting (or extended release) formulation (MPH-ER). In this work, we measure the efficacy of treatment for both presentations in one month with Conners' scales and electroencephalography (EEG). Results. for IR group, in parents and teachers Conners test, all items showed significant differences, towards improvement, except for teachers in perfectionism and emotional instability. For ER group in parent's Conners test, the items in which there were no significant differences are psychosomatic and emotional instability. For teachers, there were no significant differences in: hyperactivity and perfectionism. Comparing the Conners questionnaires (parents versus teachers) we find significant differences before and after treatment in hyperactivity, perfectionism, psychosomatics, DSM-IV hyperactive-impulsive, and DSM-IV total. In the EEG the Wilcoxon test showed a significant difference ($P < 0.0001$). As we can see, both presentations are suitable for managing the ADHD and have the same effect on the symptomatology and in the EEG.

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Pediatrics. 2015;135:e994-e1001.
PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.
Thomas R, Sanders S, Doust J, et al.
BACKGROUND AND OBJECTIVE: Overdiagnosis and underdiagnosis of attention-deficit/hyperactivity disorder (ADHD) are widely debated, fueled by variations in prevalence estimates across countries, time, and broadening diagnostic criteria. We conducted a meta-analysis to: establish a benchmark pooled prevalence for ADHD; examine whether estimates have increased with publication of different editions of

the Diagnostic and Statistical Manual of Mental Disorders (DSM); and explore the effect of study features on prevalence.
METHODS: Medline, PsycINFO, CINAHL, Embase, and Web of Science were searched for studies with point prevalence estimates of ADHD. We included studies of children that used the diagnostic criteria from DSM-III, DSM-III-R and DSM-IV in any language. Data were extracted on sampling procedure, sample characteristics, assessors, measures, and whether full or partial criteria were met.
RESULTS: The 175 eligible studies included 179 ADHD prevalence estimates with an overall pooled estimate of 7.2% (95% confidence interval: 6.7 to 7.8), and no statistically significant difference between DSM editions. In multivariable analyses, prevalence estimates for ADHD were lower when using the revised third edition of the DSM compared with the fourth edition (P =.03) and when studies were conducted in Europe compared with North America (P =.04). Few studies used population sampling with random selection. Most were from single towns or regions, thus limiting generalizability.
CONCLUSIONS: Our review provides a benchmark prevalence estimate for ADHD. If population estimates of ADHD diagnoses exceed our estimate, then overdiagnosis may have occurred for some children. If fewer, then underdiagnosis may have occurred.

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Pediatrics. 2015;135:e858-e867.

COLLABORATIVE CARE FOR CHILDREN WITH ADHD SYMPTOMS: A RANDOMIZED COMPARATIVE EFFECTIVENESS TRIAL.

Silverstein M, Hironaka LK, Walter HJ, et al.

OBJECTIVES: Although many attention-deficit/hyperactivity disorder (ADHD) care models have been studied, few have demonstrated individual-level symptom improvement. We sought to test whether complementing basic collaborative care with interventions that address common reasons for symptom persistence improves outcomes for children with inattention and hyperactivity/impulsivity.
METHODS: We conducted a randomized comparative effectiveness trial of 2 care management systems for 6- to 12-year-old children being evaluated for ADHD (n = 156). All participants received care management with decision support. Care managers in the enhanced care arm also were trained in motivational and parent management techniques to help parents engage in their child's treatment, address their own mental health needs, and manage challenging child behaviors. We used multivariable models to assess inattention, hyperactivity/impulsivity, oppositionality, and social skills over 1 year.
RESULTS: Both treatment arms generated guideline concordant diagnostic processes in 94% of cases; 40% of children had presentations consistent with ADHD. For the entire sample, there were no differences in symptom trajectories between study arms; mean differences in change scores at 12 months were -0.14 (95% confidence interval -0.34 to 0.07) for inattention; -0.13 (-0.31 to 0.05) for hyperactivity/impulsivity; -0.09 (-0.28 to 0.11) for oppositionality; and 3.30 (-1.23 to 7.82) for social skills. Among children with ADHD-consistent presentations, enhanced arm participants experienced superior change scores for hyperactivity/impulsivity of -0.36 (-0.69 to -0.03), oppositionality -0.40 (-0.75 to -0.05), and social skills 9.57 (1.85 to 17.28).
CONCLUSIONS: Among children with ADHD-consistent presentations, addressing barriers to engagement with care and challenging child behaviors has potential to improve the effectiveness of collaborative care.

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Pediatrics. 2015 Mar;135:452-59.

MENTAL HEALTH OF EXTREMELY LOW BIRTH WEIGHT SURVIVORS IN THEIR 30S.

Van Lieshout RJ, Boyle MH, Saigal S, et al.

OBJECTIVE: To determine the risk for psychiatric disorders among extremely low birth weight (ELBW) survivors in their early to mid-30s and to determine whether those born small for gestational age or those exposed to a full course of antenatal corticosteroids (ACS) were at particularly high risk.

METHODS: A prospective, longitudinal, population-based cohort of 84 ELBW survivors and 90 normal birth weight (NBW) control participants born in Ontario, Canada from 1977 to 1982 were assessed by interviewers naive to birth weight status using the Mini-International Neuropsychiatric Interview.
RESULTS: ELBW survivors had lower odds of an alcohol or substance use disorder but higher odds of current non-substance-related psychiatric problems (odds ratio [OR] = 2.47; 95% confidence interval [CI], 1.19-5.14). Those born ELBW and SGA exhibited the same patterns with larger effects. ACS-exposed ELBW survivors had even higher odds of any current non-substance-related psychiatric disorder (OR = 4.41; 95% CI, 1.65-11.82), particularly generalized anxiety disorder (OR = 3.42; 95% CI, 1.06-11.06), the generalized type of social phobia (OR = 5.80; 95% CI, 1.20-27.99), and the inattentive subtype of attention-deficit/hyperactivity disorder (OR = 11.45; 95% CI, 2.06-63.50).
CONCLUSIONS: In their early to mid-30s, ELBW survivors were less likely to have alcohol or substance use disorders but may be at greater risk for other psychiatric problems. Those exposed to ACS were at especially high risk and manifested no reduction in alcohol or substance use disorders. ELBW survivors exposed to ACS may be a special group at risk for psychopathology in adulthood.

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PLoS ONE. 2015;10.

MEASUREMENT OF THE EFFECT OF PHYSICAL EXERCISE ON THE CONCENTRATION OF INDIVIDUALS WITH ADHD.

Silva AP, Prado SOS, Scardovelli TA, et al.

Attention Deficit Hyperactivity Disorder (ADHD) mainly affects the academic performance of children and adolescents. In addition to bringing physical and mental health benefits, physical activity has been used to prevent and improve ADHD comorbidities; however, its effectiveness has not been quantified. In this study, the effect of physical activity on children's attention was measured using a computer game. Intense physical activity was promoted by a relay race, which requires a 5-min run without a rest interval. The proposed physical stimulus was performed with 28 volunteers: 14 with ADHD (GE-EF) and 14 without ADHD symptoms (GC-EF). After 5 min of rest, these volunteers accessed the computer game to accomplish the tasks in the shortest time possible. The computer game was also accessed by another 28 volunteers: 14 with ADHD (GE) and 14 without these symptoms (GC). The response time to solve the tasks that require attention was recorded. The results of the four groups were analyzed using D'Agostino statistical tests of normality, Kruskal-Wallis analyses of variance and post-hoc Dunn tests. The groups of volunteers with ADHD who performed exercise (GE-EF) showed improved performance for the tasks that require attention with a difference of 30.52% compared with the volunteers with ADHD who did not perform the exercise (GE). The (GE-EF) group showed similar performance (2.5% difference) with the volunteers in the (GC) group who have no ADHD symptoms and did not exercise. This study shows that intense exercise can improve the attention of children with ADHD and may help their school performance.

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PLoS ONE. 2015;10.

IMPROVING EXECUTIVE FUNCTIONING IN CHILDREN WITH ADHD: TRAINING MULTIPLE EXECUTIVE FUNCTIONS WITHIN THE CONTEXT OF A COMPUTER GAME. A RANDOMIZED DOUBLE-BLIND PLACEBO CONTROLLED TRIAL.

Dovis S, Van der Oord S, Wiers RW, et al.

Introduction: Executive functions (EFs) training interventions aimed at ADHD-symptom reduction have yielded mixed results. Generally, these interventions focus on training a single cognitive domain (e.g., working memory [WM], inhibition, or cognitive-flexibility). However, evidence suggests that most children with ADHD show deficits on multiple EFs, and that these EFs are largely related to different brain regions. Therefore, training multiple EFs might be a potentially more effective strategy to reduce EF-related ADHD symptoms.
Methods: Eighty-nine children with a clinical diagnosis of ADHD (aged 8-12) were randomized to either a full-active-condition where visuospatial WM, inhibition and cognitive-flexibility were trained, a partially-active-condition where inhibition and cognitive-flexibility were trained and the WM-training task was

presented in placebo-mode, or to a full placebo-condition. Short-term and long-term (3-months) effects of this gamified, 25-session, home-based computer-training were evaluated on multiple outcome domains.
Results: During training compliance was high (only 3% failed to meet compliance criteria). After training, only children in the full-active condition showed improvement on measures of visuospatial short-term-memory (STM) and WM. Inhibitory performance and interference control only improved in the full-active- and the partially-active condition. No Treatment-condition x Time interactions were found for cognitive-flexibility, verbal WM, complex-reasoning, nor for any parent-, teacher-, or child-rated ADHD behaviors, EF-behaviors, motivational behaviors, or general problem behaviors. Nonetheless, almost all measures showed main Time-effects, including the teacher-ratings.
Conclusions: Improvements on inhibition and visuospatial STM and WM were specifically related to the type of treatment received. However, transfer to untrained EFs and behaviors was mostly nonspecific (i.e., only interference control improved exclusively in the two EF training conditions). As such, in this multiple EF-training, mainly nonspecific treatment factors - as opposed to the specific effects of training EFs-seem related to far transfer effects found on EF and behavior.

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Praxis der Kinderpsychologie und Kinderpsychiatrie. 2015 Feb;64:117-34.
KOGNITIVE LEISTUNGSPROFILE VON KINDERN MIT MOTORISCHEN ENTWICKLUNGSSTÖRUNGEN UND ADHS IM VORSCHULALTER. = COGNITIVE PROFILES OF PRESCHOOL CHILDREN WITH DEVELOPMENTAL COORDINATION DISORDERS AND ADHD.
Jaščenoka J, Korsch F, Petermann F, et al.
Studies confirm that developmental coordination disorders (DCD) are often accompanied by ADHD. It is important to know why children with combined disorders show a special profile in a common intelligence test (WPPSI-III). For this purpose, the WPPSI-III results of a total of 125 children aged five to six years with diagnosed isolated DCD, isolated ADHD, combined disorders and a normative sample were compared. Children with isolated ADHD showed the best cognitive profile. Children of all three diagnosis subgroups presented significantly poorer abilities in all WPPSI-III scales than the normative sample. In comparison with preschoolers showing isolated ADHD, children with DCD and ADHD have a significant lower Processing Speed Quotient.

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Praxis der Kinderpsychologie und Kinderpsychiatrie. 2015 Feb;64:104-16.
ZUSAMMENHANG ZWISCHEN EINSCHULUNGSALTER UND VERHALTENSAUFFÄLLIGKEITEN. = RELATIONSHIP BETWEEN AGE OF SCHOOL ENTRY AND BEHAVIOUR PROBLEMS.
Schmiedeler S, Klauth L, Segerer R, et al.
Recent studies demonstrated that children who are relatively young within a school year show more behaviour problems, are at greater risk of being diagnosed with attention-deficit/hyperactivity disorder (ADHD) and treated with stimulants compared to their older classmates. In this paper we examine the association of age at school entry and behavioural problems for a German sample of elementary school children, who were enrolled in 2009 (N = 928). We used teacher ratings on the Strengths and Difficulties Questionnaire (SDQ) as well as the prevalence of ADHD diagnosis and medication. Our analyses showed that those children with a relatively younger age at school entry were judged more hyperactive than their older peers when sex was controlled for. After stratifying for sex, the effect of age at school entry on hyperactivity was now only significant for boys. No association with age at school entry could be found for the other SDQ-subscales as well as for ADHD diagnosis and medication. Although we could only partially demonstrate a significant relationship between age at school entry and behavioral problems in German elementary school-children, understanding these associations may help to consider children´s maturity differences when evaluating the child´s behavior.

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Prescriber. 2015;26:5.
ADHD DRUGS IN PRE-SCHOOL CHILDREN.
Pickett J.

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Psychiatr Serv. 2015;66:404-10.
CONCURRENT USE OF STIMULANTS AND SECOND-GENERATION ANTIPSYCHOTICS AMONG CHILDREN WITH ADHD ENROLLED IN MEDICAID.
Kamble P, Chen H, Johnson ML, et al.
Objective: This study examined the prevalence of and factors associated with concurrent use of long-acting stimulants (LAS) and second-generation antipsychotic agents among children and adolescents with attention-deficit hyperactivity disorder (ADHD).
Methods: The study involved retrospective longitudinal analysis of 2003-2007 Medicaid data from four states for children and adolescents between the ages of six and 17 years who were diagnosed as having ADHD and initiated LAS treatment. Concurrent use of LAS and second-generation antipsychotic medicationswas defined as simultaneous receipt of both medications for at least 14 days. On the basis of the conceptual framework of the Andersen behavioral model, multivariable logistic regression analysis was used to examine predisposing, enabling, and need factors associated with concurrent use.
Results: Among the 61,793 children who initiated LAS treatment for ADHD, 11,866 (19.2%) received LAS and second-generation antipsychotics concurrently for at least 14 days. Overall, the average length of concurrent use was 130(plus or minus)98 days. Multivariable logistic regression revealed that concurrent use was higher among boys, blacks, and foster care children compared with their respective counterparts. Comorbid psychiatric conditions, including disorders that are not approved indications for second-generation antipsychotic use, were associated with concurrent use of LAS and second-generation antipsychotics.
Conclusions: Almost one in five children and adolescents who initiated LAS also received second-generation antipsychotics concurrently for at least 14 days. Approved and nonapproved indications of second-generation antipsychotics influenced concurrent use in pediatric ADHD.

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Psychiatry Res 2015;227:333-338.
MIGHT THE TEMPERAMENT BE A BIAS IN CLINICAL STUDY ON ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD)?: NOVELTY SEEKING DIMENSION AS A CORE FEATURE OF ADHD.
Donfrancesco R, Di TM, Porfirio MC, et al.
Some clinical studies on attention deficit hyperactivity disorder (ADHD) have been found to overlap those of studies on personality, particularly those on the Novelty Seeking trait (NS) as measured by the Junior Temperament and Character Inventory (JTCI). The aim of this study was to evaluate the potential role of NS in clinical research on ADHD. We enroled 146 ADHD children (125 boys; mean age=9.61, S.D.=2.50) and 223 age- and gender-matched control children (178 boys; mean age=9.41, S.D.=2.30). All the parents filled in the JTCI for the evaluation of personality according to Cloninger's model. An exploratory factor analysis differentiated the NS items that concern "Impulsivity" (NS1) from those that concern other features (NS2). Multivariate Analysis of Variance (MANOVAs) revealed significant differences between ADHD children and non-ADHD children in temperamental dimensions: the scores of ADHD children were higher than those of non-ADHD children in Total NS, NS1-Impulsivity and NS2. Our results show that the NS dimension of the JTCI in ADHD children is higher than in non-ADHD children, even when a correction is made for impulsivity items. This finding suggests that the NS trait plays a central role in ADHD diagnosis even when items referred to impulsivity are removed from the NS scale.

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Psychiatry Research: Neuroimaging. 2015 Mar;231:353-56.

NEURAL MECHANISMS UNDERLYING THE THERAPEUTIC ACTIONS OF GUANFACINE TREATMENT IN YOUTH WITH ADHD: A PILOT FMRI STUDY.

Bédard AC, Schulz KP, Krone B, et al.

Twenty-five youth with attention-deficit/hyperactivity disorder (ADHD) were scanned with functional magnetic resonance imaging (fMRI) while performing a Go/No-go task before and after 6–8 weeks of randomized once-daily treatment with either the a2A-adrenergic receptor agonist guanfacine or placebo. Clinical improvement was greater for guanfacine than placebo and was differentially associated with reduced activation for guanfacine compared with placebo in the right midcingulate cortex/supplementary motor area and the left posterior cingulate cortex.

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Psychol Assess. 2014;26:1247-58.

RATINGS OF ADHD SYMPTOMS AND ACADEMIC IMPAIRMENT BY MOTHERS, FATHERS, TEACHERS, AND AIDES: CONSTRUCT VALIDITY WITHIN AND ACROSS SETTINGS AS WELL AS OCCASIONS.

Burns GL, Servera M, del Mar BM, et al.

A Multiple Indicator null Multiple Trait null Multiple Source null Multiple Occasion design was used to evaluate invariance, convergent and discriminant validity of ADHD-inattention (IN), ADHDhyperactivity/ impulsivity (HI), and academic impairment scores from the Child and Adolescent Disruptive Behavior Inventory (CADBI) using confirmatory factor analysis. Mothers, fathers, teachers, and aides completed the CADBI on 811 Spanish 1st-grade children (54% boys) twice (6-week separation). For mothers and fathers, like loadings, thresholds/intercepts, factor means, factor variances, and factor covariances/correlations were invariant across sources and occasions. All 3 factors also showed convergent (convergent correlations from .69 to .83) and significant discriminant validity. For teachers and aides, there was also invariance of parameters along with convergent and discriminant validity over sources and occasions (convergent correlations from .67 to .87). With construct validity established for home and school, it was meaningful to test construct validity between home and school. Like-item loadings and thresholds/intercepts were invariant between home and school, with the ADHD-HI factor mean being lower at school. Convergent validity of ADHD-IN, ADHD-HI, and academic impairment factors, especially ADHD-IN and ADHD-HI, was much weaker between home and school (convergent correlations from .36 to .47 for IN and HI). The strong convergent validity of ADHD-IN and ADHD-HI scores within home and school in conjunction with weak convergent validity across home and school has implications for the assessment and diagnosis of ADHD (i.e., the diagnostic criteria of symptom occurrence in 2 or more settings).

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Psychol Assess. 2015.

CROSS-CULTURAL VALIDATION OF A BEHAVIORAL SCREENER FOR EXECUTIVE FUNCTIONS: GUIDELINES FOR CLINICAL USE AMONG COLOMBIAN CHILDREN WITH AND WITHOUT ADHD.

Garcia-Barrera MA, Karr JE, Duran V, et al.

Garcia-Barrera, Kamphaus, and Bandalos (2011) derived a 25-item executive functioning screener from the Behavior Assessment System for Children (BASC), measuring 4 latent executive constructs: problem solving, attentional control, behavioral control, and emotional control. The current study included a cross-cultural examination of this screener in Colombian children with and without attention-deficit/hyperactivity disorder (ADHD). BASC teacher ratings were collected for Colombian children ages 6-11 years (848 healthy children [53% boys] and 155 children with ADHD [76% boys]). To examine the psychometric properties of the screener, a multistep procedure was implemented, including (a) confirmatory factor analysis (CFA) and factorial invariance testing across gender, age group (6-8 years, 9-11 years), and ADHD status to replicate and extend the original derivation; (b) item response theory (IRT) analysis to evaluate the information provided by individual items; and (copyright) given IRT results, a repeated CFA and invariance testing after the exclusion of 1 item from the problem-solving factor. The 24-item 4-factor model fit was adequate for controls and for ADHD participants. Results support the use of the 24-item

executive functioning screener in a cross-cultural context. In turn, in supplemental material, normative data for the Colombian sample are reported along with bilingual guidelines (i.e., Spanish/English) for implementing the screener in clinical practice. Even though the screener is useful when examining executive functions, it was not designed as a diagnostic measure for developmental disorders such as ADHD; as such, it should only inform about status of executive functioning.

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Psychol Assess. 2015;27:239-48.

PARENT-TEACHER AGREEMENT ON ADHD SYMPTOMS ACROSS DEVELOPMENT.

Narad ME, Garner AA, Peugh JL, et al.

Parent-teacher agreement on attention-deficit/hyperactivity disorder (ADHD) symptom ratings ranges from low to moderate. Most studies evaluating parent-teacher agreement have not assessed measurement invariance across raters. Hence, it is unclear whether discordance across raters is due to differing ADHD constructs across raters or other factors (e.g., subjective differences across raters). Additionally, the effect of development on parent-teacher agreement is relatively unknown. To address these limitations, the present study used parent and teacher ADHD ratings from a large (N = 6,659) developmentally diverse (ages 4-17) sample. Using exploratory structural equation modeling on half the sample, and then confirmatory factor analysis (CFA) on the other half of the sample, confirmed a 2-factor structure with significant cross-loadings for the 18 ADHD symptoms. CFA invariance analyses demonstrated that the 2-factor symptom structure was similar across raters and age groups. After confirming measurement invariance, the correlation between latent factors within and across raters was examined for each age group as well as across age groups. Parents reported greater severity of ADHD symptoms than did teachers, and both parents and teachers reported higher levels of hyperactivity/impulsivity in younger children than in older children and consistent levels of inattention across development. Finally, correlations between parent-teacher ratings of like factors were weak for inattention and moderate-strong for hyperactivity/impulsivity, and the magnitude of parent-teacher agreement did not vary across development. In conclusion, while parent and teacher ratings of ADHD behaviors are only weakly to moderately correlated, each reporter provides unique and valid clinical information as it relates to ADHD symptom presentation.

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Psychol Med. 2015 Apr;45:1195-205.

DISORDER-DISSOCIATED EFFECTS OF FLUOXETINE ON BRAIN FUNCTION OF WORKING MEMORY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER.

Chantiluke K, Barrett N, Giampietro V, et al.

Background. Attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are often co-morbid and share performance and brain dysfunctions during working memory (WM). Serotonin agonists modulate WM and there is evidence of positive behavioural effects in both disorders. We therefore used functional magnetic resonance imaging (fMRI) to investigate shared and disorder-specific brain dysfunctions of WM in these disorders, and the effects of a single dose of the selective serotonin reuptake inhibitor (SSRI) fluoxetine.

Method. Age-matched boys with ADHD (n = 17), ASD (n = 17) and controls (n = 22) were compared using fMRI during an N-back WM task. Patients were scanned twice, under either an acute dose of fluoxetine or placebo in a double-blind, placebo-controlled randomized design. Repeated-measures analyses within patients assessed drug effects on performance and brain function. To test for normalization effects of brain dysfunctions, patients under each drug condition were compared to controls.

Results. Under placebo, relative to controls, both ADHD and ASD boys shared underactivation in the right dorsolateral prefrontal cortex (DLPFC). Fluoxetine significantly normalized the DLPFC underactivation in ASD relative to controls whereas it increased posterior cingulate cortex (PCC) deactivation in ADHD relative to control boys. Within-patient analyses showed inverse effects of fluoxetine on PCC deactivation, which it enhanced in ADHD and decreased in ASD.

Conclusions. The findings show that fluoxetine modulates brain activation during WM in a disorder-specific manner by normalizing task-positive DLPFC dysfunction in ASD boys and enhancing task-negative default mode network (DMN) deactivation in ADHD.

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Psychol Med. 2015 Apr;45:977-83.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND RISK FOR DRUG USE DISORDER: A POPULATION-BASED FOLLOW-UP AND CO-RELATIVE STUDY.

Sundquist J, Ohlsson H, Sundquist K, et al.

Background. Although the association between attention-deficit/hyperactivity disorder (ADHD) and drug use disorder (DUD) is well documented, it is unclear whether it is causal or results from familial confounding.

Method. In this study we included all 551 164 individuals born in Sweden between 1991 and 1995 and used linked data from multiple nationwide registries to identify those with ADHD prior to age 15 years (1.71%). We used Cox proportional hazards models to investigate the future risk for DUD as a function of an ADHD registration and then compared the results from the entire population with the results from a co-relative design. Using the Swedish Multi-Generation Register, we identified all full-sibling, half-sibling and first-cousin pairs discordant for ADHD.

Results. In the population sample, ADHD had a substantially increased risk for future DUD with a hazard ratio (HR) of 3.34 after accounting for gender and parental education. Examining discordant cousin pairs, discordant half-siblings and discordant siblings, those with ADHD had HRs for DUD of 3.09, 2.10 and 2.38 respectively. Controlling for the number of ADHD registrations, ADHD patients with and without stimulant treatment were similarly associated with later DUD risk.

Conclusions. ADHD diagnosed before 15 years of age was strongly related to future risk for DUD. The magnitude of this association was modestly reduced in relative pairs discordant for ADHD, suggesting that the ADHD–DUD association is partly causal and partly a result of familial confounding. We found no evidence to suggest that this association resulted from stimulant treatment.

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Psychol Med. 2015 Apr;45:965-76.

DISORDER-SPECIFIC GREY MATTER DEFICITS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER RELATIVE TO AUTISM SPECTRUM DISORDER.

Lim L, Chantiluke K, Cubillo AI, et al.

Background. Attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) are two common childhood disorders that exhibit genetic and behavioural overlap and have abnormalities in similar brain systems, in particular in frontal and cerebellar regions. This study compared the two neurodevelopmental disorders to investigate shared and disorder-specific structural brain abnormalities.

Method. Forty-four predominantly medication-naïve male adolescents with ADHD, 19 medication-naïve male adolescents with ASD and 33 age-matched healthy male controls were scanned using high-resolution T1-weighted volumetric imaging in a 3-T magnetic resonance imaging (MRI) scanner. Voxel-based morphometry (VBM) was used to test for group-level differences in structural grey matter (GM) and white matter (WM) volumes.

Results. There was a significant group difference in the GM of the right posterior cerebellum and left middle/superior temporal gyrus (MTG/STG). Post-hoc analyses revealed that this was due to ADHD boys having a significantly smaller right posterior cerebellar GM volume compared to healthy controls and ASD boys, who did not differ from each other. ASD boys had a larger left MTG/STG GM volume relative to healthy controls and at a more lenient threshold relative to ADHD boys.

Conclusions. The study shows for the first time that the GM reduction in the cerebellum in ADHD is disorder specific relative to ASD whereas GM enlargement in the MTG/STG in ASD may be disorder specific relative to ADHD. This study is a first step towards elucidating disorder-specific structural biomarkers for these two related childhood disorders.

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Rev Psiquiatr Salud Ment. 2015.

EFFICACY OF CHESS TRAINING FOR THE TREATMENT OF ADHD: A PROSPECTIVE, OPEN LABEL STUDY.

Blasco-Fontecilla H, Gonzalez-Perez M, Garcia-Lopez R, et al.

Objective: To examine the effectiveness of playing chess as a treatment option for children with ADHD.

Methods: Parents of 44 children ages 6 to 17 with a primary diagnosis of ADHD consented to take part in the study. Parents completed the Spanish version of the Swanson, Nolan and Pelham Scale for parents (SNAP-IV) and the Abbreviated Conner's Rating Scales for parents (CPRS-HI) prior to an 11-week chess-training program. We used a paired t-test to compare pre- and post-intervention outcomes, and Cohen-d calculations to measure the magnitude of the effect. The statistical significance was set at P <. .05.

Results: Children with ADHD improved in both the SNAP-IV (t = 6.23; degrees of freedom (df) = 41; P <. .001) and the CPRS-HI (t = 5.39; df = 33; P <. .001). Our results suggest a large effect in decreasing the severity of ADHD as measured by the SNAP-IV (d = 0.85) and the CPRS-HI (d = 0.85). Furthermore, we found a correlation between intelligence quotient and SNAP-IV improvement (P <. .05).

Conclusions: The results of our pilot study should be interpreted with caution. This pilot project highlights the importance of carrying out larger studies with a case-control design. If our results are replicated in better designed studies, playing chess could be included within the multimodal treatment of ADHD.

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Scientific World Journal. 2015;2015.

ATTENTION DEFICIT-HYPERACTIVITY DISORDER SYMPTOMS AND DAYTIME VOIDING SYMPTOMS IN CHILDREN WITH PRIMARY ENURESIS: AN OBSERVATIONAL STUDY TO EVALUATE THE EFFECTIVENESS OF DESMOPRESSIN TREATMENT.

Yang T-K, Guo Y-J, Chang H-C, et al.

Purpose. To evaluate the effectiveness of presence of desmopressin in treating primary enuresis (PE) for children with attention deficit-hyperactivity disorder (ADHD) symptoms.

Materials and Methods. Children aged from 5 to 12 years with the chief complaint of PE treated with desmopressin were enrolled in pediatric urology clinics. The parent-reported SNAP-IV questionnaire was used to evaluate ADHD symptoms (cut-off value: 90th percentile). Voiding symptoms were assessed by the Dysfunctional Voiding Scoring System (DVSS) questionnaire. The responses to desmopressin were analyzed in children with and without ADHD symptoms.

Results. The study sample comprised 68 children; 27 (39.7%) presented with ADHD symptoms and 41 (60.3%) with non-ADHD symptoms. The children collected from a tertiary referral center may explain the high prevalence of ADHD symptoms in the present study. The total DVSS score in the ADHD symptoms group was significantly higher than in the non-ADHD symptoms group (7.72 versus 5.65, P = 0.05). In the ADHD symptoms group, there were significantly higher score in the "pee 1-2 times/day" and "can't wait" subscales of DVSS and lower sleep quality based on the Pediatric Sleep Quality questionnaire, as well as significantly lower peak flow rate and voided volume. The responses to desmopressin for enuresis were comparable between children with ADHD and non-ADHD symptoms.

Conclusions. Approximately 39.7% of PE children presented with ADHD symptoms at urologic clinics. PE children with ADHD symptoms had higher risk of daytime LUTS and comparable response to desmopressin treatment for PE. To evaluate ADHD symptoms and daytime voiding symptoms is important in children with PE

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The Spanish Journal of Psychology. 2015 Mar;18.

ATTENTION AND RESPONSE CONTROL IN ADHD. EVALUATION THROUGH INTEGRATED VISUAL AND AUDITORY CONTINUOUS PERFORMANCE TEST.

Moreno-García I, Delgado-Pardo G, Roldán-Blasco C.

This study assesses attention and response control through visual and auditory stimuli in a primary care pediatric sample. The sample consisted of 191 participants aged between 7 and 13 years old. It was divided into 2 groups: (a) 90 children with ADHD, according to diagnostic (DSM-IV-TR) (APA, 2002) and clinical (ADHD Rating Scale-IV) (DuPaul, Power, Anastopoulos, & Reid, 1998) criteria, and (b) 101 children without a history of ADHD. The aims were: (a) to determine and compare the performance of both groups in attention and response control, (b) to identify attention and response control deficits in the ADHD group. Assessments were carried out using the Integrated Visual and Auditory Continuous Performance Test (IVA/CPT, Sandford & Turner, 2002). Results showed that the ADHD group had visual and auditory attention deficits, $F(3, 170) = 14.38$; $p < .01$, deficits in fine motor regulation (Welch´s t-test = 44.768; $p < .001$) and sensory/motor activity (Welch's t-test = 95.683, $p < .001$; Welch's t-test = 79.537, $p < .001$). Both groups exhibited a similar performance in response control, $F(3, 170) = .93$, $p = .43$.Children with ADHD showed inattention, mental processing speed deficits, and loss of concentration with visual stimuli. Both groups yielded a better performance in attention with auditory stimuli.

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Value Health. 2015. [Epub ahead of print]

EVALUATION OF NEUROPSYCHIATRIC FUNCTION IN PHENYLKETONURIA: PSYCHOMETRIC PROPERTIES OF THE ADHD RATING SCALE-IV AND ADULT ADHD SELF-REPORT SCALE INATTENTION SUBSCALE IN PHENYLKETONURIA.

Wyrwich KW, Auguste P, Yu R, et al.

Background: Previous qualitative research among adults and parents of children with phenylketonuria (PKU) has identified inattention as an important psychiatric aspect of this condition. The parent-reported ADHD Rating Scale-IV (ADHD RS-IV) and the Adult ADHD Self-Report Scale (ASRS) have been validated for measuring inattention symptoms in persons with attention-deficit/hyperactivity disorder (ADHD); however, their psychometric attributes for measuring PKU-related inattention have not been established. Objective: The primary objective of this investigation was to demonstrate the reliability, validity, and responsiveness of the ADHD RS-IV and ASRS inattention symptoms subscales in a randomized controlled trial of patients with PKU aged 8 years or older.

Methods: A post hoc analysis investigated the psychometric properties (Rasch model fit, reliability, construct validity, and responsiveness) of the ADHD RS-IV and ASRS inattention subscales using data from a phase 3b, double-blind, placebo-controlled clinical trial in those with PKU aged 8 years or older.

Results: The Rasch results revealed good model fit, and reliability analyses revealed strong internal consistency reliability ((alpha) (greater-than or equal to) 0.87) and reproducibility (intraclass correlation coefficient (greater-than or equal to) 0.87) for both measures. Both inattention measures demonstrated the ability to discriminate between known groups ($P < 0.001$) created by the Clinical Global Impression-Severity scale. Correlations between the ADHD RS-IV and the ASRS with the Clinical Global Impression-Severity scale and the age-appropriate Behavior Rating Inventory of Executive Function Working Memory subscale were consistently moderate to strong (r (greater-than or equal to) 0.56). Similarly, results of the change score correlations were of moderate magnitude (r (greater-than or equal to) 0.43) for both measures when compared with changes over time in Behavior Rating Inventory of Executive Function Working Memory subscales.

Conclusions: These findings of reliability, validity, and responsiveness of both the ADHD RS-IV and the ASRS inattention scales, in addition to content validation results, support their use for the assessment of inattention symptoms among persons with PKU aged 8 years or older in both clinical and research settings.

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Zhongguo Zhen Jiu. 2014 Dec;34:1179-83.

ATTENTION DEFICIT HYPERACTIVITY DISORDER TREATED WITH SCALP ACUPUNCTURE AND EEG BIOFEEDBACK THERAPY IN CHILDREN: A RANDOMIZED CONTROLLED TRIAL.

He CD, Lang BX, Jin LQ, et al.

OBJECTIVE: To compare the difference in clinical efficacy on children attention deficit hyperactivity disorder (ADHD) between the combined therapy of scalp acupuncture and EGG biofeedback and the simple EEG biofeedback therapy so as to search the better therapeutic method for ADHD.

METHODS: One hundred patients were randomized into an observation group and a control group, 50 cases in each one. In the control group, the simple EEG biofeedback therapy was adopted. In the observation group, on the basis of biofeedback therapy, scalp acupuncture was added and applied to Dingzhongxian (MS 5), Dingpangyixian (MS 8), Baihui (GV 20), Sishencong (EX-HN 1), etc. The ten treatments made one session. After four sessions of treatment, FIQ value in Wechsler intelligence scale, CIH score in Conners children behavior questionnaire, the ratio of 0 wave and p wave in EEG, FRCQ and FAQ in the integrated visual and auditory continuous performance test (IVA-CPT) and clinical comprehensive efficacy were observed before and after treatment in the two groups separately.

RESULTS: Three cases were dropped out in the observation group and 2 cases were out in the control group. In the two groups, FIQ, FRCQ and FAQ were all increased after treatment ($P < 0.01$, $P < 0.05$); the increases in the observation group were much more significant than those in the control group after treatment (all $P < 0.05$). In the two groups, CIH score and the ratio of 0 wave and p wave were all reduced after treatment ($P < 0.01$, $P < 0.05$); the reduction in the observation group were much more apparent as compared with those in the control group (both $P< 0.05$). The total effective rate was 91.5% (43/47) in the observation group and better than 83. 3% (40/48, $P < 0.01$) in the control group.

CONCLUSION: The combined therapy of scalp acupuncture and EEG biofeedback achieves the superior efficacy on children ADHD as compared with the simple biofeedback therapy. This combined therapy rapidly relieves the essential symptoms of ADHD and improves EEG waveform in children patients. Importantly, this therapy obtains and consolidates the significant efficacy.

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AGENZIA ITALIANA DEL FARMACO

DETERMINA 27 aprile 2015

Inserimento del medicinale per uso umano «Metilfenidato (Ritalin)» nell'elenco dei medicinali erogabili a totale carico del Servizio sanitario nazionale, ai sensi della legge 23 dicembre 1996, n. 648, per il trattamento del disturbo da deficit dell'attenzione e iperattivita' (ADHD) negli adulti gia' in trattamento farmacologico prima del compimento del diciottesimo anno di eta'. (Determina n. 488/2015). (15A03435)

(GU n.107 del 11-5-2015)

IL DIRETTORE GENERALE

Visti gli articoli 8 e 9 del decreto legislativo 30 luglio 1999, n. 300;

Visto l'art. 48 del decreto-legge 30 settembre 2003 n. 269, convertito nella legge 24 novembre 2003, n. 326, che istituisce l'Agenzia italiana del farmaco ed in particolare il comma 13;

Visto il decreto del Ministro della salute di concerto con i Ministri della funzione pubblica e dell'economia e finanze in data 20 settembre 2004, n. 245 recante norme sull'organizzazione ed il funzionamento dell'Agenzia italiana del farmaco, a norma del comma 13 dell'art. 48 sopra citato, ed in particolare l'art. 19;

Visto il decreto del Ministro della salute dell'8 novembre 2011, registrato dall'Ufficio centrale del bilancio al registro «Visti semplici», foglio n. 1282, in data 14 novembre 2011, con cui e' stato nominato direttore generale dell'Agenzia italiana del farmaco il prof. Luca Pani, a decorrere dal 16 novembre 2011;

Visto il decreto del Ministro della salute 28 settembre 2004 che ha costituito la Commissione consultiva tecnico-scientifica dell'Agenzia italiana del farmaco;

Vista la legge 23 dicembre 1996 n. 648, di conversione del decreto-legge 21 ottobre 1996, n. 536, relativa alle misure per il contenimento della spesa farmaceutica e la determinazione del tetto di spesa per l'anno 1996, pubblicata nella Gazzetta Ufficiale n. 300 del 23 dicembre 1996;

Visto il provvedimento della Commissione unica del farmaco (CUF) datato 20 luglio 2000, pubblicato nella Gazzetta Ufficiale n. 219 del 19 settembre 2000 con errata-corrige nella Gazzetta Ufficiale n. 232 del 4 ottobre 2000, concernente l'istituzione dell'elenco dei medicinali innovativi la cui commercializzazione e' autorizzata in altri Stati ma non sul territorio nazionale, dei medicinali non ancora autorizzati ma sottoposti a sperimentazione clinica e dei medicinali da impiegare per una indicazione terapeutica diversa da quella autorizzata, da erogarsi a totale carico del servizio sanitario nazionale qualora non esista valida alternativa terapeutica, ai sensi dell'art. 1, comma 4, del decreto-legge 21 ottobre 1996 n. 536, convertito dalla legge 23 dicembre 1996 n. 648;

Visto ancora il provvedimento CUF datato 31 gennaio 2001 concernente il monitoraggio clinico dei medicinali inseriti nel succitato elenco, pubblicato nella Gazzetta Ufficiale n. 70 del 24 marzo 2001;

Ritenuto opportuno assicurare un'adeguata continuita' terapeutica ai pazienti adulti affetti da deficit dell'attenzione e iperattivita'

(ADHD) gia' in trattamento farmacologico prima del compimento del diciottesimo anno di eta';

Ritenuto opportuno consentire a soggetti adulti affetti da tale patologia il trattamento con detto medicinale a totale carico del Servizio sanitario nazionale;

Ritenuto necessario dettare le condizioni alle quali detto medicinale viene inserito nell'elenco di cui al citato provvedimento datato 20 luglio 2000, concernente l'istituzione dell'elenco stesso;

Tenuto conto del parere espresso dalla Commissione consultiva tecnico-scientifica (CTS) dell'AIFA nella riunione del 21-23 luglio 2014 - Stralcio Verbale n. 27;

Ritenuto pertanto di includere il medicinale «metilfenidato (Ritalin)» nell'elenco dei medicinali erogabili a totale carico del Servizio sanitario nazionale istituito ai sensi della legge 23 dicembre 1996 n. 648, per l'indicazione terapeutica citata in premessa;

Determina:

Art. 1

Il medicinale «metilfenidato (Ritalin)» e' inserito, ai sensi dell'art. 1, comma 4, del decreto-legge 21 ottobre 1996, n. 536, convertito dalla legge 23 dicembre 1996, n. 648, nell'elenco istituito col provvedimento della Commissione unica del farmaco citato in premessa.

Art. 2

Il medicinale di cui all'art. 1 e' erogabile a totale carico del Servizio sanitario nazionale alle seguenti condizioni: per il trattamento del disturbo da deficit dell'attenzione e iperattivita' (ADHD) negli adulti gia' in trattamento farmacologico prima del compimento del diciottesimo anno di eta'.

Art. 3

Presso l'Istituto superiore di sanita' e' istituito il registro nazionale ADHD secondo i criteri individuati dalla CTS. Ai fini della prescrizione del farmaco a carico del SSN, i Centri di riferimento per la diagnosi e predisposizione del piano terapeutico, specificatamente individuati dalle regioni, sono tenuti a inserire nel Registro nazionale ADHD i dati previsti dal Protocollo diagnostico e Terapeutico della sindrome di iperattivita' e deficit di attenzione. Tale programma e' finalizzato al monitoraggio dell'accuratezza diagnostica dell'ADHD e dell'appropriatezza dell'eventuale terapia farmacologica.

Ai fini delle prescrizioni a carico del SSN, i Centri dovranno compilare la scheda di arruolamento informatizzata per la raccolta dati che indica i pazienti eleggibili e la scheda di follow-up.

Art. 4

La presente determinazione ha effetto dal giorno successivo alla sua pubblicazione nella Gazzetta Ufficiale della Repubblica italiana.

Roma, 27 aprile 2015

Il direttore generale: Pani

Ospedale di Circolo

Fondazione Macchi

Facoltà di Medicina e Chirurgia

Sarzana, 16 Maggio 2015

X CONGRESSO NAZIONALE "Le nuove pratiche di intervento per l'ADHD"

FUNZIONI ESECUTIVE E PROFILI NEUROPSICOLOGICI NELL'ADHD
Uno studio caso-controllo

Chiara Luoni[1], Francesca Pavone[1], Sara Crugnola[1,2], Stefania Fontolan[1,2], Sonia Margherini[1], Giorgio Rossi[1], Cristiano Termine[1,2]

[1] S.C. Neuropsichiatria Infantile, Osp. F. Del Ponte, Varese

[2] Neuropsichiatria Infantile, Dipartimento di Medicina clinica e sperimentale, Università degli Studi dell'Insubria, Varese

FUNZIONI ESECUTIVE

È un termine ombrello, che comprende un insieme di funzioni necessarie **per guidare efficacemente il comportamento al fine di raggiungere un obiettivo**, soprattutto nelle situazioni non routinarie.

Includono il dare priorità, il seguire le sequenze, l'inibire i comportamenti famigliari o stereotipati, il creare e mantenere un'idea su quali compiti o informazioni sono più rilevanti per l'obiettivo in corso, il fornire resistenza alle informazioni che distraggono o che sono irrilevanti al fine del compito, l'utilizzare le informazioni rilevanti nella presa di decisioni, il categorizzare o l'astrarre elementi comuni da situazioni diverse, il gestire informazioni o situazioni nuove.

(Banich, 2009)

FUNZIONI ESECUTIVE

1. ATTIVAZIONE

Organizzare, dare priorità e cominciare il lavoro

2. FOCUS

Focalizzare, mantenere, spostare l'attenzione tra i task

3. SFORZO

Regolare, mantenere allerta e sforzo, processare la velocità

4. EMOZIONI

Gestire la frustrazione e modulare le emozioni

5. MEMORIA

Utilizzare la memoria di lavoro e accedere al recall

6. AZIONE

Monitorare e autoregolarsi

Schema basato sul modello di Brown, 2013

Sindrome complessa
con compromissione nello sviluppo delle **funzioni esecutive**
Brown, 2013

Le funzioni esecutive sono il **"sistema di autogestione del cervello"**,
costituito prevalentemente da operazioni inconsce.

Questa compromissione è
situazione-dipendente,
cronica,
interferisce significativamente
In molti aspetti della vita dell'individuo.

Ironicamente, una delle **manifestazioni più costanti** dell'ADHD è l'alta prevalenza di **incostanza** nelle prestazioni e di variabilità da un momento all'altro
(Castellanos et al., 2006)

Validity of the Executive Function Theory of Attention-Deficit/Hyperactivity Disorder: A Meta-Analytic Review

Erik G. Willcutt, Alysa E. Doyle, Joel T. Nigg, Stephen V. Faraone, and Bruce F. Pennington

One of the most prominent neuropsychologic theories of attention-deficit/hyperactivity disorder (ADHD) suggests that its symptoms arise from a primary deficit in executive functions (EF), defined as neurocognitive processes that maintain an appropriate problem-solving set to attain a later goal. To examine the validity of the EF theory, we conducted a meta-analysis of 83 studies that administered EF measures to groups with ADHD (total N = *3734) and without ADHD* (N = *2969). Groups with ADHD exhibited significant impairment on all EF tasks. Effect sizes for all measures fell in the medium range (.46–.69), but the strongest and most consistent effects were obtained on measures of response inhibition, vigilance, working memory, and planning. Weaknesses in EF were significant in both clinic-referred and community samples and were not explained by group differences in intelligence, academic achievement, or symptoms of other disorders. ADHD is associated with significant weaknesses in several key EF domains. However, moderate effect sizes and lack of universality of EF deficits among individuals with ADHD suggest that EF weaknesses are neither necessary nor sufficient to cause all cases of ADHD. Difficulties with EF appear to be one important component of the complex neuropsychology of ADHD.*

BIOL PSYCHIATRY 2005;57:1336–1346

Review TRENDS in Cognitive Sciences Vol.10 No.3 March 2006

Characterizing cognition in ADHD: beyond executive dysfunction

F. Xavier Castellanos[1], Edmund J.S. Sonuga-Barke[1,2], Michael P. Milham[1] and Rosemary Tannock[3]

[1]Institute for Pediatric Neuroscience, NYU Child Study Center, 215 Lexington Avenue, New York, NY 10016, USA
[2]Department of Psychology, University of Southampton, Southampton SO17 1BJ, UK
[3]Brain and Behavior Research Program, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario M5G 1X8, Canada

The hypothesis that Attention-Deficit/Hyperactivity Disorder (ADHD) reflects a primary inhibitory executive function deficit has spurred a substantial literature. However, empirical findings and methodological issues challenge the etiologic primacy of inhibitory and executive deficits in ADHD. Based on accumulating evidence of increased intra-individual variability in ADHD, we reconsider executive dysfunction in light of distinctions between 'hot' and 'cool' executive function measures. We propose an integrative model that incorporates new neuroanatomical findings and emphasizes the interactions between parallel processing pathways as potential loci for dysfunction. Such a reconceptualization provides a means to transcend the limits of current models of executive dysfunction in ADHD and suggests a plan for future research on cognition grounded in neurophysiological and developmental considerations.

In this schema, 'cool' EF is elicited by relatively abstract, decontextualized problems, such as most of the EF tasks tested so far in ADHD, including Stroop, flanker, Go/No Go, Stop, continuous performance and working memory tasks, which focus on the ability to suppress automatic processes or prepotent responses and/ or maintain task instructions or representations in working memory. 'Hot' EF 'is required for problems that are characterized by high affective involvement or demand flexible

appraisals of the affective significance of stimul

RECLUTAMENTO

Soggetti giunti consecutivamente per sospetto ADHD presso presso la S.C. di Neuropsichiatria Infantile presso l'Ospedale F. Del Ponte di Varese (centro di riferimento per l'ADHD), dal gennaio 2012 al marzo 2015.

Criteri di inclusione:

- ✓ Prima valutazione per sospetto ADHD effettuata dal bambino
- ✓ Prima diagnosi di ADHD secondo il DSM IV TR (K SADS PL)
- ✓ Età ≥ 6 anni

Criteri di esclusione

- ✓ Disabilità intellettiva
- ✓ Disturbo dello spettro autistico
- ✓ Sindromi genetiche
- ✓ Epilessia
- ✓ Alterazioni alla RM encefalo

SOGGETTI

86 casi

- 76 Maschi (88.4%)
- 10 Femmine (11.6%)
- Età 10.53 ± 2.74 (6 18)

73 controlli

- 56 Maschi (76.7%)
- 17 Femmine (23.3%)
- Età 11.16 ± 3.15 (6 16)

Differenze non significative per età, sesso e livello cognitivo

MATERIALI

Casi

- WISC IV *
- Batteria BIA
- Torre di Londra
- Fluenza grafomotoria
- Test di apprendimento
- Scale Conners *
- CBCL *
- CDI
- MASC
- K SADS PL *
- Esame obiettivo neurologico *

Controlli

- Vocabolario e Disegno con Cubi
- Batteria BIA
- Torre di Londra
- Fluenza grafomotoria

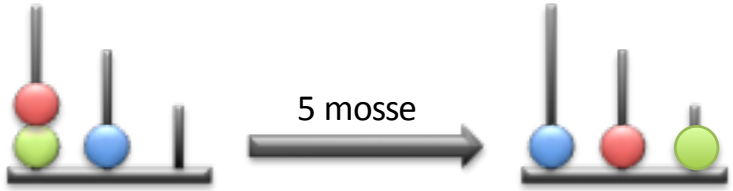
* Dati inseriti nel Registro Regionale Lombardo

PIANIFICAZIONE

Torre di Londra

Punteggio totale: capacità di pianificare

Predisporre una procedura finalizzata al raggiungimento di un obiettivo
Dipende anche dall'efficacia della memoria di lavoro e dalla capacità di inibire le risposte perseverative



Numero di mosse: efficienza della pianificazione

Maggiore è il numero di mosse, maggiori le difficoltà nella pianificazione o nella memoria di lavoro, o maggiore la perseverazione

Violazione di regole: comprensione delle regole

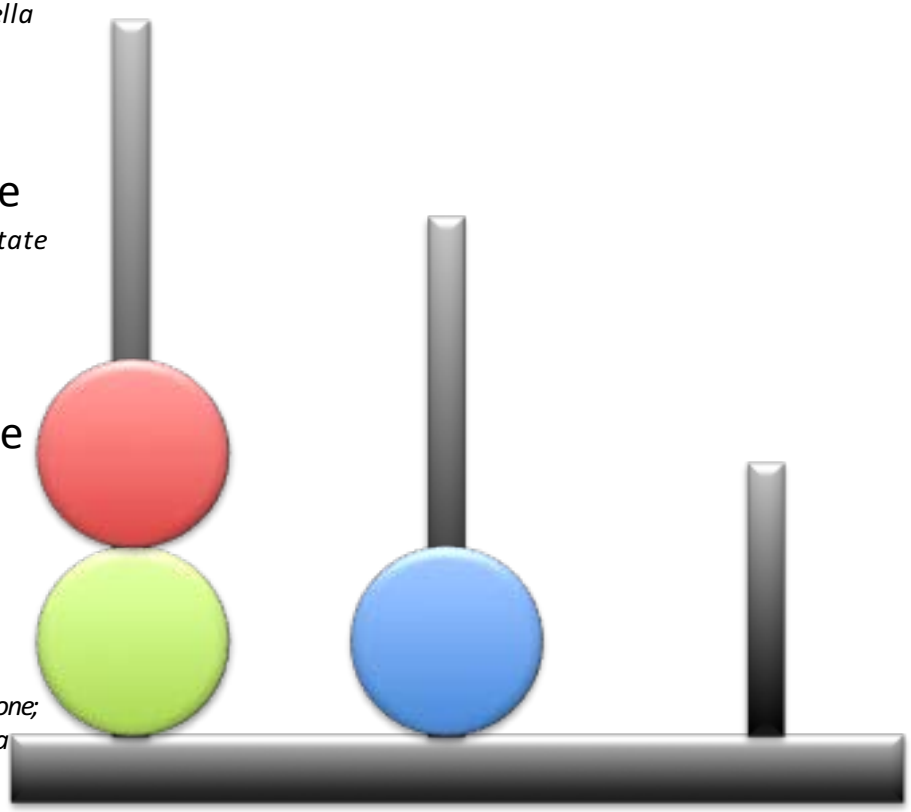
Dà indicazioni sulla capacità di comprendere e tenere a mente le regole presentate per l'esecuzione del compito

Tempo di decisione: rapidità della pianificazione

Se breve suggerisce un comportamento impulsivo; se è lungo può indicare incertezza e difficoltà nell'organizzare la pianficazione

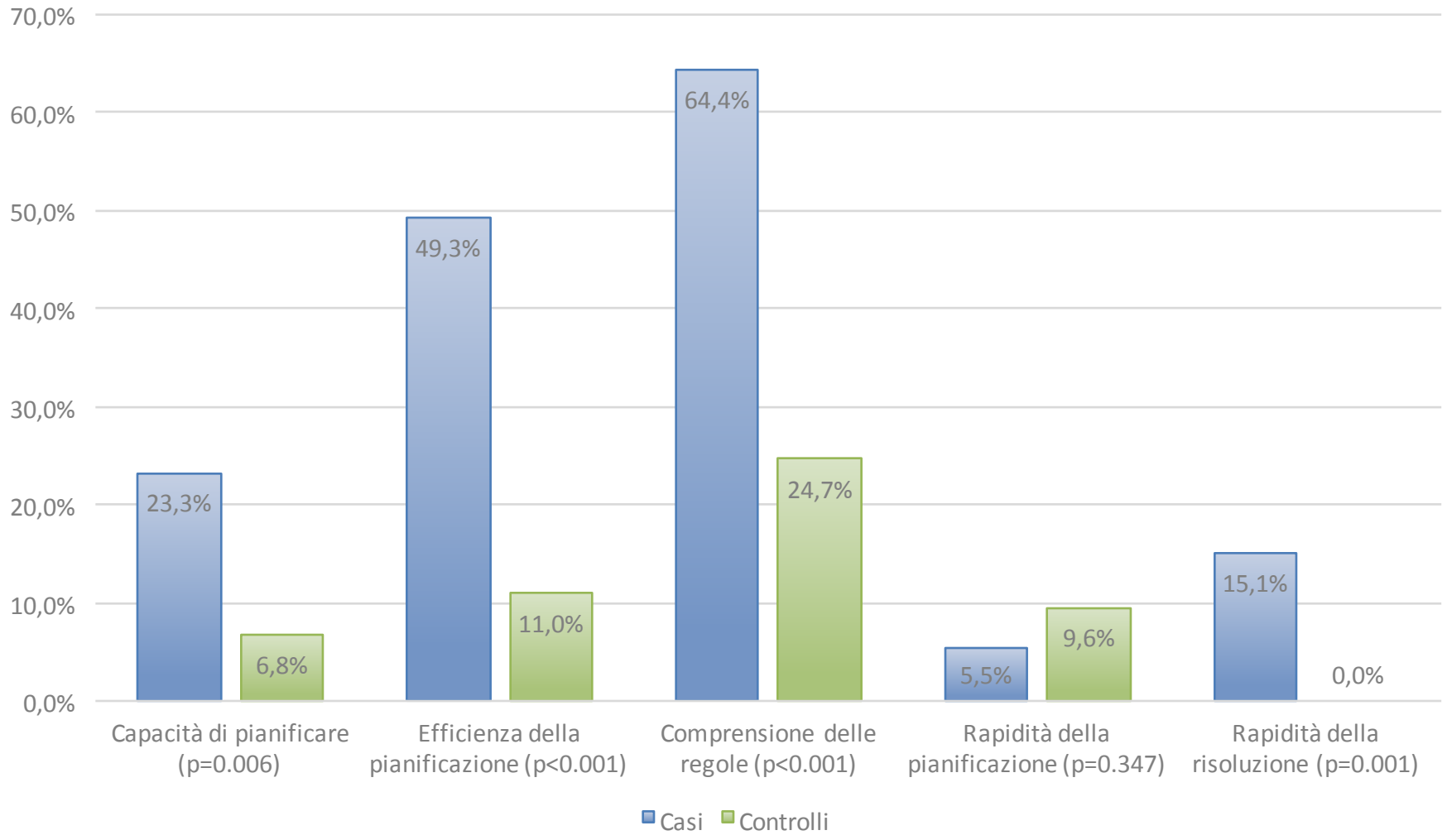
Tempo di esecuzione: rapidità della risoluzione

Se breve suggerisce un comportamento impulsivo con difficoltà nella pianificazione; se è lungo può indicare incertezza e difficoltà nell'organizzare la fase esecutiva



Abilità di pianificazione

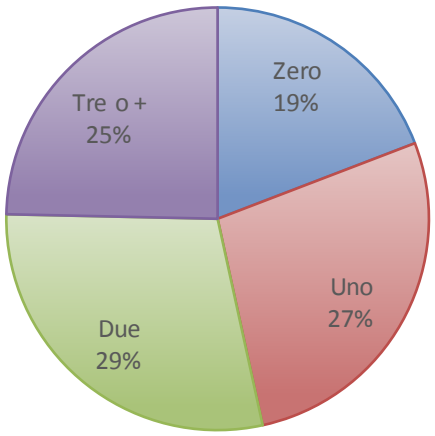
% punteggi patologici



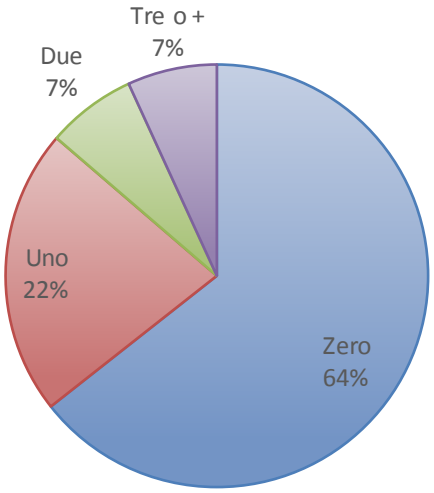
Abilità di pianificazione

N. parametri deficitari

Casi



Controlli



Almeno due punteggi deficitari:
Sensibilità: 54%
Specificità: 86%
VPP: 79.4%
VPN: 65.2%

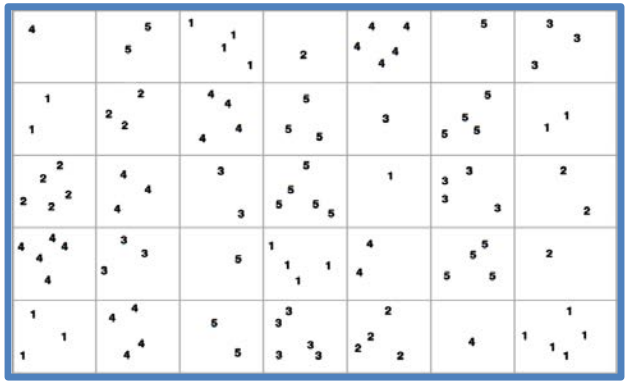
	Chi-quadrato			Regressione logistica		
Pianificazione	Casi	Controlli	p	OR	IC95%	p
Almeno 2 punteggi deficitari	54%	14%	<0.001	7,226	3,214 16,249	<0.001

PROCESSI DI INIBIZIONE

Batteria BIA

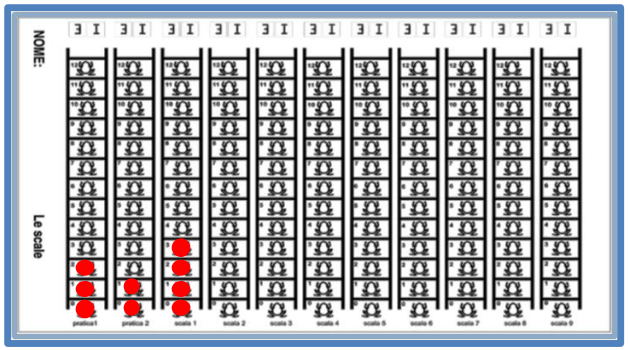
EFFETTO STROOP

Il bambino deve dire il numero di numeri presenti in ogni quadrato ignorando il loro valore



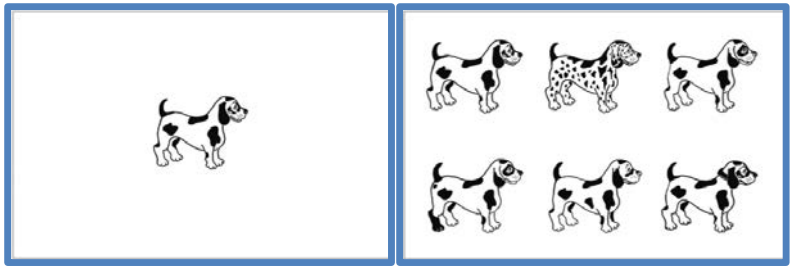
RANETTE (Go no Go)

Il bambino deve fare un segno su una ranetta quando sente il suono Go. Deve fermarsi quando sente il suono no Go.



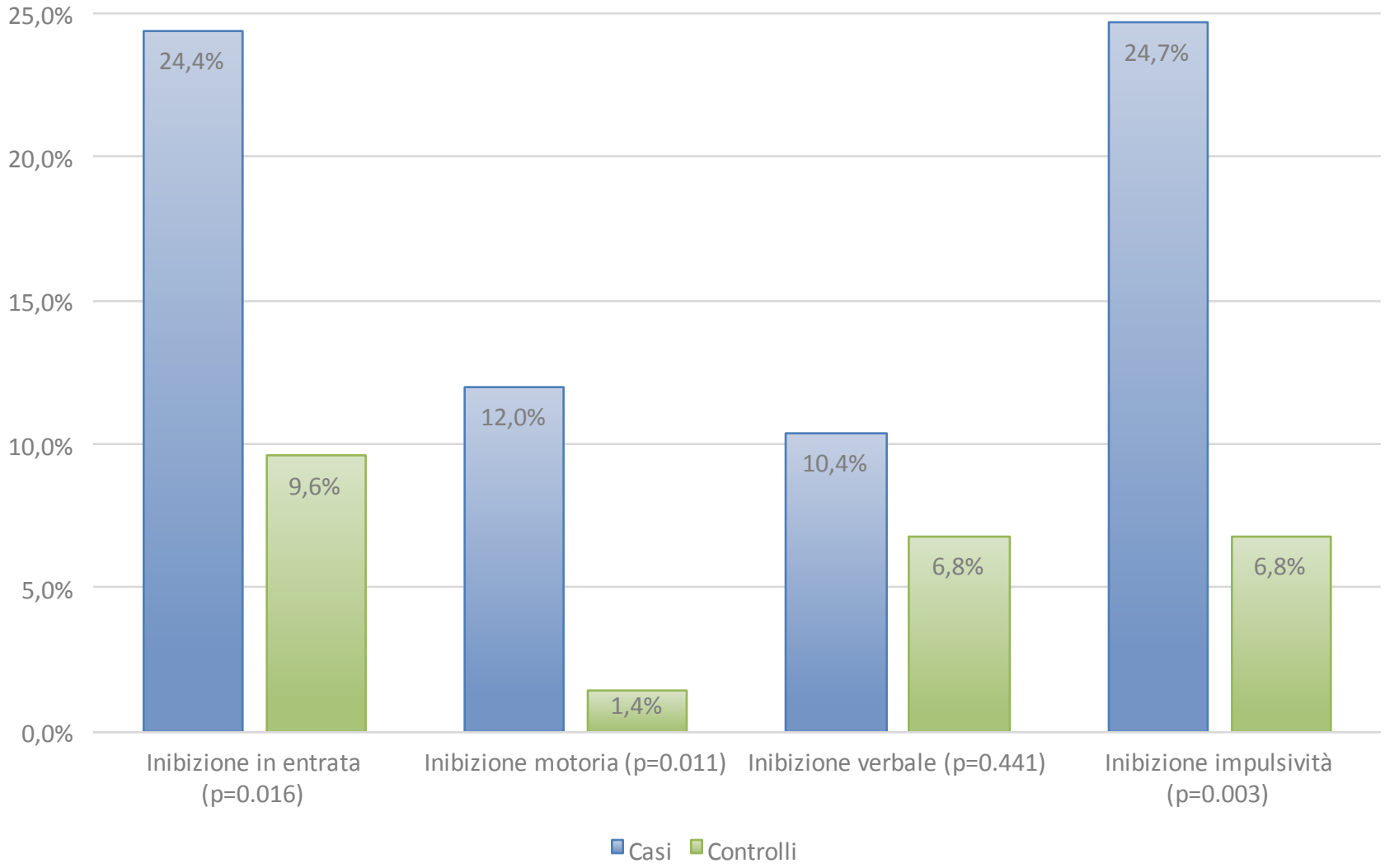
MF TEST

Il bambino deve trovare tra sei immagini quella identica allo stimolo



Processi di inibizione

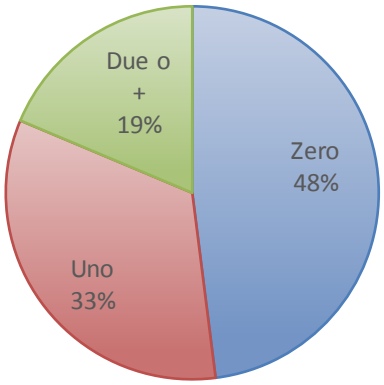
% punteggi deficitari



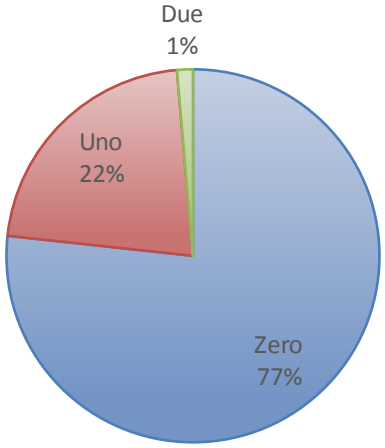
Processi di inibizione

N. punteggi patologici

Casi



Controlli



Almeno un punteggio deficitario:
Sensibilità: 52%
Specificità: 77%
VPP: 69,3%
VPN: 61,6%

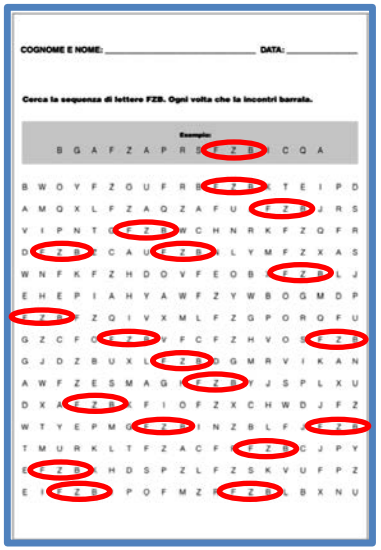
	Chi-quadrato			Regressione logistica		
Inibizione	Casi	Controlli	p	OR	IC95%	p
Almeno 1 punteggio deficitario	52%	23%	<0.001	3,569	1,760 7,236	<0.001

ATTENZIONE SOSTENUTA VISIVA E UDITIVA

Batteria BIA

TEST CP

TEST TAU



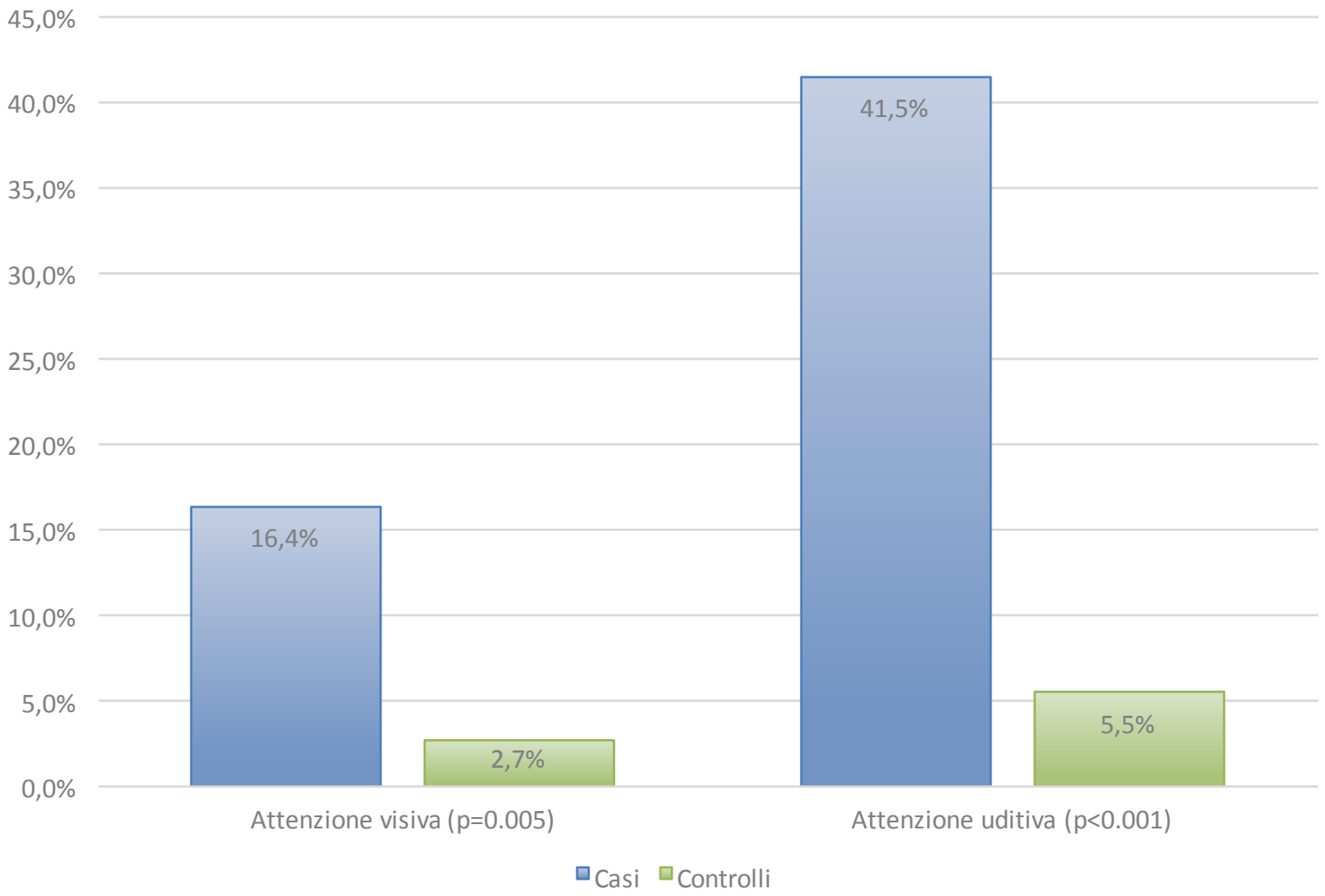
Il bambino deve trovare un insieme di lettere e segnarle (FZB).

Il bambino deve ascoltare una serie di suoni e contarli mentalmente

	Risposta Corretta	Punteggio 0/1
Pratica 1	3	10
Pratica 2	4	
Item 1	8	
Item 2	10	11
Item 3	9	
Item 4	14	
Item 5	11	
Item 6	15	
Item 7	10	
Item 8	12	
Item 9	13	
Item 10	11	
Punteggio Totale		
Percentile		
Punti Z		

Attenzione sostenuta

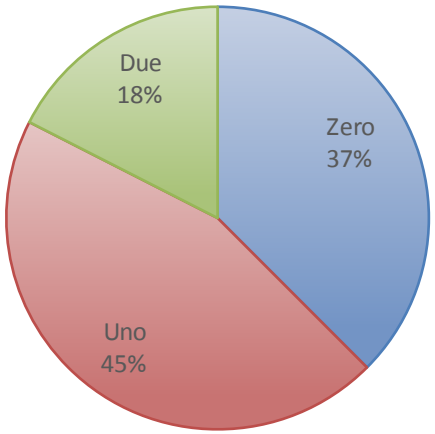
% punteggi deficitari



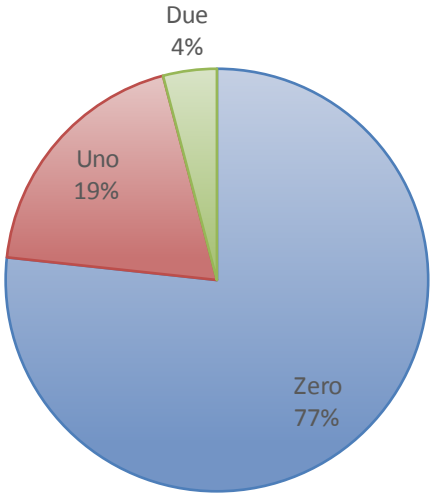
Attenzione sostenuta

N. punteggi deficitari

Casi



Controlli

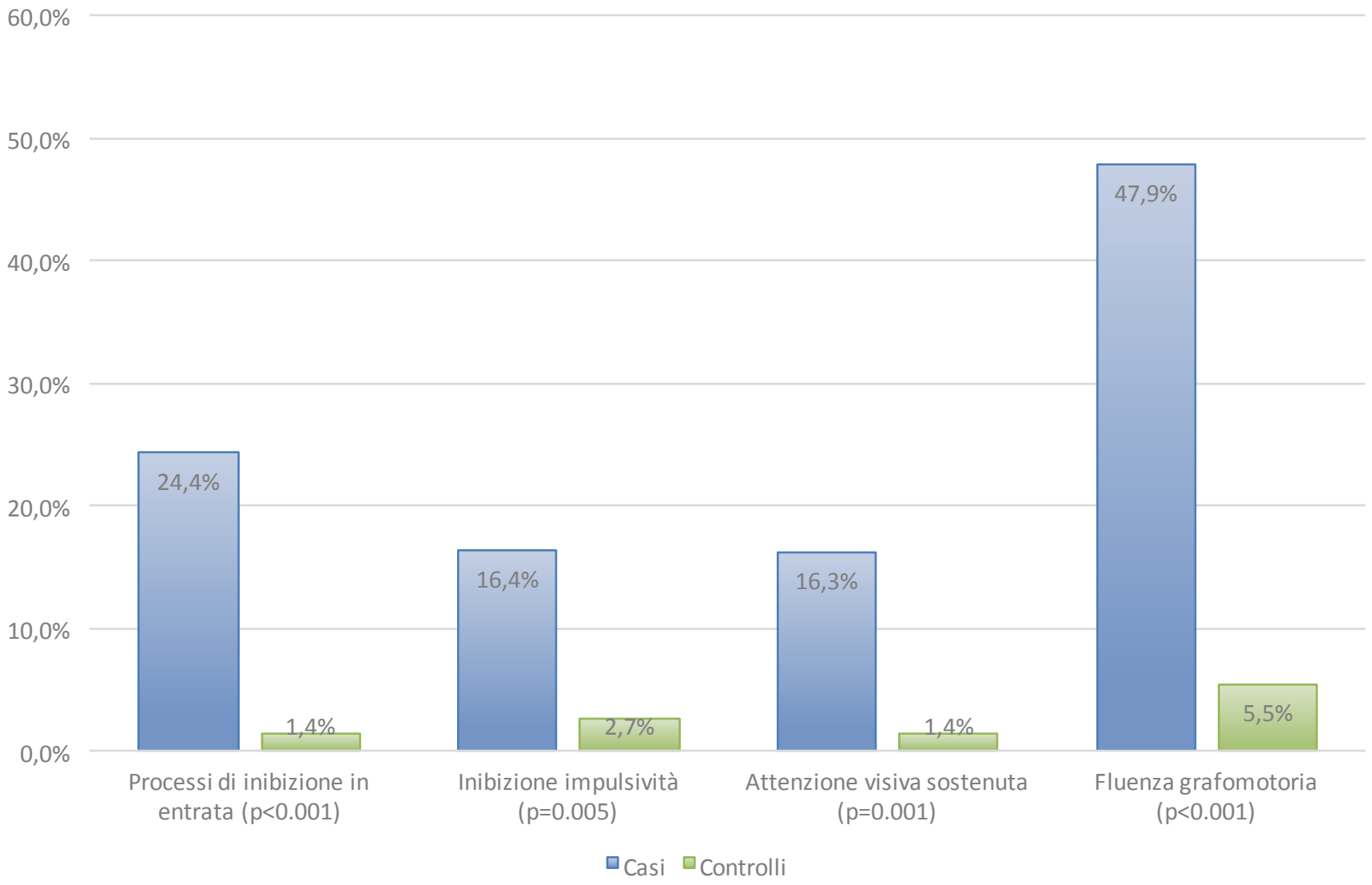


Almeno due punteggi deficitari:
Sensibilità: 63%
Specificità: 77%
VPP: 73.3%
VPN: 67.5%

	Chi-quadrato			Regressione logistica		
Attenzione sostenuta	Casi	Controlli	p	OR	IC95%	p
Almeno 1 punteggio deficitario	63%	23%	<0.001	4,949	1,360 18,007	0.015

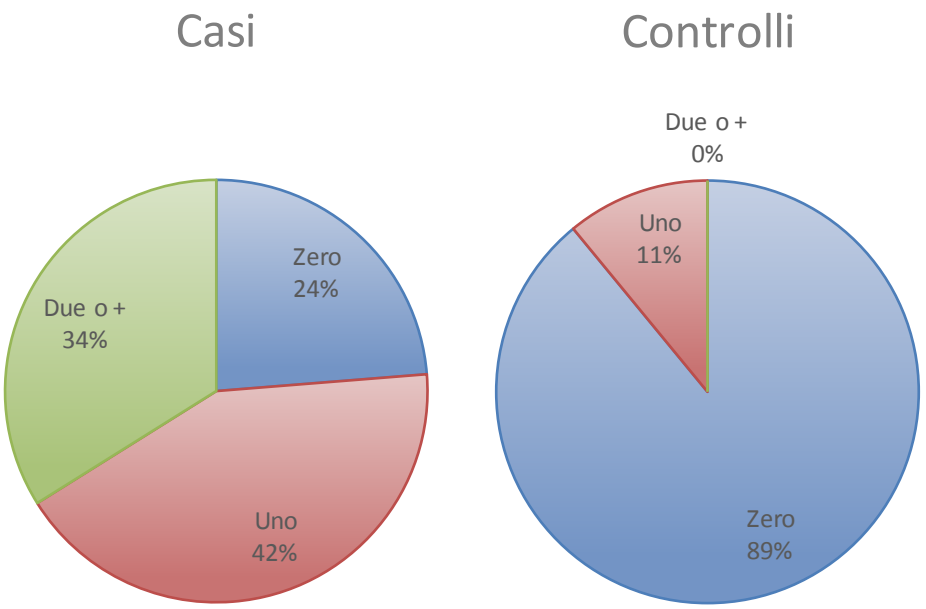
Velocità esecutiva

% punteggi deficitari



Velocità esecutiva

N. punteggi deficitari



Almeno un punteggio deficitario:
Sensibilità: 76%
Specificità: 89%
VPP: 87.4%
VPN: 78.8%

	Chi-quadrato			Regressione logistica		
Lentezza esecutiva	Casi	Controlli	p	OR	IC95%	p
Almeno 1 punteggio deficitario	76%	11%	<0.001	26,116	10,119 67,406	<0.001

Se li valutiamo insieme....

	Caratteristiche dei gruppi di test				Regressione logistica *Analisi multivariata*		
Risultati patologici	**Sensibilità**	**Specificità**	**VPP**	**VPN**	**OR**	**IC95%**	**p**
Lentezza esecutiva	76%	89%	87,4%	78,8%	34,745	10,660 113,246	**<0.001**
Pianificazione	54%	86%	79,4%	65,2%	8,947	2,597 30,825	**0.001**
Attenzione sostenuta	63%	77%	73,3%	67,5%	15,619	2,679 91,069	**0.002**
Inibizione	52%	77%	69,3%	61,6%	0,954	0,317 2,870	0.934

I parametri che possono indirizzare maggiormente la diagnosi sono, in ordine:

- ✓ Velocità esecutiva
- ✓ Abilità di pianificazione
- ✓ Attenzione sostenuta

Caratteristiche del campione clinico

76 Maschi (88.4%) e 10 Femmine (11.6%)

Età compresa tra 6 e 18 anni (10.53 ± 2.74)

66 con ADHD a presentazione combinata (76.7%)

15 con ADHD a presentazione prevalentemente inattentiva (17.5%)

5 con ADHD a presentazione prevalentemente iperattiva (5.8%)

25 soggetti appartengono a famiglie di basso livello socioeconomico (29.1%)

80 soggetti (93.0%) hanno almeno una comorbidità

WISC IV

	Media	DS	Minimo	Massimo
QI totale	99.7	16.5	62*	139
Comprensione verbale (ICV)	100.8	15.6	72	136
Ragionamento percettivo (IRP)	104.1	15.8	61	134
Memoria di lavoro (IML)	90.6	14.3	48	112
Velocità esecutiva (IVE)	92.2	14.7	59	123

- Assenza di disabilità intellettiva

- Differenza statisticamente significativa tra i punteggi IML/IVE e gli altri indici
- I punteggi medi più bassi sono registrati al Cifrario (7.9 ± 2.8) e alla Memoria di Cifre (8.5 ± 2.7)

VALUTAZIONE NEUROPSICOLOGICA

ATTENZIONE!!!

Il 22.2% dei soggetti con ADHD ottiene prestazioni nella norma in TUTTI i parametri considerati.

- ✓ Il 25% riporta punteggi patologici solo nei test che valutano la pianificazione
- ✓ Il 12.5% riporta punteggi patologici nei test che valutano la pianificazione e la velocità esecutiva
- ✓ Il 9.7% riporta punteggi patologici solo nei test che valutano l'attenzione sostenuta
- ✓ Il 5.6% riporta punteggi patologici solo nei test che valutano i processi di inibizione
- ✓ Il 5.6% riporta punteggi patologici solo nei test che valutano la velocità esecutiva

ELSEVIER

Archives of Clinical Neuropsychology
20 (2005) 457–477

Archives of CLINICAL NEUROPSYCHOLOGY

ADHD subtypes: do they differ in their executive functioning profile?

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Accepted 12 November 2004

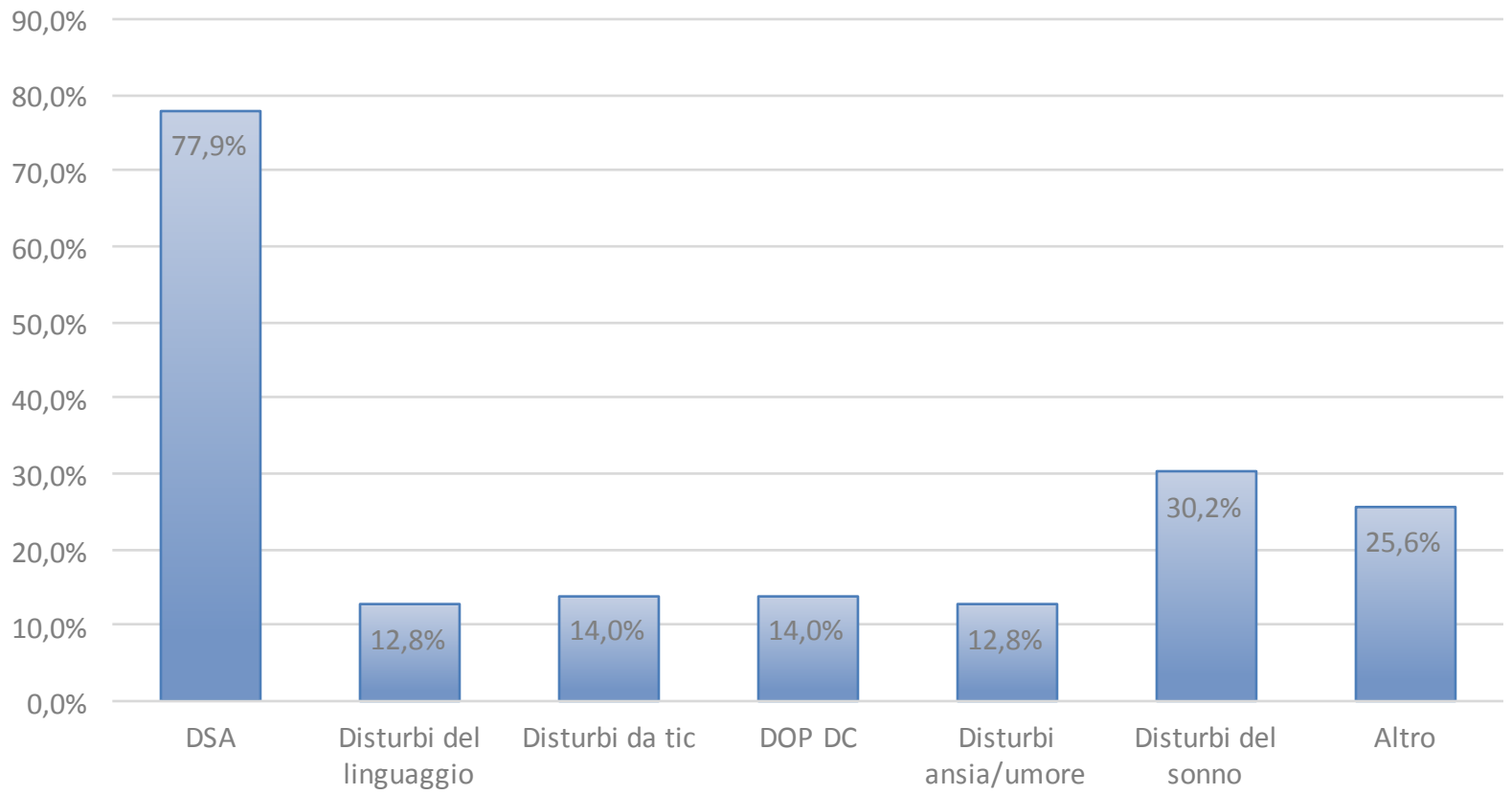
Abstract

The present study was designed to investigate the hypothesis that children with Atten... Hyperactivity Disorder combined subtype (ADHD-C) have a generalized executive functi... [Barkley, R. A. (1997). Behavioural inhibition, sustained attention, and executive functions... ing a unifying theory of AD/HD. *Psychological Bulletin, 121*, 65–94; Barkley, R. A. (19... *and the nature of self-control*. New York: The Guilford Press]. We tested whether ADHD-C and... inattentive subtype (ADHD-I) can be differentiated from each other on EF measures. We compared 1... normally developing boys with 16 boys with ADHD-C and 16 with ADHD-I on five EF domains. The boys were all matched on age, IQ, and the presence of oppositional defiant disorder (ODD)/conduct disorder (CD). Despite carefully diagnosed groups and methodological controls, the results do not support the EF-hypothesis of ADHD-C. Children with ADHD-C differed from normal controls (NC) on tasks related to inhibition; they did not exhibit EF deficits on *all* EF tasks. Children with ADHD-C also exhibited deficits on non-EF tasks. Furthermore, the ADHD-C and ADHD-I subtypes did not differ from one another. Neuropsychological findings on the domains under study did not yield evidence for the distinctiveness of ADHD-C and ADHD-I subtypes.

Keywords: ADHD; Subtypes; Neuropsychology; Executive functions; Developmental disorders

Nel nostro campione non sono rilevabili differenze significative tra i tre tipi di **presentazione** (combinata, inattentiva, iperattiva/impulsiva)

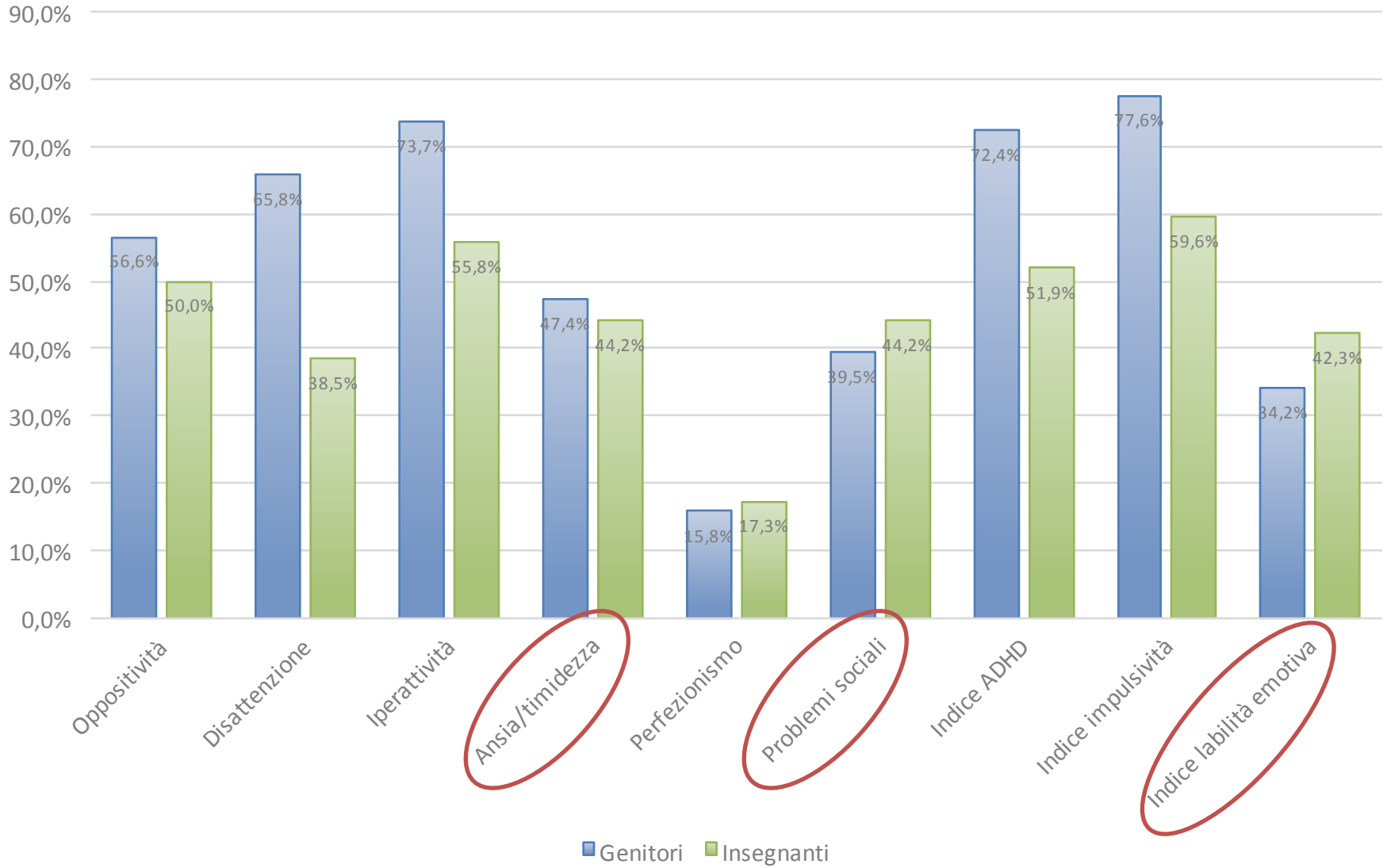
Comorbidità principali



La presenza/assenza di comorbidità non si associa a differenze significative in termini di prestazioni deficitarie nei test precedentemente esposti.

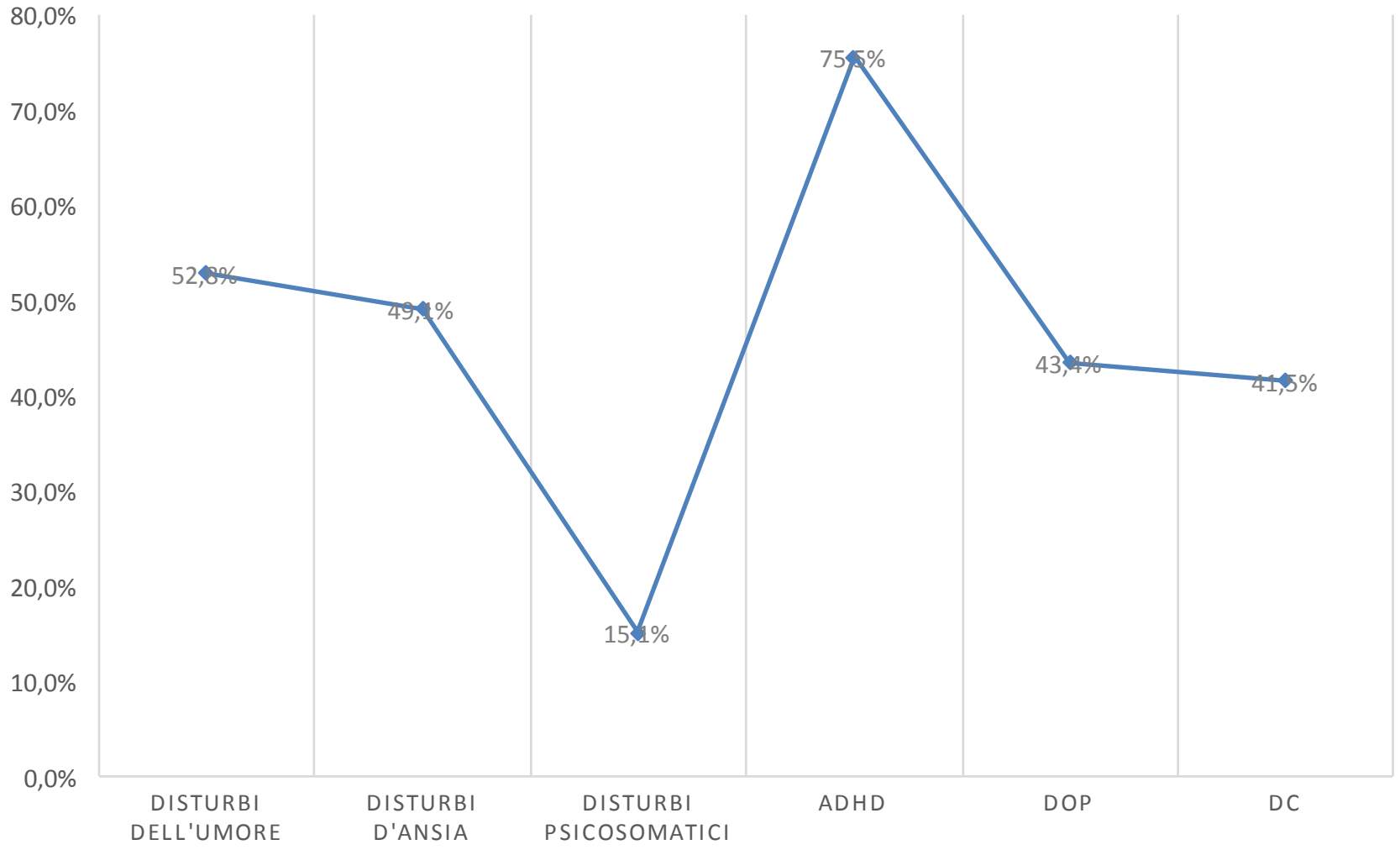
Scale Conners

% punteggi patologici (T ≥ 65)



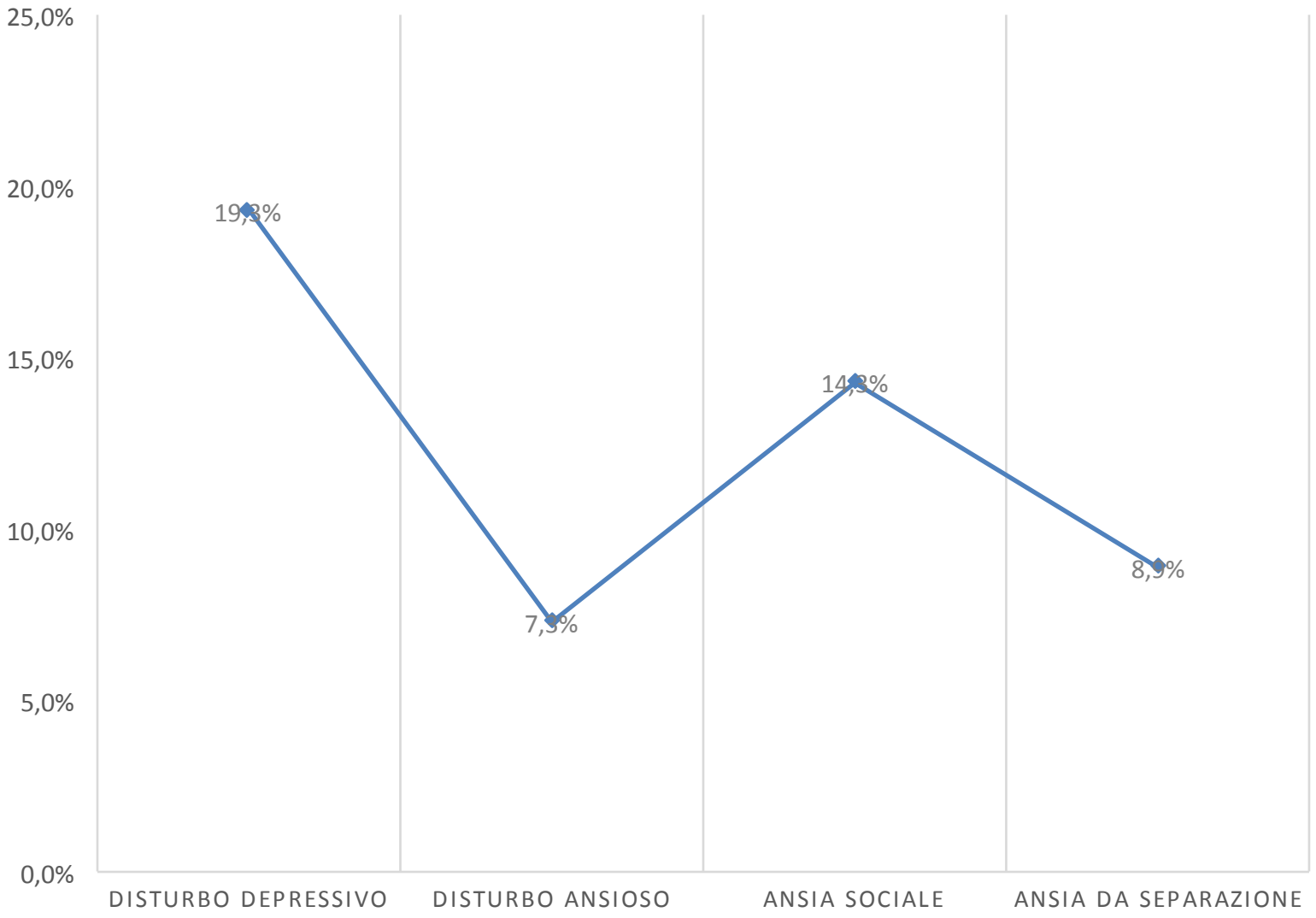
Scale CBCL DSM oriented (genitori)

% punteggi patologici (T ≥ 65)

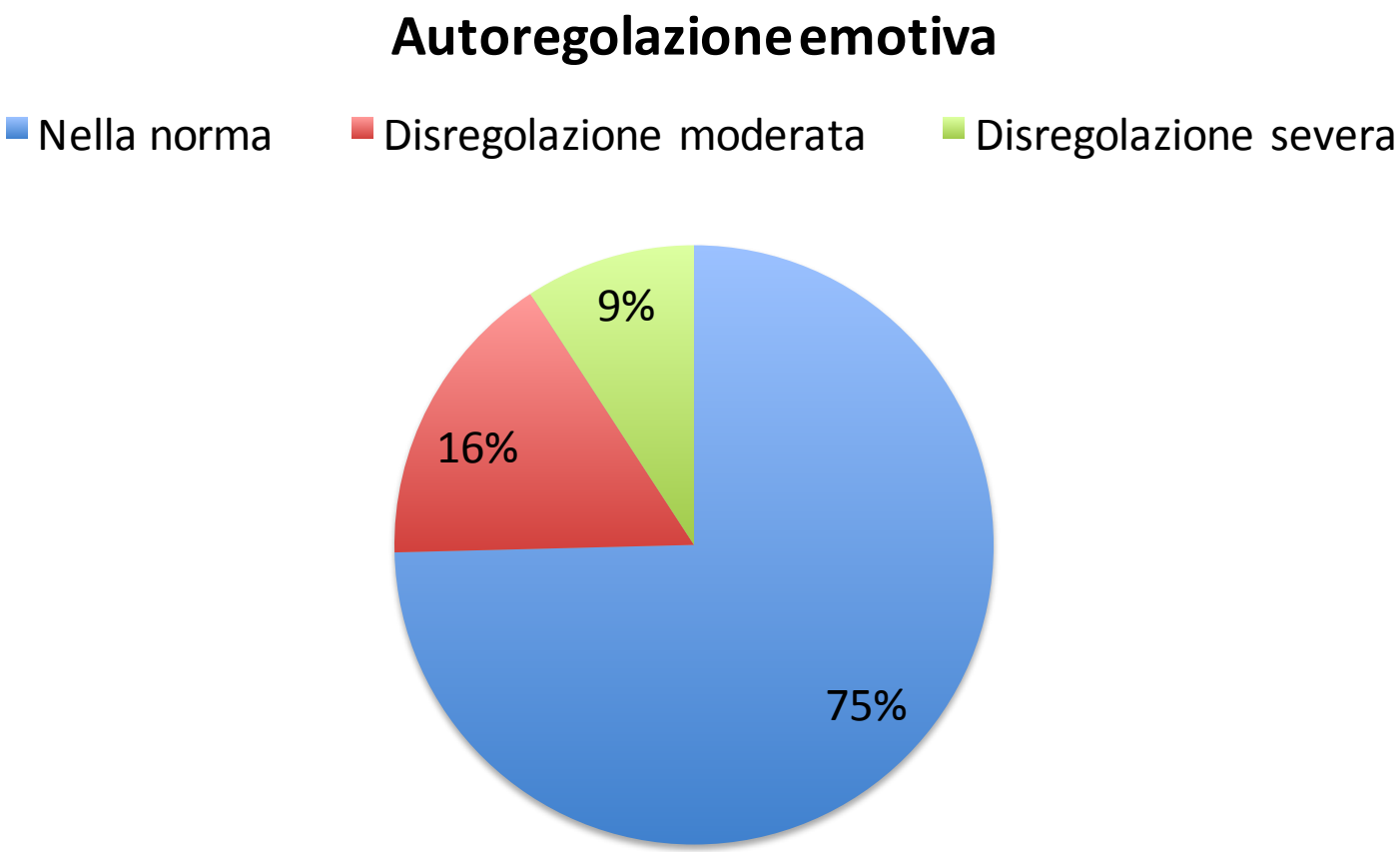


CDI e MASC (compilate dal bambino)

% punteggi patologici



CBCL: scala AAA
(Ansia/Depressione + Aggressività + Attenzione)



Più frequente nel tipo a presentazione iperattività/impulsiva (80%)
Non si associa a differenze significative nel profilo neuropsicologico

In sintesi…

✓ La negatività di test e scale non consente di escludere la diagnosi di ADHD

✓ La positività dei test sulle funzioni esecutive può essere di aiuto nell'indirizzare la diagnosi quando la clinica è dubbia

✓ I test che vanno a misurare l'attenzione sembrano essere meno sensibili e specifici rispetto ai test che valutano la velocità esecutiva e le abilità di pianificazione

✓ Durante la somministrazione di test si possono ricavare dati qualitativi su diverse caratteristiche del bambino (senso di autoefficacia, tolleranza alle frustrazioni, capacità di comprendere le regole, stile procedurale impulsivo, autostima….)

Journal of Research in Reading, ISSN 0141-0423 *DOI:10.1111/j.1467-9817.2013.01555.x*
Volume 00, Issue 00, 2013, pp 1–18

Reading difficulties and attention-deficit/ hyperactivity behaviours: evidence of an early association in a nonclinical sample

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Umberto Balottin

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Attention-deficit/hyperactivity disorder (ADHD) often co-occurs with reading disability. A cross-sectional study in an Italian-speaking, nonclinical sample was conducted in an attempt to document the existence of an early association between reading difficulties (RD) and ADHD behaviours. We recruited a sample of 369 children in their first year at primary school. Of the sample, 8.4% displayed RD; 7.0% had ADHD; 3.5% presented both RD and ADHD behaviours; 50% of the children with ADHD displayed RD; 41.9% of those with RD displayed ADHD behaviours. Low socioeconomic status was associated with a fourfold increased probability of displaying RD (odds ratio = 3.98), but not ADHD behaviours. In this nonclinical sample, we detected an early association between ADHD behaviours and RD. A key role in this association may be played by inattention symptoms, which occurred with significantly increased frequency also in the group presenting only RD.

In considerazione dell'elevata comorbidità con DSA (77.9%), dovrebbe essere sempre valutati gli apprendimenti

J Dev Behav Pediatr. 2012 April ; 33(3): 236–243. doi:10.1097/DBP.0b013e3182475267.

Severity of the Aggression/Anxiety-Depression/Attention (A-A-A) CBCL Profile Discriminates between Different Levels of Deficits in Emotional Regulation in Youth with ADHD

Joseph Biederman, M.D.[a,b], **Carter R. Petty, M.A.**[a], **Helen Day, B.A.**[a], **Rachel L. Goldin, B.A.**[a], **Thomas Spencer, M.D.**[a,b], **Stephen V. Faraone, Ph.D.**[c], **Craig B.H. Surman, M.D.**[a,b], and **Janet Wozniak, M.D.**[a,b]

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[b]Department of Psychiatry, Harvard Medical School, Cambridge, MA

Objective—We examined whether severity scores (1SD vs. 2SDs) of a unique profile Child Behavior Checklist (CBCL) consisting of the Anxiety/Depression, Aggression, a Attention (A-A-A) scales would help differentiate levels of deficits in children with AD

Study Design—Subjects were 197 children with and 224 without ADHD. We defined emotional selfregulation (DESR) as an aggregate cut-off score of >180 but <210 (1SD) o A-A scales of the CBCL (CBCL-DESR) and Severe Dysregulation as an aggregate cut-off scor of ≥210 on the same scales (CBCL-Severe Dysregulation). All subjects were assessed with structured diagnostic interviews and a range of functional measures.

Results—36% of children with ADHD had a positive CBCL-DESR profile vs. 2% of controls ($p<0.001$) and 19% had a positive CBCL-Severe Dysregulation profile vs. 0% of controls ($p<0.001$). The subjects positive for the CBCL-Severe Dysregulation profile differed selectively from those with the CBCL-DESR profile in having higher rates of unipolar and bipolar mood disorders, oppositional defiant and conduct disorders, psychiatric hospitalization at both baseline and follow up assessments, and a higher rate of the CBCL-Severe Dysregulation in siblings. In contrast, the CBCL-DESR was associated with higher rates of comorbid disruptive behavior, anxiety disorders, and impaired interpersonal functioning compared to other ADHD children.

Conclusion—Severity scores of the A-A-A CBCL profiles can help distinguish two groups of emotional regulation problems in children with ADHD.

Il 25% presenta significative difficoltà nell'autoregolazione emotiva

Neuropsychiatric Disease and Treatment

Dovepress

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ORIGINAL RESEARCH

Longitudinal course of deficient emotional self-regulation CBCL profile in youth with ADHD: prospective controlled study

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Carter Petty[1]
Laran L Hyder[1]
Katherine B O'Connor[1]
Craig BH Surman[1,2]
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Background: While symptoms of deficient emotional self-regulation (DESR) have been long associated with attention-deficit/hyperactivity disorder (ADHD), there has been limited investigation of this aspect of the clinical picture of the disorder. The main aim of this study was to examine the predictive utility of DESR in moderating the course of ADHD children into adolescence.

Methods: Subjects comprised 177 children with and 204 children without ADHD followed for an average of 4 years (aged 6–18 years at baseline, 54% male). Subjects were assessed with structured diagnostic interviews and measures of psychosocial functioning. DESR was defined by the presence (n = 79) or absence (n = 98) of Child Behavior Checklist (CBCL)-DESR profile (score $\geq 180 < 210$ total of Attention, Aggression, and Anxious/Depressed subscales) at the baseline assessment.

Results: Of subjects with DESR at baseline, 57% had DESR at follow-up. Persistent ADHD was significantly associated with DESR at follow-up ($\chi^2_{(1)} = 15.37$, $P < 0.001$). At follow-up, ADHD + DESR subjects had significantly more comorbidities ($z = 2.55$, $P = 0.01$), a higher prevalence of oppositional defiant disorder ($z = 3.01$, $P = 0.003$), and more impaired CBCL social problems t-score ($t_{(227)} = 2.41$, $P = 0.02$) versus ADHD subjects.

Conclusion: This work suggests that a positive CBCL-DESR profile predicts subsequent psychopathology and functional impairments in children with ADHD suggesting that it has the potential to help identify children with ADHD at high risk for compromised outcomes.

Keywords: attention-deficit/hyperactivity disorder, emotion, regulation, longitudinal, youth

In sintesi…

- ✓ Le funzioni esecutive sono indispensabili per la vita quotidiana e possono essere un bersaglio per l'intervento abilitativo e compensativo

- ✓ In particolare l'abilità di pianificare riveste un ruolo centrale nell'organizzare il comportamento, consentendo di programmare la vita personale e sociale, di adattarsi e di interagire efficacemente con l'ambiente, di affrontare e risolvere situazioni complesse e mutevoli

- ✓ Non va dimenticato l'aspetto relativo alla disregolazione emotiva che va evidenziato e trattato precocemente, per quanto paia il più difficile da modificare

- ✓ Le comorbidità vanno identificate e trattate!

Child and Adolescent Mental Health
a journal for all professionals working with children and young people

Child and Adolescent Mental Health Volume 15, No. 2, 2010, pp. 85–90 doi: 10.1111/j.1475-3588.2009.00538.x

Undertreatment of Motor Problems in Children with ADHD

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[7]Karakter Child and Adolescent Psychiatry University Center, 6500 HB Nijmegen, The Netherlands

Background: Motor problems occur in 30% to 50% of children with ADHD, and have a severe impact on daily life. In clinical practice there seems to be little attention for this comorbidity with the possible consequence that these motor problems go undertreated. **Method:** Clinical interview and questionnaire survey of treatment by physiotherapy and factors predicting treatment of motor problems in 235 children with ADHD and 108 controls. **Results:** Half of motor-affected children had received physiotherapy. Treated children had more severe motor problems, and less frequently presented with comorbid anxiety and conduct disorder. Treated and untreated children were similar in age, and rated similarly on ADHD inattentive and hyperactive-impulsive scales and parental socio-economic status. **Conclusion:** Currently, undertreatment of motor problems in ADHD occurs. Behavioural factors play a role in referral and intervention.

Grazie per l’attenzione!!!

http://www.usatoday.com/story/opinion/2015/05/12/adderall-addition-drug-legal-column/26135649/

America's love affair with legal amphetamine: Column

Lawrence Diller 6:02 p.m. EDT May 12, 2015

When will we be able to just say no?

I've decided to create a new psychiatric disorder. Why not? Drug companies do it all the time.

Shire, which makes Adderall, won approval recently from the Food and Drug Administration to market its amphetamine drug, Vyvanse, for the treatment of BED. You haven't heard of it? Neither had many people, until Shire funded studies to get the binge eating disorder into the DSM-5 — America's official psychiatric bible of common life dilemmas translated into mental disorders. My disorder is called achievement anxiety disorder (AAD), and it explains the increasing reports of prescription amphetamine misuse most often in the form of Adderall abuse.

Just what is achievement anxiety disorder? Like all psychiatric conditions, there are no blood tests or brain scans to make the diagnosis. But you can see it all around us — frantic people working ever harder to achieve a certain level of material satisfaction and security. Because of our country's declining position as a global economic empire, along with a widening gap between the 1% and everyone else, Americans must now work harder and make more money just to maintain the same standard of living our country enjoyed 40 years ago. And while the U.S. has produced astounding successes and accomplishments, that history has left many Americans doubting their own abilities, striving to do more and turning to drugs to cope.

A once-personal struggle for self-acceptance and success has turned into contagious angst about a collective failure to live up to our dreams. Today's Millennial generation is the first group of Americans since World War II who will not live as well as their parents did. Our young adults who are turning to Adderall are the stark casualties of this broken cultural norm that makes happiness impossible to achieve.

Adderall is not a new drug. Amphetamine (legal and illegal) has been around since 1929 and has repeatedly found its way into the mainstream culture over the years for use in treating depression,

asthma, neurasthenia, narcolepsy, weight control and now attention deficit hyperactivity disorder, ADHD — or ADD (without hyperactivity). Doctors invoke ADD as the most current reason to prescribe a chemical that, in the short term, makes anyone who takes it, child or adult, more alert, more methodical and more likely to complete tasks that are boring or difficult. There is no evidence in either children or adults that taking Adderall has long-term benefits.

Rampant Adderal use is a clear sign of our nation's epidemic of ADD or AAD — you decide. According to Drug Enforcement Administration records, in 2013 American manufacturers of prescription stimulant drugs produced 191,723 kilograms, or 211 tons, of legal speed. This translates to more than two dozen 20 mg Adderall pills for every man, woman and child in this country. AAD may be a particularly American condition. Our country makes up less than 4.5% of the world's population but produces 70% of its legal amphetamines.

Our epidemic of ADHD/ADD is the official reason for our love affair with legal amphetamine,but experts estimate that nearly a third of the stimulants prescribed in our country is diverted for illegal misuse (without a doctor's prescription). Any college student can tell you how easy it is to obtain Adderall during exam time. Knowledgeable Web surfers go to the "dark side" of the Internet and find sites such as the Silk Road, where Adderall is openly sold and traded.

However, we can't just blame drug companies and drug dealers for our love affair with Adderall. In any epidemic,one must not only examine the qualities of the virus but also consider the qualities of the host. AAD is part of our national character. Horatio Alger, George Babbitt, Jay Gatsby and Gordon Gekko are authors and fictional characters who chronicle how fundamental AAD is to the American ethos, though, as far as I know,none of them used Adderall.

Our relentless pursuit of material acquisition is our unofficial state religion. Nothing short of some natural or social catastrophe is likely to change our values soon. But at some point, our use of Adderall for AAD is certain to peak and then crash. It's a historical inevitability, with at least three waves of doctor-prescribed amphetamine abuse in our country's past. The last was in the 1970s, when many dieting women became addicted via their physicians' prescriptions. Doctors were sued, lost their licenses, and the practice stopped.

This time is different. There are mega Fortune 500 companies making $9 billion a year by selling legal speed and stimulants. Their power and influence over government regulatory agencies such as the FDA and DEA make it unlikely that the use of Adderall will decrease any time soon. Unfortunately, many more young adults will become addicted, and some will die before America says no (again) to Adderall.

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ARTICLE

Phenotypic Variability in Developmental Coordination Disorder: Clustering of Generalized Joint Hypermobility With Attention Deficit/hyperactivity Disorder, Atypical Swallowing and Narrative Difficulties

CLAUDIA CELLETTI, GIORGIA MARI, GIULIA GHIBELLINI, MAURO CELLI, MARCO CASTORI, AND FILIPPO CAMEROTA

Developmental coordination disorder (DCD) is a recognized childhood disorder mostly characterized by motor coordination difficulties. Joint hypermobility syndrome, alternatively termed Ehlers–Danlos syndrome, hypermobility type (JHS/EDS-HT), is a hereditary connective tissue disorder mainly featuring generalized joint hypermobility (gJHM), musculoskeletal pain, and minor skin features. Although these two conditions seem apparently unrelated, recent evidence highlights a high rate of motor and coordination findings in children with gJHM or JHS/EDS-HT. Here, we investigated the prevalence of gJHM in 41 Italian children with DCD in order to check for the existence of recognizable phenotypic subgroups of DCD in relation to the presence/absence of gJHM. All patients were screened for Beighton score and a set of neuropsychological tests for motor competences (Movement Assessment Battery for Children and Visual-Motor Integration tests), and language and learning difficulties (Linguistic Comprehension Test, Peabody Picture Vocabulary Test, Boston Naming Test, Bus Story Test, and Memoria-Training tests). All patients were also screening for selected JHS/EDS-HT-associated features and swallowing problems. Nineteen (46%) children showed gJHM and 22 (54%) did not. Children with DCD and gJHM showed a significant excess of frequent falls (95 vs. 18%), easy bruising (74 vs. 0%), motor impersistence (89 vs. 23%), sore hands for writing (53 vs. 9%), attention deficit/hyperactivity disorder (89 vs. 36%), constipation (53 vs. 0%), arthralgias/myalgias (58 vs. 4%), narrative difficulties (74 vs. 32%), and atypical swallowing (74 vs. 18%). This study confirms the non-causal association between DCD and gJHM, which, in turn, seems to increase the risk for non-random additional features. The excess of language, learning, and swallowing difficulties in patients with DCD and gJHM suggests a wider effect of lax tissues in the development of the nervous system.

KEY WORDS: attention deficit/hyperactivity disorder; coordination; language; hypermobility; speech; swallowing

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INTRODUCTION

The term "development coordination disorder" (DCD) is used to define the selective impairment of development of motor coordination in children [Vaivre-Douret, 2014]. Synonyms of DCD include, but are not limited to congenital clumsiness, "motor debility" and developmental dyspraxia, the latter being the result of faulty maturational processes of the central nervous system during infancy and childhood [Vaivre-Douret, 2014]. According to the diagnostic and statistical manual of mental disorders (DCM-IV) [American Psychiatric Association, 2000], DCD is an exclusion diagnosis for perturbed fine and/or global motor coordination in the absence of any cognitive, neurological, and/or sensorial deficit. The overall prevalence of DCD is close to 6% in children with an excess of affected males [American Psychiatric Association, 2000]. Motor impairments include marked delay in achieving motor milestones, clumsiness, poor sensorimotor coordination, poor balance and handwriting and poor postural control, as well as difficulties in motor learning (acquiring and automatizing new movements), execution and ideation of motor planning, timing, and sequencing of movement [Geuze, 2005]. Thus far, the etiology of DCD remains unknown, despite many hypotheses that have been suggested to explain its neurodevelopmental pathogenesis.

Kirby and Davies [2007] observed functional similarities between children with DCD and those with joint hypermobility syndrome (JHS), a connective tissue disorder diagnosed according to the Brighton criteria [Grahame et al., 2000]. This observation prompted the authors to speculate on the multisystem nature of DCD. JHS, which is now considered clinically indistinguishable from Ehlers–Danlos syndrome, hypermobility type (JHS/EDS-HT) [Tinkle et al., 2009; Castori et al., 2014], presents manifestations that span clearly beyond the integumentary and articular systems [Castori, 2012]. The proposed link between connective tissue and DCD is also supported by the observation of a high prevalence of generalized joint hypermobility (gJHM) in children with DCD [Jelsma et al., 2013]. These data corroborate what has been previously observed by Adib et al. [2005], who described clumsiness and poor coordination symptoms in 125 children with JHS. They also described speech and learning difficulties, as well as "dyspraxia" among these patients.

It is possible that the lack of recognition of a significant overlap between DCD, gJHM, and JHS/EDS-HT is due to the still widespread lack of prompt diagnosis of gJHM and related syndromes in specialized settings (i.e., among rheumatologists) [Grahame and Bird, 2001]. This is probably related to the absence of a consensus among specialists in using available diagnostic criteria for gJHM and JHS/EDS-HT [Remvig et al., 2014], as well as the absence of a reliable confirmatory test for JHS/EDS-HT [Mayer et al., 2013]. Hence, the non-random association between DCD, gJHM, and associated symptoms may represent a highly prevalent, still poorly defined, multisystem disorder in children, with unexpected consequences on various health and mental health determinants in adults.

In the short term, the early recognition of gJHM and related features may be useful for the assessment and management of the child with DCD under both the clinical and the rehabilitation perspectives. The aim of the present study is to assess the prevalence of gJHM in a group of 41 Italian children with DCD and to investigate possible phenotypic clustering in relation to additional findings, such as language disorders and learning impairments.

MATERIALS AND METHODS

From May 2012 to February 2013, 41 Italian children with DCD were assessed in a specialized setting including child neurologist, logopedist and physiatrist. The diagnosis of DCD was made according to DSM-IV [American Psychiatric Association, 2000]. Exclusion criteria were age <4 years, IQ <70 evaluated through the Wechsler Intelligence Scale for Children 4th Edition (WISC-IV) [Wechsler, 2003], as well as the presence of any neurological, rheumatic, and metabolic disease.

Motor performance was evaluated using the Movement Assessment Battery for Children (M-ABC) test [Henderson and Sugden, 1992] and the Developmental Test of Visual–Motor Integration (VMI) test [Sutton et al., 2011]:

- M-ABC is a product-oriented, norm-referenced test designed for (a) identifying children aged 4–12 years with motor difficulties; (b) clinical exploration, intervention planning; (c) program evaluation; and (d) research. It consists of eight items grouped in three sections (manual dexterity, ball skills, and balance).
- VMI is commonly used to assess handwriting dysfunction in children. VMI is a standardized, norm-referenced test designed to assess visual–motor integration. VMI requires the child to copy a series of geometric designs. Child's performance is compared with standard criteria and reference designs and a score allocated according to the accuracy of the drawing.

All the children were first evaluated for gJHM, language disorders, and learning disabilities. gJHM was assessed with the Beighton score [Beighton et al., 1973] by two trained physiatrists. This score is composed of five maneuvers: four of them are tested passively on both sides of the body and one is tested actively. The passive extension of the metacarpophalangeal joint of the little finger, elbow, and knee were measured bilaterally. When the range of motion exceeds a specified range, 1 point is given. These points are summed and the score ranges from 0 to 9 (two times four joints and 1 point for hands flat on the floor with straight knees). According to the recommendation of van der Giessen, the cut-off point for hypermobility was $\geq$5 for children aged 3–9 years and $\geq$4 points for children aged older than 10 years [van der Giessen et al., 2001].

Language and learning difficulties were assessed using the Linguistic Comprehension Test (LCT) [Rustioni, 1994], The Peabody Picture Vocabulary Test (PPVT) [Dunn and Dunn, 1981], the Boston Naming Test (BNT) [Kaplan

et al., 1976] the Bus Story Test (BST) [Renfrew, 1969], and and the Memoria-Training (MT) Test for the Assessment of reading and comprehension skills [Cornoldi and Colpo, 1998]:

- LCT is an Italian-specific and Italian-normed test of linguistic understanding; it is packaged in booklet form in a multiple-choice format, and is used to assess the understanding of grammatical contrasts in the Italian language. The child is shown a page with four picture choices and must select the picture that matches a spoken sentence. The test is administered in six different protocols depending on age, and the score is calculated as the sum of correct answers.
- PPVT measures an individual's receptive vocabulary for standard American English and provides, at the same time, a quick estimate of verbal ability or academic aptitude. It has been translated in Italian language [Stella et al., 2000]. The PPVT consists of 175 stimulus words and as many corresponding image plates. Each image plate contains four black-and-white drawings, one of which best represents the meaning of the corresponding stimulus word. The child listens to a word uttered by the interviewer and then selects one of four pictures that best describes the word's meaning.
- BNT is one of the most commonly used tests of confrontation naming. It requires subjects to provide the names of 85 drawn objects. The drawings cover a wide range of nouns, from those used very frequently (such as "house") to those that are used rarely (such as "yoke" and "hammock"). Subjects who cannot provide the correct name within 20 sec are given a semantic cue (for example, "a type of building" for "house"); if they are still unable to give the answer after additional 20 sec, they are given a phonemic cue (for example, "hou . . ." for "house"). A positive score is attributed to every correct answer given within the first 20 sec, as well as to those given after the semantic cue [Riva et al., 2000].
- BST [Renfrew, 1969], administered in the validated Italian version [Cipriani, 2012], tests the narrative skills of children in the age range between 3 years and 6 months and 8 years and 5 months. It consists of a "retelling" task: the child is asked to listen to a story and to rehearse it using verbal description and helped by pictures. For the purpose of the present study, the test was used only as a screening tool. Therefore, the result was expressed categorically as either "presence of narrative difficulties", when the child could not retell an intelligible version of the story, or "good narrative abilities".
- MT is a standardized battery of tests to assess reading and comprehension skills and was specifically designed for Italian school-age children [Cornoldi and Colpo, 1998]. MT Test consists of: (a) an evaluation of reading speed measured by the time needed to read a short passage compared with a standardized measure; (b) a test of accuracy of reading, as reflected by the number of reading errors made per passage; and (c) a text comprehension test based on the ability to provide correct answers to a defined set of questions following the reading of a short story [Levorato et al., 2004]. Owing to the lack of standardized Italian tests for the assessment of narrative skills in subjects older than 9, the subtest (c) was also used for this purpose in subjects older than 9 years, by asking them to retell a story. As with younger children receiving the BST, also in this case, subjects were categorized as having "narrative difficulties" or "good narrative abilities".

All children were also assessed by means of a custom-made questionnaire aimed to gather more in-depth information concerning different symptoms correlated with gJHM . In addition, the presence of attention deficit/hyperactivity disorder (ADHD) was checked according to DSM-IV [American Psychiatric Association, 2000]. The presence of atypical swallowing was also assessed: this condition is defined as a lingual pathological behavior, consisting of tongue pressure on the palatal and lingual surfaces of the teeth during swallowing [Melsen, 1979; Eslamian and Leilazpour, 2006].

Statistical analysis was conducted with the Medcalc software (Marienkerke, Belgium). Descriptive statistics were used for the characteristics of the samples. χ^2 test was performed to test for differences in the frequency of symptoms between the groups. Correlation between variables was expressed by the Spearman's ranking-order-correlation coefficients. An α level of 5% was adopted for analysis.

RESULTS

Among the 41 children with DCD, 31 were boys and 10 girls (mean age 8 +/- 3 years). According to the Beighton score *cut-offs*, patients were subclassified in those with DCD and gJHM (i.e. DCD-H) and those with DCD but without gJHM (i.e., DCD-NH). Nineteen (46%) patients were identified as DCD-H and 22 (54%) as DCD-NH. Comparison among selected clinical characteristics between DCD-H and DCD-NH patients are summarized in Table I.

In summary, we found statistically significant differences between groups concerning frequent falls, bruising and prolonged bleeding, motor impersistence (defined as the inability to maintain a fixed posture), arthralgias and myalgias, intestinal constipation, sore hands from writing, and ADHD that further supported phenotypic clustering around gJHM in children with DCD.

In order to further scrutinize the relationship between gJHM, language disorders, and learning disabilities, a linear regression analysis was carried out and showed a positive correlation between Beighton score and ADHD ($r = 0.59$; $P = 0.01$), whereas no statistically significant correlation was observed between Beighton score and language disorders ($r = 0.027$; $P = 0.86$).

Based on the results in the speech comprehension and production test battery, patients with a language disorder were divided into three subcategories according to DSM-IV criteria:

- "expressive", when performance was inappropriate for age in the expressive language test (BNT) and comprehension skills were normal or only mildly delayed;
- "phonological", when they performed inappropriately for age in the PPVT test while scoring normal or mildly delayed for age in all the other tests;
- "receptive–expressive", if LCT and PPVT test scores were lower than the

TABLE I. Comparison for General Features Between the Hypermobile (DCD-H) and Non-Hypermobile (DCD-NH) Groups of Children with Developmental Coordination Disorder.

Feature	DCD-NH (Total = 22)	DCD-H (Total = 19)	*P*-value
Gender	M = (17) 77%; F = (5) 23%	M = 14) 73%; F = (5) 27%	0.92
Age	79 months (± 33 months)	87 months (± 33 months)	0.23
Cesarean delivery	1 (4%)	3 (16%)	0.495
Prematurity	1 (4%)	2 (10%)	0.895
Birth problems	5 (23%)	5 (26%)	0.922
Plagiocephaly	1 (4%)	0	0.941
Crooked feet	0	1 (5%)	0.941
Congenital hip dysplasia	0	3 (16%)	0.182
Neonatal UTI	2 (9%)	2 (10%)	0.709
Delayed toddling	11 (50%)	5 (26%)	0.219
Tiptoe walking	1 (4%)	5 (26%)	0.128
Delayed ambulation	15 (68%)	11 (58%)	0.721
Clumsiness	14 (64%)	17 (89%)	0.119
Painful pronation	0	2 (10%)	0.405
Learning difficulties	5 (23%)	9 (47%)	0.184
Language delay	17 (77%)	12 (63%)	0.518
Abdominal hernias	0	4 (21%)	0.082
Frequent falls	4 (18%)	18 (95%)	**<0.001**
Bruising and prolonged bleeding	0	14 (74%)	**<0.001**
Motor impersistence	5 (23%)	17 (89%)	**<0.001**
Sore hands from writing	2 (9%)	10 (53%)	**0.007**
ADHD	8 (36%)	17 (89%)	**0.002**
Constipation	0	10 (53%)	**<0.001**
Arthralgias/myalgias	1 (4%)	11 (58%)	**<0.001**

ADHD, attention deficit/hyperactivity disorder; F, females; M, males; UTI, urinary tract infection.

expected mean score for age and if their performance was inappropriate in the expressive language test.

The speech/language assessment using the test battery showed significant differences in the incidence of narrative difficulties and atypical swallowing between groups (Table II).

DISCUSSION

In this study, we first confirmed a high rate of gJHM among children originally assessed for DCD [Kirby and Devies, 2007]. We also compared the rate of selected features, spanning from typical connective tissue features to specifically addressed neurodevelopmental attributes between a group of children with DCD and gJHM (i.e., DCD-H), and a group of non-hypermobile DCD subjects (DCD-NH). In summary, we found an excess of frequent falls (95 vs. 18%), easy bruising (74 vs. 0%), motor impersistence (89 vs. 23%), sore hands for writing (53 vs. 9%), ADHD (89 vs. 36%), constipation (53 vs. 0%), arthralgias/myalgias (58 vs. 4%), narrative difficulties (74 vs. 32%), and atypical swallowing (74 vs. 18%) in the DCD-H group compared to the DCD-NH one. Our findings suggest the existence of a highly prevalent, still poorly defined, multisystem disorder in DCD children with gJHM which could evolve in a more pronounced generalized connective tissue disorder in the later life. The eventual phenotype may be a true hereditary connective tissue disorder and, perhaps, correspond to JHS/EDS-HT. Accurate integumentary involvement was not systematically assessed in this work, because essentially conceived in a child neurology setting. Hence, we were not able to definitely confirm this hypothesis, which could represent a field for future research.

In comparison with most studies investigating the relationship between gJHM (or JHS/EDS-HT) and neurodevelopmental attributes, our observation extended such a link to language and learning difficulties. The existence of a recognizable speech impairment in patients with Ehlers-Danlos syndrome is well known in the specialized literature [Arvedson and Heintskill, 2009]. Nevertheless, evidence-based data aimed at substantiating this experience are still lacking. In this work, both groups (i.e., DCD-H and DCD-NH) showed a high rate of language disorders. More specifically, the DCD-H group displayed a significant excess of narrative difficulties with narrative competences below what is expected at their chronological age. This preliminary evidence, which needs confirmations in other studies, may share a

TABLE II. Speech and Language Results in the Hypermobile (DCD-H) and Non-Hypermobile (DCD-NH) Groups of Children with Developmental Coordination Disorder.

Feature	DCD-H	DCD-NH	χ^2	*P*-value
Gender	14 males; 5 females	17 males; 5 females	0.07	0.78
Language disorders	12/19	16/22	0.43	0.51
Type of language disorder				
Expressive	4/12	8/16	0.78	0.37
Phonological	2/12	3/16	3.07	0.88
Receptive/expressive	6/12	5/16	0.78	0.31
Narrative difficulties	14/19	7/22	7.15	**<0.001**
Atypical Swallowing	14/19	4/22	12.75	**<0.001**

common pathogenesis with the low motor competences in children with gJHM (or JHS/EDS-HT).

Now, it is well known the existence of an excess of defective proprioception in children with gJHM [Fatoye et al., 2009] and this is likely related to a recognizable neurodevelopmental pattern [Adib et al., 2005]. Stratified knowledge indicates that children organize language through action. In particular, Iverson [2010], and Iverson and Braddock [2011] suggested that emerging new motor skills affect infants' interactions with objects and people, and this is relevant for development of communication and language acquisition. In the developing child with gJHM, the (presumably) generalized lack of proprioception may affect the process of organization of spatial and temporal concepts. This phenomenon could explain the observed excess of numbers and letters reversion during writing in the DCD-H group. In fact, this may stand for a difficulty in recognizing the correct spatial orientation in the "hypermobile" child. The presumed high rate of unsatisfactory orthographic competence, dysgraphia [Adib et al., 2005], and poor pen grip in gJHM children could be explained by the same mechanism. In this work, we did not systematically assess for typical satellite symptoms, such as headache, fatigue, and specific pattern of musculoskeletal pain, of JHS/EDS-HT, and did not investigate their relationship with language impairment in the DCD-H group. However, we could hypothesize that in the symptomatic child (i.e., the gJHM child also meeting JHS/EDS-HT criteria), upper limb pain, easy fatigability of upper limb muscles, and fatigue may contribute to the poor handwriting performances.

An association between DCD and attention deficit is well known by the child neurologist, who is used to attribute the diagnosis of disorder of attention and motor perception at the mixed phenotype of DCD, AD(H)D, and oppositional defiant disorder [Gibbs et al., 2007]. Accordingly, two studies found a significant association between ADHD and gJHM in children [Koldas Doğan et al., 2011; Shiari et al., 2013]. In our work, we confirmed this association underlying the non-causal link between development of motor competence and appropriate learning skills in gJHM children. We also suggest that the presence of a (subclinical) hereditary connective tissue disorder may be an underestimated diagnosis for DCD children who also display a disorder of attention with or without an oppositional defiant disorder. The reason for an excess of ADHD in children with gJHM remains without a consistent explanation. Nevertheless, a default of the process of the organization of spatial and temporal concepts, as well as the coexistence of additional JHS/EDS-HT-related features, such as fatigue and musculoskeletal pain, could be postulated to be involved.

It is reported that low muscle tone of neck, mouth, and articulators can affect speech production, as well as swallowing in Ehlers-Danlos syndrome patients and that these subjects often have a small jaw and a highly arched palate [Shprintzen, 1997; Hunter et al., 1998, Arvedson and Heintskill, 2009]. In addition, various research groups note that the clinical absence/hypoplasia of the lingual frenulum is statistically more common in Ehlers-Danlos syndrome and JHS/EDS-HT than controls [De Felice et al., 2001; Perrinaud et al., 2007; Celletti et al., 2011]. In our study, we did not accurately assess the relationships between intraoral anatomy, tongue praxis, and speech problems. Nevertheless, DCD-H children showed a higher prevalence of atypical swallowing, a phenomenon that could be partly explained by poor tongue coordination. In this setting, we could speculate on the link between a presumed high rate of abnormal lingual frenulum in our gJHM children and atypical swallowing. Accordingly, deglutition and speech problems in gJHM (and, perhaps, JHS/EDS-HT) children may arise from the combination of short lingual frenulum and abnormal tongue pharyngeal proprioception. In turn, the evidence of a short lingual frenulum could be pathogenically unrelated to defective tongue proprioception/movement, or rather be a developmental (intrauterine) or postural (extrauterine) consequence of tongue incoordination.

In conclusion, this study highlights numerous disabling findings in hypermobile children with DCD compared to non-hypermobile subjects. Most can be treated with appropriate therapeutic plans and learning support in order to guarantee children' adequate education and attainment of proper development. Currently, the Beighton score for gJHM, although originally elaborated by studying a pediatric population, now is not considered adequate for children. Therefore, an

appropriate diagnostic work-up relying on a multidisciplinary approach is necessary [Celletti et al., 2013] during which family history and JHS/EDS-HT-related symptoms should be investigated in children originally assessed for DCD. The implementation of a rehabilitation plan working on the concept of space at a bodily level (e.g., occupational and physiotherapic training) and at a higher thoughts level (e.g., spatial organization of the setting, organization of verbal sequences, representation of graphemes) is important, as well as a lingual motility training, especially in children with difficulties in articulation and swallowing. Such a program also needs to involve children's families, as home treatment is known to improve the outcome [Mintz-Itkin, 2009]. In addition, strengthening meta-cognitive resources can support children to organize and control their movements, as well as their learning. This can be fostered with tools, such as computers and conceptual maps, in order to reach a better orthographic control and oral rehearsal.

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Self-Esteem Evaluation in Children and Adolescents Suffering from ADHD

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Abstract: *Background:* Several recent studies investigated the relationship between self-esteem and ADHD, however, the results are still controversial. In the present study we analyze the characteristics of self-esteem in a sample of children and adolescents suffering from ADHD, with a particular focus on the relationship between ADHD symptoms severity and treatment strategies.

Methods: A total of 85 patients with ADHD (44 drug-free and 41 drug-treated, 23 of which atomoxetine-treated and 18 Methylphenidate-treated) and 26 healthy controls were enrolled in the study in order to evaluate self-esteem using the Self-esteem Multidimensional Test (TMA).

Results: ADHD subjects revealed lower scores on all self-esteem domains compared to controls. Both ADHD drug-free (47.1%) and ADHD drug-treated (44.1%) groups showed significantly higher rates of subjects in the pathological range as compared to normal control group (8.8%) (p <.001) with a higher percentage of subjects in the pathological range. Among ADHD drug-treated subjects, the methylphenidate group showed higher self-esteem scores as compared to the atomoxetine group.

Conclusion: A lower self-esteem profile is more common in subjects suffering from ADHD than in healthy controls, suggesting the importance of an early detection of psychological well-being in these children in order to reduce the ADHD symptoms long-term impacts.

Keywords: Adolescents, ADHD, Atomoxetine, Children, Methylphenidate, Self-esteem.

INTRODUCTION

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common developmental disorders with a prevalence of 3-7% in the general population [1] and is associated with significant impairment symptoms. As a consequence of pervasiveness, ADHD can negatively interfere with the general well-being, as well as with social life, academic performance, and development of social skills [2-5], which in turn, can lead to low self-esteem.

Self-esteem is a complex construct that has been described in a variety of different ways [6, 7]. Generally, it can be defined as a cognitive and emotional concept of an individual about himself, and recently there has been a growing consensus that self-esteem is a multidimensional construct involving different areas such as competence, achievement, and a judgment of self-worth [6, 8-10]. Several studies investigating the relationship between self-esteem and different psychiatric disorders indicate severe inverse relationships between self-esteem and these conditions [11-13]. In line with this, the link between ADHD and low self-esteem was also demonstrated by cross-sectional studies [14-18]. An explanation for these results could be addressed to the multiple failures that these patients report in different social contests (e.g. school, family, etc.), and that drive them to experience a lower perception of their competency as compared to peers. Furthermore, recent findings from longitudinal studies also showed that children diagnosed with ADHD reported lower self-esteem in adolescence as compared to controls [16, 19, 20]. However, other studies found no differences between clinically diagnosed ADHD and controls in terms of self-esteem, showing instead that children with ADHD tend to overestimate their own competence, despite the various problems they experience, implementing a phenomenon called "positive illusory bias", a thinking style characterized by positive illusions which could also be a means of self-protection [21-24].

Independently of the controversial results, all the studies finally agreed that a positive self-esteem may help children with ADHD to cope with failures or difficulties in everyday life [16, 23], thus emphasizing the importance of self-esteem for performance and outcomes in ADHD patients [16].

However, so far, only few studies have investigated how this construct can be influenced by therapeutical treatments. Indeed, only two studies directly investigated the effect of methylphenidate on self-esteem in ADHD patients, reporting

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Table 1. Clinical Characteristics of the Sample

	ADHD Groups (N[a]=85)			Controls (N=26)
	Drug-free (N=44)	Atomoxetine (N=23)	Methilfhenydate (N=18)	
Type of ADHD				
Inattentive N(%)	7(8.2%)	-	2(2.4%)	-
Hyperactive/Impulsive N(%)	1(1.2%)	-	2(2.4%)	-
Combined N(%)	36(42.4 %)	23(27%)	14(16.5%)	-
Comorbid disorders				
SLD[b] N (%)	17(20%)	1(1.2%)	9(10.6%)	-
Anxiety Disorder N (%)	18(21.2%)	4(4.7%)	4(4.7%)	-
ODD[c] N(%)	7(8.2%)	9(10.6%)	9(10.6%)	-
Depressive Disorder N(%)	3(3.6%)	1(1.2%)	1(1.2%)	-
Other	3(3.5%)	3(3.6%)	-	-
SNAP-IV Subscales				
Inattentive M[d] (SD[e])	18.13 (4.7)	19.63 (4.3)	17.00 (5.1)	5.04 (1.1)
Hyperactive/Impulsive M (SD)	15.67 (6.4)	19.58 (4.8)	14.85 (6.3)	3.04 (1.1)
Combined M(SD)	33.80 (9.9)	39.21 (6.7)	31.84 (9.6)	8.08 (1.5)
Oppositional Defiant M(SD)	11.00 (5.0)	13.52 (5.5)	12.15 (5.2)	4.15 (1.3)

[a]Number of subjects;
[b]Specific Learning Disorder;
[c]Oppositional Defiant Disorder;
[d]Mean;
[e]Standard Deviation.

that patients treated with stimulants had significantly higher self-esteem as compared to un-medicated subjects [25, 26]. More studies have been conducted on patients treated with atomoxetine, demonstrating an improvement of self-esteem that, in turn, lead to an impact on emotional well-being and quality of life [5, 8, 27-39]. However, to our knowledge, only one of these studies used a specific tool to evaluate self-esteem [8].

In the present study we analyze the characteristics of self-esteem in a sample of children and adolescents suffering from ADHD, with a particular focus on the relationship between ADHD symptoms severity and treatment strategies.

MATERIALS AND METHODOLOGY

Participants and Procedure

A total of 85 children and adolescents (80 males and 5 females; age range 8-15 years; mean age ± SD: 10.03 ± 2.0) suffering from ADHD, referred to the Child and Adolescent Neuropsychiatry Unit of the Paediatric Department at the University of Catania (Italy) and to the Child and Adolescent Neuropsychiatry Unit of the Children's Research Hospital Bambino Gesù of Rome (Italy) throughout the year 2010 were enrolled in this study. All ADHD patients had been diagnosed according to the DSM-IV-TR criteria [1] by a psychiatry experienced with children and adolescent. Moreover, Kiddie-Schedule for Affective Disorders and Schizofrenia for School-Age Children/Present and Lifetime Version (K-SADS-PL) [40] was administered to all the patients' parents by an experienced trained clinician. An interrater reliability analysis using the Kappa statistic was performed to determine consistency among DSM-IV-TR criteria and K-SADS-PL diagnosis. The interrater reliability for the raters was found to be an almost perfect agreement (Kappa = 0.913, $p < .000$). ADHD subtypes included the following: combined type (n=73); inattentive type (n=9); hyperactive/impulsive type (n=3) (Table **1**). Variance analysis performed to evaluate ADHD symptoms severity in the presence of a comorbid Oppositional Defiant Disorder assessed by SNAP-IV [41, 42], showed significant differences between all ADHD groups and normal controls in all SNAP-IV Subscales (Inattentive: p=.000; Hyperactive/Impulsive: p=.000; Combined: p=.000; Oppositional Defiant: p=.000) with higher mean scores of symptoms severity reported by patients treated with atomoxetine as compared to drug-free patients and patients treated with methylphenidate (Table **1**). Moreover, the SNAP-IV Hyperactive/Impulsive Subscale revealed a significant difference within the ADHD group (p=.042), with higher mean scores of symptoms severity reported by patients treated with atomoxetine (19.58 ± 4.8) as compared to drug-free patients (15.67 ± 6.3) and patients treated with methylphenidate (14.85 ± 6.2) (Table **1**).

All the subjects included in the study had an intelligence quotient ≥ 80 evaluated by Leiter-R [43,44]. Of these 85 ADHD patients, 44 subjects (40 males and 4 females; age range 8-15 years; mean age ± SD: 9.97 ± 2.8) were drug-free and 41 subjects (40 males and 1 female; age range 8-15 years; mean age ± SD: 10.70 ± 2.0) received a pharmacological treatment. Among them, 23 male patients (age range 8-15 years; mean age ± SD: 10.03 ± 2.0) were treated with atomoxetine at dose of 10–110 mg/day (mean:1.28 mg/kg/day) and 18 patients (17 males and 1 female; age range 8-15 years; mean age ± SD: 9.85 ± 2.2) received methylphenidate (20-30 mg/day). All the patients included in the clinical samples had not been previously diagnosed nor treated with atomoxetine, or with stimulants and other psychotropic medications.

All the participants who received a medical treatment were assessed for self-esteem evaluation after 6 months from the beginning of the pharmacological therapy.

Twenty-six normal control male subjects (age range 8-14 years; mean age ± SD: 11.29 ± 1.4) randomly selected from a database of healthy children attending a well-being paediatric clinic for routine checks were also included in the study. All the parents and children included in the healthy control group completed the K-SADS-PL with an experienced trained clinician. None of the control subjects fulfilled the criteria for any psychiatric disorder. Moreover none of them had ever used any psychotropic medication, nor were they undergoing any psychological therapy at the time of the study.

The clinical characteristics of the subjects participating in the study are summarized in Table **1**.

All the parents of the participants who accepted to take part in the research signed a consent form, and children and adolescents assented to participation.

Assessment of Clinical Symptoms

To assess the presence of an ADHD and/or a comorbid disorder, the Kiddie-Schedule for Affective Disorders and Schizofrenia for School-Age Children/Present and Lifetime Version (K-SADS-PL) [40] was administered to the patients' parents by an experienced trained clinician.

The K-SADS-PL is a semi-structured psychiatric interview that ascertains both lifetime and current diagnostic status based on DSM-IV-TR criteria. The K-SADS-PL includes three components: introductory interview, screen interview, and five diagnostic supplements for the evaluation of psychiatric disorders. The skip-out criteria in the screen interview specify which sections of the supplements, if any, should be completed.

To evaluate the presence of a comorbidity with Oppositional Defiant Disorder, as well as the subtype and the symptoms severity of ADHD, all the parents of the clinical and control samples completed the Swanson, Nolan, and Pelham Rating Scale-IV (SNAP-IV) [41, 42].

The SNAP-IV is a 26-item questionnaire in a 4-point Likert scale that is used to evaluate ADHD symptoms and severity, and it is completed by parents and teachers. The 26 items include 18 items for ADHD symptoms (9 for inattentive, 9 for hyperactive/impulsive) and 8 items for oppositional defiant disorder (ODD) symptoms as defined in the DSM-IV-TR [1]. Each item is scored on a 0-3 scale (0 = not at all, 1 = just a little, 2 = quite a bit and 3 = very much). The SNAP-IV consists of Inattentive, and Hyperactive/Impulsive, Combined Inattentive and Hyperactive/Impulsive and Oppositional Defiant subscales.

Assessment of Self-Esteem

To assess the self-esteem all the clinical and control children and adolescents completed the Self-Esteem Multidimensional Test (TMA) [45].

The TMA is based on a hierarchical model of self-esteem: it comprises six self-esteem dimensions (Personal, Skills, Emotional, School, Family, Body, Total) that partly overlap each other and partly with the core global self-esteem. The test consists of six groups of 25 items for each dimension explored and each item requires one of 4 possible answers: absolutely true, true, not true, absolutely not true. The test provides scores in six rating scales corresponding to the six self-esteem dimensions (Personal, Skills, Emotional, School, Family, Body, Total) and a global self-esteem related score. The average scores for self-esteem in the normative sample are between 85 and 115.

Data Analysis

An interrater reliability analysis using the Kappa statistic was performed to determine consistency among DSM-IV-TR criteria and K-SADS-PL diagnosis. Standard descriptive statistics, chi-square, Student t-test, one-way ANOVA with Bonferroni comparisons, Pearson's r correlations, and linear regression models were applied to the data in order to evaluate the association between the clinical and self-esteem variables in the ADHD groups and in the normal control group. Standard descriptive statistics and Fisher's exact tests were performed to assess the association among different comorbid disorders and self-esteem domains. Moreover, comparison among ADHD groups and normal controls were performed by variance analysis to evaluate the association among ADHD symptom severity and the presence of a comorbid Oppositional Defiant Disorder. An alpha level of 0.05 was set for statistical significance. All the analyses were performed using the Statistical Package for Social Sciences (SPSS 14.0 for Windows).

RESULTS

Self-Esteem Profile in the Study Population

To evaluate self-esteem, TMA was administered to the subjects included in the study and differences between the four groups (controls, ADHD drug-free, ADHD atomoxetine-treated and ADHD methylphenidate-treated) in terms of mean scores and self-esteem profile were evaluated (Table **2** and Fig. **1**). The comparison between total ADHD patients and controls, by Student t-test, showed significantly lower self-esteem scores on all TMA Subscales (Personal, Skills, Emotional, School, Family, Body and Total) in the ADHD group (Table **2**). Among the ADHD sample, variance analysis indicated a significant difference in TMA Total Subscale (p=.049): particularly, ADHD patients treated with methyl-

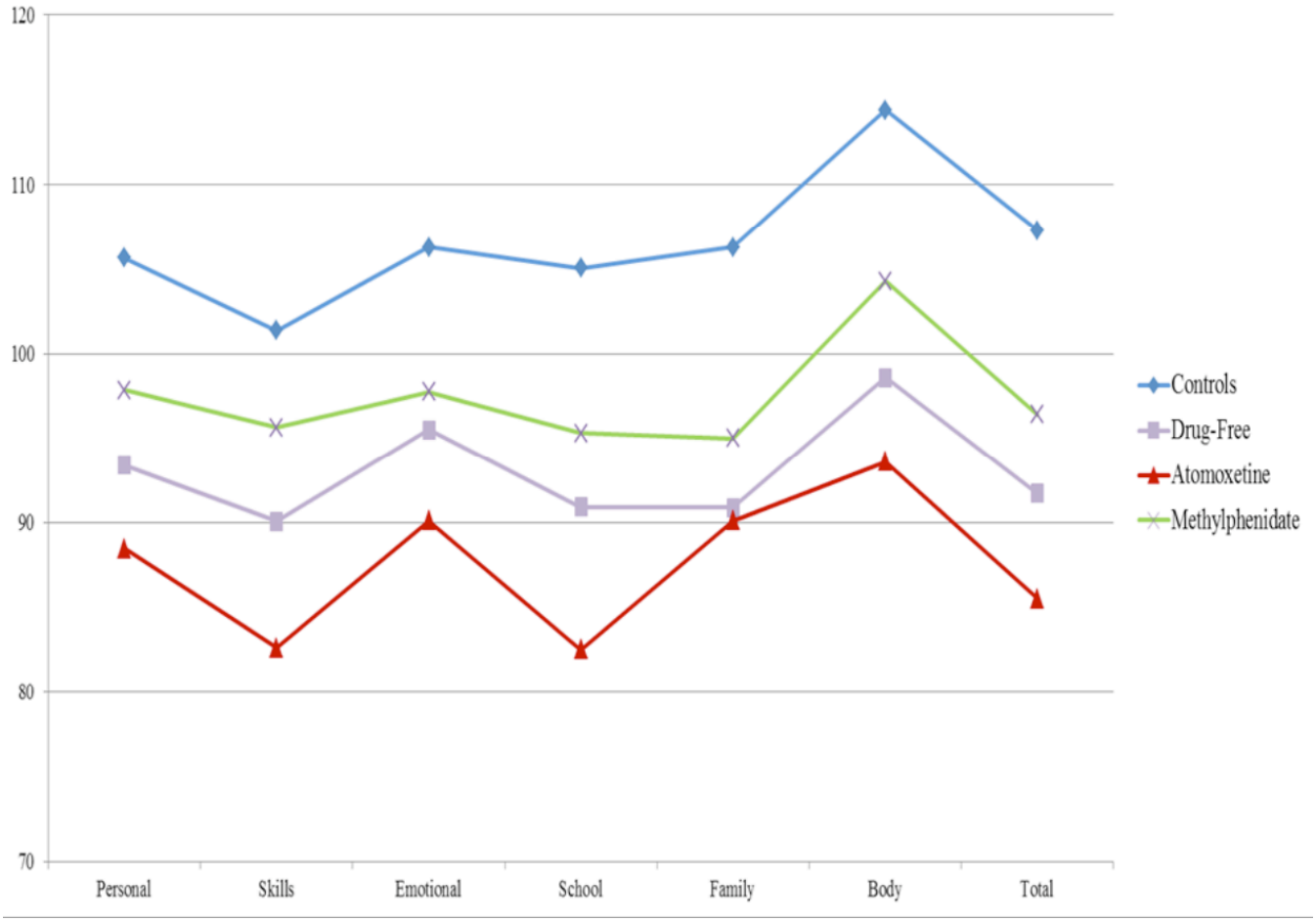

Fig. (1). Trajectories of Self-Esteem Subscales in ADHD and Control Groups.

phenidate revealed higher self-esteem mean scores in the TMA Total Subscale (96.39 ± 12.3) as compared to ADHD treated with atomoxetine (85.48 ± 9.9) as shown by Bonferroni post-hoc test (p=.048). Moreover, ADHD patients treated with Methylphenidate scored significantly higher than ADHD patients treated with atomoxetine in all TMA subscales, with the only exception of TMA Family Subscale, where the difference, albeit in the same direction, failed to reach statistical significance, by Student t-test (Table **2**).

Self-Esteem Differences According to Age and ADHD Symptoms Severity

Pearson's correlation was used to determine the relationship between age and self-esteem variables. Age was not found to correlate significantly with TMA scores in both ADHD and control groups. Similarly, no significant correlations were detected within the group of patients suffering from ADHD between TMA Total and Subscale scores and severity of ADHD symptoms, assessed by SNAP-IV.

Subjects with a Self-Esteem Below Average Range

Most of the ADHD patients had TMA Total scores within the pathological range (≤ 85), according to the established norms. Both ADHD drug-free (47.1%) and ADHD drug-treated (44.1%), of which 38.2% treated with atomoxetine and 5.9% treated with methylphenidate, groups showed significantly higher rates of subjects in the pathological range as compared to normal control group (8.8%) (p < .001), whereas no significant difference was detected between ADHD drug-free and drug-treated groups. However, within the ADHD drug-treated group, patients treated with Atomoxetine showed a significantly higher rate of pathological scores for the TMA Total score as compared to patients treated with methylphenidate (38.2% vs 5.9% respectively, p < .003).

Comorbid Disorders and Self-Esteem in the Study Population

Within the ADHD group, which comprises 85 ADHD subjects, 70 patients (80.1%) showed at least one comorbid psychiatric disorder and 21 (24.8%) had two comorbidities. In more detail, 27 children (31.8%) had a Specific Learning Disorder, 26 children (30.6%) had an Anxiety Disorder, 25 children (29.4%) had an Oppositional Defiant Disorder, 5 children (6%) had a Depressive Disorder and 6 children (7.2%) had some other comorbid diagnosis (e.g., Tourette syndrome, Tic Disorders, Bipolar Disorder, Obsessive-Compulsive Disorder, Eating Disorder) (Table **1**).

The analysis of the different comorbid diagnoses among all the domains of self-esteem, measured by TMA Test, revealed none significant differences.

Table 2. TMA Subscales in the Study Population

	TMA Subscales						
	Personal	**Skills**	**Emotional**	**School**	**Family**	**Body**	**Total**
Groups	M[a] (SD[b])	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)	M (SD)
ADHD	92.96 (14.9)	89.16 (17.3)	94.44 (12.8)	89.47 (16.1)	91.57 (10.5)	98.43 (14.3)	90.96 (14.4)
Controls	105.65 (15.2)	101.34 (14.9)	106.31 (10.9)	105.04 (15.2)	106.31 (11.6)	114.42 (21.2)	107.31 (12.2)
	t = 3.74 ***p*** = .000*	t = 3.21 ***p*** = .002*	t = 4.23 ***p*** = .000*	t = 4.33 ***p*** = .000*	t = 6.04 ***p*** = .000*	t = 4.36 ***p*** = .000*	t = 5.19 ***p***= .000*
Atomoxetine	88.43 (12.0)	82.61 (11.0)	90.08 (10.1)	82.52 (7.8)	90.09 (8.5)	93.56 (11.1)	85.48 (9.9)
Methylphenidate	97.83 (12.2)	95.61 (15.5)	97.72 (10.3)	95.28 (17.3)	95.00 (12.6)	104.28 (12.9)	96.39 (12.3)
	t = 2.46 ***p*** = .018*	t = 3.14 ***p*** = .003*	t = 2.38 ***p*** = .022*	t = 3.15 ***p*** = .003*	t = 1.49 ***p*** = .144*	t = 2.85 ***p*** = .007*	t = 3.14 ***p*** = .003*

*Student t-test;
[a]Mean;
[b]Standard Deviation.

DISCUSSION

A positive self-esteem is crucial for a healthy psychological development and indeed a positive relationship was found between self-esteem and mental health [46]. Previous studies showed that children and adolescents suffering from ADHD have low levels of social skills and self-esteem as compared to the general population [47,48] and these findings are consistent with other studies indicating that also adults with ADHD continue to have problems in many areas of functioning [49,50], thus inferring the hypothesis that social functioning and self-esteem may play a role on future outcomes in ADHD [20]. In line with this, our findings show that patients with ADHD have significantly lower scores on all the administered self-esteem rating scales (personal, skills, emotional, school, family, body) compared to healthy controls, and these results are particularly relevant in light of the crucial importance of social functioning and self-esteem for healthy functioning, that is generally impaired in ADHD individuals, during development. The ability to successfully interact with peers, one of the most important aspects of social development for all ages [51], can also be impaired in ADHD children and this deficit in peer relationships can compromise interpersonal success and happiness [52] thus leading to a low self-esteem.

Overall, ADHD subjects showed significantly higher rates of self-esteem in the pathological range as compared to healthy controls, however analysis of self-esteem with respect to treatment strategies revealed no significant differences between drug-free or drug-treated ADHD groups. However, ADHD patients treated with methylphenidate showed significantly higher self-esteem scores as compared to ADHD group treated with atomoxetine, in line with previous studies showing that stimulants were associated with significantly higher self-esteem [25, 26]. However, in another study by Frankel *et al.* [25], this relationship was not so univocal, in that only ADHD children with a comorbid diagnosis of Oppositional Defiant Disorder reported a higher self-esteem compared to pure ADHD upon treatment with stimulants. However, in our study no significant difference was detected among different comorbid disorders in terms of self-esteem. Furthermore, we also have to point out that drug treatment had a positive influence on how the teachers interacted with children affected by ADHD, and this could contribute to indirectly improve self esteem in these children [53].

Besides these significant results, the present study shows important limitations and it should be viewed in the context of the following considerations. First, in our opinion, although cross-sectional studies are extremely useful for generating hypotheses, these hypotheses need to be further confirmed by longitudinal investigations: because of the cross-sectional nature of our sample, we cannot determine the temporal relationship between ADHD and different domains of self-esteem.

Second, considering that the subjects included in the study were entirely derived from only two university clinics, this sample cannot be assumed as indicative of non-academic setting. Indeed, the sample was clinically referred and not intended to be representative of children with ADHD in the general population. Third, the control sample size was much smaller than the ADHD drug-free group limiting the generalization of our findings. Finally, self-esteem evaluation was derived from self-report questionnaires completed by the children themselves without any additional investigation of social function.

CONCLUSIONS

In conclusion the association between ADHD and self-esteem highlights the importance of early detection of children with this disorder in order to prevent the development of ADHD symptoms and to reduce long-term impacts. The development of lifespan approaches could help to clarify the role of ADHD medication either in the pathophysiological core processes or/and in the social function and self-esteem outcome.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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The Mediating Role of Aggressive Behaviour, Emotional and Behavioural Instability on the Association between ADHD Symptoms and Best Friend Conflicts

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Abstract This study examined the direct association between Attention Deficit Hyperactivity Disorder (ADHD) symptoms (i.e. inattention and hyperactivity symptoms) and children's experience of best friend conflicts, and the mediating role of aggression, emotional and behavioural instability, exploring possible gender differences. The sample consisted of 334 children (52 % female; M_{age}=9.38, SD=0.89) attending primary schools in northwest Italy. ADHD symptoms were measured with a questionnaire completed by teachers whereas others variables were assessed a self-report questionnaire completed by the children. Analyses revealed that inattention and hyperactivity symptoms were differently associated with best friend conflicts according to gender. Among boys, only hyperactivity symptoms were associated with best friend conflicts whereas among girls only inattention symptoms contributed to best friend conflicts. Aggression and emotional and behavioural instability were found to mediate these associations for both genders. These findings suggest that to understand fully the association between ADHD symptoms and best friend conflicts it might be helpful to consider the different manifestations of that association by gender, whilst also considering behavioural and emotional dimensions of children's psychosocial adjustment.

Keywords ADHD symptoms · Best friend conflicts · Gender · Mediation

Introduction

In the last years, the identification and study of Attention Deficit Hyperactivity Disorder (ADHD) symptoms in children, especially during middle childhood, has

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increased considerably. One reason for the increased interest in ADHD symptoms is that the number of children diagnosed with ADHD has increased and the difficulties associated with this disorder are becoming well-established (Hoza 2007; Hoza et al. 2005). Nonetheless both under- and over-diagnosis remain a big problem in the international context (Cuffe et al. 2005). The absence of an adequate diagnostic protocol hampers the development of appropriate interventions in which might enable better developmental outcomes for these children in many different areas of life (at school, at home, with their peers). In Italy, the attitude towards diagnosis and treatment of children ADHD differs from that in America (Frazzetto et al. 2007). Italian clinicians have not typically conceptualized ADHD as a biological syndrome and nosological entity, more often classifying ADHD as a "personality disorder", thus further complicating clinical attention and intervention. Moreover, the majority of Italian professionals do not make a definitive diagnosis of ADHD, although they usually verify the presence or absence symptoms among children.

Overall, prior work has demonstrated that children who suffer from ADHD symptoms but have not been formally diagnosed with ADHD report as many academic, social, emotional difficulties and other impairments as diagnosed children (Angold et al. 1999; Barry et al. 2002; Cornoldi et al. 2001; Polderman et al. 2010). Like children with a formal diagnosis of ADHD, children who suffer from ADHD symptoms are more disadvantaged than a matched group of peers (Abikoff et al. 2004; Bagwell et al. 2001; Frazier et al. 2007; Loe and Feldman 2007). For these reasons researchers have focused on the early identification of ADHD symptoms, investigating children with high levels of ADHD symptoms i.e. inattention (ADD symptoms) and behavioural hyperactivity (HYP symptoms) above the average level. Researchers have also examined the social and emotional impairments exclusively associated with ADHD symptomatology.

Many studies have suggested that ADHD symptoms can be associated with difficulties in peer relationships (Diamantopoulou et al. 2005, 2007). Children with ADHD symptoms were found to be rejected and neglected by peers (Abikoff et al. 2004; Bagwell et al. 2001; Blachman and Hinshaw 2002). ADHD symptoms have also been associated with low levels of social competence and poor school achievement (Biederman et al. 2004; Maedgen and Carlson 2000). ADHD symptoms are therefore assumed to be a salient factor in children's friendships and social adjustment more generally. There are however unresolved methodological and theoretical issues in the literature on ADHD symptoms and peer relationships. Firstly, most research on peer relationships of children with ADHD symptoms has examined social isolation and peer rejection, assessed by peer nominations. Significantly less research has been dedicated to the close friendship experiences of children with ADHD symptoms. The majority of ADHD and close friendship studies in fact have concentrated on friendship quality in children with a formal diagnosis of ADHD (for a review of the peer relationship of ADHD children see Mikami 2010; Normand et al. 2007). Less is known about how inattention and hyperactivity symptoms can affect boys' and girls' ability to form a close friendship and the subsequent quality of these friendships. This is important; research has shown that quality of best friendships is more important to psychosocial adjustment than the quantity of friendships (e.g. Berndt 1982, 2002; Hartup and Stevens 1997).

Friendship quality encompasses both positive (e.g. companionship, security, support) and negative (e.g. conflict, dominance, rivalry) factors (Berndt 2002; Bukowski

et al. 1994; Furman 1996). Sometimes having a close best friend may alleviate the consequences of being rejected by one's peer group (Parker and Asher 1993), it may be also associated with important indicators of overall wellbeing (Newcomb and Bagwell 1995), and may provide protection and support against various kinds of socio-emotional problems, including acting as protective factor against peer victimization (Bollmer et al. 2005). Surprisingly, although positive indicators of friendship quality have received scientific attention, negative aspects - such as conflicts within the friendship - have been under-investigated. In the present study we investigated best friend conflicts. Best friend conflicts are episodes of conflict and disagreements within close friendships, perceived by the child, which may complicate the regular course of the friendship. Although conflict is considered a negative feature of a close friendship it does not mean that children are unwilling to work things out with their peers; if they were to learn specific communication strategies - for example problem solving, negotiation and perspective taking - they might be better able to resolve such disputes (Berndt and Keefe 1995; Ladd et al. 1996; Noakes and Rinaldi 2006).

Most previous studies which have found an association between children's ADHD symptoms and the quality of their friendships have not taken into account other possible mechanisms that could explain the quality of children's friendships. During middle childhood ADHD, symptoms seem to be associated with certain behavioural and emotional problems. In particular, empirical evidence shows that girls and boys with ADHD symptoms display high levels of aggression and a lack of emotional regulation (Maedgen and Carlson 2000; Wahlstedt et al. 2008; Zalecki and Hinshaw 2004). These social and emotional problems may undermine children's peer relationships and thus cause further psychosocial difficulties (Bagwell et al. 2001; Dodge and Coie 1987). Behavioural and emotional difficulties associated with ADHD may affect a child's ability to construct friendships. Children with ADHD symptoms may have difficulties connecting emotionally with a friend, taking the friend's perspective and establishing intimacy in friendship. In accordance with this hypothesis we explored specific dimensions of children's psychosocial adjustment, hypothesizing that aggression, and emotional and behavioural instability mediate the association between ADHD symptoms and conflicts with best friends. As children with ADHD symptoms are more likely to experience social, emotional and behavioural difficulties they may also be more likely to have friendships of low quality; specifically, high levels of aggression, and emotional and behavioural instability might increase best friend conflicts.

Specifically, the present study aimed to investigate the relationship between ADHD symptoms - considering ADD and HYP symptom separately - and children's perceptions of negative friendship qualities, focusing on possible gender differences. The existing literature (for a review see Gershon 2002) has underlined the importance of gender, especially with regard to differences in the balance between HYP and ADD symptoms. In comparison to ADHD boys, ADHD girls have fewer symptoms of inattention and hyperactivity problems; however girls are more likely than boys to display ADD symptoms rather than HYP symptoms. Although research has demonstrated that ADHD symptoms lead to some impairments in children's friendships for both genders, the existing literature on friendship quality in boys and girls who suffer from ADD and HYP symptoms is instead still sparse and ambiguous (see Mikami 2010). In view of the symptom differences between genders we predicted that ADD and HYP symptom dimensions would be differently related to best friend conflicts

among boys and girls. Additionally we tested whether the association between ADD and HYP symptoms and best friend conflicts was affected by specific behavioural and emotional dimensions of psychosocial adjustment, namely aggressive behaviour and emotional and behavioural instability, in boys and girls. We expected that high levels of aggression and emotional and behavioural instability would account for the relationship between ADHD symptoms and best friend conflicts in both genders. The findings of this study could inform development of preventive interventions. Italy is a country with a low prevalence of children with ADHD symptoms (Faraone et al. 2003; Skounti et al. 2007) and Italian professionals have interpreted ADHD symptoms as a developmental disorder situated within a socio-environmental framework (for a review see Frazzetto et al. 2007). Given this perspective on ADHD, dimensions of children's psychosocial adjustment which mediate the relationship between ADHD symptoms and best friend conflicts could provide targets for clinical intervention. Identifying such mediating factors is therefore of considerable importance, and may contribute to the development of interventions aimed at improving the psychosocial adjustment of children with ADHD symptoms, including the quality of their friendships.

Method

Procedure

This study was conducted in primary schools in the northwest of Italy. The sample initially comprised 334 children attending the second, third and fourth grades in these schools. Our study was approved by the Ethical Committee of the University of Turin. Parents provided active consent for their children to participate in accordance with Italian law and the Ethical Code of the Professional Psychologist Association in Italy; the children also agreed to participate. Children completed a questionnaire, which was administered during classroom time by trained research staff (two post-doctoral researchers and two PhD students in developmental psychology). The administration of the child's questionnaires lasted approximately 1 hour. During this time the teacher (who spends many hours with that class) completed a questionnaire giving his or her assessment of the presence of ADHD symptoms in each child. Completion of the teacher's questionnaire took about 15 min. We did not offer any incentive for participation in the study. No family refused to participate.

Participants

The participants were 334 children (48 % boys, 52 % girls) who were 8 to 10 years old (M=9.38; SD=0.89) attending the second (30 %), third (53 %) and fourth (17 %) grades of primary schools in urban and suburban areas of northern Italy. The participants were representative of the population of children attending primary school in this part of Italy. Our sample was comparable to the general Italian population (ISTAT [National Institute of Statistics], 2012). Ninety-three percent of the children were born in the same region, 5 % in other Italian regions and 2 % abroad. Ninety-one percent of the children had two Italian parents, 7 % had two non-Italian parents and 2 % were from mixed families; 80 % of the children lived with both married parents. In terms of

parental education 20 % of the parents had completed basic school, 40 % had finished high school, 20 % had some vocational specialization and 20 % had graduated from university. Ninety-four percent of the parents completed the questionnaire about socio-demographic information and returned it to school the following week in a sealed envelope. We did not find any difference in the study variables between the children whose parents completed the parental questionnaire and those whose parents did not. The parental questionnaires were completed by mothers (70 %), fathers (10 %), or both parents (20 %).

Measures

ADHD Symptoms To measure ADHD symptoms we used the ADHD Rating Scale for Teachers (SDAI) in an Italian version developed and validated by Marzocchi and Cornoldi (2000). The SDAI Scale was designed for use in screening, not for clinical diagnosis, and includes 18 items based on the eighteen-item list of ADHD symptoms in the fourth edition of the *Diagnostic and Statistic Manual of Mental Disorders* (American Psychological Association 2000). Half the items relate to inattention (ADD subscale) e.g. '*Has difficulty sustaining attention in tasks or play activities*' and half relate to hyperactivity (HYP subscale) e.g. '*Is on the go or acts as if driven by a motor*'. The questionnaire was administered to teachers who were asked to assess the frequency of the appearance of the given behaviours, using a four-point Likert scale ranging from 0 to 3, where 0 = *child never shows this behaviour*); 1 = *child sometimes shows this behaviour*; 2 = *child often shows this behaviour*); 3 = *child very often shows this behaviour*. A higher score indicates that the given behaviour occurs more frequently. Cronbach's α for the ADD and HYP subscales was 0.94 and 0.93 respectively.

Aggressive Behaviour To measure aggressive behaviour, child participants completed a fifteen-item Likert scale ranging from 1 (*almost never*) to 3 (*many times*) based on the number of times they had engaged in each of the listed behaviours e.g. non-play fighting, kicking, punching, teasing others or hurting others during the last year. An Italian version of this scale with good internal consistency (Cronbach's α=0.86) was developed and validated by Caprara and Pastorelli (1993). The scale was used as in previous studies (Caprara et al. 1997; Pastorelli et al. 1997) as a general indicator of the behaviours of interest. A higher score indicates higher frequency of a given behaviour.

Emotional and Behavioural Instability To measure emotional and behavioural instability, participants completed a seventeen-item Likert scale with response ranging from 1 (*almost never*) to 3 (*many times*). Items included 'I shout, I interrupt someone when he/she is talking', 'I play noisy games', 'I disturb someone', 'I do not stay quiet', 'I play dangerous games', 'I cry frequently'. The Italian version of this scale was developed and validated by Caprara and Pastorelli (1993). The scale was used as in previous studies (Caprara et al. 1997; Pastorelli et al. 1997) as a general indicator of the behaviours of interest. Internal consistency, measured by Cronbach's alpha, was 0.75. A higher score indicates a higher frequency of a given behaviour.

Best Friend Conflicts To measure best friend conflicts we used the Italian version, validated by Fonzi and colleagues (1996), of the Conflict Scale of the Friendship Quality Scale originally developed by Bukowski and colleagues (1994); it has

Cronbach's α=0.66 and consists of 4 items, with responses on a four-point Likert scale ranged from 1 (*not at all*) to 4 (*very much*), and assesses feelings about frequent fighting, being angry even after the fight is over, disagreeing about many things, and reciprocal teasing of one's best friend. A higher score indicates a higher frequency of a given behaviour.

Statistical Analyses

Baron and Kenny's method was used to test whether putative mediating factors - aggressive behaviour and emotional and behavioural instability - affected the association between ADD and HYP symptom dimensions (predictors) and best friend conflicts (outcome) (Baron and Kenny 1986; MacKinnon and Dwyer 1993). In a preliminary analysis we checked whether the main predictors were associated with the outcome. Next the mediators were examined separately in two parallel models. A series of linear regression models were run, entering the predictors (ADD and HYP symptoms) in the first step, and the selected mediators (aggressive behaviour, emotional and behavioural instability) in the next step. Finally, Sobel tests were conducted to determine the statistical significance of mediation effects (Preacher and Leonardelli 2009).

Results

Descriptive Results

Descriptive statistics and correlations for all the study variables are presented in Tables 1 and 2 respectively. Boys were found to have more ADD (t[330]=4,53; p<0.01) and HYP (t[330]=2,24; p<0.05) symptoms than girls. Means for aggressive behaviour and emotional and behavioural instability appeared to be significantly higher for boys than girls (t[330]=2,502; p<0.05 and t[330]=4,148; p<0.05 respectively; see Table 1). Correlation scores indicated that the outcome (best friend conflicts) was differently associated with the predictors (ADD and HYP symptoms) according to gender. For boys best friend conflicts were associated with HYP symptoms but not ADD symptoms, whereas for girls best friend conflicts were associated with ADD but not HYP symptoms (Table 2). A precondition for testing mediation (Baron and Kenny 1986) is a main effect of the predictor variable on the outcome variable, as this main effect differed according to gender we decided to test the mediation models separately for boys and girls.

Mediator Effects on the Association Between HYP Symptoms and Best Friend Conflicts Among Boys

Results indicated that high HYP symptom scores were significantly associated with a high probability of reporting best friend conflicts, controlling for age (B=0.074; p<0.01; Table 3). The precondition of mediation, namely that HYP symptom scores were significantly associated with our mediator factors, was fulfilled: HYP symptoms were positively associated with aggressive behaviour (B=0.35; p<0.05) and emotional

Table 1 Descriptive statistic for all study variables

Variable	Boys Mean (SD)	Girls Mean (SD)	t
Best friend conflicts	6.9 (2.6)	6.7 (2.6)	0.697
ADD	7.5**(6.6)	5.9 (6.3)	4.532**
HYP	5.8*(5.9)	3.2 (4.6)	2.241*
Aggressive behaviour	22.8*(4.9)	20.2 (3.4)	2.502*
Emotional/Behavioural instability	25.4*(6.2)	23.3 (5.3)	4.148*

N=334

* $p<0.05$

** $p<0.01$

and behavioural instability (B=0.21; $p<0.05$). In the first mediation model, when the aggressive behaviour variable was added into the analyses, HYP symptoms scores were no longer associated with best friend conflicts (B=0.016; $p>0.05$), controlling for age (Table 3). A Sobel test revealed that the inclusion of aggressive behaviour fully mediated the association between HYP symptoms scores and best friend conflicts (z=2.25; $p<0.01$).

The second mediation model showed that when emotional and behavioural instability (the putative mediator) was added to the equation HYP symptoms scores were no longer associated with the outcome (best friend conflicts) (B=0.044; $p>0.05$), controlling for age (Table 4). Again, the Sobel test indicated that emotional and behavioural instability fully mediated the relationship between HYP symptoms scores and best friend conflicts (z=2.20; $p<0.01$).

Mediator Effects on the Association Between ADD Symptoms and Best Friend Conflicts Among Girls

Results indicated that high ADD symptoms scores were significantly associated with a high probability of reporting best friend conflicts, controlling for age (B=0.082;

Table 2 Correlations among variables for girls (below the diagonal) and for boys (above the diagonal)

Variable	1	2	3	4	5
1. Best friend conflicts	–	0.10	0.17**	0.41**	0.21**
2. ADD	0.20**	–	0.76**	0.24**	0.15
3. HYP	0.13	0.69**	–	0.33**	0.25**
4. Aggressive behaviour	0.23**	0.15*	0.18*	–	0.57**
5. Emotional/Behavioural instability	0.14*	0.15*	0.17*	0.56**	–

N=334

* $p<0.05$

** $p<0.01$

Table 3 Unstandardized regression coefficients (controlling for age) of best friend conflicts (outcome), HYP (predictor), aggressive behaviour (mediator) among boys

Variable	B	SE β	β
Step 1			
HYP	0.074	0.035	0.169**
R^2	0.022		
F	4.508*		
Step 2			
HYP	0.016	0.034	0.037
Aggressive behaviour	0.214	0.041	0.404**
R^2	0.163		
F	16.116**		
ΔR^2	0.141		
ΔF	11.608		

N=161

* $p<0.05$

** $p<0.01$

Step 1: $R^2=0.022$, $p<0.05$; Step 2: $\Delta R^2=0.141$, $p<0.001$

$p<0.01$; Table 5). The precondition of mediation, that ADD symptoms scores were significantly associated with our mediator factors, was fulfilled: ADD symptoms scores were positively associated with aggressive behaviour (B=0.23; $p<0.01$) and emotional

Table 4 Unstandardized regression coefficients (controlling for age) of best friend conflicts (outcome), HYP (predictor), emotional/behavioural instability (mediator) among boys

Variable	B	SE β	β
Step 1			
HYP	0.074	0.035	0.169**
R^2	0.022		
F	4.508*		
Step 2			
HYP	0.044	0.039	0.095
Emotional/Behavioural instability	0.079	0.035	0.187*
R^2	0.040		
F	4.094**		
ΔR^2	0.018		
Δ F	0.414		

N=161

* $p<0.05$

** $p<0.01$

Step 1: $R^2=0.022$, $p<0.05$; Step 2: $\Delta R^2=0.018$, $p<0.01$

and behavioural instability (B=0.14; $p<0.05$). In the first mediation model, when the aggressive behaviour variable was added into the analyses, there was a decrease in the coefficient of the predictor (ADD symptoms) and the outcome (best friend conflicts) (B=0.068; $p<0.05$), controlling for age (Table 5). A Sobel test revealed that the inclusion of aggressive behaviour partially mediated the association between HYP symptoms scores and best friend conflicts (z=2.15; $p<0.05$).

The second mediation model showed that when emotional and behavioural instability (mediator) was added to the model there was a decrease in the coefficient of the predictor (ADD symptoms) and the outcome (best friend conflicts) (B=0.029; $p<0.05$) controlling for age (Table 6). Again, the Sobel test indicated that emotional and behavioural instability partially mediated the relationship between ADHD symptoms scores and best friend conflicts (z=2.18; $p<0.05$).

Conclusions

This study examined the association between ADHD symptoms (i.e. ADD and HYP symptoms) and children's best friend conflicts, investigating the possible mediating role of behavioural and emotional dimensions of children's psychosocial adjustment, and also considering potential gender differences. The study has added to existing research on friendship quality in the peer relationships of girls and boys with ADD and HYP symptoms, issues which have thus far received little attention. The study has highlighted how the association between specific social and behavioural dimensions - namely aggressive behaviour and emotional and behavioural instability - and ADD and HYP symptoms helps to explain the presence of peer-related socio-behavioural impairments amongst these children.

Table 5 Unstandardized regression coefficients (controlling for age) of best friend conflicts (outcome), ADD (predictor), aggressive behaviour (mediator) among girls

Variable	B	SE β	β
Step 1			
ADD	0.082	0.031	0.196**
R^2	0.033		
F	6.820*		
Step 2			
ADD	0.068	0.031	0.164*
Aggressive behaviour	0.166	0.061	0.204**
R^2	0.067		
F	7.131**		
ΔR^2	0.34		
ΔF	0.311		

N=173

* $p<0.05$

** $p<0.01$

Step 1: R^2 =0.033, $p<0.01$; Step 2: ΔR^2 =0.34, $p<0.001$

Table 6 Unstandardized regression coefficients (controlling for age) of best friend conflicts (outcome), ADD Symptoms (predictor), emotional/behavioural instability (mediator) among girls

Variable	B	SE β	β
Step 1			
ADD	0.082	0.031	0.196**
R^2	0.033		
F	6.820*		
Step 2			
ADD	0.029	0.014	0.117*
Emotional/Behavioural instability	0.064	0.025	0.143*
R^2	0.041		
F	7.780**		
ΔR^2	0.008		
Δ F	0.96		

N=173

* $p<0.05$

** $p<0.01$

*** $p<0.001$

Step 1: R^2 =0.033, $p<0.01$; Step 2: ΔR^2 =0.008, $p<0.01$

Overall, our results confirm the gendered manifestation of ADHD symptomatology: girls had lower levels of ADD and HYP symptoms than boys. However our study highlighted gender differences in the relationship between these symptoms and best friend conflicts. In boys, best friend conflicts were related to the presence of HYP symptoms but not ADD symptoms, whereas in girls best friend conflicts were associated only with ADD symptoms. This latter result is not surprising; it is consistent with a previous study of ADHD girls' friendships (Blachman and Hinshaw 2002). This study demonstrated that inattentive girls tend to report fewer friendships and less stable peer relationships. Our study extends these results by providing evidence that girls who suffer from ADD symptoms also experience best friend conflicts. A possible explanation for this is that the presence of ADD symptoms is bound up with social withdrawal and disinterest, behaviours which - especially in girls - are responsible for less positive friendship engagement and more peer disagreements (Wheeler and Carlson 1994). Our results in boys seems are also consistent with the existing literature suggesting that impairments in boys' friendships relate primarily to the level of hyperactivity, which is often linked to disruptive and impulsive behaviour. HYP symptoms, which mainly affect boys, increase the likelihood of disagreement and conflicts between friends. Extending previous research which concentrated on general social functioning and peer status (Abikoff et al. 2004; Bagwell et al. 2001; Diamantopoulou et al. 2005, 2007), our findings suggest that boys and girls who suffer from HYP and ADD symptoms respectively, reported high levels of negative friendship qualities, specifically, a high level of best friend conflicts. ADD and HYP symptoms are therefore not only a risk factor for isolation and rejection by peers; they are also a risk factor for jeopardizing close friendships, because they are associated with a higher incidence of conflicts and disagreement between friends. If children do not learn strategies to resolve peer

conflicts they could be at significant risk for certain developmental problems e.g. poor school achievement; anxiety (Berndt 2002).

Our findings also revealed that the association between ADD and HYP symptoms and best friend conflicts was mediated by aggressive behaviour, and emotional and behavioural instability in both boys and girls. In other words, certain dimensions of children's psychosocial adjustment are important factors in understanding the peer-related socio-behavioural impairments of children who suffer from ADHD symptoms. Together with our first result on the association between ADHD symptoms and conflict in close friendship, this seems to provide additional evidence of the behavioural and emotional deficits of children with ADHD symptoms. Perhaps these children perceive more conflicts with the best friend as they experience aggressive behaviour and a lack of behavioural and emotional stability. Thus the association between ADHD symptoms and best friend conflicts simply becomes apparent in how high children with ADHD symptoms perceive their behavioural and emotional difficulties. A possible explanation for this finding (Bagwell et al. 2001; Barkley 1997; Hoza et al. 2005) is that these children often show poor behavioural control, emotional instability and aggressive behaviours when compared with their developmentally typical peers. These kinds of behaviours are likely to interfere with the skills needed to establish and consolidate a close and secure friendship and could subsequently increase the likelihood of conflict episodes and disputes between friends. This process can also be explained in terms of the social information processing model that was used recently to explain the social problems experienced by children with ADHD (King et al. 2009). This model suggests that aggressive behaviour is due to an impairment in children's social cognitive processes (e.g. encoding social cues, evaluation and response decisions); aggression in impulsive and hyperactive children is thus explained in terms of biases in the cognitive processing of ambiguous social information and situations. Children who are more aggressive and display a higher level of ADHD symptoms also tend to have the most severe peer relationship difficulties, displaying inappropriate behaviour with peers (Dodge and Coie 1987; Bagwell et al. 2001). The best friend conflicts experienced by children in our study who suffered from ADHD symptoms and emotional and behavioural difficulties may have been a manifestation of their deficient processing of social information, but this hypothesis should be tested by investigating explicitly the social information processing abilities of children with ADHD symptoms. Establishing which ADHD symptoms are associated with impairments in peer relationships, describing the processes underlying this association in terms of psychosocial impairments and exploring potential gender differences is a subject for future studies.

Some limitations of the present study must be emphasized. The study used a cross-sectional design which precluded the investigation of long-term patterns in peer relationships and causal inferences. It may be that, rather than aggression and emotional and behavioural instability affecting conflict within friendships, experiencing this kind of conflict may affect the emotional and behavioural stability of children. The next step in this line of research is to investigate the associations we have uncovered over a longer period of time. We relied on teachers' ratings of the children's ADHD symptoms and so we had no information about the age at symptom onset or about the symptomatology across contexts e.g. at home etc. Using a combination of parents' and teachers' assessment of ADHD symptoms might offer the most practical assessment for clinical intervention programmes.

Moreover, it should be noted the nature speculative of our results about the role of aggressive behaviour, emotional and behavioural instability on the association between ADHD symptoms and best friend conflicts. Our results in fact cannot be adopted to individuals in countries where a formal diagnosis of ADHD is provided by medical professionals, because the present study refers only to children who suffer from ADHD symptomatology reported by teachers. Future researches could investigate if our results can be applied also to children into clinical and medical groups. The present results must therefore be interpreted with caution, as the measures relied on teachers' perceptions of hyperactivity and inattention children symptoms. Furthermore, the use of only child's self-report questionnaire (about friendship quality, aggression, emotional and behavioural instability) should be noted as a shortcoming of our research. Although other studies underlined that school-aged children are able to provide reliable information about their friendship and behaviour (Ladd et al. 1996; Riley 2004), responses may be affected by virtue of children immaturity and lack of insight. So, the use of objective measures about children friendship and adjustment could add validity to our study. Also, we did not collect information about reciprocity in children's friendships. Adopting a dyadic approach would allow us to circumvent the fact that some children who suffer from ADHD may not report the quality of their friendships accurately. Nonetheless, problems with biased self-report data have been reported in studies that analyzed perceptions of friendship in children with a formal diagnosis of ADHD (for a review see Mikami 2010), but not in studies that examined children with ADHD symptoms. Finally, the low Cronbach alpha of the Best Friend Conflicts Scale should be noted.

Despite these limitations, this study adds to the literature an interesting description of perceptions of friendship quality in children with ADHD symptoms, and an investigation the role of aggressive behaviour and emotional and behavioural instability in the relationship between ADHD symptoms and best friend conflicts. We uncovered important gender differences in the association of ADHD symptoms with conflict within close friendships. This study contributes to a better understanding of gender differences in peer-related socio-behavioural impairments of children who suffer from ADHD symptoms. Future research should explore this line of research. Our findings have provided indirect evidence of the developmental importance of social and emotional impairments in ADHD symptomatology; a number of studies have already underlined the importance of further examining the development of social and emotional skills in children with ADHD symptoms, and suggested that deficits in specific social skills may account for many of the difficulties in peer relationships experienced by children with ADHD symptoms (Blachman and Hinshaw 2002). Finally, this study contributes to the small body of literature on Italian children with ADHD symptoms. Although some effects may be culturally specific, for example the discrepancies between Italy and United States in the qualitative and quantitative classification of ADHD symptoms (Frazzetto et al. 2007), the direction of the relationship between ADHD symptoms and social, behavioural and emotional dimensions of children's functioning reported in this study is consistent with the international consensus. Future research should continue to examine children with ADHD symptoms, not only to improve the definition of the disorder, but to develop interventions to prevent some difficulties, such as peer conflicts, which are differently associated with the symptomatology in boys and girls.

In summary, successful peer relationships are important for all children both in terms of current and future wellbeing. Children who do not succeed in the peer relationship

domain are at risk for a multitude of problems throughout their life span. Further clarification of how children with ADHD symptoms perceive their best friendships and how certain behavioural and emotional dimensions of children's psychosocial adjustment are related to close friendships appears necessary and might enable the development of specific interventions targeting dyadic friendship (see Hoza et al. 2003) to ameliorate the problematic and adverse peer relationships of Italian boys and girls with ADHD symptoms.

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ORIGINAL CONTRIBUTION

The role of *DCDC2* genetic variants and low socioeconomic status in vulnerability to attention problems

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Abstract Both genetic and socio-demographic factors influence the risk for behavioral problems in the developmental age. Genetic studies indicate that shared genetic factors partially contribute to behavioral and learning problems, in particular reading disabilities (RD). For the first time, we explore the conjoint role of *DCDC2* gene, an identified RD candidate gene, and socioeconomic status (SES) upon behavioral phenotypes in a general population of Italian children. Two of the most replicated *DCDC2* markers [i.e., regulatory element associated with dyslexia 1 (READ1), rs793862] were genotyped in 631 children (boys = 314; girls = 317) aged 11–14 years belonging to a community-based sample. Main and interactive effects were tested by MANOVA for each combination of *DCDC2* genotypes and socioeconomic status upon emotional and behavioral phenotypes, assessed by Child Behavior Check-List/6–18. The two-way MANOVA (Bonferroni corrected p value = 0.01) revealed a trend toward significance of READ1(4) effect ($F = 2.39$; $p = 0.016$), a significant main effect of SES ($F = 3.01$; $p = 0.003$) and interactive effect of READ1(4) × SES ($F = 2.65$; $p = 0.007$) upon behavioral measures, showing higher attention problems scores among subjects 'READ1(4+) and low SES' compared to all other groups (p values range 0.00003–0.0004). ANOVAs stratified by gender confirmed main and interactive effects among girls, but not boys. Among children exposed to low socioeconomic level, READ1 genetic variant targets the worst outcome in children's attention.

Keywords Children · Behavior · DCDC2 · Socioeconomic status · Gene-by-environment interaction

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Introduction

It is now widely recognized that complex behavioral phenotypes have a multi-factorial etiology, and both genetic and environmental factors influence psychopathological traits [1].

Twin and adoptive studies found substantial genetic contribution to emotional/behavioral traits in middle childhood, with heritability estimates ranging between 51 and 65 % for externalizing and 37–50 % for internalizing behaviors [2–5].

In childhood, behavioral problems have usually been shown to co-occur often with learning disabilities [6]. Children referred for learning problems also show an excess of social problems [7], and are reported by teachers, parents and peers as having problematic interpersonal

relationship [8]. The significance of the association between behavioral problems and learning disabilities remains unknown. Preexisting problems such as poor concentration, anxiety, distractibility and poor motivation may be detrimental for attaining adequate learning skills. Conversely, the academic failure due to learning problems enhances the vulnerability to developing psychopathology through low self-esteem, low motivation and social isolation. Aggressive behavior with antisocial traits has been reported to frequently co-occur with learning disabilities in childhood, both in urban [9] and rural settings [10]. On the other hand, a bulk of literature concerns the relationship of learning disabilities and internalizing symptoms [11, 12]. Interestingly, up to 40 % of children with attention-deficit/hyperactivity disorder (ADHD) or reading disabilities (RD) also meet criteria for the other disorder [13]. The links between ADHD and RD, or ADHD and global measures of learning disability are widely studied in the literature [14, 15].

Genetic studies suggested that ADHD and RD co-occur in the same individuals as a consequence of at least partial sharing of the same genetic determinants. The same genes may contribute to a portion of the susceptibility to both ADHD and RD causing heightened risk of manifestation of either or both disorders [16–18]. Given the evidence for overlapping heritability between RD and ADHD, many studies have begun to investigate the molecular basis of this comorbidity. Based on well-established linkage findings in RD involving chromosome 6 loci [19–24], Willcutt and colleagues [25] investigated the linkage between chromosome 6 and ADHD phenotype in RD-ascertained sibling pairs. The results showed linkage between ADHD phenotype and D6S276 and D6S105 markers, located on 6p22.1 and 6p22.2 loci. Interestingly, the results remained significant after controlling for reading measures, suggesting that the linkage findings are not a secondary consequence of reading impairment. A gene located in the 6p22 region, the *DCDC2* gene, has been repeatedly associated with RD [23, 26–35], though negative associations have also been reported [36–38].

To test whether *DCDC2* also contributes to ADHD, Couto and colleagues [39] investigated the association between *DCDC2* and both ADHD dimensions (i.e., inattention and hyperactivity/impulsivity) in an ADHD-ascertained sample. The strongest associations were found between both ADHD symptoms and two markers (i.e., rs793862 and rs807701) of the *DCDC2* gene. The same *DCDC2* markers were also tested for association with measures of RD; however, no association was found. These findings were consistent with Willcutt et al.'s [25] study and emphasize the role of *DCDC2* gene as a candidate gene for ADHD.

The *DCDC2* gene is involved in neural development, specifically in the neuronal migration to the neocortex. In the brain, *DCDC2* is expressed in many regions, including entorhinal cortex, inferior and medial temporal cortex, hypothalamus, amygdala and hippocampus [27, 40]. More interestingly, it has been recently found [29, 41] that a short tandem repeat (STR) in intron 2 of *DCDC2* (i.e., BV677278) is a regulatory element, binding a brain-expressed nuclear protein with very high specificity. It seems that more common BV677278 alleles change the expression level of *DCDC2*, and that BV677278 may function as an enhancer of *DCDC2* and as a regulatory element that influences reading skills. On the basis of this data, BV677278 was renamed regulatory element associated with dyslexia 1 (READ1 [29]).

Given the evidence for overlapping heritability between ADHD and RD and the recent findings about the relevance of *DCDC2* gene in behavioral disorders [39], we are interested in testing if *DCDC2* gene, one of the most replicated for RD, is a susceptibility gene for behavioral traits in a general population of Italian children.

In addition, the genetic liability is likely to interact with non-genetic elements, playing a role in explaining a sizable proportion of variance. Specifically, although limited by the fact of being a generic, broad, distal risk variable, socioeconomic status (SES) has been found to be one of the most powerful predictors for child psychopathology [42]. Previous studies have shown that the rates of psychopathology are higher among individuals with lower SES than those with higher SES [43, 44]. In a nationally representative study of children aged 8–17 [45], low SES was significantly associated with elevated scores on anxious/depressed, somatic complaints, thought problems, attention problems and aggressive syndromes, as measured by parental responses on Child Behavior Checklist form [46].

Thus, given the evidence that SES as well as *DCDC2* gene are independently associated with behavioral problems, we hypothesize that *DCDC2* gene and SES may exert a conjoint role on behavioral and emotional difficulties. To test this hypothesis, in a community-based cohort of 631 Italian children aged 11–14 years, we assessed the role of two among the most replicated markers of *DCDC2* gene (i.e., READ1 and rs793862) and SES in influencing several behaviors, as measured by Child Behavior Check-List/6–18 (CBCL/6–18), the most widely adopted instrument for the assessment of behavioral problems in adolescence. We used a gene-by-environment interplay (G × E) approach to identify subjects at heightened risk for unfavorable developmental outcomes.

Methods

Sample

Participants in the present study were subjects involved in two epidemiological studies of mental health in youth, aged 11–14 years. Subjects from sample 1 ($n = 460$; mean age $= 12.08 \pm 0.86$) were from Lecco and Conegliano—two average-sized, urban areas among the seven participating units in the Italian Project on Pre-adolescent Mental Health (PrISMA—Progetto Italiano Salute Mentale Adolescenti). Full details of the methods used in the original epidemiological study are given elsewhere [47]. Subjects from sample 2 ($n = 171$; mean age $= 11.89 \pm 0.90$) were participants in a longitudinal study of emotional and behavioral problems in childhood carried out in Ponte Lambro (PL), a small-sized area near Lecco. The PL and PrISMA samples have no overlapping subjects.

Inclusion criteria were: (1) belonging to Caucasian families; (2) having no certification of handicap; (3) having a written informed consent signed by both parents. The study protocol was approved by the Eugenio Medea scientific institute ethical and scientific committees.

Behavioral measures

Subjects' behavioral and emotional profiles were rated by the parent-administered CBCL/6–18 [46]. The Italian translation of the CBCL was found reliable and valid in previous epidemiological work. We employed the eight CBCL/6–18 subscales (anxious/depressed, withdrawn/depressed, somatic complaints, rule-breaking, aggressive behavior, social, thought and attention problems). In this study, we used the *T* scores based on the set of multicultural norms ''group 2'', which applies to the normative sample of the Italian population as suggested by the multicultural supplement to the manual for the ASEBA [48].

Socioeconomic status (SES)

Parental socioeconomic status was scored according to the Hollingshead 90-point scale [49], whereby a score ranging 10–90 was assigned to each parental job, and the higher of two scores was used when both parents were employed. Since analysis and interpretation of interactions are more straightforward with dichotomous factors [50], SES was split into two classes of risk, namely 'low' (SES 10–30) and 'middle/high' (SES 40–90), based on theoretically meaningful cutoff points as available from existent literature [51, 52].

Isolation of DNA and marker genotyping

Genomic DNA was extracted from mouthwash samples collected in 4 % sucrose using the DNAzol Genomic DNA Isolation reagent (Molecular Research Center, Cincinnati, OH). DNA concentration and quality of each sample were determined on a Nanodrop 1000 spectrophotometer (Thermo Scientific). Within intron 2 of the *DCDC2* gene, Meng et al. [27] identified a 168-bp purine-rich region containing a polymorphic compound short tandem repeat (STR) comprising the alleles containing variable copy numbers of (GAGAGGAAGGAAA)n and (GGAA)n repeat units.

The compound STR, BV677278, in intron 2 was genotyped by sequencing PCR products generated with forward primer (TGTTGAATCCCAGACCACAA) and reverse primer (ATCCCGATGAAATGAAAAGG). The sequencing method has been described elsewhere [27]. Chromatograms were analyzed and alleles assigned with Mutation Surveyor version 3.1 (SoftGenetics, State College), by comparing samples to reference traces after alignment. The 2,445 bp BV677278 deletion was genotyped by allele-specific PCR amplification with a combination of three primers in one reaction as previously described [27]. rs793862 marker was typed by PCR amplification with primers F (5′-AGG GCA CTG GAA TGG AAA ATG A-3′) and R (5′-GCC TTT CTA GCT GTT CTG CCT-3′) followed by sequencing. Table 1 shows the distribution of BV677278 and rs793862 markers

Table 1 Allele frequencies of the *DCDC2* markers (i.e., READ1 and rs793862)

	Allele	Frequency
READ1	1	0.587
	3	0.069
	4	0.101
	5	0.035
	6	0.052
	8	0.001
	9	0.002
	10	0.050
	Deletion	0.093
	15	0.003
	18	0.002
	19	0.001
	20	0.005
	22	0.001
rs793862	A	0.285
	G	0.715

in the sample. Hardy–Weinberg equilibrium (HWE) analyses were performed in R statistical analysis package (HWpval [53]) for all markers in the total sample and in girls and boys separately. The genotype frequencies of two markers were checked for HWE in all groups using a Chi-square test for rs793862 and a root-mean-square statistic for READ1.

Statistical analyses

Since in the PrISMA project, parents were let free to participate through simple behavioral assessments or behavioral assessment plus DNA collection, for PrISMA sample it was possible to control for possible participation biases. We performed preliminary analyses by ANOVA to check for possible participation biases in the original sample.

To overcome the loss of power related to the small number of observations in analyses and to allow comparison across previous studies [27, 31, 36, 54], READ1 alleles were grouped as proposed by Meng et al. [27]: the deletion and minor alleles (frequency ≤5 %, i.e., 2, 5, 6, 8, 9, 10, 15, 18, 19, 20, 22 alleles) were combined into category '2' (see Table 1). We therefore considered '1', '2',' 3',' 4', categories in further analysis. A genotype-based approach was considered for *DCDC2* markers. We tested a dominant model of each READ1 allele by treating the heterozygote and the homozygote genotypes as a single category. Thus, two-level genotype analyses were performed, separately comparing the presence of 1–2 copies of alleles '1', '2', '3', '4', to the absence of that same allele—READ1(1+)–READ1(1−); READ1(2+)–READ1(2−); READ1(3+)–READ1(3−); READ1(4+)–READ1(4−). Similarly, rs793862 genotypes were grouped into two-level variables (coded '0', '1'), with each level representing, respectively, 0, and 1–2 minor allele frequency. Table 2 shows frequencies of genotype categories both for READ1 and rs793862. Independence between *DCDC2* markers and SES was tested by Pearson's Chi-square statistics.

In the light of the observed degrees of intercorrelation among the eight behavioral dependent variables (average correlation coefficient = 0.44), main and interactive G × E effects were jointly analyzed by five multivariate analysis of variance (MANOVA) for each combination of *DCDC2* genotypes [i.e., READ1(1), READ1(2), READ1(3), READ1(4), rs793862] and SES, which were entered as independent variables. Since the sex ratio (boys:girls) in behavioral and emotional disorders was different [55, 56], gender effect was taken into account in the analyses. Significant interactions were tested with subsequent ANOVA in the total sample, and then in boys and girls separately. Post hoc analyses of significant interactions were carried out by the Tukey-HSD method. When dealing with multiple comparisons, we adjusted the p value threshold of significance by the Bonferroni's method. All analyses were performed using SPSS version 21.0 software package and R statistical analysis package.

Table 2 Genotype frequencies of the *DCDC2* markers (i.e., READ1 and rs793862)

	Genotype	Frequency (*n*)
READ1	1−	0.156 (84)
	1+	0.844 (454)
	2−[a]	0.576 (310)
	2+[a]	0.424 (228)
	3−	0.870 (468)
	3+	0.130 (70)
	4−	0.810 (436)
	4+	0.190 (102)
rs793862	G/G	0.511 (316)
	A/G-A/A	0.489 (302)

[a] The deletion and minor alleles (frequency ≤5 %) were combined into category '2'

Results

There were no significant differences owing to SES ($t = 0.72$, $p = 0.47$), age ($t = 1.34$, $p = 0.18$), and gender ($\chi^2 = 0.64$, $p = 0.42$) between children who belonged to families who agreed vs. those who belonged to families who did not agree to participate in the genetic study. When we compared the CBCL syndrome subscales, we found that there were no significant differences in 'somatic complaints', 'social problems', 'attention problems', 'rule-breaking behavior', and 'aggressive behavior'. However, when we compared 'anxious/depressed' 'withdrawn/depressed' and 'thought problems' scores of children who belonged to families who agreed vs. those who belonged to families who did not agree to participate in the genetic study, we found that the former group had significantly higher scores (see Online Resource 1). These slight differences were expected, since it is known that children and their families who agree to participate in behavioral/genetic psychiatry study may to some extent deviate from the population's mean value of psychopathology/adaptation.

Complete emotional and behavioral data, successful DNA collection, and SES information were available for 171 subjects from PL and 460 subjects from PrISMA. Although all children were attending the same school grades, children in the PrISMA sample were significantly older than children in the PL sample ($t = 3.51$, $p < 0.001$) owing to a modest difference in the timing of recruitment of the two samples (winter–spring for the PrISMA sample and autumn for the PL sample).

Table 3 Descriptive statistics of behavioral and socioeconomic status (SES) in boys ($n = 314$) and girls ($n = 317$) subgroups and in the total sample ($n = 631$)

CBCL/6–18[a]	PrISMA		PL		Combined sample		
	Boys ($n = 232$) Mean (SD)	Girls ($n = 226$) Mean (SD)	Boys ($n = 80$) Mean (SD)	Girls ($n = 70$) Mean (SD)	Boys ($n = 314$) Mean (SD)	Girls ($n = 317$) Mean (SD)	p values*
Anxious/depressed	57.26 (7.16)	55.58 (6.44)	56.76 (8.24)	55.36 (6.74)	57.13 (7.44)	55.52 (6.50)	<0.001
Withdrawn/depressed	57.23 (7.02)	55.23 (6.68)	56.54 (7.36)	56.04 (6.29)	57.05 (7.10)	55.47 (6.56)	<0.001
Somatic complaints	55.54 (5.51)	54.86 (5.37)	54.45 (5.39)	55.92 (5.50)	55.26 (5.49)	55.16 (5.41)	0.740
Social problems	56.16 (6.36)	55.01 (5.82)	54.73 (6.39)	54.63 (6.08)	55.79 (6.13)	54.89 (5.88)	0.008
Thought problems	54.06 (5.47)	53.83 (5.03)	54.74 (6.39)	54.19 (5.42)	54.23 (5.72)	53.94 (5.13)	0.342
Attention problems	56.11 (6.43)	56.60 (7.37)	55.23 (5.90)	55.04 (5.80)	55.88 (6.30)	56.14 (5.97)	0.487
Rule-breaking behavior	52.62 (3.81)	52.42 (3.75)	53.53 (4.18)	52.50 (3.54)	52.85 (4.13)	52.44 (3.68)	0.062
Aggressive behavior	55.07 (5.73)	53.78 (5.31)	55.19 (6.23)	53.66 (4.66)	55.10 (5.85)	53.74 (5.11)	<0.001
SES	57.72 (21.89)	59.49 (22.06)	54.88 (22.45)	53.03 (23.08)	56.96 (22.04)	57.59 (22.52)	0.727
% Low SES[b] (n)	14.20 (31)	17.30 (37)	25.00 (20)	22.70 (20)	17.10 (51)	18.80 (57)	

* p values obtained from t test for gender in behavioral phenotypes

[a] Child Behavior Check-List/6–18 subscales, expressed in normed T scores (mean = 50, SD = 10)

[b] SES ≤30 points (Hollingshead [50])

Both polymorphisms were in Hardy–Weinberg equilibrium in the total sample and in boys and girls subsamples (see Online Resource 2). Allele frequencies were equally distributed between gender (READ1 $\chi^2 = 0.62$, $p = 0.891$; rs793862 $\chi^2 = 1.46$, $p = 0.228$), SES (READ1 $\chi^2 = 3.47$, $p = 0.325$; rs793862 $\chi^2 = 1.29$, $p = 0.255$) and across the PrISMA and PL samples (READ1 $\chi^2 = 3.75$, $p = 0.289$; rs793862 $\chi^2 = 0.06$, $p = 0.806$).

Socio-demographic and behavioral characteristics of the sample are shown in Table 3, in the total sample, in PrISMA and PL samples and in boys and girls separately. All distributions approached normality, with acceptable skewness (range 1.11–2.08) and kurtosis (range 0.74–2.07) values.

Distribution of behavioral measures across children's gender showed significant differences upon anxious/depressed, withdrawn/depressed, social problems and aggressive behavior, with significant higher scores among boys (see Table 3).

To evaluate the relationship between READ1, rs793862 markers and SES, Chi-square analyses were performed. No significant p values were found for both READ1 and rs793862 markers ($\chi^2 = 18.93$, $p = 0.125$; $\chi^2 = 1.29$, $p = 0.255$), suggesting negligible G–E correlations in our data set.

Bonferroni corrected p value threshold for significance was set at 0.01 (0.05/5). The two-way MANOVA revealed no significant main or interaction effects of rs793862 markers and SES on behavioral measures. Furthermore, we found no significant main and interaction effects of READ1(1), READ1(2), READ1(3) genotypes, and SES on behavioral measures. The two-way MANOVA revealed a trend toward significance of READ1(4), a significant main effect of SES and interactive effect of READ1(4) × SES (see Table 4). The subsequent ANOVA showed a significant main effect of READ1(4): observed power = 0.92, partial $\eta^2 = 0.02$; a significant main effect of SES: observed power = 0.99, partial $\eta^2 = 0.04$; and a significant interactive effect of READ1(4) × SES: observed power = 0.98, partial $\eta^2 = 0.03$ upon attention problems subscale (see Table 5; Fig. 1). Post hoc analyses of the significant interaction in the ANOVA showed significantly higher attention problem scores in the 'READ1(4+) genotypes and low SES' group compared to all other groups (p values range 0.00003–0.0004). We then performed the ANOVAs of the significant interaction upon CBCL/6–18 attention problems in boys and girls separately. Girls showed main significant READ1(4) effect

Table 4 Interactive effects between READ1(4) and socioeconomic status (SES) from two-way MANOVA upon behavioral phenotypes ($n = 631$)

	F statistic[a]	p value	Effect size[b]	Observed power[c]
READ1(4)	2.39	0.016	0.04	0.90
SES	3.01	0.003	0.04	0.96
READ1(4) × SES	2.65	0.007	0.04	0.93

Dependent variables in each MANOVA were the eight CBCL/6–18 subscales: anxious/depressed, withdrawn/depressed, somatic complaints, thought problems, attention problems, aggressive behavior. Bonferroni corrected p value threshold for significance = 0.01

[a] Roy's largest root

[b] Partial eta-squared

[c] Observed power

Table 5 Main and interactive significant effects between READ1(4) and socioeconomic status (SES) upon CBCL/6–18 attention problems in the total sample ($n = 631$)

		READ1(4−)	READ1(4+)	READ1(4), F (p)	SES, F (p)	READ1(4) × SES , F (p)
SES	Low	56.20 ± 6.52 (80)	63.11 ± 10.70 (18)	11.31 (0.001)	19.25 (0.00001)	15.46 (0.0001)
	Middle/high	55.77 ± 6.58 (349)	55.23 ± 5.42 (83)			

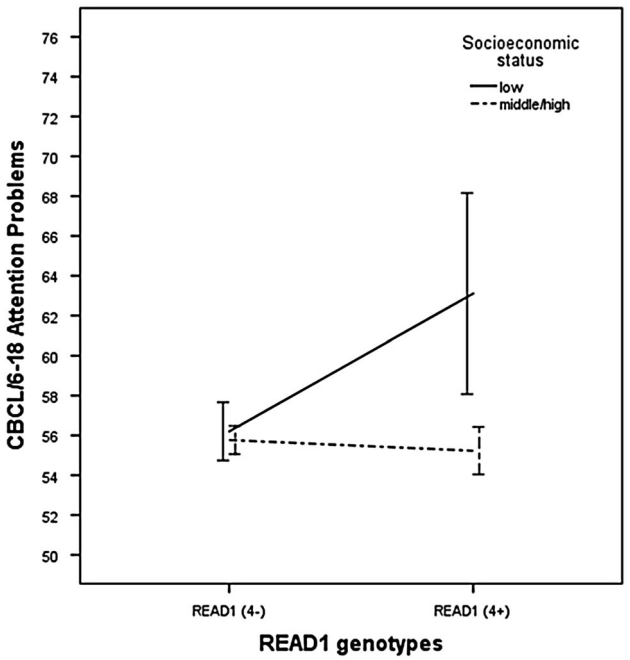

Fig. 1 Results of univariate analysis of variance estimating mean differences of attention problems as a function of SES and READ1(4) genotypes

($F = 23.13$; $p = 0.000003$; observed power = 0.99, partial $\eta^2 = 0.08$), main significant SES effect ($F = 17.21$; $p = 0.00005$; observed power = 0.99, partial $\eta^2 = 0.06$), and significant interactive effect ($F = 23.94$; $p = 0.000002$; observed power = 0.99, partial $\eta^2 = 0.08$). Among boys, there were no significant genetic ($F = 0.47$; $p = 0.49$), SES ($F = 1.78$; $p = 0.18$), or interactive effects ($F = 0.002$; $p = 0.96$; see Table 6; Fig. 2). The post hoc analyses of the statistically significant interaction showed that girls with low SES and READ1(4+) genotypes obtained significantly higher attention problems scores compared to all other groups (p values range 0.000001–0.000005).

Given that the *DCDC2* gene is one of the most replicated candidate genes for specific learning impairment (especially reading disabilities), to test if our findings were due to an underlying association with learning variables, the main and interaction effects between READ1(4) and SES upon attention problems were repeated using a proxy measure of learning disabilities as covariate, i.e., CBCL/6–18 school competence, which is a composite measure of scholastic performance in reading, writing, and arithmetic. Two-way ANCOVA showed significant main and interactive effects [main READ1(4) $F = 10.26$; $p = 0.001$; observed power = 0.89, partial $\eta^2 = 0.02$; SES $F = 7.84$; $p = 0.005$; observed power = 0.80, partial $\eta^2 = 0.02$; READ1(4) × SES $F = 12.99$; $p = 0.0003$; observed power = 0.95, partial $\eta^2 = 0.02$), suggesting that the association of READ1(4+) genotypes with attention problems could be independent from RD-related difficulties. We then analyzed the ANCOVA of the significant interaction in boys and girls separately: girls showed significant main and interactive effects [READ1(4) $F = 20.39$; $p = 0.00001$; observed power = 0.99, partial $\eta^2 = 0.07$; SES $F = 5.81$; $p = 0.017$; observed power = 0.67, partial $\eta^2 = 0.02$; READ1(4) × SES $F = 17.02$; $p = 0.00005$; observed power = 0.98, partial $\eta^2 = 0.06$), while there were no significant genetic ($F = 0.27$; $p = 0.61$), SES ($F = 0.85$; $p = 0.36$), or interactive effects ($F = 0.08$; $p = 0.77$) among boys.

Discussion

We found first evidence that belonging to low SES and having READ1(4+) genotypes are associated, both alone and in gene-by-environment interaction, with higher scores of CBCL/6–18 attention problems subscale.

The attention problems subscale includes items of inattention, impulsivity and hyperactivity that have been associated with *DCDC2* gene in two independent studies [25, 39]. Since the etiopathology of ADHD has been considered to be neurodevelopmental [57], it could be plausible that *DCDC2* gene, playing a role in neural migration which is the first step in cortical development, is considered a susceptibility gene for ADHD. Specifically, having READ1 allele-4 may cause heightened risk of manifestation of attention problems. It has been suggested that READ1 has an effect on gene expression regulation and binds a brain-expressed nuclear protein with very high specificity and that it is capable of modulating reporter-gene expression from the *DCDC2* promoter in an allele-specific manner [29, 41]. Based on our findings we can hypothesize that the associations are based on functional mechanisms and that differential, allele-dependent

Table 6 Interactive significant effects between READ1(4) and socioeconomic status (SES) upon CBCL/6–18 attention problems in girls and boys separately

Boys ($n = 314$)					GIRLS ($n = 317$)				
		READ1(4−)	READ1(4+)	READ1(4) × SES, F (p)			READ1(4−)	READ1(4+)	READ1(4) × SES, F (p)
SES	Low	57.61 ± 7.00 (38)	56.57 ± 6.66 (7)	0.81 (0.96)	SES	Low	54.93 ± 5.85 (42)	67.27 ± 10.92 (11)	23.94 (0.000002)
	Middle/high	55.66 ± 6.44 (172)	54.75 ± 5.24 (44)			Middle/high	55.88 ± 6.72 (177)	55.77 ± 5.63 (39)	

expression of *DCDC2* due to READ1(4+) genotypes may influence brain activation patterns in ADHD-related traits. However, since previous studies [29, 41] on functional role of READ1 found no significant results with allele-4, the results need to be interpreted cautiously, until replicated by at least one additional independent study. In addition, since the coverage of the *DCDC2* region by the markers employed in this study is limited, caution should be applied in addressing the functional mechanism underlying this association.

On the other hand, we did not find significant support for association of behavioral phenotypes with rs793862. This marker has been found associated with ADHD only in a previous study [39]. This discrepancy could be due to different populations' characteristics (family based vs. population based) and/or statistical methodologies (TDT vs. MANOVA). Since ADHD is a heterogeneous disorder, these results need replication in different study populations.

Interestingly, we found an association between READ1, per se or in interaction with SES, and attention but no other behavioral trait. Although our results require cautious consideration, they may contribute to assess the etiological relevance of the *DCDC2* gene in a specific and defined behavioral phenotype, i.e., attention problems.

Furthermore, we found significant association between *DCDC2* and attention, after controlling for learning problems. This result is in agreement with a previous study [25] that found a significant association between ADHD phenotype and a chromosome 6p22 locus in a sib-pair sample with RD; this result remained significant after controlling for reading, suggesting that association with ADHD was not a consequence of reading impairment. It seems that, irrespective of reading disability, the causal variants for ADHD might be found in the *DCDC2* region.

Perhaps of greater importance, our findings showed significant interactive effect, specifically *DCDC2*-by-SES, whereby the co-presence of one or two copies of allele-4 with low SES multiplies the risk for attention problems.

Low SES—alone or in interaction with genes—has been found to influence several behavioral traits/disorders, including attention [51, 52]; these children have an increased incidence of poor school outcomes and a greater need for special education. Low SES may have a crucial role in attention problems, either directly or indirectly, through detrimental effects onto more proximal child-specific factors, such as parenting [58].

While the biological pathways through which SES interacts with *DCDC2* in our study population remain unknown, low SES may act as enhancer of the genetic influence of *DCDC2* variant upon attention problems in the preadolescence years. By providing a more comprehensive

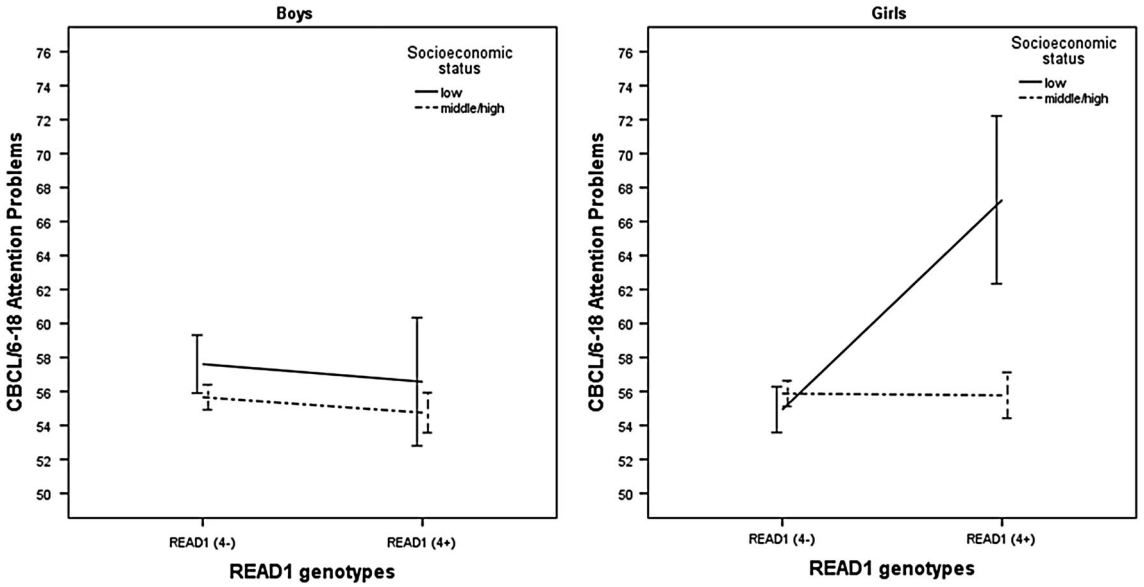

Fig. 2 Results of univariate analysis of variance estimating mean differences of attention problems as a function of SES and READ1(4) genotypes in boys ($n = 314$) and girls ($n = 317$)

analysis of influences at play, the interactive effect we found adds newer and stronger insights into the effects of *DCDC2* polymorphisms across differential and environmental niches.

Finally, our data suggest that the effects of *DCDC2* would appear only in girls. It is well established by animal and molecular studies that developmental programming has different effects in boys and girls [59].

The sex differences may reflect the distinctive sexual dimorphism of the brain, including hormonal and structural factors, which emerge during development. Thus, it is conceivable that READ1 involved in cortical morphogenesis and neurogenesis [60], if combined with low SES, could potentiate different genetic vulnerabilities for boys and girls, looking specifically at ADHD problems. Since the exact meaning of these differences is not well understood, understanding the mechanisms underlying sex differences is not only fundamental per se, but might also contribute to understand the known sex differences in prevalence, age of onset, and severity seen in ADHD-related problems [61].

Nevertheless, our results must be viewed in light of some limitations. Firstly, due to the small sample size of the 'at-risk' category (i.e., READ1(4+) + low SES), especially for gender effect analyses, a sampling error could be involved. The current findings should be interpreted cautiously until further replication is obtained in a larger sample. Secondly, while direct interviews in the general population subjects elicit more information of possible clinical relevance, these studies are by definition based on children who are mostly healthy and relying on paper-and-pencil instruments is still viable in face of realistic cost-effectiveness considerations. Thirdly, we studied a Caucasian population of Italian ancestry which may limit the generalizability of our results due to population-specific allelic frequencies or cultural background. Fourthly, we used parental employment as a measure of SES coded according to the Hollingshead 90-point scale for parental occupation. However, SES is a complex and distal variable. As such, it is likely to incorporate other measures/indexes and is also indirectly related to many other variables (education, income, nutrition), some of which may be partially genetic in origin. Therefore, the possibility remains that part of what we have interpreted as a gene-by-environment interaction could in fact encompass a gene-by-gene interaction. Finally, we used CBCL/6–18 school competence as a proxy measure for RD. A direct assessment of reading skills through standardized tests should be more appropriate.

While these findings need replication in independent samples, we have provided the first evidence of the joint effects of the *DCDC2* gene and low SES upon attention in an Italian sample of pre-adolescents. With careful consideration of the potential limitations, our study can be important for primary prevention and early intervention risk in the area of ADHD. Based on these data, probabilistic profiles of risk can be tailored and used to identify early subjects at heightened risk for attention problems. This yields considerable advantages in terms of cost-effective strategies for targeted preventive/therapeutic programs.

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Conflict of interest The authors declare that they have no conflict of interest.

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Reading difficulties and attention-deficit/hyperactivity behaviours: evidence of an early association in a nonclinical sample

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Attention-deficit/hyperactivity disorder (ADHD) often co-occurs with reading disability. A cross-sectional study in an Italian-speaking, nonclinical sample was conducted in an attempt to document the existence of an early association between reading difficulties (RD) and ADHD behaviours. We recruited a sample of 369 children in their first year at primary school. Of the sample, 8.4% displayed RD; 7.0% had ADHD; 3.5% presented both RD and ADHD behaviours; 50% of the children with ADHD displayed RD; 41.9% of those with RD displayed ADHD behaviours. Low socioeconomic status was associated with a fourfold increased probability of displaying RD (odds ratio = 3.98), but not ADHD behaviours. In this nonclinical sample, we detected an early association between ADHD behaviours and RD. A key role in this association may be played by inattention symptoms, which occurred with significantly increased frequency also in the group presenting only RD.

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a common childhood disorder that occurs in approximately 5% of the population. Characterised by developmentally disproportionate levels of inattention, impulsivity and hyperactivity (American Psychiatric Association, 2007), ADHD often co-occurs with reading disability, another common disorder of childhood reported in both clinical (Dykman & Ackerman, 1991; Semrud-Clikeman, Biederman, Sprich-Buckminster, Lehman, Faraone & Norman, 1992) and population-based (Carroll, Maughan, Goodman & Meltzer, 2005; Willcutt & Pennington, 2000; Willcutt, Pennington, Olson, Chhabildas & Hulslander, 2005) samples. Reading disability is a

specific learning disability affecting 3–6% of the population. It is characterised by difficulties with accurate and/or fluent word recognition and by poor spelling and decoding abilities. These difficulties occur despite adequate cognitive abilities and educational opportunities (American Psychiatric Association, 2007). In ADHD samples, the rate of comorbid reading disability is between 25% and 40% (Dykman & Ackerman, 1991), whereas in samples selected for reading disability, the rate of comorbid ADHD ranges from 15% to 26% (Gilger, Pennington & DeFries, 1992).

The role of orthographic opacity

The main published studies evaluating the association between reading disability and ADHD refer to populations of English-speaking children (e.g., Carroll, Maughan, Goodman & Meltzer, 2005; Semrud-Clikeman, Biederman, Sprich-Buckminster, Lehman, Faraone & Norman, 1992; Willcutt, Pennington, Olson, Chhabildas & Hulslander, 2005), whereas evidence relating to speakers of Italian, which – unlike English – has a transparent orthography, is lacking.

This discrepancy is important because dyslexia has been found to show increased incidence and increased severity, particularly in terms of reading accuracy (Cheung, Chen, Lai, Wong & Hills, 2001; Landerl, Wimmer & Frith, 1997; Lindgren, De Renzi & Richman, 1985; Paulesu et al., 2001; Ziegler, Perry, Ma-Wyatt, Ladner & Schulte-Körne, 2003), in countries where the language spoken has an opaque orthography.

As shown by a cross-linguistic study conducted by Seymour, Aro and Erskine (2003), the time needed to become accurate and fluent in foundation-level reading varies between European languages, ranging from around 1 year for transparent orthographies (such as Italian) to 2–3 years for opaque orthographies (such as English). Remarking that the 'effects appear not to be attributable to differences in age of starting or letter knowledge' (p. 143), the authors argued that fundamental linguistic differences in syllabic complexity and orthographic depth are responsible.

In this regard, Paulesu et al. (2001), comparing Italian, French and English subjects with dyslexia, found, in the presence of comparable positron emission tomography scans in the three populations (i.e., 'reduced activity at the level of the left middle, inferior and superior temporal cortex and in the middle occipital gyrus' [p. 2165]), that the Italians, favoured by the orthographic transparency of their language, showed significantly more rapid and accurate reading of words and nonwords.

Indeed, the acquisition of a shallow orthography may be based on a single (alphabetic) process, whereas the acquisition of a deep orthography requires the formation of a dual (alphabetic + logographic) foundation. It can be hypothesised that learning under conditions where attention and processing resources are divided between two functions will occur more slowly than learning under conditions where all resources are focused on a single function. In addition, dual-process learning will demand the employment of a wider range of cognitive skills (including attention) than single-process learning and might therefore increase the prevalence of comorbid reading disability and ADHD in populations whose language has an opaque as opposed to transparent orthography, but at present there are no data supporting or refuting this hypothesis.

The role of socioeconomic status

Socioeconomic status (SES), typically indexed by parental education, occupation and income, is probably the most widely used contextual variable in education research: many studies show

that SES is associated with a wide array of health, cognitive and socio-emotional outcomes in children (Bradley & Corwyn, 2002). Numerous studies have documented that poverty and low parental education are associated with lower levels of school achievement and IQ later in childhood (e.g., Alexander, Entwisle & Dauber, 2000; Duncan, Brooks-Gunn & Klebanov, 1994; Escalona, 1982). In their recent review, Hackman and Farah (2009) reported that different neuro-cognitive systems are affected by SES, in particular language and executive function.

SES also appears to affect school attendance, number of years of schooling completed and academic achievement. A recent meta-analytic review (Sirin, 2005), focusing on studies published between 1990 and 2000, examined the relationship between students' SES and their academic achievement. Its overall finding was that parents' position in the socioeconomic structure has a strong impact on students' academic achievement. Family SES sets the stage for students' academic performance both directly (by providing resources at home) and indirectly (by providing the social capital that is necessary to succeed at school).

But the relationship between SES, IQ and academic achievement may be quite complex and bidirectional. Indeed, Herrnstein and Murray (1994) speculated that it is heritable traits, such as intelligence and cognitive abilities, that allow people to reach higher levels of education and obtain more prestigious jobs; this correlation may lead high-IQ individuals into higher social strata.

SES and reading disability. SES is also a robust predictor of children's reading achievement, with a higher SES associated with higher levels of reading skills. Evidence has suggested that SES is predictive of multiple components of reading ability and development, including decoding, print knowledge and comprehension (Bowey, 1995; Hecht, Burgess, Torgesen, Wagner & Rashotte, 2000; Lonigan, Burgess, Anthony & Barker, 1998; Noble & McCandliss, 2005; Raz & Bryant, 1990). Carroll et al. (2005) found that specific literacy difficulties were associated with social class and parental education: children in the lowest social class were almost 10 times more likely to have specific literacy problems than children from the highest social class.

SES and ADHD. Very few studies have investigated the relationship between socioenvironmental factors and ADHD. Lasky-Su et al. (2007) suggested a direct interaction between genetic and environmental factors in the development of ADHD. In fact, family SES was found to predict inattentive, but not hyperactive–impulsive, symptom counts in children exposed to brain-derived neurotrophic factor, a genetic risk factor for ADHD. Hjern, Weitoft and Lindblad (2010), in a Swedish cohort study of more than 1 million children of primary and secondary school age, demonstrated that socioeconomic indicators such as education, single parenthood and receipt of social welfare assistance were associated with medicated ADHD. Low maternal education alone predicted 33% of cases of medicated ADHD, single parenthood 14% and social welfare 10%, whereas psychiatric or addictive disorder in the parents predicted less than 4% of cases.

SES measurement. Although there is general consensus that income, education and occupation together represent SES better than any of these variables alone (White, 1982), there is no consensus on: (a) how best to composite the set of indicators; (b) whether the relationship between SES and child outcomes is best examined using a composite, statistical procedure that includes all indicators, or each indicator singly; or (c) how best to measure each component (Krieger, Williams & Moss, 1997).

Many measures of SES are available (e.g., Blishen, Carroll & Moore, 1987; Entwislea & Astone, 1994; Hollingshead, 1975; Nakao & Treas, 1992). The Hollingshead (1975) Four-Factor Index of Social Status has been one of the most frequently used, proving valuable as

a predictor/covariate and/or outcome measure in studies of dyslexia (e.g., Felton, Naylor & Wood, 1990; Shaywitz et al., 1999), premature infants (Barratt, 1996) and psychiatric disorders such as major depression (e.g., Cuffe, Waller, Cuccaro, Pumariega & Garrison, 1995).

Cirino et al. (2002) found a high inter-measure agreement (range $r = .81$ to .88) across three SES measures (the Hollingshead Four-Factor Index, the Nakao and Treas Scale and the Blishen, Carroll and Moore Scale) using data from two countries (United States and Canada). This finding suggests that SES-based comparisons might justifiably be made across studies that employ different SES measures.

The current study

In light of all these considerations, we conducted a cross-sectional study in a general-population sample, employing a multivariate design that included gender and measures of SES, IQ, reading abilities and ADHD symptoms. The study had the following aims:

1. to document the existence of an early association (at the end of the first year of school) between reading difficulties (RD) and ADHD behaviours in an Italian-speaking (transparent orthography), nonclinical sample, thereby verifying the reproducibility of the results so far obtained mainly in English-speaking populations (opaque orthography);
2. to evaluate the role and importance of SES, gender and IQ in this association;
3. to confirm the existence of substantially greater correlations between RD and symptoms of inattention than between RD and symptoms of hyperactivity/impulsivity.

Method

Subjects

As a part of a programme of early identification and treatment of learning disabilities, over a 2-month period (March and April 2005), we met the parents and teachers of 396 native Italian, first-year primary school children from 13 primary schools (22 classes) in four districts of the Italian city of Varese, a small provincial capital with about 80,000 inhabitants.

To obtain the parents' informed consent to their children's participation in the study (which had local ethics committee approval) and also to collect, by means of a semi-structured interview, information relating to each family's SES (e.g., parents' profession and years of education), the aims of the study were first clearly explained to them.

Children with mental retardation or other known neurological or psychiatric disorders ($n = 9$) or whose parents withheld their consent ($n = 8$) were excluded from the study; we also excluded children with low intelligence (<10th percentile on the Raven Coloured Progressive Matrices [CPM] – 'Materials' section; $n = 10$). The study sample was thus made up of 369 children (202 boys and 167 girls) aged between 6.05 and 7.25 years (mean age 6.73 ± 0.34 years).

Materials

Nonverbal intelligence was assessed using the Raven CPM (Raven, 1996). Each of this instrument's 36 items consists of an incomplete abstract pattern. Subjects are required to select, from a set of six, the figure needed to complete the pattern correctly.

Reading abilities were assessed on the basis of the child's reading aloud of an age-appropriate passage (Cornoldi, Colpo & Gruppo, 1998; Cornoldi, Tressoldi and Perini, 2010): a short story comprising 140 syllables. This reading task was discontinued if the child exceeded the 240-second time limit. Normative data for this test were collected between 1977 and 1980 and updated between 1995 and 1998; they refer to a sample of 5,700 students attending 127 schools in 18 Italian regions. Conducted individually, this test allowed us to establish, with reference to Italian normative data for the age group, each child's reading fluency (number of syllables read per second) and reading accuracy (number of mistakes made). These are key parameters in transparent orthographies, such as Italian. The reliability of the test ranges from .752 to .869 for accuracy and from .943 to .967 for fluency.

The presence of *ADHD behaviours* was assessed using two structured rating scales suitable for screening purposes: the 27-item Conners' Parent Rating Scales, Revised: Short Version (CPRS-R:S), and the 28-item Conners' Teacher Rating Scales, Revised: Short Version (CTRS-R:S). These scales, which are derived from the long forms of these questionnaires (CRS-R:L), ask parents and teachers to rate a child's behaviour in relation to a series of problems commonly present in children. These short-version scales are made up of four subscales: oppositional, inattention, hyperactivity and Conners' ADHD index. The raw scores recorded on these rating scales were converted to *T* scores in accordance with Italian normative data obtained from a sample of 2,414 subjects, including 641 children aged 6–8 years, evenly distributed across the whole of the country (northern, central and southern Italy). Internal consistency reliability (Cronbach's α) was good, ranging from .745 (hyperactivity subscale) to .897 (ADHD index) for the CPRS-R:S and from .847 (oppositional) to .924 (ADHD index) for the CTRS-R:S (Conners, 2007).

Higher *T* scores reflect a higher number and/or frequency of problems reported. *T* scores below 66 are recorded by children without significant difficulties ('normal'); *T* scores between 66 and 69 indicate children who are 'at risk' of behavioural problems, whereas *T* scores above the clinical cut-off ($T \geq 70$) identify children with significant behavioural problems ('clinical').

Procedures

Each child was tested individually in a single 45-minute session conducted during school hours in a room set apart from the rest of the class. At the end of the first school year (May 2005), a child neuropsychiatrist and/or a psychologist individually administered a battery of standardised neuropsychological tests ('Materials' section) to assess nonverbal intelligence and reading abilities.

In relation to age-based Italian normative data, children with insufficient passage reading scores (i.e., <10th percentile) for both speed and accuracy were classified as reading disabled (i.e., as presenting RD); continuous scores were also used for correlational analyses.

Children whose mother and teacher both assigned *T* scores >65 on one or more Conners' subscales were classified as presenting ADHD behaviours (hereinafter ADHD); again, continuous scores were used for correlational analyses.

To assess SES, we computed the Hollingshead Four-Factor Index of Social Status (Hollingshead, 1975), a measure that uses education and occupation to determine a family's composite social status. The higher the index, the higher is the SES. In families with both parents in employment, the scores were averaged to obtain a single score per family.

On the basis of the scores obtained, the children were grouped into three categories: *low* (8–22), *medium* (23–50) and *high SES* (51–66). The parents of the low-SES children were manual workers or in unskilled occupations or precarious employment and had a low level of education (elementary or middle school); the parents of the high-SES children had a high level of education (university degree) and occupied managerial positions or were in intellectual, scientific or highly specialised professions. The parents of the children in the medium-SES group had an intermediate level of education (high school) and did office work or had skilled jobs in the business and services sector or technical professions.

Statistical analysis

The statistical analysis of the data was performed using the PASW (SPSS) Statistics 17.0.3 package for Macintosh. *P* values $<.05$ were considered statistically significant. Before beginning the statistical analysis, we used the Kolmogorov–Smirnov test to verify the normal distribution of the variables. Differences in scores (quantitative variables) between boys and girls and SES categories were assessed by performing independent-samples *t*-tests and one-way ANOVAs (Scheffe's post hoc test). The chi-square test was used to analyse categorical and nominal variables and to compare the frequencies of the qualitative variables. Bivariate correlations (Spearman's *rho*) were performed between Conners' *T* scores and the reading test results, IQ and SES index. In addition, a logistic regression model was used that included gender and SES, IQ, reading abilities and ADHD symptoms. The results are presented as odds ratios with 95% confidence intervals.

Results

All the children included in this study were found to have a normal nonverbal IQ (108.01 ± 8.82; range: 81–135); SES was high in 11.4%, medium in 57.7% and low in 30.9% of the sample. Post hoc tests carried out using Scheffe's method revealed no differences between the medium-SES and high-SES groups for all the variables considered. Therefore, in the multivariate analysis and presentation of the results, only two groups are considered: low SES and medium–high SES.

RD were found in 8.4% ($n = 31$, 11 girls and 20 boys) of our sample: risk factors for RD were found to be low SES (odds ratio [OR] = 3.89, $p = .004$) and the concomitant presence of ADHD behaviours (OR = 18.13, $p < .001$). There emerged no significant Gender×SES, ADHD×SES or Gender×SES×ADHD interactions (Table 1).

The proportion of children with ADHD behaviours (those placed, by both parents and teachers, in the 'at risk'/'clinical' range on at least one subscale) was 7.0% ($n = 26$, 18 boys and 8 girls). The results of the logistic regression analysis showed that only the presence of RD significantly increased the odds of a child presenting ADHD behaviours (OR = 17.97, $p < .001$). There were no significant Gender×SES, RD×SES or Gender×SES×RD interactions (Table 2).

The prevalence of coexistent RD and ADHD behaviours was 3.5% ($n = 13$, seven boys and six girls). On the basis of the presence of these disorders (neither, one or both), the children were divided into four groups (Table 3): children without difficulties (N group, $n = 325$, 171 boys and 154 girls), children showing only RD (RD group, $n = 18$, 13 boys and 5 girls), children showing only ADHD behaviours (ADHD group, $n = 13$, 11 boys and 2 girls) and children with both RD and ADHD behaviours (RD + ADHD group, n = 13, seven boys and six girls). A higher prevalence of male children was found in the

Table 1. Characteristics of the RD group and risk factors.

	RD, *n* (%)				
	Yes, 31 (8.4)	No, 338 (91.6)	Univariate *p*	Multivariate *p*	OR (95% CI)
Low SES, *n* (%)	19 (61.3)	91 (28.3)	<.001	.004	3.89 (1.55–9.76)
Boys, *n* (%)	20 (64.5)	182 (53.8)	.253	.217	
Nonverbal IQ, *M* (*SD*)	104.79 (8.27)	108.29 (8.82)	.037	.488	
ADHD behaviours, *n* (%)	13 (41.9)	13 (3.8)	<.001	<.001	18.13 (6.87–37.85)

ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; OR, odds ratio; SES, socioeconomic status.

Table 2. Characteristics of the children with ADHD behaviours and risk factors.

	ADHD behaviours, *n* (%)		Univariate	Multivariate	
	Yes, 26 (7.0)	No, 343 (93.0)	*p*	*p*	OR (95% CI)
Low SES, *n* (%)	11 (42.3)	103 (30.2)	.199	.744	
Boys, *n* (%)	18 (69.2)	184 (53.6)	.124	.298	
Nonverbal IQ, *M* (*SD*)	105.50 (7.25)	108.19 (8.91)	.134	.978	
Reading difficulties, *n* (%)	13 (50.0)	18 (5.2)	<.001	<.001	17.97 (6.79–37.59)

ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; OR, odds ratio; SES, socioeconomic status.

ADHD group and in the RD group, but the difference was not statistically significant ($p = .058$), probably partly on account of the small size of the groups. No significant differences in IQ were found between the groups ($p = .159$). A significantly higher prevalence of low SES ($p = .002$) was found in the RD (66.7%) and RD + ADHD (53.8%) groups compared with the N (28.2%) and ADHD (30.8%) groups.

The analysis of reading speed showed that the children in the ADHD group, despite not meeting the RD criteria, recorded significantly lower results than the N group (0.67 ± 0.40 vs 1.12 ± 0.52, $p < .001$), whereas their performance did not differ significantly from those of the RD (0.28 ± 0.14, $p = .201$) and RD + ADHD (0.25 ± 0.11, $p = .233$) groups. The level of reading accuracy was found to be comparable in the N and ADHD children, who made significantly fewer mistakes ($p < .001$) than the RD and RD + ADHD children.

The mean Conners' scale scores recorded in the four groups were compared by means of a one-way ANOVA ($p < .001$ for all the variables considered). On the inattention subscale (compiled by teachers), the RD group obtained a score very similar to that of the ADHD children (65.72 ± 12.92 and 65.69 ± 8.34), which was significantly lower than the score of the RD + ADHD group (73.69 ± 5.63, Scheffe's post hoc $p = .043$) and significantly higher than that of the N group (48.41 ± 7.28, Scheffe's post hoc $p < .001$). There were no significant differences between Conners' scale scores of the ADHD and RD + ADHD groups.

The percentages of pathological ('at risk'/'clinical') Conners' scale scores differed significantly in the four groups ($p < .001$). The children in the RD group, compared with those in the N group, more frequently recorded pathological *T* scores on the inattention subscale compiled by teachers (50.0% vs 4.9%) and on the ADHD index compiled both by parents (11.1% vs 3.4%)

Table 3. Data on the demographic and ability variables for the four groups.

Variable		N group (325)	RD group (18)	ADHD group (13)	RD + ADHD group (13)
Age, *M* (*SD*)		6.74 (0.35)	6.62 (0.32)	6.76 (0.31)	6.56 (0.19)
Gender	Girls, *N* (%)	154 (47.4)	5 (27.8)	2 (15.4)	6 (46.2)
	Boys, *N* (%)	171 (52.6)	13 (72.2)	11 (84.6)	7 (53.8)
Socioeconomic status	Low, *N* (%)	91 (28.2)	12 (66.7)	4 (30.8)	7 (53.8)
	Medium, *N* (%)	194 (59.7)	6 (33.3)	7 (53.8)	6 (46.2)
	High, *N* (%)	40 (12.1)	0 (0.0)	2 (15.4)	0 (0.0)
Nonverbal IQ, *M* (*SD*)		108.38 (8.89)	104.69 (7.76)	106.09 (6.96)	104.90 (7.76)
Reading ability	Fluency, *M* (*SD*)*	1.12 (0.52)	0.28 (0.14)	0.67 (0.40)	0.25 (0.11)
	Accuracy, *M* (*SD*)**	4.86 (4.44)	10.97 (4.62)	7.15 (6.35)	11.88 (6.81)
Teachers' Conners***	Oppositional, *M* (*SD*)	47.58 (7.45)	48.11 (6.53)	55.77 (18.07)	56.23 (17.58)
	Inattention, *M* (*SD*)	48.41 (7.28)	65.72 (12.92)	65.69 (8.34)	73.69 (5.63)
	Hyperactivity, *M* (*SD*)	47.07 (6.35)	48.50 (6.16)	60.54 (14.64)	57.15 (12.27)
	ADHD index, *M* (*SD*)	47.18 (6.55)	53.61 (8.29)	62.31 (12.25)	62.92 (10.75)
Parents' Conners ***	Oppositional, *M* (*SD*)	45.76 (7.68)	44.78 (7.56)	55.08 (11.89)	57.15 (9.56)
	Inattention, *M* (*SD*)	48.17 (7.47)	53.50 (10.23)	66.62 (12.29)	72.01 (8.91)
	Hyperactivity, *M* (*SD*)	49.36 (9.27)	45.94 (5.89)	69.69 (14.76)	66.85 (12.99)
	ADHD index, *M* (*SD*)	48.85 (8.21)	50.67 (9.55)	69.62 (9.57)	67.15 (5.54)

M, mean; *SD*, standard deviation.
*Syllables per second; **errors; ***T scores.

and by teachers (16.7% vs 3.1%). The RD + ADHD group, compared with the ADHD group, more frequently had 'at risk/clinical' scores on the inattention subscale, compiled both by parents (76.9% vs 69.2%) and by teachers (100.0% vs 61.5%), whereas they less frequently had pathological scores on the oppositional, hyperactivity and ADHD index subscales.

Table 4 details the correlations (Spearman's *rho*) between Conners' scale T scores, SES, IQ and the results of the reading tests. The highest correlation was found between the teacher-compiled inattention subscale score and reading ability, both reading speed ($rho = -.580$) and reading accuracy ($rho = .447$); this subscale was also significantly correlated with IQ and SES (Table 4).

A logistic regression analysis failed to identify significant risk factors for the development of RD + ADHD as opposed to just one of the two disorders (Table 5). This was probably due to the small size of the groups.

Discussion

Association between RD and ADHD behaviours

In this study of a nonclinical sample of schoolchildren, RD was found in 8.4% of the children at the end of their first year at school. This percentage falls within the worldwide RD prevalence range for school-age children, estimated to be between 1% and 11%

Table 4. Correlations between Conners' scale scores, the reading test results and SES index.

	rho p							
	TC inattention	Inattention	TC hyperactivity	PC hyperactivity	TC ADHD index	PC ADHD index	TC oppositional	PC oppositional
Nonverbal IQ	**−.317**	**−.182**	−.033	−.022	**−.173**	−.083	−.010	.021
	<.001	**<.001**	.497	.668	**<.001**	.112	.841	.694
Reading fluency	**−.580**	**−.361**	**−.194**	**−.122**	**−.398**	**−.264**	**−.149**	−.071
	<.001	**<.001**	**<.001**	**.019**	**<.001**	**<.001**	**.002**	.173
Reading accuracy	**.447**	**.288**	**.129**	**.142**	**.278**	**.198**	.069	.082
	<.001	**<.001**	**.008**	**.007**	**<.001**	**<.001**	.157	.117
SES index	**−.305**	**−.118**	−.042	−.076	**−.208**	−.061	−.007	−.006
	<.001	**.024**	.388	.145	**<.001**	.246	.894	.890

PC, parents' Conners; TC, teachers' Conners.
Note: For each item, the *rho* coefficients are given on the upper line and the relative *p* values underneath. Significant correlations are shown in bold.

Table 5. Characteristics of the 'ADHD + RD' group and the 'ADHD or RD' group.

	Group, *n* (%)				
	ADHD + RD, 13 (29.5)	ADHD or RD, 31 (70.5)	Univariate *p*	Multivariate *p*	OR (95% CI)
Low SES, *n* (%)	7 (53.8)	16 (51.6)	0.892	0.710	
Boys, *n* (%)	7 (53.8)	24 (77.4)	0.118	0.086	
Nonverbal IQ, *M* (*SD*)	104.90 (7.76)	105.30 (8.00)	0.881	0.825	

ADHD, attention-deficit/hyperactivity disorder; CI, confidence interval; *M*, mean; OR, odds ratio; RD, reading disorder; *SD*, standard deviation; SES, socioeconomic status.

(American Psychiatric Association, 2007). At present, the only official figure on the prevalence of dyslexia in Italy is that found in the study by Lindgren et al. (1985), who reported a value of 3.6%. However, this finding cannot be compared with the result of our study, given that it was drawn from a larger sample of children who, moreover, had reached the end of their fifth year of schooling and were thus older than the ones included in our study; furthermore, the parameter used by Lindgren et al. to diagnose dyslexia, that is, 'reading comprehension', is no longer accepted in Italy as a valid diagnostic criterion for dyslexia (Associazione Italiana Dislessia, 1993). In our sample, the odds of encountering RD were 18.13 times greater in children with ADHD behaviours than in their normal-reading peers.

The prevalence of ADHD symptoms in our sample was 7.0%, which is in line with the American Psychiatric Association (2007) range of 3% to 7%. Most of our ADHD subjects were male children (84.6%), a finding consistent with a recent population-based birth cohort study (Yoshimasu et al., 2010). The odds of encountering attention problems or signs of hyperactivity were 17.97 times greater in the poor readers than in their normal-reading peers.

In our sample, the prevalence of coexistent RD and ADHD behaviours was 3.5%. In children with ADHD behaviours, the rate of comorbid RD was 50%, whereas in subjects with RD, the rate of comorbid ADHD symptoms was 41.9%. These rates, too, are consistent with the findings of Yoshimasu et al. (2010), even though their study is not directly comparable with ours as it was conducted in youngsters falling within a much broader age range (5–19 years) and used different criteria for the definition of the groups. There are no Italian data available for comparison.

Role and importance of gender, IQ and SES

In our sample, the presence of ADHD behaviours alone or RD alone was greater in male children; this difference came close to the threshold of statistical significance ($p = .058$). Its failure to reach statistical significance may be due to the small size of the sample. Conversely, no gender difference was found in the RD + ADHD group (boys 53.8% and girls 46.2%). Therefore, consistent with previous reports (Paloyelis, Rijsdijk, Wood, Asherson & Kuntsi, 2010; Saudino & Plomin, 2007; Willcutt, Pennington & DeFries, 2000; Yoshimasu et al., 2010), our findings did not provide any evidence for gender difference in the aetiology of the association between RD and ADHD symptoms.

Furthermore, the children with both disorders (RD + ADHD) did not differ, in IQ, from the other subjects. It is therefore possible that the association of RD and ADHD behaviours

is independent of IQ; some authors found that early inattention symptoms predicted later reading achievement even after controlling for prior reading ability and IQ (Rabiner & Coie, 2000; Rabiner, Malone & Conduct Problems Prevention Research Group, 2004).

Moreover, our results demonstrated that a low SES increases a child's risk of presenting RD (OR = 3.89) but not ADHD behaviours (i.e., of being placed, both by parents and by teachers, in the 'at risk'/'clinical' range on at least one subscale). However, SES was found to be significantly correlated (inversely) with *T* scores on the inattention subscale, compiled both by teachers ($rho = -.305$, $p < .001$) and by parents ($rho = -.118$, $p = .024$), and with the teacher-compiled ADHD index subscale score ($rho = -.208$, $p < .001$). Indeed, the RD + ADHD group, compared with the ADHD group, showed a significantly higher prevalence of low SES (53.8% vs 30.8%, $p < .001$). These data suggest that common environmental factors play a significant role in determining the association between RD and ADHD behaviours.

Disparities in SES between children could be mediated by many factors: aspects of the home literacy environment, the degree of early print exposure, the quality of early schooling, the level of cognitive stimulation, nutrition and parenting styles. Moreover, a lower SES is associated with higher levels of stress and with changes in the function of physiological stress response systems in children and adults (Evans & Marcynyszyn, 2004; Goodman, McEwen, Dolan, Schafer-Kalkhoff & Adler, 2005; Lantz, House, Mero & Williams, 2005; Levine, 2005). There is substantial evidence that low-SES children more often manifest symptoms of psychiatric disorders and maladaptive social functioning than children from more affluent backgrounds (Bradley & Corwyn, 2002; Carroll et al., 2005). However, it is not yet entirely clear whether low SES results in increased rates of psychiatric illness or whether the burden of psychiatric illness results in a decrease in SES.

Childhood environments and experiences in different socioeconomic strata also seem to be responsible, at least in part, for differences in children's neuro-cognitive outcomes, including their reading ability and attention (Noble, McCandliss & Farah, 2007).

Shonkoff and Phillips (2000) reported that high-SES parents are more inclined to engage children in conversation, read to them more and provide them with more teaching experiences; furthermore, their conversations are richer, contain more contingent responsiveness and include more efforts to elicit child speech. Their teaching style is more structured and richer in complex verbal strategies and their children have been found to manifest more advanced verbal competence. Such differences in parenting practice are strongly implicated in the relationship between SES and children's intellectual and academic performance (Sirin, 2005). Bradley and Corwyn (2002) also found that access to stimulating materials and experiences mediated the relationship between SES and children's behavioural problems. The connection between SES, stimulating experiences and children's cognitive functioning is well established (Brooks-Gunn & Duncan, 1997; McLoyd, 1998). Such experiences provide both direct and indirect (i.e., mediated through more capable peers and adults) learning opportunities for children, as well as serving as a motivational basis for continued learning. Low-SES parents are less likely to buy reading and learning materials for their children, less likely to take their children to educational and cultural events and less likely to regulate the amount of TV their children watch. As a result, low-SES children more frequently experience school failure (even in the early years), which can set them on a trajectory of either conduct problems or withdrawal behaviours (Bradley & Corwyn, 2002). Teacher attitudes and expectations may also be part of a complex set of mediators linking low SES to school failure and behavioural problems. McLoyd (1998) has argued that teachers tend to perceive low-SES pupils less positively (in terms of both their academic and their

self-regulatory skills) and to give these children less positive attention and less reinforcement for good performance. If children, both prior to school entry and during their school years, are less exposed to cognitively stimulating materials and experiences at home, they are more likely to fulfil these teachers' negative stereotypes, thereby further increasing the likelihood of negative interactions with teachers. Over time, the frustration connected with school failure and negative exchanges with teachers is likely to increase acting-out behaviours (or depression in some cases). It also increases the likelihood that children will affiliate with deviant peers.

However, it is also necessary to consider that traits such as attention and reading ability may also be, in part, inherited. As pointed out by Rowe, Vesterdal and Rodgers (1999), social science studies have largely tended to ignore the possible genetic component of 'environmental' variables in the interpretation of the effects of family and other social environments on intellectual and social development. Indeed, measures of social class, such as 'years of education' and 'income', are most often treated as strictly environmental variables, yet genotypes may influence the phenotypic associations between IQ, education and income. The authors, on the basis of the findings of the National Longitudinal Survey of Youth, affirmed that the origins of social differences may lie both in genetically based traits and in different environmental backgrounds (Rowe et al., 1999).

Herrnstein and Murray (1994) argued that heritable traits such as intelligence influence social success. Intelligence, as measured by IQ tests, influences the rate at which individuals learn and the complexity of the intellectual problems they are able to solve (Gottfredson, 1997; Rowe, 1997). It is thus possible that a high IQ enables some individuals to occupy social niches that are difficult, if not impossible, for low-IQ individuals to enter. Furthermore, the same genes that affect parental behaviour (or abilities or family circumstances) may affect children's phenotypes, and heritable traits in the child can evoke responses from parents (or other interactive partners) that cause environmental influences to be correlated with genotypes: for example, parents who like to read tend to have children who like to read, and parents are more likely to buy books for children who like to read. These processes may make the social status variables themselves heritable through the heritable traits that produce variation in social status (Rowe et al., 1999). SES effects may be moderated by children's own characteristics, family characteristics and external support systems: children with different genetic attributes will respond differentially to the same environmental circumstances; on the other hand, environments help to determine how genes express themselves (Bradley & Corwyn, 2002).

RD and ADHD inattention symptoms

The RD and ADHD groups obtained very similar scores on the teacher-compiled inattention subscale, which shows that in the school setting there are no differences between these two groups in terms of attention difficulties; conversely, the latter group showed a higher prevalence of hyperactivity–impulsivity symptoms. At school, the RD + ADHD group, compared with the ADHD group, more frequently presented inattention symptoms (100% vs 61.5%, $p < .001$) but less often showed hyperactivity–impulsivity symptoms (30.8% vs 46.2%). Finally, the ADHD group, compared with the N group, showed a significantly slower reading speed (a key parameter in transparent orthographies, such as Italian).

In our sample, RD were found to be more highly correlated with ADHD inattention symptoms than with hyperactivity–impulsivity symptoms, which is in line with the results of others (Carroll et al., 2005; Martin, Levy, Pieka & Hay, 2006; Paloyelis et al., 2010; Sexton, Gelhorn, Bell & Classi, 2011; Willcutt & Pennington, 2000; Willcutt, Pennington, Olson & DeFries, 2007).

Silva-Pereyra et al. (2010), in their study, used standardised low-resolution brain electromagnetic tomography to locate sources of P2 and P3 event-related potential components in normal versus poor readers (children) performing a cued continuous performance task: during the presentation on a personal computer of a sequence of 600 arrows, the participants were instructed to respond (by clicking on the left mouse button) to the designated target arrow, but only if a specific arrow (warning stimulus) had immediately preceded it (go trial). On the basis of the results they obtained, the authors hypothesised that the poor readers may have impaired ability to focus their attention when a new stimulus is expected (lack of superior parietal activation), which could produce an imbalance in the processes that normally inhibit unnecessary information (greater prefrontal cortex activation). This condition may leave them less prepared to decode graphemes and could create other problems in the reading processing continuum, such as phonological processing deficits.

The association between inattention and RD is unlikely to derive solely from the behavioural sphere; indeed, it is now increasingly recognised that cognitive attentional processes are involved in many stages of the reading process (Bosse, Tainturier & Valdois, 2007; Paloyelis et al., 2010; Reynolds & Besner, 2006; Shaywitz & Shaywitz, 2008; Vidyasagar & Pammer, 2010).

Limitations of the study

To be fully representative of the Italian school population, our sample would have to have been recruited across the various Italian regions. That said, the schools involved in the study are located in different parts of the city of Varese (centre, residential areas and outskirts) and also take children from small outlying communities. This made the sample as representative as possible of the variety of areas (urban/nonurban) that feed Italian schools.

It is possible that some of the children who met our criteria for RD at the end of their first school year are simply slower than their peers in acquiring reading skills and would probably not present significant RD were they to be reassessed later on. Some authors argued that classifying children as reading disabled (on the basis of IQ and reading tests) in their first year of school is inappropriate, given that such assessments might, in some cases, overidentify children who have not been adequately exposed to reading (Shaywitz, Escobar, Shaywitz, Fletcher & Makuch, 1992).

The prevalence data on ADHD behaviours in our study should be interpreted in light of several limitations. It is possible that our use of rating scales, rather than a full, structured interview, to assess ADHD symptoms could have resulted in an overestimation of their prevalence. To overcome, in part, this problem, ADHD behaviours were considered present only when there was agreement between the parent and teacher ratings.

Furthermore, the data collection method did not allow us to detect possible comorbidities (motor problems, language disorders, etc.), which could further influence the association between RD and ADHD symptoms.

On the other hand, the use of an unselected, general-population sample avoided possible selection biases associated with clinic-referred or selected community samples and means that the findings we obtained can be extended to the general population, albeit with caution given the small size of the RD and ADHD groups.

Finally, given the absence of validated Italian scales, sociocultural level was assessed using an American scale (Hollingshead, 1975). We deliberately chose a scale that does not include income as a variable as this seems to be the parameter most influenced by country of origin, currency and level of inflation. The seven-group classification of level of education and the grouping of occupation into nine categories are characteristics very similar to the Italian National Institute of Statistics classifications (Istituto Nazionale di Statistica, 2005, 2006). It is reasonable to assume that the subdivision of the final score into three categories was sufficient to ensure that any small inconsistencies, between countries, in the status of certain occupations were overcome. Moreover, Cirino et al. (2002) found that studies using the Hollingshead scale to derive SES scores can be compared with studies using more recently developed measures, which also take income into account.

Conclusion

In this study, we detected the existence of an early association (i.e., at the end of the first year at school) between RD and ADHD behaviours, in an Italian-speaking nonclinical sample. A significant role in the development of this association seems to be played by sociocultural factors (which could, in part, be genetically mediated). Finally, we detected greater correlations between RD and symptoms of inattention than between RD and symptoms of hyperactivity–impulsivity. Furthermore, inattention symptoms were also found in subjects with RD alone. These findings show that there is a need for better understanding of the aetiology of the association between ADHD inattention symptoms and RD and also of the role played in this association by genetic and environmental factors.

Recent findings in fact indicate that other cognitive processes are involved in reading, particularly attentional mechanisms, and that disruption of these attentional mechanisms may play a causal role in RD. Recognition of the role of attentional mechanisms in reading may open up the way for the development of new strategies of intervention in dyslexia (Shaywitz & Shaywitz, 2008).

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Might the temperament be a bias in clinical study on attention-deficit hyperactivity disorder (ADHD)?: Novelty Seeking dimension as a core feature of ADHD

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ABSTRACT

Some clinical studies on attention deficit hyperactivity disorder (ADHD) have been found to overlap those of studies on personality, particularly those on the Novelty Seeking trait (NS) as measured by the Junior Temperament and Character Inventory (JTCI). The aim of this study was to evaluate the potential role of NS in clinical research on ADHD. We enroled 146 ADHD children (125 boys; mean age=9.61, S.D.=2.50) and 223 age- and gender-matched control children (178 boys; mean age=9.41, S.D.=2.30). All the parents filled in the JTCI for the evaluation of personality according to Cloninger's model. An exploratory factor analysis differentiated the NS items that concern "Impulsivity" (NS1) from those that concern other features (NS2). Multivariate Analysis of Variance (MANOVAs) revealed significant differences between ADHD children and non-ADHD children in temperamental dimensions: the scores of ADHD children were higher than those of non-ADHD children in Total NS, NS1-Impulsivity and NS2. Our results show that the NS dimension of the JTCI in ADHD children is higher than in non-ADHD children, even when a correction is made for impulsivity items. This finding suggests that the NS trait plays a central role in ADHD diagnosis even when items referred to impulsivity are removed from the NS scale.

1. Introduction

Cloninger (1987) and Cloninger et al. (1993) developed a psychobiological model according to which personality is composed of both temperament and character traits. This model contains four dimensions of temperament: Harm Avoidance (HA) involves the inhibition of behaviour by anxiety-provoking stimuli; Novelty Seeking (NS) entails the activation of behaviour due to a desire to explore novelty or complexity, as well as excitability owing to frustration and boredom; Reward Dependence (RD) refers to the need for social approval and attachment; Persistence (P) implies perseverance in behaviour despite frustration and fatigue. Hence, temperament involves individual differences in basic emotional impulses, such as fear (related to high HA), anger (related to high NS), disgust (related to high RD) and ambition (related to high P) (Cloninger and Zohar, 2011).

These basic emotional drivers of temperament are regulated by three character traits in Cloninger's model of personality development. Self-directedness (SD) is a person's ability to self-regulate his/her behaviour according to specific goals and values in such a way as to make the person responsible, purposeful and resourceful. Cooperativeness (C) is the ability to get along with other people by being tolerant, empathic, helpful and forgiving. Self-Transcendence (ST) is a person's ability to identify with nature and the world as a whole, which means a person seeks to understand what is beyond their individual human existence and is able to sublimate and act altruistically. To quantify those seven dimensions, Cloninger developed the Temperament and Character Inventory (Cloninger, 1999, 1994; Martinotti et al., 2008), a widely used self-report measure of personality. To evaluate temperament and character in paediatric age, according to Cloninger's model, two specific tools were constructed

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and validated: the Pre-schooler Temperament and Character Inventory (Ps-TCI: Constantino et al., 2002) and the Junior Temperament and Character Inventory (JTCI: Luby et al., 1999; Andriola et al., 2012). Unlike the adult version of the TCI, the questionnaires for children do not include subscales for each factor.

International studies on temperament and psychopathology have consistently suggested that there is a strong correlation between temperament and psychopathology in children and adolescents (Rothbart et al., 2000; Kuo et al., 2004). For example, a high degree of NS has been associated with externalizing problems, as well as with the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (Copeland et al., 2004; Rettew et al., 2004), including early onset antisocial behaviour (Tremblay et al., 1994) and conduct disorder (Schmeck and Goth, 2001). Moreover, JTCI scales designed to assess Novelty Seeking and Harm Avoidance discriminate between internalizing and externalizing problems (Copeland et al., 2004; Rettew et al., 2004). Moreover, measures of low persistence have been linked to disruptive behaviour (Schmeck and Poustka, 2001). By contrast, high levels of HA in children and adolescents have been linked above all to internalizing disorders (Biederman et al., 1993; Schwartz et al., 1999).

On the basis of this evidence, we believe that temperamental features in children with attention-deficit/hyperactivity disorder (ADHD), a chronic pervasive childhood disorder, deserve further attention. Few studies have assessed the relationship between dimensions of temperament/character and ADHD using the JTCI in clinical samples. Cho et al. (2008) reported higher NS scores and lower SD scores in ADHD children than in healthy subjects. Other studies on ADHD children (Yoo et al., 2005) have shown that patients have higher NS levels than control subjects. These studies confirm the presence of a typical temperament trait in ADHD children, i.e. NS.

One objection that has been raised regarding the results of the aforementioned studies is that seven of the 18 NS items in the JTCI assess impulsivity. Although impulsivity in adolescents in general is not fully comparable to that of ADHD children, it is possible that ADHD children score higher on these items, which would result in a statistical bias (i.e. an increase in the Total NS scores). It may be possible to avoid this bias by separating the NS items of impulsivity from the other NS items and by assessing whether the NS dimension is represented to a greater degree in ADHD. If so, it might be possible to correct for the NS variable in clinical studies on ADHD. Few authors have highlighted the following methodological consequence: unless the NS dimension is equally represented in the ADHD group and in the control group, the differences between groups for the variables taken into consideration (e.g. smoking, obesity, gambling, internet addiction) may be overestimated or may appear to result from the temperament (NS) dimension as opposed to psychopathology (ADHD).

This may be the case in a series of studies on NS that revealed a correlation with addictions such as alcohol and nicotine (Martin et al., 2002), substance abuse (Wills et al., 1994), gambling (MacLaren et al., 2011) and obesity (Sullivan et al., 2007). However, the fact that similar results emerged from studies on ADHD suggests that individuals with this disorder are more susceptible to alcohol and substance abuse (Ohlmeier et al., 2008), nicotine abuse (Fuemmeler et al., 2007), gambling (Breyer et al., 2009) and obesity (Cortese and Morcillo, 2010). Are the latter findings due to the NS dimension being more marked in ADHD children than in controls? Thus, reliable results can only be obtained by modifying the research design so as to correct for the temperament variable: the results of one interesting study, which compared internet addictive behaviours and temperament in ADHD adolescents, suggest that internet addiction is related to ADHD symptoms, though not to a higher degree of NS (Cho et al., 2008).

The aim of this study was investigate the relationship between ADHD and NS. We separated the NS items that evaluate "Impulsivity" from the NS items that evaluate other characteristics, and then compared each of these NS scores in ADHD children and non-ADHD children. This separation is based on empirical data that derive from previous factorial analyses, described in the following sections.

2. Methods

2.1. Participants

We enroled a total of 369 Caucasian children between 6 and 19 years of age, divided as follows:

- 146 children had a diagnosis of ADHD (125 boys and 21 girls; mean age=9.61, S.D.=2.50).
- 223 children, who were matched for age and gender with the ADHD group but did not have psychiatric disorders (178 boys and 45 girls; mean age=9.41, S.D.=2.30).

The children with ADHD were outpatients enroled consecutively at the ASL RM/A, a regional public Developmental Neurological and Psychiatric Disorders Clinic that specialises in the diagnosis and treatment of ADHD.

The non-clinical sample was recruited in primary and secondary schools of the Lazio region. After each student in each classroom had been assigned a number, a random number generator was used to extrapolate the subjects for the control group. We obtained permission from the principals of each of these schools to ask parents for their written informed consent to administer the questionnaires to their children for research purposes. We were not refused permission by any of the principals or parents. In order to ensure that none of the children in the control group had psychiatric disorders, those with symptom scores in the clinical range in the Strengths and Difficulties Questionnaire (SDQ, see below) were excluded. All the children with ADHD were stimulant naïve since none had previously been diagnosed with this disorder. Children with mental retardation were excluded by using the Wechsler Intelligence Scale for Children (WISC-III). The mean Total IQ scores were 98.75 (S.D.=21.24) in the ADHD group and 99.16 (S.D.=19.89) in the control group. A score <70 was used as an exclusion criterion.

The diagnosis of ADHD was based on the Kiddie-Schedule for Affective Disorders and Schizophrenia (Kaufman et al., 1997), administered by the same experienced child psychiatrist (RD), and on the DSM-IV TR criteria for ADHD (American Psychiatric Association, 2000). A medical history was collected, and neurological and physical examinations, including an electroencephalogram, were performed in all the ADHD participants to exclude comorbid medical and neurological conditions.

2.2. Measures

2.2.1. Junior Temperament and Character Inventory

The JTCI assesses temperament in children between 6 and 16 years of age. It was developed in three versions by Cloninger: the JTCI-parent version, which is filled in by the parent; the JTCI-he/she version, which is filled in by the teacher or by another rater who knows the child well; and the JTCI-self-report version for subjects who are at least 10 years old, but may need to be older if their level of understanding and literacy is low (Luby et al., 1999). All the versions contain 108 statements to which the respondent has to answer "true" or "false". The 108 items measure the seven dimensions of the Cloninger psychobiological model of personality. The JTCI has been translated and validated into numerous other languages in addition to the language in which it was originally written, including American English (Copeland et al., 2004; Rettew et al., 2004), Spanish (Sancho et al., 2008), French (Asch et al., 2009), German (Schmeck and Poustka, 2001), Swedish (Kerekes et al., 2011), Hungarian (Csorba et al., 2010), Korean (Lyoo et al., 2004) and Japanese (Hiramura et al., 2011). In the present study, we used the Italian version of the JTCI parent version (Andriola et al., 2012), validated on 459 children from 6 to 16 years of age. The factor structure confirmed that the same personality dimensions as in the original version of the questionnaire emerged: four temperament traits, i.e. Harm Avoidance, Novelty Seeking, Reward Dependence, Persistence; three character traits, i.e. Self-directedness, Cooperativeness and Self-Transcendence. The correlational architecture of the JTCI closely corresponds to the findings yielded by other measures of the psychobiological model of personality in adults and children (for the JTCI, two confirmatory factor analyses for the temperament and character scales were performed separately: temperament scales GFI of 0.73 and RMSEA of 0.07; character scales GFI of 0.76 and RMSEA of 0.07), with an acceptable level of internal consistency (Cronbach's Alpha: Harm Avoidance=0.80; Novelty Seeking=0.66; Reward Dependence=0.43; Persistence=0.58; Self-directedness=0.78; Cooperativeness=0.68; Self-Transcendence=0.59). Although a multi-informant assessment of personality would have been more suited to this study, we used the parent-version of the JTCI (Luby

et al., 1999). In order to assess various aspects of NS in ADHD children, we divided the NS trait into two subscales referred to as NS1-Impulsivity and NS2-Other items. The NS1-Impulsivity included items in the Total NS that are comparable to the TCI-R/Impulsivity subscale.

2.2.2. Strengths and Difficulties Questionnaire

To exclude the presence of psychopathological symptoms in the control group, we used another instrument, which had previously been validated in English and Italian, to screen childhood behaviours, i.e. the Strengths and Difficulties Questionnaire (SDQ; Goodman, 2001; Italian version Marzocchi, 2002). The SDQ, which is based on 25 questions that are answered by parents, is designed to assess five variables: emotional problems, conduct problems, hyperactivity/inattention, peer relationship problems, and prosocial behaviour.

2.3. Statistical analysis

Differences in socio-demographic characteristics (age, gender, socio-economic level) were evaluated in the two groups (ADHD group, non-ADHD group) by means of Chi-square analysis on categorical variables and One-way ANOVAs on continuous variables. An exploratory non-parametric factor analysis, with Oblimin rotation, was performed on the polychoric correlations between the items of the Inventory, using the Mplus V5 statistical package (Muthén and Muthén, 2007) on 223 non-ADHD children.

In order to assess inter-group differences in the dimensions of temperament and character, Multivariate Analysis of Variance MANOVAs were also performed on the JTCI scores (dependent variables), including groups and gender (in order to control the effect of gender) as independent variables in all the analyses. Significance levels were corrected according to Bonferroni's procedure.

Pearson's *r* correlations between different temperament and character dimensions were performed separately for the ADHD and non-ADHD groups. Lastly, Logistic Regressions were used to verify the predictive role of the demographic variables and temperamental and character traits on the presence/absence of a diagnosis of ADHD, and were codified as *dummy* variables. In particular, the presence/absence of ADHD was included as dependent variables in different sets of analyses and three models were run: the first model included age, gender, socio-economic level and temperament dimensions as independent variables; the second included age, gender, socio-economic level and NS subscales (NS1-Impulsivity, NS2) as independent variables; the third included age, gender, socio-economic level and character dimensions as independent variables. Wald statistics were used to rely *B* significance.

Table 1
Demographic data.

	ADHD group $N=146$	Non-ADHD group $N=223$	χ^2/F	p
Boys	125	178	2.02	n.s.
Age; mean, S.D.	9.61, 2.50	9.41, 2.30	0.59	n.s.
SES: mean; S.D.	74.96; 17.00	74.82; 13.17	0.00	n.s.

3. Results

No differences in gender distribution, age or socio-economic level were observed between the ADHD group and the non-ADHD group (see Table 1).

We performed an exploratory non-parametric factor analysis, with Oblimin rotation. Visual inspection of the screen graph revealed the extraction of two factors, explaining 28.80% of the variance. The pattern matrix of the factor loadings is presented in Table 2.

Oblique rotation was chosen with the intent of allowing factors to correlate freely. In the interpretation and labelling of the factors, we decided to consider as "salient" item loadings >0.30 on the factor, accompanied by secondary loadings differing by at least 0.10. An exception was made for item 47, which yielded a loading of 0.23 on Factor 1. The item was retained in Factor 1 because it appeared to be highly congruent with the content of the factor.

With regard to the factor structure of the NS factors, items 26, 11, 20, 58 and 47 fall within the first factor called "NS1-Impulsivity" (the items are all negative loadings). In addition, items 53 and 8, which refer to the tendency to save money, fall within the impulsivity factor. The other items in the NS dimensions were considered as one aspect, called NS2, even if they did not fall within a single alternative factor (owing to mixed or low saturations). This decision was taken because the objective of the analysis was not to identify the subdimensions of the NS but simply to test the hypothesis of the existence of an aspect of impulsivity among the items that make up the NS. The factorial structure we identified was in keeping with our initial hypothesis derived from the adult version of the TCI, which includes four subscales: Impulsivity, Exploratory/excitability, Extravagance and Disorderliness.

With regard to the JTCI scores, MANOVAs yielded significant differences between the two groups in several temperamental and character dimensions (principal effects, see Table 3).

With regard to the temperamental dimensions, ADHD children displayed higher scores than the non-ADHD children in Total NS ($p=0.00$; $\eta=0.18$), NS1-Impulsivity ($p=0.00$; $\eta=0.12$) and NS2 ($p=0.00$; $\eta=0.06$), and a lower score in P ($p=0.00$; $\eta=0.56$); with regard to the character dimensions, ADHD children displayed lower scores than non-ADHD children in SD ($p=0.00$; $\eta=0.17$) and C ($p=0.00$; $\eta=0.06$). With regard to gender-by-group interaction effects, the results yielded significant effects only on NS1-Impulsivity ($p=0.01$; $\eta=0.02$): in particular, ADHD males (NS1-Impulsivity mean=5.30, S.D.=1.43) and females (NS1-Impulsivity mean=5.52, S.D.=2.04) scored

Table 2
Exploratory non-parametric factor analysis, Oblimin rotation, on JTCI Novelty Seeking items.

	NS1-Impulsivity	NS2
Item_26 My child prefers to make choices only after reviewing the options.	−0.63	−0.15
Item_11 My child likes to plan a lot even for ordinary things.	−0.59	−0.11
Item_20 My child thinks about things a lot before making a decision.	−0.58	0.08
Item_53 My child likes to save money rather than to spend it.	−0.53	0.17
Item_8 Even when my child has plenty of money, he/she would rather save it than spend it on him/herself.	−0.50	0.12
Item_58 My child wants things to be done in a strict and orderly way.	−0.42	0.06
Item_47 My child usually checks with someone else before starting an activity.	−0.23	−0.15
Item_86 My child usually waits for other kids to take the lead when something has to be done.	0.18	0.11
Item_98 My child is good at exaggerating or stretching the truth.	0.10	0.62
Item_3 My child loses his/her temper more easily than other children.	0.03	0.58
Item_33 My child usually follows the rules.	0.10	0.42
Item_75 My child will break rules if he/she can get away with it.	0.25	0.41
Item_42 My child is very bossy.	−0.12	0.41
Item_103 Even when my child is aware of potential danger, he/she will still take risks.	−0.04	0.36
Item_71 My child makes decisions quickly because he/she doesn't like to wait.	0.29	0.32
Item_92 If a quick decision is needed, my child has more trouble than most children.	−0.01	−0.27
Item_7 My child often needs naps or extra rest periods because he/she gets tired easily.	0.02	0.11
Item_65 It is easier for my child to do new and fun things when close people are with him/her.	0.01	−0.09

Table 3
Multivariate Analysis of Variance-principal effects: comparison of ADHD group and non-ADHD group on JTCI temperamental and character dimensions.

	ADHD group Mean, S.D.	Non-ADHD group Mean, S.D.	*F*	*p*
Harm Avoidance	8.42, 4.29	8.93, 4.44	1.21	n.s.
Total Novelty Seeking	11.54, 3.48	7.22, 3.18	150.34	0.00
Novelty Seeking 2	6.18, 2.63	3.29, 2.12	51.32	0.00
Novelty Seeking 1-Impulsivity	5.34, 1.52	4.13, 2.93	23.91	0.00
Reward Dependence	5.66, 2.10	5.93, 1.76	1.84	n.s.
Persistence	1.47, 1.37	3.04, 1.57	97.39	0.00
Self-directedness	9.11, 4.21	14.15, 3.87	139.64	0.00
Cooperativeness	13.40, 4.32	16.42, 2.47	72.27	0.00
Self-Transcendence	5.14, 2.06	5.64, 1.90	5.80	n.s.

higher than non-ADHD males (NS1-Impulsivity mean=4.43, S.D.=2.98) and females (NS1-Impulsivity mean=2.96, S.D.=2.41).

With regard to the relationship between temperament and character dimensions in the two groups, results yielded several significant correlations (see Table 4). In particular, Total NS in the ADHD group was correlated with SD and C, NS1-Impulsivity was correlated with C, and NS2 was correlated with SD and C. Moreover, significant correlations emerged in the non-ADHD group among Total NS and SD and C, among NS1-Impulsivity and SD and C, as well as between NS2 and C.

Logistic Regression Analysis on the JTCI temperament dimensions ($\chi^2=30.69$, $p=0.00$) revealed that Total NS ($B=0.33$, Exp-B=1.38, $p<0.01$) and P ($B=-0.48$, Exp-B=0.61, $p<0.01$) were significant predictors of the presence of ADHD in children (Cox and Snell $R^2=0.34$). Indeed, both the NS subscales emerged as significant predictors of ADHD ($\chi^2=114.74$, $p=0.00$; Cox and Snell $R^2=0.31$, NS1-Impulsivity: $B=0.32$, Exp-B=1.30, $p<0.01$; NS2: $B=0.40$, Exp-B=1.69, $p<0.01$). With regard to the character dimensions ($\chi^2=14.77$, $p=0.00$), low SD ($B=-0.28$, Exp-B=0.75, $p<0.01$) and low ST ($B=-0.27$, Exp-B=0.76, $p<0.01$) were found to be significant predictors of ADHD (Cox and Snell $R^2=0.31$).

Table 4
Pearson's correlations between temperament and character dimensions in the two groups (ADHD and non-ADHD).

	Self-directedness	Cooperativeness	Self-Transcendence
ADHD group			
Harm Avoidance	−0.13	−0.19*	−0.21*
Total Novelty Seeking	−0.34**	−0.40**	−0.11
Novelty Seeking 1-Impulsivity	−0.11	−0.16*	−0.09
Novelty Seeking 2	−0.37**	−0.41**	0.02
Reward Dependence	0.22*	0.42**	0.04
Persistence	0.38**	0.16	0.01
Non-ADHD group			
Harm Avoidance	−0.24**	−0.03	0.19*
Total Novelty Seeking	−0.44**	−0.36**	−0.09
Novelty Seeking 1-Impulsivity	−0.29**	−0.23**	−0.00
Novelty Seeking 2	−0.12	−0.13*	0.01
Reward Dependence	0.13	0.23**	0.09
Persistence	0.48**	0.21**	−0.11

* $p<0.05$.
** $p<0.01$.

4. Discussion

The statistical analysis shows that the scores of ADHD children were higher than those of non-ADHD children in Total NS, NS1-Impulsivity and NS2.

Our results thus confirm that by separating the Impulsivity Symptoms from the NS scale, the differences between the ADHD group and control group in the Total NS score remain significant, as reported in previous studies. NS is more marked in the ADHD group even when we correct for impulsivity items by separating the latter from the other items of the scale. This finding adds an important element to previous studies on the association between personality (according to Cloninger's model) and ADHD by highlighting the important role played by the NS dimension in this clinical category.

In our clinical sample, other personality traits that differ from the control group are low persistence, low self-directedness and low cooperativeness. This finding is in agreement with the results of previous studies (Tillmann et al., 2003; Jang et al., 2006). Regarding the relationship between NS items and other personality factors, our data show, as expected, an inverse correlation between HA and NS, NS and P, and C and NS. This correlation persists even if we separate the items in NS1-Impulsivity and NS2.

SD instead negatively correlated only with Total NS and NS2. This may be explained by considering that the NS2 factor contains items that relate to the inability of self-regulation and imprudence. These aspects are clearly implicated in the structuring of the character trait of Self-directedness, which identifies persons who are mature, strong, self-sufficient, responsible, reliable, goal-oriented and constructive (Cloninger et al., 1993). If we consider this aspect of character, the data reveal a significant difference between the ADHD group and the control group. This result is to be expected because emotional self-regulation is an important component of SD. Self-directedness is reduced in a large percentage of children with ADHD, who have been reported to Manifest a "Deficit of Emotional Self-Regulation" (DESR), as reported by several authors (Barkley, 2010; Anastopoulos et al., 2011; Spencer et al., 2011).

The correlation between temperament and character dimensions, which yielded comparable data in both groups, is in agreement with studies in the literature (Andriola et al., 2012; Copeland et al., 2004; Cloninger et al., 1993). In particular, a significant negative correlation emerged between NS and C, which can be explained by the exploratory and sensation seeking that prevent a person from adhering to the rules of a group. HA was negatively related to SD and C, as if the inhibition and caution typical of an introverted personality do not allow the subject to develop adequate coping abilities and social skills. RD, SD and C were positively correlated. Lastly, P and SD, two traits that share aspects such as responsibility, organization and commitment, were also positively correlated.

The statistical analyses on the gender variable did not reveal any significant differences between males and females: both male and female ADHD subjects display higher scores in the Total NS scores, as well as in NS1-Impulsivity and NS2, than males and females in the control group.

The data that emerge from the present study confirm the need to introduce a corrective element in clinical studies, i.e. that control groups should also be matched for temperament dimensions, particularly for NS. What results would consequently emerge from a study on obesity if we were to compare a group of ADHD children with a group of non-ADHD children who have the same mean score in NS? Or in a study on gambling, nicotine use or addiction? The results of such a study would be in contrast to previous studies. Indeed, the statistical differences found in previous studies between an ADHD group and a control group with different NS scores would very likely be attributed not to the ADHD syndrome but to the higher NS level. If we were instead to use a control group whose NS levels were similar to those of the ADHD group, any differences between the groups in the variable studied would either not be statistically significant or, if statistically significant, would be attributed to other factors. We realize that it would be difficult to find a clinical group

with values in the NS dimension comparable to those of an ADHD cohort. In addition, the difficulty would further increase if we needed to compare the groups for the NS dimension even after excluding impulsiveness, according to the procedures used in this paper. However, the results that we obtained here suggest that the method we propose would provide data that might prove useful in a clinical context. For clinical assessment and rehabilitation purposes, it would be useful to know whether addictive behaviour or hyperalimentation/obesity is due to a clinical disorder or to a temperament trait.

Lastly, with regard to the character dimensions, SD appears to be more closely linked to ADHD in children: impulsiveness, inattention and lack of acceptance of rules may induce poor self-acceptance, an inability to choose, selective attention to negative aspects of the self and lack of resources. Our ADHD sample also displayed lower cooperativeness levels, a finding that may be ascribed to poor social ability: impulsivity, an inability to await one's turn in communication and interaction and the tendency to be excluded by one's peers all cause the hyperactive child not to feel at ease within the group and not to expect to be treated well by others. All these variables either reduce the social interactions that are required to become skilled or make them intermittent and superficial. High NS, low SD and low C therefore appear to identify the personality architecture of ADHD subjects. This may translate into important clinical implications in the treatment of this disorder. It may be possible to alter the behaviour and improve the quality of life of ADHD subjects by increasing their degree of cooperativeness and by attempting to enhance their self-control and self-regulation, according to Cloninger's model of well-being based on the development of the character (Cloninger, 2006).

The strong correlation between NS and ADHD highlights another important psychopathological aspect: the continuity/discontinuity of ADHD through developmental stages. Recent empirical data (Carlotta et al., 2013) point to the role of temperament (NS) in mediating the relationship between ADHD and personality disorders, such as Borderline Personality Disorders (BPD). ADHD could thus be a point on a continuous line that ranges from normative personality traits, such as NS, to severe impairment of functioning, such as personality disorders. Presuming that there is a continuum, ADHD might be a risk factor in the development of a personality disorder such as BPD, just as a high NS score is a risk factor in the development of ADHD. However, future studies are needed to confirm these hypotheses.

This study has several limitations. First, the presence of ADHD in the control group was ruled out by means of the SDQ, though a semi-structured interview such as the K-SADS might have been more suitable and should be recommended in future studies. Second, the sample was collected in a single city in central Italy; a wider catchment area that includes rural areas and is not limited to one city would lend more weight to our findings and would provide a broader sample. Third, the personality assessment could be improved by using subscales of seven factors, which are adopted in the more elaborate adult version of the Cloninger model though not for the JTCI, which contains a smaller number of items. In addition, the use of a multi-informant assessment of personality, using a self-report form in the personality assessment, would provide more reliable data in future studies. Another limitation, which lies in our statistical analysis, is the use of a combination of all non-impulsive items as a single factor (NS2). Although this decision is not supported by factor analysis, it was required to isolate and study the impulsivity items.

Lastly, an interesting extension of our study might be an analysis, based for example on the ADHD Rating Scale, of how the Total NS and NS-Impulsivity scores vary according to the intensity of ADHD symptoms.

In conclusion, the evaluation of personality dimensions in ADHD children using a control group that is matched for sex, age and personality profile may shed light on the overlap between psychopathology and temperament and reveal any reciprocal influences. Moreover, our findings suggest that temperamental profiles should be included in studies on the developmental trajectories of psychopathology.

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