NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

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BIBLIOGRAFIA ADHD LUGLIO 2014

Acta Chir Orthop Traumatol Cech. 2014;81:221-26.

IS ATTENTION DEFICIT AND HYPERACTIVITY DISORDER A RISK FACTOR FOR SUSTAINING FRACTURES OF PROXIMAL HUMERUS?

Erdogan M, Desteli EE, Imren Y, et al.

PURPOSE OF THE STUDY To evaluate whether or not children with displaced proximal humerus fractures are more likely to have attention deficit and hyperactivity disorder (ADHD).

PATIENTS AND METHOD Between January 2010 and February 2013, we retrospectively evaluated 42 children with proximal humerus fractures. Requirements for inclusion were an open epiphyseal plate and a non-pathological fracture of the proximal humerus. Fractures were classified according to Saiter-Harris, Neer and Horwitz. Following orthopaedic examination, all of the children were consulted to child psychiatry department of our hospital. Orthopaedic examination included a detailed physical examination; the assessment of the overall shoulder functions using the Constant score. Diagnostic and Statistical Manual of Mental Disorders, Text Revisions (DSM-IV-TR) were used for psychiatric examination.

RESULTS 9 of the 42 children with proximal humerus fractures consulted to child psychiatry were put ADHD diagnoses (21 %). Of the remaining 33 children without ADHD diagnosis, 5 children were operated; percentage of surgery was 15%. We found statistically significant difference between the rates of ADHD diagnosed children with proximal humerus fractures and ADHD diagnoses in normal population ($p<0.01$). There was also statistically significant difference between operation rates of children with or without ADHD diagnosis (55 % vs. 15 %) ($p<0,01$).

CONCLUSIONS ADHD can be accepted as a risk factor for sustaining high energy trauma and rate of ADHD children who were operated was significantly more than normal children. This might be due to more displaced, open fractures or polytrauma - higher energy trauma- they sustained. Deciding on the treatment method, surgery may be treatment of choice in certain children with severely displaced, irreducable, fractures or polytrauma with accompanying ADHD due to the potential difficulties during follow up period.

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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 Neuropsychiatr. 2014;26:202-08.

IMPROVEMENT OF FACIAL AFFECT RECOGNITION IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER UNDER METHYLPHENIDATE.

Beyer Von MS, Becker I, Sinzig J.

Introduction and Hypothesis Some authors draw a connection between the dopaminergic pathways and emotional perception. The present study is based on that association and addresses the question whether methylphenidate and the resulting amelioration of the disturbed dopamine metabolism lead to an improvement of the facial affect recognition abilities in children with attention-deficit/hyperactivity disorder (ADHD).

Methods A computer test was conducted on 21 participants, aged 7-14 years and with a diagnosis of ADHD - some with comorbid oppositional defiant disorder - conducted the FEFA (Frankfurt Test and Training of Facial Affect), a computer test to examine their facial affect recognition abilities. It consists of two subtests, one with faces and one with eye pairs. All participants were tested in a double-blind cross-over study, once under placebo and once under methylphenidate.

Results and Discussion The collected data showed that methylphenidate leads to amelioration of facial affect recognition abilities, but not on a significant level. Reasons for missing significance may be the small sample size or the fact that there exists some overlapping in cerebral connections and metabolic pathways of the site of action of methylphenidate and the affected dopaminergic areas in ADHD. However, consistent with the endophenotype concept, certain gene locations of the dopaminergic metabolism as both an aetiological factor for ADHD and the deficient facial affect recognition abilities with these individuals were considered. Consulting current literature they were found to be not concordant. Therefore, we conclude that the lacking significance of the methylphenidate affect on facial affect recognition is based on this fact.

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Acta Neuropsychol. 2014;12:27-52.

NEUROPSYCHOLOGICAL TESTING OF AD/HD SUBTYPES AS AN INDICATOR FOR NEUROMETRICS AND THERAPY: CURRENT STATE AND FURTHER CONSIDERATIONS.

Pachalska M, Borkowska AR, Kropotov JD.

Background: The research presented in this chapter reflects some current trends in neuropsychological research on AD/HD children, with the goal of exploring the structure of the mental deficits that shape the clinical picture. The purpose of this research was to ascertain the specific nature of the disturbances of mental function in various sub types of AD/HD, and on that basis to reach some conclusions regarding the differentiation of the neuronal basis.

Material/ Methods: We examined 132 children, 9 to 12 years of age, divided into two groups. The first group, which included children with the combined subtype of AD/HD, consisted of 64 children, 59 boys and 5 girls; the second group, with the inattentive sub-type, consisted of 21 children, 17 boys and 4 girls. There was also a control group, made up of 47 children (40 boys and 7 girls) without AD/HD symptoms. For our research we used the neuropsychological instruments most often applied in AD/HD, so that the results could be compared and discussed.

Results: We found different dimensions of functioning which can be used to characterize children with combined-type AD/HD, i.e. with manifest symptoms of inattentive, impulsive, and hyperactive behavior. De -ficits in the inhibition of a motor response after a stop signal, when the response has already been evoked by a stimulus; deficits in the inhibition of a response to a stimulus that should not evoke any reaction (over-reactions); reduced readiness (preparation) for motor response; deficits in maintaining attention; in inhibiting a cognitive response; reduced concentration, deficits in divided attention and working memory; deficits in planning and monitoring motor performance. This list of characteristics suggests that children with combined-type AD/HD show differentiated deficits in behavior control.

Conclusions: Fuller cooperation is necessary between neuropsychologists and psychophysiologists, which will help the latter in understanding the problems of a person with AD/HD, and help the former evaluate the results of new programs of neurotherapy.

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ADHD Atten Deficit Hyperact Disord. 2014.

HYPERACTIVITY AND SENSATION SEEKING AS AUTOREGULATORY ATTEMPTS TO STABILIZE BRAIN AROUSAL IN ADHD AND MANIA?

Geissler J, Romanos M, Hegerl U, et al.

Hypoarousal as indicated by skin conductance and electroencephalography (EEG) has been discussed as a pathogenetic factor in attention-deficit/hyperactivity disorder (ADHD). The aim of this paper was to review these arousal-related pathogenetic concepts and to present the more recently proposed vigilance regulation model of affective disorders and ADHD. The latter builds on methodological advances in classifying short EEG segments into vigilance stages (Vigilance Algorithm Leipzig, VIGALL), indicating different states of global brain function ("brain arousal"). VIGALL allows the objective assessment of vigilance regulation under defined conditions, e.g. how fast vigilance declines to lower vigilance stages associated with drowsiness during 15-20-min EEG recordings under resting conditions with eyes closed. According to the vigilance regulation model, the hyperactivity and sensation seeking observed in overtired children, ADHD and mania may be interpreted as an autoregulatory attempt to create a stimulating environment in order to stabilize vigilance. The unstable regulation of vigilance observed in both mania and ADHD may thus explain the attention deficits, which become especially prominent in monotonous sustained attention tasks. Among the arguments supporting the vigilance regulation model are the facts that destabilizing vigilance (e.g. via sleep deprivation) can trigger or exacerbate symptoms of ADHD or mania, whereas stabilizing vigilance (e.g. via psychostimulants, reducing sleep deficits) alleviates these symptoms. The potential antimanic effects of methylphenidate are presently being studied in an international randomized controlled trial. We propose vigilance regulation as a converging biomarker, which could be useful for identifying treatment responders to psychostimulants and forming pathophysiologically more homogeneous ADHD subgroups for research purposes.

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Adm Policy Ment Health. 2014 Jul;41:503-13.

LATINO PARENTAL HELP SEEKING FOR CHILDHOOD ADHD.

Gerdes AC, Lawton KE, Haack LM, et al.

To better understand the help seeking process that occurs within Latino families when a child is exhibiting behaviors consistent with attention-deficit/hyperactivity disorder (ADHD), qualitative and quantitative data from 73 Latino parents were examined. Findings suggest that most Latino parents in the current sample recognized ADHD symptoms as concerning and in need of professional help and reported being motivated to seek help. Unfortunately, they also appeared to lack knowledge about the etiology of and effective treatment for ADHD, and many identified barriers to seeking help. Future research must involve community collaborations aimed at increasing awareness and knowledge of ADHD and decreasing barriers to seeking help in targeted Latino communities.

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Am J Health Syst Pharm. 2014 Jul;71:1163-70.

METHYLPHENIDATE AND DEXMETHYLPHENIDATE FORMULATIONS FOR CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Sugrue D, Bogner R, Ehret MJ.

PURPOSE: Current literature on the safety and efficacy of various intermediate- and long-acting preparations of methylphenidate and dexmethylphenidate for pediatric attention-deficit/hyperactivity disorder (ADHD) is reviewed.

SUMMARY: The efficacy of methylphenidate in controlling ADHD symptoms is firmly established. Given the drug's relatively short half-life in pediatric patients (about 2.5 hours), a number of intermediate- and long-acting products have been developed; these extended-release methylphenidate products provide the same efficacy as immediate-release (IR) formulations, with the convenience of less frequent dosing. Intermediate-acting methylphenidate preparations have effects lasting as long as 8 hours, but peak concentrations are not attained for up to 5 hours, and many patients may require twice-daily dosing. Long-

acting methylphenidate products developed to address these challenges include a controlled-release tablet and bimodal-delivery capsules containing mixtures of IR and extended-release beads (durations of effect, 8-12 hours). Options for patients with difficulty swallowing tablets or capsules include a once-daily transdermal delivery system and a once-daily liquid formulation. Dexmethylphenidate (the more pharmacologically active d-isomer of racemic methylphenidate) can provide efficacy comparable to that of IR methylphenidate at half the dose; an extended-release form of dexmethylphenidate can provide less fluctuation in peak and trough concentrations than the IR form. Methylphenidate and dexmethylphenidate products in capsule form can be opened and sprinkled on applesauce.
CONCLUSION: The various formulations of IR and intermediate- and extended-release methylphenidate and dexmethylphenidate can be useful options in satisfying patients' individual needs in the management of ADHD. All are equally efficacious in controlling ADHD symptoms.

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Am J Med Genet Part B Neuropsychiatr Genet. 2014.
POLYGENIC SCORES ASSOCIATED WITH EDUCATIONAL ATTAINMENT IN ADULTS PREDICT EDUCATIONAL ACHIEVEMENT AND ADHD SYMPTOMS IN CHILDREN.
De Zeeuw EL, van Beijsterveldt CE, Glasner TJ, et al.
The American Psychiatric Association estimates that 3 to 7 per cent of all school aged children are diagnosed with attention deficit hyperactivity disorder (ADHD). Even after correcting for general cognitive ability, numerous studies report a negative association between ADHD and educational achievement. With polygenic scores we examined whether genetic variants that have a positive influence on educational attainment have a protective effect against ADHD. The effect sizes from a large GWA meta-analysis of educational attainment in adults were used to calculate polygenic scores in an independent sample of 12-year-old children from the Netherlands Twin Register. Linear mixed models showed that the polygenic scores significantly predicted educational achievement, school performance, ADHD symptoms and attention problems in children. These results confirm the genetic overlap between ADHD and educational achievement, indicating that one way to gain insight into genetic variants responsible for variation in ADHD is to include data on educational achievement, which are available at a larger scale.

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Am J Orthopsychiatry. 2014;84:209-17.
ADOLESCENTS' ADHD SYMPTOMS AND ADJUSTMENT: THE ROLE OF ATTACHMENT AND REJECTION SENSITIVITY.
Scharf M, Oshri A, Eshkol V, et al.
The associations between attachment style, ADHD symptoms, and social adjustments were examined in a community sample of adolescents. Five hundred and eight junior high school students completed questionnaires pertaining to attachment style, ADHD symptoms (inattention and hyperactivity), and rejection sensitivity, and were rated by homeroom teachers on social adjustment. Analyses supported a 3-profile pattern of attachment styles: secure, dismissing, and preoccupied. The 3 attachment profiles showed differential risk on adolescents' social adjustment, as well as on ADHD symptoms. The secure profile showed the most adaptive outcomes on all of the examined adjustment outcomes, compared with the other 2 profiles. In contrast, the preoccupied attachment profile showed the highest levels of ADHD problems, angry and anxious expectations, while displaying a similar level of maladjustment to the dismissing profile. In addition, structural equation modeling was used and supported a model that tested an indirect link between attachment security and adolescent adjustment via an ADHD latent factor. Findings suggest that clinicians and educators should pay attention to relational patterns (attachment styles) in adolescence, as these may serve as a developmental precursor for ADHD and a range of adjustment problems in school.

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Anadolu Psikiyatr Derg. 2014;15:265-71.

AN EVALUATION OF THE QUALITY OF LIFE OF CHILDREN WITH ADHD AND THEIR FAMILIES.

Kandemir H, Kilic BG, Ekinci S, et al.

Objective: This study evaluated the quality of life of children with attention-deficit/hyperactivity disorder (ADHD) and their families to identify the effects of the psychosocial distress associated with the disorder.

Methods: Seventy-six children and adolescents aged 7 to 16 with ADHD who had been referred to the Ankara University School of Medicine Department of Child and Adolescent Psychiatry and 59 age and gender matched control children who had never been referred to a child psychiatric clinic were included in the study. The Pediatric Quality of Life Inventory (PedsQL), Short Form-36, Strengths and Difficulties Questionnaire, Turgay's Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV)-Based Child and Adolescent Behavior Disorders Screening and Rating Scale, and the McMaster Family Assessment Device (FAD) were administered.

Results: The children with ADHD showed lower school achievements and had more school absences than the control group. In SF-36, parents of the children with ADHD showed statistically significant differences in their pain, gener-al health, vital energy, and mental health subscale scores compared to the control group. The PedsQL-child scale psychosocial health subscale and total scale scores of the ADHD patients were significantly lower than the control group. The PedsQL-parent psychosocial health and total scale scores of the ADHD group were significantly lower than the control group. In the McMaster (FAD) results, there were significant differences in the problem-solving, communication, roles, affective responsiveness, and affective involvement subscale scores.

Conclusion: The re-sults of this study suggest that children with ADHD and their families have poorer quality of life in some domains. In child and adolescent psychiatric clinics, the psychosocial and clinical aspects of ADHD must be taken into account.

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Arch Pediatr. 2014 Aug;21:852-59.

PRESCRIPTION OF METHYLPHENIDATE FOR CHILDREN: IMPORTANCE OF RECOMMENDATIONS TO LIMIT MISUSE.

Cheron-Blumel A, Grall-Bronnec M, Victorri-Vigneau C, et al.

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder appearing during childhood. Multimodal strategies have been developed to treat this disorder, some of them including medication. To this day in France, prescriptions are mainly based on methylphenidate. Ever since this drug was marketed in France in 1995, it has been subject to enhanced monitoring, mainly because of the risk of dependence, abuse, and misuse. The present study aims at assessing (1) whether the recommendations on methylphenidate use for children are being respected, (2) the extent of problematic use of methylphenidate, and (3) the impact of said recommendations being respected on the development of problematic consumption. We studied patients who were treated with methylphenidate in an academic child psychiatry department. We specifically developed a semistructured interview grid for this study. Both parents and children were interviewed. In almost three out of four cases, at least one recommendation had not been followed (52 % of patients did not follow the recommendation of stopping use during weekends and holidays). We found an average of 1.6 (range, 0-5) recommendations that were not respected. In almost two out of three cases, the consumption of methylphenidate was problematic; for 40 % of children, this meant the search for at least one effect other than the expected therapeutic effects, such as an intellectual, creative, or athletic boosting effect. Approximately one-third of parents also sought an effect other than therapeutic for their child. Conversely, if all of the prescription recommendations were followed, less problematic consumption was observed. Methylphenidate-based treatments must therefore be implemented after a specialist has evaluated the patient and be prescribed following the recommendations. In this context, the treatment's benefits are undeniable.

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Atten Defic Hyperact Disord. 2014 Jul.

OXYTOCIN PLASMA CONCENTRATIONS IN CHILDREN AND ADOLESCENTS WITH AUTISM SPECTRUM DISORDER: CORRELATION WITH AUTISTIC SYMPTOMATOLOGY.

Taurines R, Schwenck C, Lyttwin B, et al.

Findings from research in animal models and humans have shown a clear role for the neuropeptide oxytocin (OT) on complex social behaviors. This is also true in the context of autism spectrum disorder (ASD). Previous studies on peripheral OT concentrations in children and young adults have reported conflicting results with the initial studies presenting mainly decreased OT plasma levels in ASD compared to healthy controls. Our study therefore aimed to further investigate changes in peripheral OT concentrations as a potential surrogate for the effects observed in the central nervous system (CNS) in ASD. OT plasma concentrations were assessed in 19 male children and adolescents with ASD, all with an IQ > 70 (age 10.7 +/- 3.8 years), 17 healthy male children (age 13.6 +/- 2.1 years) and 19 young male patients with attention deficit hyperactivity disorder (ADHD) as a clinical control group (age 10.4 +/- 1.9 years) using a validated radioimmunoassay. Analysis of covariance revealed significant group differences in OT plasma concentrations ($F(2, 48) = 9.574$, $p < 0.001$, eta 2 = 0.285; plasma concentrations ASD 19.61 +/- 7.12 pg/ml, ADHD 8.05 +/- 5.49 pg/ml, healthy controls 14.43 +/- 9.64 pg/ml). Post hoc analyses showed significantly higher concentrations in children with ASD compared to ADHD ($p < 0.001$). After Bonferroni correction, there was no significant difference in ASD in comparison with healthy controls ($p = 0.132$). A significant strong correlation between plasma OT and autistic symptomatology, assessed by the Autism Diagnostic Observation Schedule, was observed in the ASD group ($p = 0.013$, $r = 0.603$). Patients with ADHD differed from healthy control children by significantly decreased OT concentrations ($p = 0.014$). No significant influences of the covariates age, IQ, medication and comorbidity could be seen. Our preliminary results point to a correlation of OT plasma concentrations with autistic symptom load in children with ASD and a modulation of the OT system also in the etiologically and phenotypically overlapping disorder ADHD. Further studies in humans and animal models are warranted to clarify the complex association of the OT system with social impairments as well as stress-related and depressive behavior and whether peripheral findings reflect primary changes of OT synthesis and/or release in relevant areas of the CNS.

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Atten Defic Hyperact Disord. 2014 Jul.

BARRIERS TO EVIDENCE-BASED TREATMENT FOR CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Corkum P, Bessey M, McGonnell M, et al.

A number of evidence-based treatments are available for attention-deficit/hyperactivity disorder (ADHD), including pharmacological, psychosocial, or a combination of the two treatments. For a significant number of children diagnosed with ADHD, however, these treatments are not utilized or adhered to for the recommended time period. Given that adherence to treatment regimens is necessary for reducing the symptoms of ADHD, it is crucial to develop a comprehensive understanding of why adherence rates are so low. The current review examines the literature to date that has directly explored utilization and adherence issues related to the treatment of ADHD in order to identify the key barriers to treatment. This review focused on four main factors that could account for the poor rates of treatment utilization and adherence: personal characteristics (socio-demographic characteristics and diagnostic issues), structural barriers, barriers related to the perception of ADHD, and barriers related to perceptions of treatment for ADHD. This review included 63 papers and covered a variety of barriers to treatment that have been found in research to have an impact on treatment adherence. Based on this review, we conclude that there are complex and interactive relationships among a variety of factors that influence treatment utilization and adherence. Four main gaps in the literature were identified: (1) there is limited information about barriers to psychosocial interventions, compared to pharmacological interventions; (2) there is a limited variety of research methodology being utilized; (3) treatment barrier knowledge is mostly from parents' perspectives; and (4) treatment utilization and treatment adherence are often studied jointly. Information from this review can help practitioners to identify potential barriers to their clients being adherent to treatment recommendations.

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Aust New Zealand J Psychiatry. 2013;47:61.

DISENTANGLING DISORDER AND DISABILITY: ADHD IN INTELLECTUAL DISABILITY.

O'Brien G.

Background: ADHD is more common among people with intellectual disability but there is little familiarity among treating clinicians of the appropriate diagnostic, assessment and treatment approaches applicable to this population.

Objectives: This presentation will review the current approaches to the clinical assessment and treatment of ADHD among children with intellectual disability.

Summary: Children with intellectual disability demonstrate high levels of over-active behaviour and impaired attention. Disentangling out those children with intellectual disability who suffer from ADHD is a major challenge to the clinician. As regards establishing the diagnosis, the clinical insights from the UK DCLD (Diagnostic Criteria for Learning Disability) are useful in distinguishing those individuals whose behavioural and attentional characteristics are qualitatively different from other children with intellectual disabilities. Also, some of the standard assessment schedules have proven to be applicable to intellectually disabled children. Looking forward, the changes proposed in DSM-5 may be promising. The management plan for ADHD in children with intellectual disability needs to reflect the myriad underlying causes which can contribute to the clinical presentation. In particular, children with more severe intellectual disability often do not respond to stimulant medication. Furthermore, the established neuropsychiatric side effects of stimulant medication are more common among children with intellectual disabilities. Consequently, while stimulant medication and other standard drugs used in ADHD do have an important role to play in the treatment of ADHD among children with intellectual disabilities, other treatment approaches - both drug and non-drug - are more often applicable in this population, than among children in general.

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Aust New Zealand J Psychiatry. 2013;47:44-45.

ADULT ADHD-MY APPROACH TO ASSESSMENTS: THE EXPERIENCE OF ADULT ADHD IN NEW ZEALAND.

Edwards R.

The identification and management of adult ADHD poses several challenges for NZ health services. There is limited access to specialists for diagnostic assessment, treatment options and facilities. Attention deficit hyperactivity disorder (ADHD) is a chronic and heritable disorder characterised by inattention, hyperactivity and impulsive behaviour. While onset is in childhood, the disorder frequently persists into adulthood. ADHD has a high comorbidity rate with other psychiatric disorders. Many adults with ADHD experience significant psychosocial problems leading to high levels of personal distress and can contribute to an economic cost for society if left unidentified and untreated. Research indicates that around 30-70% of children diagnosed with ADHD will continue to experience some or all symptoms into adulthood. It is increasingly recognised that a number of adults are suffering from ADHD in whom the disorder was never diagnosed in childhood. It is not known if the prevalence of adult ADHD differs in the Maori population or across other cultural groups. In 2009, more than 1700 adult New Zealanders over 25 years of age received medication for ADHD, with almost 1300 young adults in the 18-25-year age range also on medication. In this presentation I discuss my approach to ADHD with the hope of increasing awareness of this disorder in adults, reducing stigma and to improve the care for adults with ADHD.

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Behav Sleep Med. 2014 Sep;12:373-88.

SLEEP IN CHILDREN WITH DISRUPTIVE BEHAVIORAL DISORDERS.

Aronen ET, Lampenius T, Fontell T, et al.

This study compared sleep in patients with Conduct Disorder/Oppositional Defiant Disorder (CD/ODD) and normative children and evaluated the associations between sleep and behavioral symptoms in patients. Participants were 30 patients, aged 7 to 12 years, with diagnoses of CD/ODD and their age and gender matched controls. Patients with CD/ODD and their parents reported significantly more sleep problems than did the control children and their parents (p values < 0.01). By actigraphy, CD/ODD children with comorbid

ADHD slept significantly less than did the patients with CD/ODD alone and the controls. In patients, low sleep amount and efficiency associated with increased amount of parent-reported externalizing symptoms (r = -0.72, 0.66, p values < 0.001). Results highlight the need of evaluating sleep in children with CD/ODD. Improving their sleep may ease their symptoms.

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Behav Brain Funct. 2014 May;10.

DOES IQ INFLUENCE ASSOCIATIONS BETWEEN ADHD SYMPTOMS AND OTHER COGNITIVE FUNCTIONS IN YOUNG PRESCHOOLERS?

Rohrer-Baumgartner N, Zeiner P, Egeland J, et al.

Background: Working memory, inhibition, and expressive language are often impaired in ADHD and many children with ADHD have lower IQ-scores than typically developing children. The aim of this study was to test whether IQ-score influences associations between ADHD symptoms and verbal and nonverbal working memory, inhibition, and expressive language, respectively, in a nonclinical sample of preschool children.
Methods: In all, 1181 children recruited from the Norwegian Mother and Child Cohort Study were clinically assessed at the age of 36 to 46 months. IQ-score and working memory were assessed with subtasks from the Stanford Binet test battery, expressive language was reported by preschool teachers (Child Development Inventory), response inhibition was assessed with a subtask from the NEPSY test, and ADHD symptoms were assessed by parent interview (Preschool Age Psychiatric Assessment).
Results: The results showed an interaction between ADHD symptoms and IQ-score on teacher-reported expressive language. In children with below median IQ-score, a larger number of ADHD symptoms were more likely to be accompanied by reports of lower expressive language skills, while the level of ADHD symptoms exerted a smaller effect on reported language skills in children with above median IQ-score. The associations between ADHD symptoms and working memory and response inhibition, respectively, were not influenced by IQ-score.
Conclusions: Level of IQ-score affected the relation between ADHD symptoms and teacher-reported expressive language, whereas associations between ADHD symptoms and working memory and response inhibition, respectively, were significant and of similar sizes regardless of IQ-score. Thus, in preschoolers, working memory and response inhibition should be considered during an ADHD assessment regardless of IQ-score, while language skills of young children are especially important to consider when IQ-scores are average or low.

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Behav Neurol. 2014;2014.

ATTENTION DEFICIT HYPERACTIVITY DISORDER: A NEGLECTED ISSUE IN THE DEVELOPING WORLD.

Chinawa JM, Odetunde OI, Obu HA, et al.

Background. Attention deficit hyperactivity disorder (ADHD) is a neglected illness in a developing country. Objectives. The objectives of this study are to investigate the prevalence and pattern of ADHD among children in a Nigeria.
Methods. A structured self-administered questionnaire was used to collect information from the parents of children (and older children) who attended children outpatients' clinic during the study period. The DSM-IV-TR diagnostic criteria for attention deficit hyperactivity disorder were used.
Results. Two hundred and seventy-three (273) out of 282 questionnaires were filled completely, giving a response rate of 96.8%. Nine (9) children fulfilled the stated criteria for ADHD giving a prevalence rate of 3.2%. There is no association between gender and ADHD (P=0.784).
Conclusions. The prevalence of ADHD in our setting is 3.2%, which is similar to that obtained elsewhere in the world.

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BMJ (Online). 2014;348.

DRUG TREATMENT FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND SUICIDAL BEHAVIOUR: REGISTER BASED STUDY.

Chen Q, Sjolander A, Runeson B, et al .

Objective: To investigate the association between drug treatment for attention-deficit/hyperactivity disorder (ADHD) and risk of concomitant suicidal behaviour among patients with ADHD. Design: Register based longitudinal study using within patient design. Setting: Linkage of multiple national registers in Sweden. Participants: 37 936 patients with ADHD born between 1960 and 1996 and followed from 2006 to 2009 for treatment status by ADHD drug treatment and suicide related events (suicide attempt and completed suicide). Main outcome measure: Incidence rate of suicide related events during ADHD drug treatment periods compared with that during non-treatment periods. Results: Among 37 936 patients with ADHD, 7019 suicide related events occurred during 150 721 person years of follow-up. At the population level, drug treatment of ADHD was associated with an increased rate of suicide related events (hazard ratio 1.31, 95% confidence interval 1.19 to 1.44). However, the within patient comparison showed a reverse association between ADHD drug treatment and rate of suicide related events (0.89, 0.79 to 1.00). Among stimulant users, a reduced within patient rate of suicide related events was seen during treatment periods (0.81, 0.70 to 0.94). Among non-stimulant/mixed users, no significantly increased within patient rate of suicide related events during non-stimulant treatment periods was seen (0.96, 0.72 to 1.30). Conclusions: This study found no evidence for a positive association between the use of drug treatments for ADHD and the risk of concomitant suicidal behaviour among patients with ADHD. If anything, the results pointed to a potential protective effect of drugs for ADHD on suicidal behaviour, particularly for stimulant drugs. The study highlights the importance of using within patient designs to control for confounding in future pharmacoepidemiological studies.

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Braz J Phys Ther. 2014 Jul;0:0.

SENSORY PROCESSING ABILITIES OF CHILDREN WITH ADHD.

Shimizu VT, Bueno OF, Miranda MC.

OBJECTIVE: To assess and compare the sensory processing abilities of children with Attention Deficit/Hyperactivity Disorder (ADHD) and children without disabilities, and to analyze the relationship between sensory processing difficulties and behavioural symptoms presented by children with ADHD. METHOD: Thirty-seven children with ADHD were compared with thirty-seven controls using a translated and adapted version of the "Sensory Profile" answered by the parents/caregivers. For the ADHD group, Sensory Profile scores were correlated to behavioural symptoms assessed using the Child Behaviour Check List (CBCL) and the Behavioural Teacher Rating Scale (EACI-P). The statistical analyses were conducted using the Mann Whitney test and Pearson correlation coefficients. RESULTS: Children with ADHD showed significant impairments compared to the control group in sensory processing and modulation, as well as in behavioural and emotional responses as observed in 11 out of 14 sections and 6 out of 9 factors. Differences in all Sensory Profile response patterns were also observed between the two groups of children. Sensory Profile scores showed a moderately negative correlation with CBCL and EACI-P scores in the ADHD group. CONCLUSION: These results indicate that children with ADHD may present sensory processing impairments, which may contribute to the inappropriate behavioural and learning responses displayed by children with ADHD. It also suggests the importance of understanding the sensory processing difficulties and its possible contribution to the ADHD symptomatology.

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Child Adolesc Psychiatr Clin N Am. 2014 Jul;23:427-64.

QUANTITATIVE EEG AND NEUROFEEDBACK IN CHILDREN AND ADOLESCENTS: ANXIETY DISORDERS, DEPRESSIVE DISORDERS, COMORBID ADDICTION AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, AND BRAIN INJURY.

Simkin DR, Thatcher RW, Lubar J.

This article explores the science surrounding neurofeedback. Both surface neurofeedback (using 2-4 electrodes) and newer interventions, such as real-time z-score neurofeedback (electroencephalogram [EEG] biofeedback) and low-resolution electromagnetic tomography neurofeedback, are reviewed. The limited literature on neurofeedback research in children and adolescents is discussed regarding treatment of anxiety, mood, addiction (with comorbid attention-deficit/hyperactivity disorder), and traumatic brain injury. Future potential applications, the use of quantitative EEG for determining which patients will be responsive to medications, the role of randomized controlled studies in neurofeedback research, and sensible clinical guidelines are considered.

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Child Psychiatry Hum Dev. 2014 Jun;45:318-28.

SUSTAINED IMPACT OF INATTENTION AND HYPERACTIVITY-IMPULSIVITY ON PEER PROBLEMS: MEDIATING ROLES OF PROSOCIAL SKILLS AND CONDUCT PROBLEMS IN A COMMUNITY SAMPLE OF CHILDREN.

Andrade BF, Tannock R.

This prospective 2-year longitudinal study tested whether inattentive and hyperactive/impulsive symptom dimensions predicted future peer problems, when accounting for concurrent conduct problems and prosocial skills. A community sample of 492 children (49 % female) who ranged in age from 6 to 10 years (M = 8.6, SD = .93) was recruited. Teacher reports of children's inattention, and hyperactivity/impulsivity symptoms, conduct problems, prosocial skills and peer problems were collected in two consecutive school years. Elevated inattention and hyperactivity/impulsivity in Year-1 predicted greater peer problems in Year-2. Conduct problems in the first and second years of the study were associated with more peer problems, and explained a portion of the relationship between inattention and hyperactivity/impulsivity with peer problems. However, prosocial skills were associated with fewer peer problems in children with elevated inattention and hyperactivity/impulsivity. Inattention and hyperactivity/impulsivity have negative effects on children's peer functioning after 1-year, but concurrent conduct problems and prosocial skills have important and opposing impacts on these associations.

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Child Neuropsychol. 2013 Sep;19(5):495-515. doi: 10.1080/09297049.2012.696603. Epub 2012 Jun 27.

BEYOND INTERFERENCE CONTROL IMPAIRMENT IN ADHD: EVIDENCE FROM INCREASED INTRAINDIVIDUAL VARIABILITY IN THE COLOR-STROOP TEST.

Borella E, de Ribaupierre A, Cornoldi C, Chicherio C.

The present study investigates intraindividual variability (IIV) in the Color-Stroop test and in a simple reaction time (SRT) task. Performance level and variability in reaction times (RTs)-quantified with different measures such as individual standard deviation (ISD) and coefficient of variation (ICV), as well as ex-Gaussian parameters (mu, sigma, tau)-were analyzed in 24 children with attention deficit/hyperactivity disorder (ADHD) and 24 typically developing children (TDC). Children with ADHD and TDC presented equivalent Color-Stroop interference effects when mean RTs were considered, and the two groups did not differ in the SRT task. Interestingly, compared to TDC, children with ADHD were more variable in their responses, showing increased ISD and ICV in the Color-Stroop interference condition and in the SRT task. Moreover, children with ADHD exhibited higher tau values-that is, more frequent abnormally long RTs-in the Color-Stroop interference condition than did the TDC, but comparable tau values in the SRT, suggesting more variable responses. These results speak in favor of a general deficit in more basic and central processes that only secondarily may affect the efficiency of inhibitory processes in children with

ADHD. Overall the present findings confirm the role of IIV as a cornerstone in the ADHD cognitive profile and support the search for fine-grained analysis of performance fluctuations.

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Clinical Child and Family Psychology Review. 2014 Jun;17:157-72.

CO-OCCURRING AGGRESSIVE AND DEPRESSIVE SYMPTOMS AS RELATED TO OVERESTIMATIONS OF COMPETENCE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Jiang Y, Johnston C.

Research indicates that on average, children with attention-deficit/hyperactivity disorder (ADHD) overestimate their competence in various domains. ADHD also frequently co-occurs with disorders involving aggressive and depressive symptoms, which themselves seem to influence estimations of self-competence in social, academic, and behavioral domains. In particular, high levels of aggressive behavior are generally associated with overestimations of competence, and high levels of depressive symptoms are related to underestimations of competence. This paper reviews studies of overestimations of competence among children with ADHD and examines the extent to which comorbid aggressive or depressive symptoms may be influencing these estimates. Although significant challenges arise due to limited information regarding comorbidities and problematic methods used to assess overestimations of competence, existing evidence suggests that ADHD may be associated with overestimations of competence over and above co-occurring aggression. As well, studies suggest that comorbid depression may reduce the appearance of overestimations of competence in children with ADHD. Underlying mechanisms (e.g., neuropsychological deficits or self-protection) of overestimations in children with ADHD are discussed, each with particular clinical implications for the assessment and treatment of ADHD. Future research would do well to carefully consider and explicitly describe the comorbid aggressive and depressive characteristics among individuals with ADHD when overestimations of competence are examined.

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Clin Neurophysiol. 2014;125:1626-38.

AGE DEPENDENT ELECTROENCEPHALOGRAPHIC CHANGES IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Poil S-S, Bollmann S, Ghisleni C, et al.

Objective: Objective biomarkers for attention-deficit/hyperactivity disorder (ADHD) could improve diagnostics or treatment monitoring of this psychiatric disorder. The resting electroencephalogram (EEG) provides non-invasive spectral markers of brain function and development. Their accuracy as ADHD markers is increasingly questioned but may improve with pattern classification. Methods: This study provides an integrated analysis of ADHD and developmental effects in children and adults using regression analysis and support vector machine classification of spectral resting (eyes-closed) EEG biomarkers in order to clarify their diagnostic value. Results: ADHD effects on EEG strongly depend on age and frequency. We observed typical non-linear developmental decreases in delta and theta power for both ADHD and control groups. However, for ADHD adults we found a slowing in alpha frequency combined with a higher power in alpha-1 (8-10. Hz) and beta (13-30. Hz). Support vector machine classification of ADHD adults versus controls yielded a notable cross validated sensitivity of 67% and specificity of 83% using power and central frequency from all frequency bands. ADHD children were not classified convincingly with these markers. Conclusions: Resting state electrophysiology is altered in ADHD, and these electrophysiological impairments persist into adulthood. Significance: Spectral biomarkers may have both diagnostic and prognostic value.

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Clin Pharmacol Drug Dev. 2014;3:252-61.

PHARMACOKINETICS AND PHARMACODYNAMICS OF GUANFACINE EXTENDED RELEASE IN ADOLESCENTS AGED 13-17 YEARS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Martin P, Satin L, Vince BD, et al.

The safety and efficacy of guanfacine extended release (up to 4mg/day) for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents aged 6-17 years is well documented. Data suggest that weight-adjusted doses of guanfacine extended release >0.08mg/kg but (less-than or equal to)0.12mg/kg, if tolerated, may provide additional clinical benefits. For many adolescents, such dosing would exceed 4mg/day, the highest approved dose. This open-label multicenter study evaluated the safety, tolerability, and steady-state pharmacokinetics of guanfacine extended release at escalated forced doses (less-than or equal to)9mg/day in adolescents (N=31) aged 13-17 years with ADHD. Following doses of approximately 0.12mg/kg, the highest weight group (>70-90kg) exhibited lower mean clearance at steady-state than the lowest weight group ((greater-than or equal to)30-50kg). Consistent with its known antihypertensive effects, guanfacine extended release was associated with dose-dependent decreases in blood pressure (BP) and heart rate (HR). The physiologic response of increased BP upon standing was blunted in a dose-related manner while the physiologic response of increased HR upon standing was not substantively affected. The most common treatment-emergent adverse events were somnolence, dizziness, and sinus bradycardia. These results, and those from prior studies, support further examination of the efficacy and safety of higher weight-adjusted doses of guanfacine extended release for ADHD.

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Clin Pract. 2014;11:289-94.

REINTRODUCTION OF STIMULANT TREATMENT FOR PATIENTS WITH ADHD, AFTER STIMULANT-RELATED PSYCHOSIS.

Chammas M, Ahronheim GA, Hechtman L.

ADHD is a common condition that affects a large proportion of the child, adolescent and adult population. One of the most widely used medications for treating this illness are psychostimulants, which are generally well tolerated. Nevertheless, one of the rare side effects includes the development of psychotic symptoms. Generally, these symptoms are cleared when the medication is discontinued. There have been several case reports in the literature pertaining to these side effects. Most of them solely involve discontinuation of the medication, but there are four case reports where rechallenging with stimulant medication occurred, with only two of these resulting in recurrence of psychotic symptoms. We report three additional cases where rechallenging with stimulant medication did not result in reappearance of psychotic symptoms. Possible risk factors for developing such side effects and hypothesized mechanisms are discussed.

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CNS Drugs. 2014.

DOES PHARMACOLOGICAL TREATMENT OF ADHD IN ADULTS ENHANCE PARENTING PERFORMANCE? RESULTS OF A DOUBLE-BLIND RANDOMIZED TRIAL.

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

Objective This study examines the effects of parental lisdexamfetamine (LDX) treatment on parent-child interactions. Methods Participants were 30 parents (27 % were male) and their children aged 5-12 years, both diagnosed with DSM-IV attention-deficit/hyperactivity disorder (ADHD). Optimal LDX dose (30, 50, or 70 mg/day) was determined for parents during a 3-week open-label titration, followed by a within-subjects trial of the acute impact of LDX and placebo on observable parent-child interactions. Two laboratory-based, parent-child interactions simulating typical family tasks (e.g., homework, joint play) were conducted within 2 weeks, once with the adult on a blinded optimal dose of LDX and once on placebo (phase I). Parents were then randomly assigned to continue blinded treatment with LDX or placebo for another month followed by a third interaction task (phase II) to assess the ongoing effects of LDX on parent-child interactions. The primary outcome was the change in rate of parenting behaviors coded during the parent-child interaction tasks. Secondary outcomes included observed rates of children's inappropriate behaviors during the

laboratory tasks and changes in parental ADHD symptom severity (ADHD-Rating Scale). Results Twenty parents (67 %) completed the trial. In phase I, medication was associated with a significant reduction in negative talk by parents (p = 0.0066, d = -0.47). There was a Medication null Task interaction (p = 0.0235) with a reduction in children's negative behaviors in the homework phase only (p = 0.0154, d = -0.58). In phase II, LDX was associated with significant increases in praise by parents (d = 0.81) and reductions in parental commands (d = -0.88) and children's inappropriate behaviors (d = -0.84) (all p-values < 0.05). While not reaching statistical significance, LDX was also associated with large reductions in parental verbalizations (d = -0.82), moderate increases in parental responsiveness (d = 0.55), and large reductions in the ratio of commands to verbalizations during the non-homework task (d = -1.05) (all p-values < 0.10). Significant reductions in parental ADHD symptoms vs. placebo were observed (p < 0.005). Loss of appetite, dry mouth, headaches, and delayed sleep onset were the most common adverse events. Conclusions Improvements in parent-child interactions emerged over time with LDX treatment of parental ADHD. Results suggest that pharmacological treatment of parental ADHD may improve outcomes in parents and their children.

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CNS Drugs. 2014.

TREATMENT RESPONSE AND REMISSION IN A DOUBLE-BLIND, RANDOMIZED, HEAD-TO-HEAD STUDY OF LISDEXAMFETAMINE DIMESYLATE AND ATOMOXETINE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Dittmann RW, Cardo E, Nagy P, et al.

Objectives A secondary objective of this head-to-head study of lisdexamfetamine dimesylate (LDX) and atomoxetine (ATX) was to assess treatment response rates in children and adolescents with attention-deficit hyperactivity disorder (ADHD) and an inadequate response to methylphenidate (MPH). The primary efficacy and safety outcomes of the study, SPD489-317 (ClinicalTrials.gov NCT01106430), have been published previously. Methods In this 9-week, double-blind, active-controlled study, patients aged 6-17 years with a previous inadequate response to MPH were randomized (1:1) to dose-optimized LDX (30, 50 or 70 mg/day) or ATX (patients <70 kg: 0.5-1.2 mg/kg/day, not to exceed 1.4 mg/kg/day; patients (greater-than or equal to)70 kg: 40, 80 or 100 mg/day). Treatment response was a secondary efficacy outcome and was predefined as a reduction from baseline in ADHD Rating Scale IV (ADHD-RS-IV) total score of at least 25, 30 or 50 %. Sustained response was predefined as a reduction from baseline in ADHD-RS-IV total score ((greater-than or equal to)25, (greater-than or equal to)30 or (greater-than or equal to)50 %) or a Clinical Global Impressions (CGI)-Improvement (CGI-I) score of 1 or 2 throughout weeks 4-9. CGI-Severity (CGI-S) scores were also assessed, as an indicator of remission. Results A total of 267 patients were enrolled (LDX, n = 133; ATX, n = 134) and 200 completed the study (LDX, n = 99; ATX, n = 101). By week 9, significantly (p < 0.01) greater proportions of patients receiving LDX than ATX met the response criteria of a reduction from baseline in ADHD-RS-IV total score of at least 25 % (90.5 vs. 76.7 %), 30 % (88.1 vs. 73.7 %) or 50 % (73.0 vs. 50.4 %). Sustained response rates were also significantly (p < 0.05) higher among LDX-treated patients (ADHD-RS-IV (greater-than or equal to)25, 66.1 %; ADHD-RS-IV (greater-than or equal to)30, 61.4 %; ADHD-RS-IV (greater-than or equal to)50, 41.7 %; CGI-I, 52.0 %) than among ATX-treated individuals (ADHD-RS-IV (greater-than or equal to)25, 51.1 %; ADHD-RS-IV (greater-than or equal to)30, 47.4 %; ADHD-RS-IV (greater-than or equal to)50, 23.7 %; CGI-I, 39.3 %). Finally, by week 9, 60.7 % of patients receiving LDX and 46.3 % of those receiving ATX had a CGI-S score of 1 (normal, not at all ill) or 2 (borderline mentally ill), and greater proportions of patients in the LDX group than the ATX group experienced a reduction from baseline of at least one CGI-S category. Conclusions Both LDX and ATX treatment were associated with high levels of treatment response in children and adolescents with ADHD and a previous inadequate response to MPH. However, within the parameters of the study, LDX was associated with significantly higher treatment response rates than ATX across all response criteria examined. In addition, higher proportions of patients in the LDX group than the ATX group had a CGI-S score of 1 or 2 by week 9, indicating remission of symptoms. Both treatments were generally well tolerated, with safety profiles consistent with those observed in previous studies.

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Compr Psychiatry. 2014.

THE SEVERITY OF ATTENTION DEFICIT HYPERACTIVITY SYMPTOMS AND ITS RELATIONSHIP WITH LIFETIME SUBSTANCE USE AND PSYCHOLOGICAL VARIABLES AMONG 10TH GRADE STUDENTS IN ISTANBUL.

Evren C, Dalbudak E, Evren B, et al.

Aim: The aim of this study was to determine the severity of attention deficit hyperactivity symptoms (ADHS) and related psychological and behavioral variables among 10th grade students in Istanbul/Turkey. Methods: Cross-sectional online self-report survey conducted in 45 schools in 15 districts Istanbul. The questionnaire included sections about demographic data and use of substances including tobacco, alcohol and drugs. Also ADHS, depression, anxiety, anger and sensation seeking subscales of Psychological Screening Test for Adolescents (PSTA) were used. The analyses were conducted based on the 4938 subjects. Results: Mean ADHS score was higher in females and among those with a lifetime use of tobacco, alcohol and drug, and having self-harming behavior and suicidal thoughts. ADHS score was correlated with depression, anxiety, anger and sensation seeking scores. In univariate covariance analysis (ANCOVA); depression, anxiety, anger, sensation seeking, lifetime alcohol use and suicidal thoughts predicted the severity of ADHS. Conclusions: The findings suggest that, since ADHS is associated with depression, anxiety, anger, sensation seeking, lifetime alcohol use and suicidal thoughts among 10th grade students, clinicians should screen suicidality and comorbid psychiatric symptoms routinely in adolescents with ADHS.

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Contemporary Family Therapy: An International Journal. 2014 Jun;36:260-80.

"THERE IS SOMETHING NOT QUITE RIGHT WITH BRAD…": THE WAYS IN WHICH FAMILIES CONSTRUCT ADHD BEFORE RECEIVING A DIAGNOSIS.

Lewis-Morton R, Dallos R, McClelland L, et al.

This study explored how four families who were in the midst of the process of a potential diagnosis of 'Attention Deficit Hyperactivity Disorder' (ADHD) for their child negotiated competing explanations of the problems. The research drew on a social constructionist, systemic and attachment lens to understand; (a) the constellations of meanings that are constructed by the families to explain the difficulties and (b) how families use strategies in their talk to account for or contest these constellations of meaning. A discursive analysis revealed that the families in this study, following initial explorations, adopted a sequential and cumulative dismissal of psychosocial explanations. Hence, the thrust of the conversation implicitly added up to the only possibility, the inevitable conclusion that it was ADHD. The malleability and flexibility in which the families explored these explanations varied and for some families the process of closure towards 'illness' as a dominant explanation sealed alternative conversations more than in others. The findings also revealed a complexity for the parents in balancing the need to offer discipline versus another response and this has clinical implications and highlights the need for further research in this area.

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Curr Opin Pediatr. 2014 Aug;26:466-71.

2014 UPDATE ON ATOPIC DERMATITIS IN CHILDREN.

Totri CR, Diaz L, Eichenfield LF.

PURPOSE OF REVIEW: The prevalence of pediatric atopic dermatitis (AD) has increased throughout the world, now ranging from 10 to 20% in developed countries. Pediatric patients with AD make up a substantial proportion of patients seen by general pediatricians, allergists, dermatologists, and other specialists. As such, there is a need to optimize understanding and management of AD. RECENT FINDINGS: The traditional atopic comorbidities of AD have now expanded to include associations with nonatopic conditions such as attention deficit hyperactivity disorder. Furthermore, with insights from basic, translational, and clinical research, experts have a more comprehensive knowledge of the genetic, immunological, and environmental factors influencing the development of AD. With this new perception, innovative approaches to the management of AD have developed with an emphasis on preventive rather than reactive care. The role of biological agents in the treatment of this common, yet chronic, disease of the

skin has not been clearly elucidated. SUMMARY: There have been several recent breakthroughs in the diagnosis, pathophysiology, and management of AD. Despite these advances, much work is still needed in order to ensure optimal care for AD sufferers.

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Dev Psychol. 2014 Jul.

MEDIA USE AND ADHD-RELATED BEHAVIORS IN CHILDREN AND ADOLESCENTS: A META-ANALYSIS.

Nikkelen SW, Valkenburg PM, Huizinga M, et al.

There are several theoretical reasons to believe that media use might be related to attention-deficit/hyperactivity disorder (ADHD) or ADHD-related behaviors (i.e., attention problems, hyperactivity, and impulsivity). Although studies into the media-ADHD relationship have accumulated, they have yielded inconsistent results. Therefore, we still do not know whether children's media use and ADHD-related behaviors are related and, if so, under which conditions. To fill this gap in the literature, we first identified 6 different hypotheses that may explain why media use in general and viewing fast-paced or violent media content might be related to 1 or more ADHD-related behaviors. Subsequently, we conducted a meta-analysis of 45 empirical studies investigating the relationship between media use and ADHD-related behaviors in children and adolescents. Our results indicated a small significant relationship between media use and ADHD-related behaviors (r+=.12). Finally, we identified several specific gaps in the existing literature and presented 5 crucial directions for future research.

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Dev Psychopathol. 2014 Aug;26:817-30.

PREDICTING BORDERLINE PERSONALITY DISORDER SYMPTOMS IN ADOLESCENTS FROM CHILDHOOD PHYSICAL AND RELATIONAL AGGRESSION, DEPRESSION, AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Vaillancourt T, Brittain HL, McDougall P, et al.

Developmental cascade models linking childhood physical and relational aggression with symptoms of depression and attention-deficit/hyperactivity disorder (ADHD; assessed at ages 10, 11, 12, 13, and 14) to borderline personality disorder (BPD) features (assessed at age 14) were examined in a community sample of 484 youth. Results indicated that, when controlling for within-time covariance and across-time stability in the examination of cross-lagged relations among study variables, BPD features at age 14 were predicted by childhood relational aggression and symptoms of depression for boys, and physical and relational aggression, symptoms of depression, and symptoms of ADHD for girls. Moreover, for boys BPD features were predicted from age 10 ADHD through age 12 depression, whereas for girls the pathway to elevated BPD features at age 14 was from depression at age 10 through physical aggression symptoms at age 12. Controlling for earlier associations among variables, we found that for girls the strongest predictor of BPD features at age 14 was physical aggression, whereas for boys all the risk indicators shared a similar predictive impact. This study adds to the growing literature showing that physical and relational aggression ought to be considered when examining early precursors of BPD features.

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Early Hum Dev. 2014;90:399-405.

PRESCHOOL REGULATORY PROBLEMS AND ATTENTION-DEFICIT/HYPERACTIVITY AND COGNITIVE DEFICITS AT SCHOOL AGE IN CHILDREN BORN AT RISK: DIFFERENT PHENOTYPES OF DYSREGULATION?

Schmid G, Wolke D.

Background: Early regulatory problems (RP), i.e., excessive crying, feeding, and sleeping difficulties, have been reported to be predictors of cognitive and attention-deficit/hyperactivity problems. However, previous studies had limitations such as small sample size or retrospective design.

Aim: To investigate whether persistent RP from infancy until preschool age are precursors of ADHD problems and cognitive deficits at school age. Study design: A prospective study from birth to 8.5. years of age.

Subjects: 1120 infants born at risk.
Measures: RP were assessed at 5. months (i.e., excessive crying, feeding, and sleeping problems), 20, and 56. months (i.e., eating and sleeping problems) via parent interviews and neurological examination. At 8.5. years of age, IQ was assessed by a standard test (K-ABC), and ADHD problems by direct observations in the test situation and by the Mannheimer Parent Interview (MPI, DSM-IV diagnosis of ADHD).
Results: 23.8% of the sample born at risk had RP at least at two measurement points until preschool age. Persistent RP predicted lower IQ ((beta)= - .17; 95% CI (- .21; - .10)), behaviour problems ((beta)= - .10; 95% CI (- .15; - .03)), attention (OR 2.43; 95% CI (1.16; 5.09)) and hyperactivity problems (OR 3.10; 95% CI (1.29; 7.48)), and an ADHD diagnosis (OR 3.32; 95% CI (1.23; 8.98)) at school age, even when controlled for psychosocial and neurological confounders.
Conclusions: Early persistent RP increased the odds of ADHD and associated problems at school age, indicating a cascade model of development, i.e., infant behaviour problems provide the starting point of a trajectory of dysregulation through time.

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Eas As A Psyc. 2010;20:53.

SOCIO-DEMOGRAPHIC AND CLINICAL PROFILES OF CHILDREN WITH ADHD IN INDIA.

Gopalan RT, Oommen A, Srinath S.

Introduction: Attention-deficit hyperactivity disorder (ADHD) is the most commonly diagnosed behavioural disorder of childhood. Various factors like pre-, peri- and post-natal developments, temperamental factors, genetics and parental and sibling psychopathologies are associated with ADHD.
Objective: To assess the socio-demographic, clinical, and parental and siblings profiles of children with ADHD in Indian setup.
Methods: The data were collected randomly as part of multimodal intervention study. Forty children with ADHD with or without co-morbidities were selected. They were assessed by Binet-Kamat Test of Intelligence (BKT), and their parents were interviewed by using Missouri Assessment of Genetics Interview for Children-Parent version (MAGIC-P) and Detailed Evaluation Schedule for Children and Adolescents (DESCA-1).
Results: The results showed predominance of male children, presence of dijficult temperament, developmental delays, educational dijficulties, and parental psychopathologies.
Conclusion: The clinical and socio-demographic features of children with ADHD in India are in line with the fiindings of existing literature.

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Eas As A Psyc. 2010;20:52-53.

PREFRONTAL CORTEX NEUROPLASTICITY IN CHILDREN WITH ADHD; A 1H MAGNETIC RESONANCE SPECTROSCOPY (MRS) STUDY.

Wiguna T, Wibisono S, Susworo, et al.

Background: Approximately 4 to 15% of primary school-aged children are diagnosed with attention-deficit hyperactivity disorder (ADHD) worldwide. Nowadays, ADHD is serious public mental health issue that results in diverse negative outcomes. A prominent theory of ADHD is that, there is a dysfunction of dopamine (DA) neurotransmission with a consequent dysregulation of DA-modulated in prefrontal area. Treatment of methylphenidate amplifies DA signals by blocking DA transporters, and strengthens the dopamine firing rate on prefrontal neuron.
Objectives: To identify the effect of 20-mg long-acting methylphenidate in enhancing the DA signal in prefrontal cortex, which indicated by changing of neuro-metabolite detected by 1H magnetic resonance spectroscopy (MRS).
Methods: This was a 1-group pre-test and post-test study. We examined 21 ADHD children without any co-morbidity aged 7 to 10 years who were drug-naive. Low echo time (TE) MRS scans were acquired from the right and left prefrontal cortex in all subjects. Compounds which can be visualised with MRS included

N-acetylaspartate (NAA), glutamate / glutamine (Glu), creatine / phosphocreatine (Cr), cholin (Cho), and myo-Inositol (mI). Paired t test was used to analyse the mean difference of the ratios of NAA / Cr, Glu / Cr, Cho / Cr and mI / Cr, before and after the subjects took the medication for 12 weeks. Parents were also asked to fill out the Indonesian Hyperactive Behaviour Assessment Scale for kids every 2 weeks, and repeated measures test was used to analyse the data.
Results: There was significantly decrease of Glu / Cr and Cho / Cr ratios, both in the right and left prefrontal cortex ($p < 0.05$) after the subjects took 20-mg long-acting methylphenidate for 12 weeks. In this finding, NAA / Cr ratio increased significantly ($p < 0.05$) as well. Parents reported a significant reduction of the ADHD symptoms of their child ($p < 0.001$).
Conclusions: These findings suggest that prefrontal neuron showed a functional plasticity after administering 12-week 20-mg long-acting methylphenidate, which is also indicated by a decrease in total score of the Indonesian Hyperactive Behaviour Assessment Scale.

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Eas As A Psyc. 2010;20:42.

A THREE-YEAR REVIEW OF PARENT MANAGEMENT TRAINING PROGRAMME FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER CHILDREN.

Chan P, Chow V, Fung C, et al.

Introduction: The aim of this paper is to evaluate the effectiveness of parent management training carried out from 2007 to 2009 at Child and Adolescent Psychiatric Day Centre, Queen Mary Hospital. The parent management training aims at educating parents of effective parenting. The training involves issues in fostering child compliance, handling defiant behaviours, and investing in positive parent child interactions. The parenting characteristics in children with attention-deficit hyperactivity disorder (ADHD) and disruptive behaviours are commonly described as reinforcement of mutually coercive behaviours, inconsistent parenting practices across time and between parents, poor problem-solving skills, and ineffective parental controls. Poor attention of these problems will cause families to suffer, leading to later problems such as child abuse, juvenile delinquency, family breakdown, and adult mental illness. Therefore, early intervention such as training of parenting skills is essential to prevent continual suffering and growing problems. Moreover, parent management training is one of the most extensively studied therapies for children, and it has been shown to be effective in decreasing oppositional, aggressive, and antisocial behaviour (Kazdin, 1985; Forehand and Long, 1988; Webster-Stratton, 1989).
Methods: The content of treatment was designed to target coercive parenting commonly found in children with ADHD. The parent training programme consisted of 92-hour weekly sessions with 10 families. Each session consisted of video demonstration of parenting techniques, modelling, therapist-lead group discussion, and homework assignment. Effectiveness of the training was evaluated by laboratory observation of parent-child interaction and a set of questionnaires assessing patients' behaviours.
Results and Conclusion: From 2007 to 2009, there were 89 families participated in the training and 73% of participants had completed the pre-treatment, post-treatment and follow-up assessments. Preliminary analysis of the data revealed that the parent management training was effective. Moreover, there was good response from the satisfaction survey from the participants. The findings support that the parent management training is a promising and cost-effective treatment for children with disruptive behaviour disorder in the local setting. In this presentation, the findings will be discussed with implications for future practice and research.

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Eas As A Psyc. 2010;20:53-54.

THE ROLE OF COUNTERFACTUAL THINKING IN LEARNING DEFICIENCY OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER-DIAGNOSED CHILDREN.

Hur T, Kim HY.

Objective: The present study aimed to examine the relationship between attention-deficit hyperactivity disorder (ADHD) and counterfactual thinking, specifically the roles of counterfactual thinking in learning deficiency of ADHD children.

Methods: Twenty ADHD-diagnosed (based on K-ARS and K-PRC) and 20 normal children (grades 1-6; mean age = 10.7 years) participated in this study. They were presented with 3 scenarios describing the troubles that any children could face in everyday life and need to learn behavioural corrections through. They were then given 2 minutes to talk freely about the scenarios. Finally they were asked to answer the causes of the troubles, generate counterfactuals specifically, and rate future-behavioural intention in trouble situations (K-CBCL).

Results: As hypothesised, ADHD children reported less counterfactuals than normal children did in the free-talk task (mean = 1.20 and 2.50 respectively; $t = -2.13$, $p < 0.05$). Also, the number of children who reported at least a counterfactual was relatively smaller in ADHD children (40%) than in normal children (85%; $X2 = 8.64$, $p < 0.05$). Furthermore, a significant negative correlation was found between the number of counterfactuals and the severity of ADHD (the score of K-ARS) [$r = -0.34$, $p < 0.05$]. More importantly, when the contents in the induced counterfactual list focused more on the causes of the troubles, the behavioural intentions for future positive behaviours were higher ($r = 0.38$, $p < 0.05$).

Conclusions: The results found that ADHD children would engage in counterfactual thinking less than normal children would do, and the tendency was stronger as the severity of ADHD was higher. In addition, when ADHD children generated counterfactual thoughts that focused on the causes of troubles, their intentions for positive behaviours in future were improved. The present findings supported our proposition that counterfactual thinking could play a major role in the learning deficiency of ADHD children.

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Environ Int. 2014 Sep;70:125-31.

PRENATAL EXPOSURE TO ORGANOPHOSPHATE PESTICIDES AND RECIPROCAL SOCIAL BEHAVIOR IN CHILDHOOD.

Furlong MA, Engel SM, Barr DB, et al.

Prenatal exposure to organophosphate pesticides (OPs) has been associated with adverse neurodevelopmental outcomes in childhood, including low IQ, pervasive developmental disorder (PDD), attention problems and ADHD. Many of these disorders involve impairments in social functioning. Thus, we investigated the relationship between biomarkers of prenatal OP exposure and impaired reciprocal social behavior in childhood, as measured by the Social Responsiveness Scale (SRS). Using a multi-ethnic urban prospective cohort of mother-infant pairs in New York City recruited between 1998 and 2002 (n=404) we examined the relation between third trimester maternal urinary levels of dialkylphosphate (SigmaDAP) OP metabolites and SRS scores among 136 children who returned for the 7-9year visit. Overall, there was no association between OPs and SRS scores, although in multivariate adjusted models, associations were heterogeneous by race and by sex. Among blacks, each 10-fold increase in total diethylphosphates (SigmaDEP) was associated with poorer social responsiveness (beta=5.1 points, 95% confidence interval (CI) 0.8, 9.4). There was no association among whites or Hispanics, or for total SigmaDAP or total dimethylphosphate (SigmaDMP) biomarker levels. Additionally, stratum-specific models supported a stronger negative association among boys for SigmaDEPs (beta=3.5 points, 95% CI 0.2, 6.8), with no notable association among girls. Our results support an association of prenatal OP exposure with deficits in social functioning among blacks and among boys, although this may be in part reflective of differences in exposure patterns.

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Epilepsia. 2014;55:71.

CHARACTERISTICS OF EPILEPSY CHILDRENWHO OVERLAP WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD).

Lee IG, Choi HY, Hahn JY, et al.

Purpose: To investigate the prevalence of ADHD in children with epilepsy and to determine the difference of characteristics in patients with epilepsy and concomitant ADHD as opposed to the patients without ADHD for better management.

Method: 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. Their ages ranged from 6 to 18 years. The subject were included in the study those who made a regular visit for more than a year.

Results: 1 Out of 184 patients, 69 patients (37.5%) had both ADHD and epilepsy (male 46: female 23). 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, epileptiform discharges on EEG was focused in central regions in 39% of them (p=0.014). 4 In 56% of patients without ADHD, their seizures remained under the control with single anticonvulsant, as opposed to 36% of patients with both ADHD and epilepsy (p=0.001).

Conclusion: The incidence of ADHD in epilepsy children was 37.5%, and patients with epilepsy and concomitant ADHD showed a significant difference and poor response to epilepsy treatment, as opposed to patients without ADHD. Therefore, early detection and establishment of countermeasures for ADHD is necessary.

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Epilepsia. 2014;55:66.

FRONTAL RHYTHMIC BETA ACTIVITY IN CHILDREN WITH ASD OR ADHD.

Nakagawa E, Koichihara R, Sugai K, et al.

Purpose: Frontal spindle of the sleep period is seen at 11-12 Hz from an infant. We frequently experience the frontal rhythmic beta activity (FRBA) like frontal spindle, but which has high amplitude and high frequency in frontal predominance including frontal pole areas. The major aim of this work was to clarify the FRBA in children with Autism spectrum disorders (ASD), attention-deficit hyperactivity disorder (ADHD) or intellectual disability (ID) and assessment of neurophysiology of ASD and ADHD.

Method: 126 children (92 boys, 34 girls, mean age 13.1 years) with ASD (77), ADHD (19) and/or ID (45) were studied. Conventional electroencephalogram (EEG) recording and assessment of FRBA more than 13 Hz frequency during the sleep stage 2 were performed.

Results: In 36 children (29 boys, 7 girls, mean age 8.6 years) presenting FRBA (28.5%), the EEG was found characteristic FRBA. 25 of them (69.5%) presented ASD, 11 of them (30.5%) ADHD, 21 of them ID. The characteristic of the FRBA was high frequency with a mean average 15 Hz (13-18) and high amplitude with a mean amplitude 63.8 (mu)V (62.5-185). In 30 children presenting FRBA (83.3%), the EEG was found abnormal (paroxysmal of spikes and sharp waves) in the frontal dominant areas.

Conclusion: 28.5% of children with ASD or ADHD exhibited EEG patterns with the FRBA. These children also showed high percentage of abnormal epileptic-like activity in the frontal dominant areas. The assessment of FRBA indicated that the excitability of frontal lobe and lead to shed light on the neurophysiology of ASD and ADHD.

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Epilepsy Behav. 2014.

FOCUSING ON ADHD AND ATTENTION IN CHILDREN WITH EPILEPSY.

Dunn DW .

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Epilepsy Behav. 2014;37:54-58.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ATTENTION IMPAIRMENT IN CHILDREN WITH BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES.

Kim E-H, Yum M-S, Kim H-W, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common comorbidity in children with epilepsy and has a negative impact on behavior and learning. The purposes of this study were to quantify the prevalence of ADHD in benign childhood epilepsy with centrotemporal spikes (BCECTS) and to identify clinical factors that affect ADHD or attention impairment in patients with BCECTS.The medical records of 74 children (44 males) with neuropsychological examination from a total of 198 children diagnosed with BCECTS at Asan Medical Center were retrospectively reviewed. Electroclinical factors were compared across patients with ADHD and those without ADHD. Mean T-scores of the continuous performance test were compared across patients grouped according to various epilepsy characteristics.Forty-eight (64.9%) patients had ADHD. A history of febrile convulsion was more common in patients with ADHD than in patients without ADHD (p=0.049). Bilateral centrotemporal spikes on electroencephalogram were more common in patients receiving ADHD medication than in patients with untreated ADHD (p=0.004). Male patients, patients with frequent seizures prior to diagnosis, and patients with a high spike index ((greater-than or equal to). 40/min) on sleep EEG at diagnosis had significantly lower visual selective attention (p<. 0.05).Children with BCECTS had a high prevalence of ADHD, and frequent seizures or interictal epileptiform abnormalities were closely related to impairment of visual selective attention in children with BCECTS, indicating the need for ADHD or attention impairment screening in children with BCECTS.

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Epilepsy Behav. 2014 Jul.

TREATING ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS WITH EPILEPSY: WHAT DO WE KNOW?

Jones JE.

Children with epilepsy are at significant risk of psychiatric disorders, which can in turn negatively impact social skills development, academic achievement, and quality of life. The most commonly reported psychiatric comorbidities in pediatric epilepsy are ADHD, depression, and anxiety. The prevalence rates of anxiety disorders in pediatric epilepsy range from 5 to 49%, and in the general population, anxiety disorders are the most common psychiatric disorder in childhood. For the purposes of this review, anxiety disorders will be examined in order to 1) examine rates of anxiety disorders in children and adolescents with epilepsy, 2) review treatment options for anxiety disorders in children with epilepsy, and 3) identify future avenues for the development of evidence-based practices for the treatment of anxiety disorders in youth with epilepsy.

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Eur Child Adolesc Psychiatry. 2014 Jul.

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

von RD, Mennes M, van EH, 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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European Child & Adolescent Psychiatry. 2014.

COMORBIDITY OF ADHD AND INCONTINENCE IN CHILDREN.

von GA, Equit M.

ADHD and incontinence are common childhood disorders which co-occur at much higher rates than expected by chance. The aim of this review was to provide an overview both of the comorbidity of nocturnal enuresis (NE), daytime urinary incontinence (DUI) and faecal incontinence (FI) in children with ADHD; and, vice versa, of the co-occurrence of ADHD in children with NE, DUI and FI. Most clinical studies have focussed on the association of ADHD and NE. Population-based studies have shown that children with DUI have an even greater risk for ADHD than those with NE. While children with FI have the highest overall comorbidity rates of psychological disorders, these are heterogeneous with a wide range of internalising and externalising disorders-not necessarily of ADHD. Genetic studies indicate that ADHD and NE, DUI and FI do not share the same genetic basis. The comorbidity is conferred by non-genetic factors. Possible aetiological and pathogenetic links between ADHD and incontinence are provided by neurophysiological, imaging and pharmacological studies. The co-occurrence has clinical implications: children with ADHD and NE, DUI and FI are more difficult to treat, show lower compliance and have less favourable treatment outcomes for incontinence. Therefore, both groups of disorders have to be assessed and treated specifically.

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Eur Child Adolesc Psychiatry. 2014;23:437-50.

A PARENT-BASED INTERVENTION PROGRAMME INVOLVING PRESCHOOLERS WITH AD/HD BEHAVIOURS: ARE CHILDREN'S AND MOTHERS' EFFECTS SUSTAINED OVER TIME?

Azevedo AF, Seabra-Santos MJ, Gaspar MF, et al.

To evaluate the 12-month efficacy of a parent-based intervention programme on children's and mothers' outcomes in a sample of Portuguese preschoolers displaying early hyperactive and inattentive behaviours (AD/HD behaviours), 52 preschool children whose mothers had received the Incredible Years basic parent training (IY) were followed from baseline to 12 months of follow-up. Reported and observational measures were used. Effects were found in the children's reported AD/HD behaviours at home and at school after 12 months. Large effect sizes were also found in mothers' variables: a decrease in self-reported dysfunctional parenting practices and an improved sense of competence and observed positive parenting. However, the improvements in coaching skills that have been observed after 6 months of follow-up decreased over time. No other significant differences were found between 6 and 12 months follow-up, with small effect sizes indicating that the significant post-intervention changes in child and parenting measures were maintained. After 12 months of follow-up, there was a clinically important reduction of over 30 % in reported AD/HD behaviours in 59 % of children. The sustained effects observed both for children and their mothers suggest long-term benefits of IY. Therefore, efforts should be made by Portuguese policy makers and professionals to deliver IY as an early preventive intervention for children displaying early AD/HD behaviours.

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Eur J Neurol. 2014;21:561.

EEG MARKERS IN A SAMPLE OF CHILDREN WITH ATTENTION DEFICIT HYPER ACTIVITY DISORDER.

Awad EA, Shorb EM, Hendawy HMF.

Introduction: Recent studies demonstrated that children with Attention Deficit Hyper Activity Disorder (ADHD) have different Electroencephalographic activity compared to non ADHD children. In this study we aimed to find possible EEG markers for ADHD patients.

Methods: Sleeping Electroencephalography (EEG) was recorded for 39 children with ADHD and 17 children without ADHD of 5-8-years-old. They were recruited from the outpatient child clinic in Ain Shams university institute of psychiatry, Cairo, Egypt. Subjects had no history of medical, neurological or IQ abnormalities that might cause EEG changes. Analysis of the quantitative EEG data was done by 2 different methods. The first method aimed at finding and comparing the different rhythm in both ADHD and non ADHD groups using True Scan Deymed version 6.42 software. The negative wave amplitude analysis was done using BESA EEG software version 11. Data was analyzed statistically with two-sided student t-test for nonequal variance. Differences expressing $p<0.05$ were considered significant.

Results: Results showed increase in the EEG theta activity in ADHD group compared to the control group. Moreover, we found statistically significant difference in the negative wave amplitudes at several frontal electrodes especially F10 ($p=0.01$), F3, F8 and F9 ($p=0.03$). However, negative wave amplitudes at other frontal electrodes showed no statistically significant difference.

Conclusions: Children with ADHD have prominently increased theta activity, more in the frontal areas and high negative wave amplitudes in many frontal EEG electrodes which may be used as markers for ADHD patients.

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Eur J Neurol. 2014;21:558.

TRANSCRANIAL DIRECT CURRENT STIMULATION IN THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN CHILDREN AGED 7-12-YEARS.

Shugar O, Bronnikov V.

Introduction: ADHD is a prevalent neurodevelopmental disorder. Pharmacological treatment of ADHD may be associated with a range of serious adverse effects (seizures, psychotic symptoms, cardioiovascular events), so nonpharmacological treatment without adverse effects is needed to develop. Transcranial direct current stimulation (tDCS) is a non-invasive technique for brain stimulation and it increasingly being used in the treatments of some neurological disorders.

Methods: With tDCS, cortical neurons excitability increases in the vicinity of the anodal electrode and suppressed near the cathodal electrode. There is EEG and neuropsychological evidence that ADHD is associated with hyperactivity in right and left dorsolateral prefrontal cortex (DLPFC) , in right and left frontal cortex (FC) , in left anterior temporal region (ATR). tDCS has a potential in facilitating inter- and intra-hemispheric balance.

Results: We investigated the efficacy of the method tDCS by proof assay and by EEG processed by method of transitional probabilities one EEG wave by another on the symptoms of ADHD comparing the data before and after the treatment. 70 children with ADHD were included in this study . All subjects completed the tDCS for 25-30 min/day 2-3 times a week for 2.5 weeks. A tDCS protocol is proposed applying anode electrodes over the most problem zones of the brain (right FC,right DLPFC, left ATR).

Conclusions: By treated of such tDCS protocol alleviated the symptoms of ADHD and improved executive functions and general condition in children with ADHD for a long period of time (6-18 month) without any adverse effects (in catamnesis data).

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Eur J Pediatr. 2014.

AARSKOG-SCOTT SYNDROME: A NOVEL MUTATION IN THE FGD1 GENE ASSOCIATED WITH SEVERE CRANIOFACIAL DYSPLASIA.

Volter C, Martinez R, Hagen R, et al.

Aarskog syndrome (AAS) is an X-linked human disease that affects the skeletal formation and embryonic morphogenesis and is caused by mutations in the FGD1 gene. Patients typically show distinctive skeletal and genital developmental abnormalities, but a broad spectrum of clinical phenotypes has been observed. We report here on the clinical and molecular analysis of a family that reveals a novel FGD1 mutation in a 9-year-old boy displaying extreme craniofacial dysplasia associated with attention deficit hyperactivity disorder. Sequencing of FGD1 revealed a novel mutation in exon 7 at position c.1468 C > T in the index patient, leading to a stop codon in the highly conserved RhoGEF gene domain. His mother and maternal grandmother were also found to be heterozygous for this FGD1 mutation. Conclusion: Our results identify a novel mutation of FDG1 in a family with Aarskog syndrome and underscore the phenotypical variability of this condition.

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Expert Opin Pharmacother. 2014 Aug;15:1601-10.

GUANFACINE EXTENDED RELEASE FOR THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS.

Connor DF, Arnsten AF, Pearson GS, et al.

Introduction: Guanfacine extended release (GXR) is a selective alpha2A-adrenoreceptor agonist originally developed as an antihypertensive agent and now FDA approved for the treatment of attention-deficit/hyperactivity disorder (ADHD) as monotherapy and as adjunctive to psychostimulants in children and adolescents 6 - 17 years old.

Areas covered: Search of the PubMed and PsycInfo databases from 1990 to 2014 using the search term 'guanfacine'. Studies selected for review were either controlled or open trials of guanfacine or GXR. Shire Pharmaceuticals, Inc. was contacted and supplied a synopsis of all available ADHD studies on GXR for review.

Expert opinion: GXR is an evidence-based treatment for ADHD in children and adolescents. Because this compound has a smaller effect size than psychostimulants for the symptoms of ADHD, it is generally considered a second-line treatment after the psychostimulants or in combination with psychostimulants. Evidence for efficacy is more robust in children than for adolescents. Because of its pharmacodynamic actions in prefrontal cortex, GXR shows considerable promise for other behavioral conditions frequently comorbid with ADHD and potential promise for emotional and behavioral dysregulation secondary to traumatic stress.

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Front Human Neurosci. 2014;8.

ELEVATING HOPE AMONG CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER THROUGH VIRTUAL REALITY.

Shiri S, Tenenbaum A, Sapir-Budnero O, et al.

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Front Human Neurosci. 2014;8.

NOVEL METHOD TO CLASSIFY HEMODYNAMIC RESPONSE OBTAINED USING MULTI-CHANNEL fNIRS MEASUREMENTS INTO TWO GROUPS: EXPLORING THE COMBINATIONS OF CHANNELS.

Ichikawa H, Kitazono J, Nagata K, et al.

Near-infrared spectroscopy (NIRS) in psychiatric studies has widely demonstrated that cerebral hemodynamics differs among psychiatric patients. Recently we found that children with attention-deficit/hyperactivity disorder (ADHD) and children with autism spectrum disorders (ASD) showed different

hemodynamic responses to their own mother's face. Based on this finding, we may be able to classify the hemodynamic data into two those groups and predict to which diagnostic group an unknown participant belongs. In the present study, we proposed a novel statistical method for classifying the hemodynamic data of these two groups. By applying a support vector machine (SVM), we searched the combination of measurement channels at which the hemodynamic response differed between the ADHD and the ASD children. The SVM found the optimal subset of channels in each data set and successfully classified the ADHD data from the ASD data. For the 24-dimensional hemodynamic data, two optimal subsets classified the hemodynamic data with 84% classification accuracy, while the subset contained all 24 channels classified with 62% classification accuracy. These results indicate the potential application of our novel method for classifying the hemodynamic data into two groups and revealing the combinations of channels that efficiently differentiate the two groups.

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Front Neural Circuits. 2014;8.

ATTRIBUTED GRAPH DISTANCE MEASURE FOR AUTOMATIC DETECTION OF ATTENTION DEFICIT HYPERACTIVE DISORDERED SUBJECTS.

Dey S, Rao R, Shah M.

Deficit Hyperactive Disorder (ADHD) is getting a lot of attention recently for two reasons. First, it is one of the most commonly found childhood disorders and second, the root cause of the problem is still unknown. Functional Magnetic Resonance Imaging (fMRI) data has become a popular tool for the analysis of ADHD, which is the focus of our current research. In this paper we propose a novel framework for the automatic classification of the ADHD subjects using their resting state fMRI (rs-fMRI) data of the brain. We construct brain functional connectivity networks for all the subjects. The nodes of the network are constructed with clusters of highly active voxels and edges between any pair of nodes represent the correlations between their average fMRI time series. The activity level of the voxels are measured based on the average power of their corresponding fMRI time-series. For each node of the networks, a local descriptor comprising of a set of attributes of the node is computed. Next, the Multi-Dimensional Scaling (MDS) technique is used to project all the subjects from the unknown graph-space to a low dimensional space based on their inter-graph distance measures. Finally, the Support Vector Machine (SVM) classifier is used on the low dimensional projected space for automatic classification of the ADHD subjects. Exhaustive experimental validation of the proposed method is performed using the data set released for the ADHD-200 competition. Our method shows promise as we achieve impressive classification accuracies on the training (70.49%) and test data sets (73.55%). Our results reveal that the detection rates are higher when classification is performed separately on the male and female groups of subjects.

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Front Psychiatry. 2014;5.

VISUAL NETWORK ASYMMETRY AND DEFAULT MODE NETWORK FUNCTION IN ADHD: AN FMRI STUDY.

Sigi HT, Kane AM, Kaminsky O, et al.

Background: A growing body of research has identified abnormal visual information processing in attention-deficit hyperactivity disorder (ADHD). In particular, slow processing speed and increased reliance on visuo-perceptual strategies have become evident.

Objective: The current study used recently developed fMRI methods to replicate and further examine abnormal rightward biased visual information processing in ADHD and to further characterize the nature of this effect; we tested its association with several large-scale distributed network systems.

Method: We examined fMRI BOLD response during letter and location judgment tasks, and directly assessed visual network asymmetry and its association with large-scale networks using both a voxelwise and an averaged signal approach.

Results: Initial within-group analyses revealed a pattern of left-lateralized visual cortical activity in controls but right-lateralized visual cortical activity in ADHD children. Direct analyses of visual network asymmetry confirmed atypical rightward bias in ADHD children compared to controls. This ADHD characteristic was

atypically associated with reduced activation across several extra-visual networks, including the default mode network (DMN). We also found atypical associations between DMN activation and ADHD subjects' inattentive symptoms and task performance.
Conclusion: The current study demonstrated rightward VNA in ADHD during a simple letter discrimination task. This result adds an important novel consideration to the growing literature identifying abnormal visual processing in ADHD. We postulate that this characteristic reflects greater perceptual engagement of task-extraneous content, and that it may be a basic feature of less efficient top-down task-directed control over visual processing. We additionally argue that abnormal DMN function may contribute to this characteristic.

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Genes Brain Behav. 2014;13:535-42.
ASSOCIATION OF THE KCNJ5 GENE WITH TOURETTE SYNDROME AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Gomez L, Wigg K, Zhang K, et al.
Linkage and association of Tourette Syndrome (TS) and Attention-Deficit/Hyperactivity Disorder (ADHD) have previously been reported in the 11q24 chromosomal region. To identify the risk gene within the region we studied the potassium inwardly-rectifying channel J5 (KCNJ5) gene in a sample of 170 nuclear families with TS. We genotyped eight markers across the gene and observed biased transmission of haplotypes from parents to probands in this sample. We then tested these markers in an independent sample of 242 nuclear families with ADHD and found the same haplotype was significantly over transmitted to ADHD probands. Screening of the coding region of KCNJ5 in 48 probands with TS did not identify any variation that could explain the association of the haplotype. We also genotyped two microsatellite markers, one in the promoter and the other in the 3' region and found no evidence for association for either marker for TS, however, we found significant evidence for association with the 3' repeat and ADHD. A small gene (c11orf45) of unknown function lies within the first intron of KCNJ5 that is transcribed in the opposite orientation and this gene may regulate the expression of KCNJ5. We studied the correlation of the expression of KCNJ5 and the antisense transcript in brain tissues from control individuals and found that the antisense transcript and the short KCNJ5 isoform are co-expressed in three brain regions. The results of this study indicate that KCNJ5 is associated with TS and ADHD in our samples, however, the functional variant(s) remain to be identified.

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Gent Test and Mol Biomarkers. 2014;18:505-09.
ASSOCIATION BETWEEN MONOAMINE OXIDASE GENE POLYMORPHISMS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN KOREAN CHILDREN.
Kwon HJ, Jin HJ, Lim MH.
Attention deficit hyperactivity disorder (ADHD) is a common disorder of the school-age population. ADHD is familial and genetic studies estimate heritability at 80-90%. The aim of the present study was to investigate the association between the genetic type and alleles for the monoamine oxidase (MAO) gene in Korean children with ADHD. The sample consisted of 180 ADHD children and 159 control children. We diagnosed ADHD according to DSM-IV. ADHD symptoms were evaluated with Conners' Parent Rating Scales and Dupaul Parent ADHD Rating Scales. Blood samples were taken from the 339 subjects, DNA was extracted from blood lymphocytes, and polymerase chain reaction was performed for MAO polymorphism. Allele and genotype frequencies were compared using the chi-square test. We compared the allele and genotype frequencies of MAO gene polymorphism in the ADHD and control groups. This study showed that there was a significant correlation among the frequencies of the rs5906883 (odds ratio [OR]=1.47, 95% confidence interval [CI]=1.08-2.00, p=0.014) and the rs3027407 (OR=1.41, 95% CI=1.03-1.91, p=0.029) alleles of MAO, but the final conclusions are not definite. Follow-up studies with larger patient or pure subgroups are expected. These results suggested that MAO might be related to ADHD symptoms.

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Harv Rev Psychiatry. 2014 May;22:179-92.

ALTERNATIVE NATIONAL GUIDELINES FOR TREATING ATTENTION AND DEPRESSION PROBLEMS IN CHILDREN: COMPARISON OF TREATMENT APPROACHES AND PRESCRIBING RATES IN THE UNITED KINGDOM AND UNITED STATES.

Murphy JM, McCarthy AE, Baer L, et al.

The use of psychotropic medications for children and adolescents with attention and depression problems continues to generate both attention in the news media and controversy within the field. Given that the United Kingdom has recently issued guidelines for its national health service that differ substantially from those in the United States, the time is ripe to reexamine the evidence. The purpose of this article is to describe the UK's new "stepped care" guidelines for treating attention and depression problems in children and to compare them to the US guidelines issued by the American Academy of Pediatrics and the American Academy of Child and Adolescent Psychiatry. Our findings are that, despite many similarities, the UK guidelines are generally more conservative in their recommendations for medication use, especially for children experiencing only moderate impairment. Our article also compares prescription and diagnosis rates in the UK and the US, and reports evidence for lower rates of prescribing in the UK, despite some evidence that the rates of problems may not differ substantially. We conclude by noting that the existence of an alternative standard provides validation for clinicians or families who prefer to take a more conservative approach to medication use. The two different approaches to care also provide a valuable opportunity for research to determine whether the approaches result in different treatment outcomes.

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Int J Psychiatry Clin Pract. 2014 Jul;1-34.

EFFECT OF METHYLPHENIDATE TREATMENT ON APPETITE AND LEVELS OF LEPTIN, GHRELIN, ADIPONECTIN, AND BRAIN-DERIVED NEUROTROPHIC FACTOR IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT AND HYPERACTIVITY DISORDER.

Sahin S, Yuce M, Alacam H, et al.

Abstract

Objectives: We aimed to explore whether use of methylphenidate relates leptin, ghrelin, adiponectin, and brain-derived neurotrophic factor (BDNF). In addition, the relationship between methylphenidate related weight loss in attention deficit hyperactivity disorder (ADHD) patients and these biomolecules were evaluated.

Methods: Thirty ADHD patients receiving methylphenidate and 20 healthy controls were included. Leptin, ghrelin, adiponectin, and BDNF levels were measured at baseline and after 2-month treatment in both groups.

Results: At baseline, leptin, ghrelin, adiponectin, and BDNF levels were similar in the ADHD and control groups. The most common adverse events occurring in the ADHD group after 2-month treatment included loss of appetite (70%) and weight loss (66.7%). A significant difference was found in body weight, BMI, and CGI scores of the ADHD patients after the treatment. While posttreatment ghrelin and adiponectin levels were significantly higher in the ADHD group, BDNF level was significantly lower. Posttreatment decrease in leptin levels was not significant.

Conclusions: Leptin and BDNF were not associated with poor appetite and/or weight loss due to methylphenidate treatment. However, ghrelin and adiponectin might be biomolecules that played a role in underlying neurobiological mechanisms of methylphenidate-related appetite or weight loss.

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Int J Environ Res Public Health. 2014;11:6743-56.

ASSOCIATION BETWEEN URINE PHTHALATE LEVELS AND POOR ATTENTIONAL PERFORMANCE IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER WITH EVIDENCE OF DOPAMINE GENE-PHTHALATE INTERACTION.

Park S, Kim B-N, Cho S-C, et al.

Although there is some evidence supporting the existence of an association between prenatal maternal or postnatal child's urine phthalate metabolite concentrations and poor attentional performances, the

interaction between urine phthalate metabolite levels and genetic variation for neuropsychological deficit of attention-deficit hyperactivity disorder (ADHD) has not been examined. The aim of this study was to determine whether phthalate metabolites in urine are associated with poor neuropsychological performance in children with ADHD, and whether such association is affected by genotype-phthalate interaction. A cross-sectional examination of urine phthalate metabolite concentrations and the continuous performance test (CPT) were performed in 179 Korean children with ADHD recruited from department of psychiatry of university hospital. Correlations between urine phthalate metabolite concentrations and the CPT scores were investigated, and the interaction of phthalate metabolite levels with the selected polymorphisms at major candidate genes for ADHD, namely dopamine receptor D4 (DRD4), dopamine transporter, (alpha)-2A-adrenergic receptor, and norepinephrine transporter genes. For the subjects with the DRD4 4/4 genotype, there were significant associations of the urine phthalate metabolite concentrations with the number of omission errors, the number of commission errors, and the response time variability scores on the CPT. However, for the subjects without the DRD4 4/4 genotype, no significant associations were found. The results of this study suggest a possible association between phthalate metabolite concentrations and poor attentional performances of ADHD as well as a genetic influence on this association. Further prospective and epigenetic studies are needed to investigate causality and pathophysiological mechanisms.

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Int J Hum Gen. 2014;14:59-66.

T102C AND 1438 G/A POLYMORPHISMS OF THE SEROTONIN 2A RECEPTOR GENE IN ETIOLOGY AND COURSE OF ADHD.

Guney E, Iseri E, Ergun SG, et al.

The aim of this study was to investigate the -1438A>G and T102C polymorphisms of serotonin 2A (5-HT2A) receptor gene frequencies in patients with ADHD compared with a healthy control group, and to determine the effects of these polymorphisms on the course and outcome of ADHD. Fifty adolescents and young adults diagnosed with ADHD in childhood (between 1994 and 2001) were included in this study. The 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 adolescents and young adults who were healthy both physically and mentally. In adolescence and adulthood, a diagnosis was reached after a semistructured interview based on the DSM-IV criteria. A genetic evaluation was carried out using the Polymerase Chain Reaction method. 50 adolescents and young adults (39 males, 11 females; age range 16-25 years) who were diagnosed with ADHD during childhood (age range at the time of diagnosis 6-10 years) and 50 healthy adolescents and young adults (33 males, 17 females; age range 16-25 years) were evaluated. In adolescence and adulthood, the diagnosis of ADHD remained in 44 (88%) of the cases, whereas six (12%) were in remission after the 7-14-year follow-up.* No 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 found between the ADHD and control groups. No significant difference was found between ADHD patients with CC, CT, or TT genotypes in terms of the outcome of the illness ((chi)2=0.114, p=0.94). Similarly, there was no difference between ADHD patients with AA, AG, and GG genotypes in terms of the outcome ((chi)2=0.530, p=0.76). No significant association between -1438A>G and T102C polymorphisms of the 5-HT2A receptor gene and ADHD was found in the present study. No significant effect of these two polymorphisms on the outcome of ADHD in adolescence was detected. The results of this study do not support a role for the serotonergic system in the development and course of ADHD.

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Iran J Psychiatry. 2014;9:47-54.

BARKLEY'S PARENT TRAINING PROGRAM, WORKING MEMORY TRAINING AND THEIR COMBINATION FOR CHILDREN WITH ADHD: ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Maleki ZH, Mashhadi A, Soltanifar A, et al.

Objective: The aim of the current study was to examine the effectiveness of Barkley's parent training program, working memory training and the combination of these two interventions for children with Attention deficit hyperactivity disorder (ADHD).

Methods: In this study, 36 participants with ADHD (aged 6 to 12 years) were selected by convenience sampling. Revision of the Swanson, Nolan and Pelham (SNAP) questionnaire (SNAP-IV), Child Behavior Checklist (CBCL) and clinical interviews were employed to diagnose ADHD. Wechsler Intelligence Scale for Children-Fourth Edition was also implemented. The participants were randomly assigned to the three intervention groups of Barkley's parent training program, working memory training and the combined group. SNAP-IV and CBCL were used as pre-tests and post-tests across all three groups. Data were analyzed using MANCOVA (SPSS version18).

Results: There was a significant difference ($p < 0.05$) in the decline of attention deficit and hyperactivity /impulsivity symptoms between the combined treatment group and working memory training group and also between the combined treatment group and the parent training group in SNAP. In terms of attention problems (experience-based subscales) of CBCL, there was a significant difference ($p < 0.001$) between the combined treatment group and working memory training group. Furthermore, compared to the working memory training and parent training groups, the combined group demonstrated a significant decline ($p < 0.01$) in clinical symptoms of ADHD (based on DSM).

Conclusion: It was revealed that combined treatment in comparison with the other two methods suppressed the clinical symptoms of ADHD more significantly.

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J Abnorm Child Psychol. 2014 Aug;42:1005-17.

EFFECTS OF A SUMMER TREATMENT PROGRAM ON FUNCTIONAL SPORTS OUTCOMES IN YOUNG CHILDREN WITH ADHD.

O'connor BC, Fabiano GA, Waschbusch DA, et al.

Participation in youth sports can be very beneficial, but children with Attention Deficit Hyperactivity Disorder (ADHD) may participate less often and less successfully. The current study evaluated functional sports outcomes for children with ADHD who attended an intensive behavioral treatment program that included a sports training component, and it compared outcomes to children with ADHD who did not attend the program. Results suggest that treatment resulted in significant improvements in many aspects of children's sports functioning, including knowledge of game rules, in vivo game performance, and fundamental skill tasks (motor proficiency, ability to trap a soccer ball appropriately, reduced handball penalties in soccer, and improved ability to catch a baseball). Parents also reported improved sports skills and good sportsmanship in the treatment group. No differences between groups were evident on additional skill tasks evaluating accurately kicking a soccer ball, throwing a baseball, or hitting a baseball off a tee. These results suggest intensive behavioral intervention that includes sports training can significantly improve functional sports outcomes for young children with ADHD

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J Atten Disord. 2014 Jul.

INTERACTIONS BETWEEN EARLY TRAUMA AND CATECHOL-O-METHYLTRANSFERASE GENES ON INHIBITORY DEFICITS IN CHILDREN WITH ADHD.

Park S, Kim BN, Kim JW, et al.

OBJECTIVE: To investigate the interaction between childhood trauma exposure with the catechol-O-methyltransferase (COMT) and dopamine receptor D4 (DRD4) polymorphisms in relation to neuropsychological measures in children with ADHD.

METHOD: A cross-sectional examination of early traumatic experiences and the continuous performance test (CPT) were performed in 55 children with ADHD. Participants were also genotyped for the DRD4 exon III 48-bp variable number of tandem repeats (VNTR) polymorphism and the COMT Val158-Met (rs4680) polymorphism.
RESULTS: There was significant interaction between the effects of the COMT genotype and trauma in commission errors. In participants with ADHD carrying the COMT Val/Val genotype, the group exposed to trauma showed significantly higher commission errors than the non-traumatized group. However, for the participants with other genotypes, no significant differences were found.
CONCLUSION: This study suggests that there exists a genetic influence on the association between childhood trauma and the severity of inhibitory deficits in children with ADHD.

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J Atten Disord. 2014 Jul.
BIPOLAR DISORDER IN CHILDREN WITH ADHD: A CLINICAL SAMPLE STUDY.
Donfrancesco R, Di TM, Andriola E, et al.
OBJECTIVE: To explore the impact of early-onset bipolar disorder (pediatric bipolar disorder [PBD]) on ADHD.
METHOD: We compared ADHD symptom severity, ADHD subtype distribution, and rates of comorbid and familial psychiatric disorders between 49 ADHD children with comorbid PBD and 320 ADHD children without PBD.
RESULTS: Children with ADHD and PBD showed higher scores in the Hyperactive and Inattentive subscales of the ADHD Rating Scale, than children with ADHD alone. The frequency of combined subtype was significantly higher in ADHD children with PBD, than in those with ADHD alone. ADHD children with PBD showed a higher rate of familial psychiatric disorders than ADHD children without PBD. The rate of conduct disorder was significantly greater in children with PBD and ADHD compared with children with ADHD alone.
CONCLUSION: ADHD along with PBD presents with several characteristics that distinguish it from ADHD alone, suggesting that these may be distinct disorders

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J Atten Disord. 2014 Jul.
SELF- AND PARENT-RATED QUALITY OF LIFE OF A TREATMENT NAIVE SAMPLE OF CHILDREN WITH ADHD: THE IMPACT OF AGE, GENDER, TYPE OF ADHD, AND COMORBID PSYCHIATRIC CONDITIONS ACCORDING TO BOTH A CATEGORICAL AND A DIMENSIONAL APPROACH.
Dallos G, Miklosi M, Kereszteny A, et al.
OBJECTIVE: Our aim was to evaluate the Quality of Life (QoL) of treatment naive children with ADHD.
METHOD: Data from 178 parent-child dyads were analyzed using multiple regression to assess the relationships between QoL, and characteristics of ADHD and comorbid psychopathology.
RESULTS: Lower self-reported QoL was associated with female gender, higher age, more symptoms of anxiety and trauma-related disorders in dimensional approach, and with the comorbid diagnoses of trauma-related disorders and oppositional defiant disorder (ODD)/conduct disorder (CD) in categorical approach. Lower parent-reported QoL was related to older age and increasing number of symptoms of mood and anxiety disorders on one hand, and any diagnosis of mood and anxiety disorders and ODD/CD on the other.
CONCLUSION: Our results draw the attention to the importance of taking into account age, gender, and both self- and parent reports when measuring QoL of children with ADHD and both dimensional and categorical approaches should be used.

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J Atten Disord. 2014 Jul.

THE PARENTAL EMOTIONAL RESPONSE TO CHILDREN INDEX: A QUESTIONNAIRE MEASURE OF PARENTS' REACTIONS TO ADHD.

Lambek R, Sonuga-Barke E, Psychogiou L, et al.

OBJECTIVE: The current study introduces the Parental Emotional Response to Children Index (PERCI), a new questionnaire specifically designed to measure parents' emotional response to ADHD and related behaviors (delay discounting and delay aversion).

METHOD: The PERCI was completed by parents of 6- to 14-year-old children with (n = 126) and without (n = 160) ADHD.

RESULTS: Factor analysis confirmed five separate subscales with acceptable psychometric properties. Parents of children with ADHD reported a stronger emotional response to ADHD behaviors than parents of typically developing children and inattention symptoms evoked the strongest emotional response in parents regardless of child diagnostic status.

CONCLUSION: Parents' emotional responses appear to be differentiated in terms of specific ADHD-related triggers mapping onto the different domains of ADHD and delay-related responses. Further research is required to understand changes in parental emotional responses over time and their impact on children's developmental trajectories.

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J Atten Disord. 2014 Jul.

PERSISTENCE OF PARENT-REPORTED ADHD SYMPTOMS FROM CHILDHOOD THROUGH ADOLESCENCE IN A COMMUNITY SAMPLE.

Holbrook JR, Cuffe SP, Cai B, et al.

OBJECTIVE: To examine ADHD symptom persistence and factors associated with elevated symptom counts in a diverse, longitudinal community-based sample.

METHOD: Parents reported demographics and completed a diagnostic interview repeatedly over a 6-year period. At Time 1, 481 interviews were completed about children (5-13 years); all participants were invited to four annual follow-up interviews, and 379 (79%) completed at least one. Inattentive (IA) and hyperactive-impulsive (HI) symptom counts were modeled with logistic quantile regression, while accounting for study design complexities.

RESULTS: The prevalence of seven IA symptoms remained stable from early childhood through late adolescence. The prevalence of eight HI symptoms decreased by more than half over time. After demographic adjustment, the upper quartile of HI symptom counts decreased with age ($p<.01$). High HI symptom counts persisted more among those with high IA symptom counts ($p = .05$).

CONCLUSION: This study further characterizes and provides insights into ADHD symptom trajectory through adolescence.

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J Atten Disord. 2014 Jul.

ADHD DRUG PRESCRIBING TREND IS INCREASING AMONG CHILDREN AND ADOLESCENTS IN HONG KONG.

Man KK, Ip P, Hsia Y, et al.

OBJECTIVE: To investigate the prevalence of ADHD medication prescribing of school-aged children in Hong Kong (HK) from 2001 to 2013 and to compare with other countries.

METHOD: Using the Hong Kong Hospital Authority Clinical Data Analysis and Reporting System, we investigated the epidemiology and prevalence of ADHD medication prescribing.

RESULTS: The prevalence of children on ADHD medication increased 14 times throughout the study period-0.072% in 2001 (95% confidence interval [CI] = [0.068%, 0.077%]) to 1.027% (95% CI = [1.008%, 1.047%]) in 2013. Prevalence in females increased at a faster rate than in males. The prescribing trend in kindergarten children (3- to 5-year-old) was relatively steady from 2001 to 2008-0.025% (95% CI = [0.019%, 0.033%]) in 2001-until a marked increase from 2009 to 2013-0.121% (95% CI = [0.105%, 0.139%]) in 2013.

CONCLUSION: The prevalence of ADHD medication prescribing in Hong Kong is increasing but remains lower than most Western countries. However, the prevalence of ADHD medication prescribing for kindergarten children should be monitored to ensure appropriate use.

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J Atten Disord. 2014 Jul.

SLEEP PROBLEMS AND DAILY FUNCTIONING IN CHILDREN WITH ADHD: AN INVESTIGATION OF THE ROLE OF IMPAIRMENT, ADHD PRESENTATIONS, AND PSYCHIATRIC COMORBIDITY.

Virring A, Lambek R, Jennum PJ, et al.

OBJECTIVE: Little systematic information is available regarding how sleep problems influence daytime functioning in children with ADHD, as the role of ADHD presentations and comorbidity is unclear.
METHOD: In total, 397 children were assessed with the Children's Sleep Habits Questionnaire, the Weiss Functional Impairment Rating Scale, and the ADHD Rating Scale.
RESULTS: We found a moderate, positive correlation between sleep problems and impaired functioning in both children with ADHD and in typically developed children. ADHD presentations did not differ significantly with respect to sleep problem profile, but having a comorbid internalizing or autistic disorder lead to higher sleep problem score.
CONCLUSION: Sleep problems and impaired daily functioning were more common in children with ADHD, but the overall association between sleep problems and impaired daily functioning was similar in clinical and nonclinical children. Internalizing or autistic comorbid disorders added significantly to the sleep problems.

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J Atten Disord. 2014 Jul.

CO-OCCURRENCE OF ODD AND CD IN PRESCHOOL CHILDREN WITH SYMPTOMS OF ADHD.

Bendiksen B, Svensson E, Aase H, et al.

OBJECTIVE: Patterns of co-occurrence between ADHD, Oppositional Defiant Disorder (ODD), and Conduct Disorder (CD) were examined in a sample of non-referred preschool children. ADHD subtypes and sex differences were also explored.
METHOD: Children aged 3.5 years (n=1,048) with high scores on ADHD characteristics were recruited from the Norwegian Mother and Child Cohort Study and clinically assessed, including a semi-structured psychiatric interview.
RESULTS: In children with ADHD, concurrent ODD was present more often than CD (31% vs. 10%), but having ADHD gave higher increase in the odds of CD than of ODD (ODD: odds ratio [OR] = 6.7, 95% confidence interval [CI] = [4.2, 10.8]; CD: OR = 17.6, 95% CI = [5.9, 52.9]). We found a greater proportion of children having the combined ADHD subtype as well as more severe inattentiveness among children with co-occurring CD compared with ODD. Sex differences were minor.
CONCLUSION: There are important differences in co-occurring patterns of ODD and CD in preschool children with ADHD.

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J Atten Disord. 2014 Jul.

ADHD AMONG RURAL SOUTHEASTERN NIGERIAN PRIMARY SCHOOL CHILDREN: PREVALENCE AND PSYCHOSOCIAL FACTORS.

Ndukuba AC, Odinka PC, Muomah RC, et al.

OBJECTIVE: To determine the prevalence of ADHD among primary school pupils in a rural community in Southeastern Nigeria and to determine the psychosocial factors associated with the condition.
METHOD: One hundred eighty-one randomly selected participants had their teachers complete the school version of ADHD Rating Scale-IV. Their parents also completed a sociodemographic questionnaire, the

clinical interview form for the child and adolescent ADHD patients, and home version of the ADHD Rating Scale-IV.
RESULTS: Twelve (6.6%) of the children met the criteria for diagnosis. A history of prolonged labor (odds ratio [OR] = 14.1; 95% confidence interval [CI] = [2.13, 93.1]), and parents' negative assessment of their marriages (OR = 0.1; CI = [0.017, 0.567]) were the most predominant factors which independently associated with the ADHD in the children.
CONCLUSION: There is, therefore, a need for the care of rural dwelling African children, who otherwise would have difficulties accessing health care that is concentrated in the cities.

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J Child Adolesc Psychopharmacol. 2014 Jul.
MEDICATION PERSISTENCE IN TURKISH CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Ayaz M, Ayaz AB, Soylu N, et al.
Abstract
Objective: The aim of this study was to investigate medication persistence in Turkish children and adolescents with attention-deficit/hyperactivity disorder (ADHD). The effects of sociodemographic characteristics, symptom severity of ADHD, comorbidity, and treatment-related factors influencing medication persistence in children diagnosed with ADHD were studied.
Methods: Medication persistence over a continuous 12 month period was evaluated for 877 children and adolescents between 6 and 18 years of age, who were diagnosed with ADHD for the first time and started to receive medication. Medication persistence was determined according to whether or not taking the prescribed medication continued for 12 months after the initiation of treatment. Whereas the symptom severity of ADHD was assessed by using the Turgay Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV)-based Child and Adolescent Behaviour Disorders Screening and Rating Scale-Parents Form (T-DSM-IV-S), perceived medication efficacy after the first treatment was evaluated by the Clinical Global Impressions-Improvement Scale (CGI-I).
Results: In this study, medication persistence over a continuous 12 month period occurred at a rate of 30.2% (n=265) in the subjects studied. The hierarchical regression analysis conducted in this research revealed that younger age, higher hyperactivity/impulsivity symptom severity, use of long-acting methylphenidate, addition of another ADHD medication, addition of other psychotropic medications, absence of side effects, and perceived medication efficacy were associated with successful medication persistence over a continuous 12 month period.
Conclusions: Understanding the factors that affect medication persistence in ADHD may improve treatment efficacy and symptom control, while minimizing future risks.

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J Int Neuropsychol Soc. 2014 Jul;1-13.
THE CLINICAL UTILITY AND SPECIFICITY OF PARENT REPORT OF EXECUTIVE FUNCTION AMONG CHILDREN WITH PRENATAL ALCOHOL EXPOSURE.
Nguyen TT, Glass L, Coles CD, et al.
Prenatal alcohol exposure and attention-deficit/hyperactivity disorder (ADHD) result in behavioral issues related to poor executive function (EF). This overlap may hinder clinical identification of alcohol-exposed children. This study examined the relation between parent and neuropsychological measures of EF and whether parent ratings aid in differential diagnosis. Neuropsychological measures of EF, including the Delis-Kaplan Executive Function System (D-KEFS), were administered to four groups of children (8-16 years): alcohol-exposed with ADHD (AE+, n=80), alcohol-exposed without ADHD (AE-, n=36), non-exposed with ADHD (ADHD, n=93), and controls (CON, n=167). Primary caregivers completed the Behavior Rating Inventory of Executive Function (BRIEF). For parent ratings, multivariate analyses of variance revealed main effects of Exposure and ADHD and an interaction between these factors, with significant differences between all groups on nearly all BRIEF scales. For neuropsychological measures,

results indicated main effects of Exposure and ADHD, but no interaction. Discriminant function analysis indicated the BRIEF accurately classifies groups. These findings confirm compounded behavioral, but not neuropsychological, effects in the AE+ group over the other clinical groups. Parent-report was not correlated with neuropsychological performance in the clinical groups and may provide unique information about neurobehavior. Parent-report measures are clinically useful in predicting alcohol exposure regardless of ADHD. Results contribute to a neurobehavioral profile of prenatal alcohol exposure. (JINS, 2014, 20, 1-13).

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J Pediatr. 2014 Jul.

CARDIAC AUTONOMIC DYSFUNCTION AND ARTERIAL STIFFNESS AMONG CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER TREATED WITH STIMULANTS.

Kelly AS, Rudser KD, Dengel DR, et al.

OBJECTIVE: To compare markers of cardiovascular health in youth diagnosed with attention deficit hyperactivity disorder (ADHD) by the use of stimulant medication with healthy controls.

STUDY DESIGN: Children and adolescents (n=85; mean age 11.2 +/- 2.8 years; 66 boys) diagnosed with ADHD using a stimulant and 53 siblings without ADHD (mean age 11.1 +/- 3.8 years; 28 boys) were included in this cross-sectional study. Measured variables included blood pressure, heart rate (HR), HR variability: SD of the RR interval and low frequency to high frequency ratio, carotid-radial pulse wave velocity, carotid artery augmentation index (AIx), radial artery AIx, brachial artery flow-mediated dilation, and digital reactive hyperemic index.

RESULTS: Compared with control patients, participants with ADHD had greater resting systolic blood pressure (3.9 mm Hg, 95% CI [1.2-6.7], P = .005), diastolic blood pressure (5.5 mm Hg, 95% CI [3.2-7.8], P < .001), HR (9.2 beats/min, 95% CI [6.0-12.3], P < .001), low frequency to high frequency ratio (0.55, 95% CI [0.22-0.89], P = .001), carotid AIx (7.2%, 95% CI [1.9-12.5], P = .008), and pulse wave velocity (0.36 m/s, 95% CI [-0.05, 0.78], P = .089), and lower SD of the RR interval (-33.7 milliseconds, 95% CI [-46.1, -21.3], P < .001). Neither flow-mediated dilation nor reactive hyperemic index was significantly different.

CONCLUSIONS: Children and adolescents being treated with a stimulant medication for ADHD exhibited signs of altered cardiac autonomic function, characterized by increased sympathetic tone, and showed evidence of arterial stiffening

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JDDG J German Soc Dermatol. 2014;12:6-7.

ATTENTIVENESS AND IGE-LEVELS ARE ALTERED IN CHILDREN WITH ATOPIC DERMATITIS AND CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: SIMILARITIES AND DIFFERENCES.

Wolfer W, Krauel K, Bonnekoh B, et al.

Atopic dermatitis (AD) is supposed to be an independent risk factor for attention deficit hyperactivity disorder (ADHD). The molecular basis of this connection remains to be elucidated. Among other phenomena, AD-pathophysiology is characterized by a reduction of intracellular storage organelles and disturbed granule release mechanisms in several cell systems. This results in an often adequate but not sustained reaction to stimulation. We hypothesized that CNSreactions requiring sustained granule release (from neurons) may be impaired in AD-patients as well. Therefore, we compared the reaction of children with AD in several neuropsychological tests to ADHD-patients which are known to be unable to keep up an enduring CNS-response. 14 ADHD-inpatients with confirmed diagnosis (13 m, 1f), 11 ADchildren (8 m, 3f) and 8 healthy individuals (HI; 6 m, 2f) without any atopic/psychiatric background were studied in three modules: A) child psychiatry, B) dermato-allergology, C) laboratory. In A, using a neuropsychological computer-based test battery [Psytest 2.2, Herzogenrath, Germany], short term (120 signals / 4 min, nullsprintnull) and long term (900 signals / 30 min, nullendurancenull) attentiveness towards visual and acoustic stimuli was tested. ADHD symptoms, emotional/ behavioural difficulties and personality traits (e.g. novelty seeking) were assessed employing questionnaires (CBCL, DISYPS II-ADHD, JTCI). In B, Erlanger Atopie Score (EAS), SCORAD and a prick test with common aero allergens were performed. In C, total

serum IgE, eosinophilic cationic protein (ECP) and differential blood count were determined. A) 2 AD-children were omitted from analysis since parents reported a significant number of ADHD symptoms. In the short term attentiveness test, AD-children reacted comparable to the ADHD-group: significantly slower with more mistakes than HI. this was most pronounced in AD-children with exacerbated disease. In the long term attentiveness test, AD-children showed again prolonged reaction times which slowed down even more over time as compared to HI, but did not make as many errors as ADHD-patients. B) 12/14 ADHD-children did not have any AD-symptoms nor any history of atopy, 13/14 showed a white dermographism, EAS was 9 (plus or minus) 3 (atopic skin diathesis unclear). 5/11 AD-patients showed exac- erbated disease at the timepoint of the study (SCORAD > 10, mean EAS 12 (plus or minus) 3). C) ADHD- and AD-patients had elevated IgE levels (500 (plus or minus) 420 kU/l and 653 (plus or minus) 950 kU/l), eosinophila (8.7 (plus or minus) 9% and 7 (plus or minus) 6%) and high ECP-levels (31 (plus or minus) 30 and 39 (plus or minus) 33 (mu)g/l). Our results confirm the hypothesis that CNS-reactions requiring sustained granule release are impaired in AD. Thus, having in mind the well known granule defects in epidermis and immune system of AD, granule alterations seem to be a general cell biologic AD-phenomenon. Similarities in neurophysiological tests were mirrored by similar ECP- and IgE-levels among AD-/ ADHS-children. This may suggest a common cell biological basis for these phenomena

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J Anxiety Disord. 2014;28:530-36.

PSYCHOTROPIC DRUG UTILIZATION IN CHILDREN WITH CONCURRENT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ANXIETY.

Liu X, Kubilis P, Xu D, et al.

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J Child Adolesc Psychopharmacol. 2014;24:269-74.

CONCORDANCE BETWEEN PARENT AND PHYSICIAN MEDICATION HISTORIES FOR CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Kuriyan AB, Pelham WE, Molina BSG, et al.

Objective: It is necessary for both clinicians and researchers who study attention-deficit/hyperactivity disorder (ADHD) to obtain a medication history for patients/participants for a variety of purposes. Because of the complexity of constructing medication histories using official records, parental report of medication for children with ADHD is the most commonly used source of information. However, the reliability and validity of parent reports of medication history have not been thoroughly studied. Previous studies have only examined the psychometrics of interview assessments of medication use for a maximum of a 12 month recall period. The current study compares parent report provided by a questionnaire and physician records for children and adolescents with ADHD. This is the first study to examine validity of retrospective recall for an extended medication history (prekindergarten-12th grade) using a questionnaire, and the first to examine validity of parental report of dosage.

Methods: Participants with ADHD were part of the Pittsburgh ADHD Longitudinal Study. The current study utilized data from those in the ADHD group who had at least 1 year of data from the physician's records and corresponding records from the parent (n=178).

Results: Percent agreement for medication use was >80%. Intraclass correlation coefficients for parent-provider agreement on total daily dosage of ADHD medications were in the good to excellent range. There were no significant predictors of agreement.

Conclusions: Our findings indicate that it is acceptable for clinics and research studies to obtain information about medication use for children with ADHD retrospectively solely based on parental report.

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J Child Adolesc Psychopharmacol. 2014;24:245-52.

GUANFACINE EXTENDED RELEASE ADJUNCTIVE TO A PSYCHOSTIMULANT IN THE TREATMENT OF COMORBID OPPOSITIONAL SYMPTOMS IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Findling RL, McBurnett K, White C, et al.

Objective: The purpose of this study was to assess the effect of guanfacine extended release (GXR) adjunctive to a psychostimulant on oppositional symptoms in children and adolescents with attention-deficit/hyperactivity disorder (ADHD).

Methods: A multicenter, double-blind, placebo-controlled dose-optimization study of GXR (1-4 mg/d) or placebo administered morning (a.m.) or evening (p.m.) adjunctive to psychostimulant was conducted in subjects ages 6-17 with suboptimal response to psychostimulant alone. Suboptimal response was defined as treatment with a stable dose of psychostimulant for (greater-than or equal to) 4 weeks with ADHD Rating Scale IV total score (greater-than or equal to) 24 and Clinical Global Impressions-Severity of Illness score (greater-than or equal to) 3, as well as investigator opinion. Primary efficacy and safety results have been reported previously. Secondary efficacy measures included the oppositional subscale of the Conners' Parent Rating Scale-Revised: Long Form (CPRS-R:L); these are reported herein.

Results: Significant reductions from baseline to the final on-treatment assessment on the oppositional subscale of the CPRS-R:L were seen with GXR plus psychostimulant compared with placebo plus psychostimulant, both in the overall study population (placebo-adjusted least squares [LS] mean change from baseline to the final on-treatment assessment: GXR a.m.+psychostimulant, -2.4, p=0.001; GXR p.m.+psychostimulant, -2.2, p=0.003) as well as in the subgroup of subjects with significant baseline oppositional symptoms (GXR a.m.+psychostimulant, -3.6, p=0.001; GXR p.m.+psychostimulant, -2.7, p=0.013). Treatment-emergent adverse events were reported by 77.3%, 76.3%, and 63.4% of subjects in the GXR a.m., GXR p.m., and placebo groups, respectively, in the overall study population.

Conclusions: GXR adjunctive to a psychostimulant significantly reduced oppositional symptoms compared with placebo plus a psychostimulant in subjects with ADHD and a suboptimal response to psychostimulant alone.

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Journal of Child Psychology and Psychiatry. 2014 May;55:505-15.

PATHWAYS TO SELF-HARMFUL BEHAVIORS IN YOUNG WOMEN WITH AND WITHOUT ADHD: A LONGITUDINAL EXAMINATION OF MEDIATING FACTORS.

Swanson EN, Owens EB, Hinshaw SP.

Background: Rates of suicide attempts and nonsuicidal self-injury [(NSSI); e.g., cutting, burning] peak in adolescence and early adulthood; females and individuals with psychiatric symptoms and diagnoses appear to be at particular risk. Hinshaw et al. [Journal of Consulting and ClinicalPsychology, ([Hinshaw, S.P., 2012]), 80, 1041] reported that young women with histories of childhood ADHD diagnoses reported higher rates of suicide attempts and NSSI than nondiagnosed, comparison women.

Methods: Via analyses of an ongoing longitudinal investigation, our aims are to examine, with respect to both aspects of self-harmful behavior, (a) ADHD subtype differences and effects of diagnostic persistence (vs. transient and nondiagnosed classifications) and (b) potential mediating effects of impulsivity and comorbid psychopathology, ascertained during adolescence.

Results: Young adult women with a childhood diagnosis of ADHD-Combined type were at highest risk for suicide attempts as well as the most varied and severe forms of NSSI compared with those with ADHD-Inattentive type and those in the comparison group; participants with a persistent ADHD diagnosis were at higher risk than those with a transient diagnosis or those never meeting criteria for ADHD. Mediator analyses revealed that, during adolescence, an objective measure of impulsivity plus comorbid externalizing symptoms were simultaneous, partial mediators of the childhood ADHD-young adult NSSI linkage. Adolescent internalizing symptoms emerged as a partial mediator of the childhood ADHD-young adult suicide attempt linkage.

Conclusions: ADHD in females, especially when featuring childhood impulsivity and especially with persistent symptomatology, carries high risk for self-harm. Psychiatric comorbidity and response inhibition are important mediators of this clinically important longitudinal association. We discuss limitations and implications for prevention and intervention.

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Journal of Child Psychology and Psychiatry. 2014 Jul;55:819-27.

SHARED FAMILIAL TRANSMISSION OF AUTISM SPECTRUM AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDERS.

Musser ED, Hawkey E, Kachan-Liu SS, et al.

Background To determine whether familial transmission is shared between autism spectrum disorders and attention-deficit/hyperactivity disorder, we assessed the prevalence, rates of comorbidity, and familial transmission of both disorders in a large population-based sample of children during a recent 7 year period.
Methods Study participants included all children born to parents with the Kaiser Permanente Northwest (KPNW) Health Plan between 1 January 1998 and 31 December 2004 (n = 35,073). Children and mothers with physician-identified autism spectrum disorders (ASD) and/or attention-deficit/hyperactivity disorder (ADHD) were identified via electronic medical records maintained for all KPNW members.
Results Among children aged 6–12 years, prevalence was 2.0% for ADHD and 0.8% for ASD; within those groups, 0.2% of the full sample (19% of the ASD sample and 9.6% of the ADHD sample) had co-occurring ASD and ADHD, when all children were included. When mothers had a diagnosis of ADHD, first born offspring were at 6-fold risk of ADHD alone (OR = 5.02, p < .0001) and at 2.5-fold risk of ASD alone (OR = 2.52, p < .01). Results were not accounted for by maternal age, child gestational age, child gender, and child race.
Conclusions Autism spectrum disorders shares familial transmission with ADHD. ADHD and ASD have a partially overlapping diathesis.

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Journal of Child Psychology and Psychiatry. 2014 May;55:436-45.

THE ASSOCIATION OF ATTENTION DEFICIT HYPERACTIVITY DISORDER WITH SOCIOECONOMIC DISADVANTAGE: ALTERNATIVE EXPLANATIONS AND EVIDENCE.

Russell G, Ford T, Rosenberg R, et al.

Background: Studies throughout Northern Europe, the United States and Australia have found an association between childhood attention deficit hyperactivity disorder (ADHD) and family socioeconomic disadvantage. We report further evidence for the association and review potential causal pathways that might explain the link.
Method: Secondary analysis of a UK birth cohort (the Millennium Cohort Study, N = 19,519) was used to model the association of ADHD with socioeconomic disadvantage and assess evidence for several potential explanatory pathways. The case definition of ADHD was a parent-report of whether ADHD had been identified by a medical doctor or health professional when children were 7 years old.
Results: ADHD was associated with a range of indicators of social and economic disadvantage including poverty, housing tenure, maternal education, income, lone parenthood and younger motherhood. There was no evidence to suggest childhood ADHD was a causal factor of socioeconomic disadvantage: income did not decrease for parents of children with ADHD compared to controls over the 7-year study period. No clinical bias towards labelling ADHD in low SES groups was detected. There was evidence to suggest that parent attachment/family conflict mediated the relationship between ADHD and SES. Conclusion: Although genetic and neurological determinants may be the primary predictors of difficulties with activity level and attention, aetiology appears to be influenced by socioeconomic situation.

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J Clin Psychopharmacol. 2014;34:467-74.

EFFECT OF METHYLPHENIDATE ON NEUROCOGNITIVE TEST BATTERY: AN EVALUATION ACCORDING TO THE DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS, FOURTH EDITION, SUBTYPES.

Durak S, Ercan ES, Ardic UA, et al.

The aims of this study were to evaluate the neuropsychological characteristics of the restrictive (R) subtype according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition and the attention-deficit/hyperactivity disorder (ADHD) combined (CB) type and predominantly inattentive (PI) type subtypes and to evaluate whether methylphenidate (MPH) affects neurocognitive test battery scores according to these subtypes. This study included 360 children and adolescents (277 boys, 83 girls) between 7 and 15 years of age who had been diagnosed with ADHD and compared the neuropsychological characteristics and MPH treatment responses of patients with the R subtype - which has been suggested for inclusion among the ADHD subtypes in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition - with those of patients with the PI and CB subtypes. They did not differ from the control subjects in the complex attention domain, which includes Continuous Performance Test, Stroop test, and Shifting Attention Test, which suggests that the R subtype displayed a lower level of deterioration in these domains compared with the PI and CB subtypes. The patients with the CB and PI subtypes did not differ from the control subjects in the Continuous Performance Test correct response domain, whereas those with the R subtype presented a poorer performance than the control subjects. The R subtype requires a more detailed evaluation because it presented similar results in the remaining neuropsychological evaluations and MPH responses.

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J Intellect Disabil Res. 2014.

ASD, ADHD, MENTAL HEALTH CONDITIONS AND PSYCHOPHARMACOLOGY IN NEUROGENETIC SYNDROMES: PARENT SURVEY.

Reilly C, Senior J, Murtalgh L.

Background: There are a number of neurogenetic syndromes with well described behavioural phenotypes including fragile X syndrome, Prader-Willi syndrome, Williams syndrome and velo-cardio-facial syndrome (VCFS). Autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD) and psychiatric conditions are often associated with the syndromes.

Method: Parents (n=381) of school-aged children with one of the four syndromes in the UK and Ireland were asked whether their child had been professionally diagnosed with ASD, ADHD or a mental health condition. Parents were also asked whether their child had been prescribed medication for behavioural or psychiatric reasons.

Results: The highest level of reported diagnoses of ASD and ADHD was in fragile X syndrome. In all syndrome groups, lower rates of diagnosis were reported in comparison to previously published research. Prescribing of medication for behavioural/psychiatric reasons was highest in fragile X syndrome although the highest usage of melatonin was in Williams syndrome.

Conclusion: Reasons for a lower recognition of ASD, ADHD and mental health conditions in clinical practice compared with research studies may include 'diagnostic overshadowing' due to presence of intellectual disability and a genetic syndrome. However, there may also be a lack of belief in the utility of such diagnoses in neurogenetic syndromes among relevant professionals and/or lack of access to professionals with sufficient expertise in the recognition of such diagnoses in those with neurogenetic syndromes. The low rates of prescribing of medication for behavioural/psychiatric reasons may reflect the low level of clinical diagnoses or lack of belief in the utility of psychopharmacology in this population.

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J Neuroimmunol. 2014;273:111-14.

INCREASED LEVELS OF SERUM NEOPTERIN IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Ceylan MF, Uneri OS, Guney E, et al.

Attention deficit/hyperactivity disorder (ADHD) is the most frequently occurring neuropsychiatric disorder in childhood with an etiology that is not fully understood. A number of reviews that have addressed the neurobiology of ADHD have focused on imaging and genetics. Relatively little attention has been given to factors/mechanisms involved in the brain dysfunction. We suggest that changes in cellular immunity may be involved. Neopterin is a good indicator of cellular immunity, and we evaluated serum levels of neopterin in patients with ADHD. The study group consisted of 49 patients with ADHD. An age- and gender-matched control group was composed of 31 healthy subjects. Venous blood samples were collected, and the levels of neopterin were measured. The levels of neopterin were significantly higher in ADHD than in the comparison subjects. Cellular immunity may have a role in the etiopathogenesis of ADHD.

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J Psychopathol Behav Assess. 2014 Jun;36:237-45.

PERSONALITY TRAITS ELUCIDATE SEX DIFFERENCES IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMORBIDITY DURING EARLY CHILDHOOD.

Martel MM, Gremillion ML, Tackett JL.

Attention-Deficit/Hyperactivity Disorder (ADHD) is highly comorbid with other childhood disorders, and there are striking sex differences in this comorbidity, particularly during early childhood. For example, boys with ADHD are more likely to exhibit comorbid disruptive behavior and neurodevelopmental disorders, compared to girls, during early childhood. Yet, explanations for these well-established sex differences remain in short supply. The current study evaluated the novel hypothesis that personality traits may serve as intermediate phenotypes that help explain sex differences in common ADHD comorbidity profiles during early childhood. Study participants were 109 children between the ages of 3 and 6 and their primary caregivers and teachers/daycare providers, recruited from the community and over-recruited for ADHD-related problems. Primary caregivers completed the Child Behavior Checklist, and teachers/daycare providers completed the Teacher Report Form as a measure of child behavior problems. Examiners completed the California Q-Sort as a measure of child personality traits. Moderated mediation analyses suggested that personality traits explain associations between ADHD and oppositional-defiance, aggression, and language problems in a sex-specific manner. While high neuroticism mediated associations between ADHD and oppositional-defiance in girls, disagreeableness mediated associations between ADHD and aggression and low conscientiousness mediated associations between ADHD and neurodevelopmental language problems in boys. Sex differences in trait-psychopathology associations may help explain sex differences in comorbidity profiles with possible implications for child assessment and personalized early intervention.

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J Am Acad Child Adolesc Psychiatry. 2014;53:780-89.

MAPPING THE DEVELOPMENT OF THE BASAL GANGLIA IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Shaw P, de RP, Watson B, et al.

Objective The basal ganglia are implicated in the pathophysiology of attention-deficit/hyperactivity disorder (ADHD), but little is known of their development in the disorder. Here, we mapped basal ganglia development from childhood into late adolescence using methods that define surface morphology with an exquisite level of spatial resolution.

Method Surface morphology of the basal ganglia was defined from neuroanatomic magnetic resonance images acquired in 270 youth with DSM-IV-defined ADHD and 270 age- and sex-matched typically developing controls; 220 individuals were scanned at least twice. Using linear mixed model regression, we mapped developmental trajectories from age 4 through 19 years at approximately 7,500 surface vertices in the striatum and globus pallidus.

Results In the ventral striatal surfaces, there was a diagnostic difference in developmental trajectories (t = 5.6, p <.0001). Here, the typically developing group showed surface area expansion with age (estimated rate of increase of 0.54 mm2 per year, standard error [SE] 0.29 mm2 per year), whereas the ADHD group showed progressive contraction (decrease of 1.75 mm2 per year, SE 0.28 mm2 per year). The ADHD group also showed significant, fixed surface area reductions in dorsal striatal regions, which were detected in childhood at study entry and persisted into adolescence. There was no significant association between history of psychostimulant treatment and developmental trajectories.
Conclusions Progressive, atypical contraction of the ventral striatal surfaces characterizes ADHD, localizing to regions pivotal in reward processing. This contrasts with fixed, nonprogressive contraction of dorsal striatal surfaces in regions that support executive function and motor planning.

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J Am Acad Child Adolesc Psychiatry. 2014;53:745-60.

THREE-YEAR LATENT CLASS TRAJECTORIES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) SYMPTOMS IN A CLINICAL SAMPLE NOT SELECTED FOR ADHD.

Arnold LE, Ganocy SJ, Mount K, et al.

Objective This study aims to examine trajectories of attention-deficit/ hyperactivity disorder (ADHD) symptoms in the Longitudinal Assessment of Manic Symptoms (LAMS) sample.
Method The LAMS study assessed 684 children aged 6 to 12 years with the Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS) and rating scales semi-annually for 3 years. Although they were selected for elevated manic symptoms, 526 children had baseline ADHD diagnoses. With growth mixture modeling (GMM), we separately analyzed inattentive and hyperactive/impulsive symptoms, covarying baseline age. Multiple standard methods determined optimal fit. The (chi)2 and Kruskal-Wallis analysis of variance compared resulting latent classes/trajectories on clinical characteristics and medication.
Results Three latent class trajectories best described inattentive symptoms, and 4 classes best described hyperactive/impulsive symptoms. Inattentive trajectories maintained their relative position over time. Hyperactive/impulsive symptoms had 2 consistent trajectories (least and most severe). A third trajectory (4.5%) started mild, then escalated; and a fourth (14%) started severe but improved dramatically. The improving trajectory was associated with the highest rate of ADHD and lowest rate of bipolar diagnoses. Three-fourths of the mildest inattention class were also in the mildest hyperactive/impulsive class; 72% of the severest inattentive class were in the severest hyperactive/impulsive class, but the severest inattention class also included 62% of the improving hyperactive-impulsive class.
Conclusion An ADHD rather than bipolar diagnosis prognosticates a better course of hyperactive/impulsive, but not inattentive, symptoms. High overlap of relative severity between inattention and hyperactivity/impulsivity confirms the link between these symptom clusters. Hyperactive/impulsive symptoms wane more over time. Group means are insufficient to understand individual ADHD prognosis. A small subgroup deteriorates over time in hyperactivity/impulsivity and needs better treatments than currently provided.

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J Am Acad Child Adolesc Psychiatry. 2014;53:736-44.

IMPACT OF THE DSM-5 ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AGE-OF-ONSET CRITERION IN THE US ADOLESCENT POPULATION.

Vande Voort JL, He J-P, Jameson ND, et al.

Objective The present study aims to compare the prevalence and clinical correlates of DSM-IV versus DSM-5-defined attention-deficit/hyperactivity disorder (ADHD) and subtypes in a nationally representative sample of US youth based on the age-of-onset criterion.
Method The sample includes 1,894 participants 12 to 15 years of age from cross-sectional National Health and Nutrition Examination Survey (NHANES) surveys conducted from 2001 to 2004. Data on DSM-IV and DSM-5 criteria for ADHD were derived from administration of the parental ADHD module of the National Institute of Mental Health (NIMH) Diagnostic Interview Schedule for Children, Version IV (DISC-IV).

Results Extension of the age-of-onset criterion from 7 to 12 years led to an increase in the prevalence rate of ADHD from 7.38% (DSM-IV) to 10.84% (DSM-5). Youth with later age of onset did not differ from those with earlier age of onset in terms of severity and patterns of comorbidity. However, the group with later age of onset was more likely to be from lower income and ethnic minority families.
Conclusion The comparability of the clinical significance of the early and later age-of-onset groups supports the DSM-5 extension of the age-of-onset criterion in ADHD

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Korean J Pediatr. 2014;57:317-22.
PREVALENCE OF RESTLESS LEGS SYNDROME AND SLEEP PROBLEMS IN KOREAN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SINGLE INSTITUTION STUDY.
Kwon S, Sohn Y, Jeong S-H, et al.
Purpose: Attention deficit hyperactivity disorder (ADHD) is a common disorder in school-aged children. Patients with restless legs syndrome (RLS) often present with ADHD symptoms and vice versa. This study was the first to attempt to identify the prevalence of RLS and sleep problems in children with ADHD in Korea.
Methods: Patients diagnosed with ADHD were asked to complete a sleep questionnaire. The sleep questionnaire included items to help identify the presence of four typical symptoms that are used as diagnostic criteria for RLS.
Results: A total of 56 patients, including 51 boys and 5 girls (mean age, 10.7 years old) participated. Of these, 24 complained of pain, discomfort, or an unpleasant sensation in the legs. Based on the RLS diagnostic criteria, 2 patients were diagnosed with definite RLS and 4 with probable RLS. There were no significant differences in age, medication dosage, or neuropsychological test scores between the patients with and without RLS symptoms.
Conclusion: Approximately 42.9% of patients with ADHD presented with RLS symptoms and 7.1% of these were diagnosed with RLS. Patients with ADHD also experienced various other sleep disorders. Thus, appropriate assessment and treatment for sleep disorders in patients with ADHD is essential.

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Lancet. 2014 Jul;384:104.
THE REALITIES AND NEEDS OF CHILDREN LIVING WITH ADHD.
Anon.

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Neurologia. 2014.
PREVALENCE OF SLEEP DISORDERS IN PATIENTS WITH NEUROFIBROMATOSIS TYPE 1.
Marana Perez AI, Duat RA, Soto I, V, et al.
Introduction: Neurofibromatosis type 1 (NF1) is frequently associated with neurological disorders unrelated to neurofibromas, including sleep disorders.
Objectives: This article reviews the prevalence of sleep disorders in patients with NF1, compares rates to data reported in the literature, and analyses the relationship between cognitive disorder and attention deficit hyperactivity disorder (ADHD) in these patients.
Material and methods: Comparative retrospective study reviewing data collected between January 2010 and January 2012 from patients diagnosed with NF1 in a tertiary hospital.
Results: We included 95 paediatric patients with NF1 who completed the Bruni Sleep Disturbance Scale in Children. The overall prevalence of sleep disorders was 6.3%, which was lower than in the general paediatric population. Patients with NF1 and ADHD had a higher prevalence of sleep onset and maintenance disorders (18% vs 6.3%), sleep-wake transition disorders (12.5% vs 6.3%), and daytime sleepiness (12.5% vs 7.9%); differences were not statistically significant. A statistically significant difference was found in the subdomain of nocturnal hyperhidrosis (21.9% vs 6.3%, $P < 0.05$). Patients with NF1 and

IQ < 85 showed higher prevalence rates of daytime sleepiness (20% vs 6.7%) and of sleep hyperhidrosis (11% vs 0%).
Conclusions: The prevalence of sleep disorders in our cohort of patients with NF1 was no higher than in the general paediatric population, although some of these disorders are more common in cases with cognitive disorders or ADHD.

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Neurology. 2014;83:151-59.
VARIATIONS IN EEG DISCHARGES PREDICT ADHD SEVERITY WITHIN INDIVIDUAL SMITH-LEMLI-OPITZ PATIENTS.
Schreiber JM, Lanham DC, Trescher WH, et al.
Objective: We sought to examine the prevalence of EEG abnormalities in Smith-Lemli-Opitz syndrome (SLOS) as well as the relationship between interictal epileptiform discharges (IEDs) and within-subject variations in attentional symptom severity.
Methods: In the context of a clinical trial for SLOS, we performed cross-sectional and repeatedmeasure observational studies of the relationship between EEG findings and cognitive/behavioral factors on 23 children (aged 4-17 years). EEGs were reviewed for clinical abnormalities, including IEDs, by readers blinded to participants' behavioral symptoms. Between-group differences in baseline characteristics of participants with and without IEDs were analyzed. Within-subject analyses examined the association between the presence of IEDs and changes in attentiondeficit/ hyperactivity disorder (ADHD) symptoms.
Results: Of 85 EEGs, 43 (51%) were abnormal, predominantly because of IEDs. Only one subject had documented clinical seizures. IEDs clustered in 13 subjects (57%), whereas 9 subjects (39%) had EEGs consistently free of IEDs. While there were no significant group differences in sex, age, intellectual disability, language level, or baseline ADHD symptoms, autistic symptoms tended to be more prevalent in the "IED" group (according to Autism Diagnostic Observation Schedule-2 criteria). Within individuals, the presence of IEDs on a particular EEG predicted, on average, a 27% increase in ADHD symptom severity.
Conclusions: Epileptiform discharges are common in SLOS, despite a relatively low prevalence of epilepsy. Fluctuations in the presence of epileptiform discharges within individual children with a developmental disability syndrome may be associated with fluctuations in ADHD symptomatology, even in the absence of clinical seizures.

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Neuropsychiatr Dis Treat. 2014;10:1081-92.
CLUSTER-RANDOMIZED, CONTROLLED 12-MONTH TRIAL TO EVALUATE THE EFFECT OF A PARENTAL PSYCHOEDUCATION PROGRAM ON MEDICATION PERSISTENCE IN CHILDREN WITH ATTENTION-DEFCIT/HYPERACTIVITY DISORDER.
Montoya A, Hervas A, Fuentes J, et al.
Background: This multicenter, cluster-randomized, nonblinded study evaluated the effect of parental psychoeducation on medication persistence among children and adolescents with newly diagnosed attention-defcit/hyperactivity disorder (ADHD).
Methods: Patients received standard medication alone or medication plus a parental psychoeducation program, and were followed for 12 months. The primary endpoint was time to withdrawal or termination of medication due to any cause. Secondary endpoints included change in ADHD symptom severity, functional outcome, program satisfaction, and safety.
Results: A total of 208 patients completed the study, which was terminated early because recruitment had ceased. At 12 months, there was no significant difference between the psycho-education and control groups in the proportion of patients who discontinued pharmacologic treatment (13.2% versus 14.3%, respectively; size effect -0.3, P=0.34; hazard ratio 0.72, 95% confidence interval 0.36-1.43). Psychoeducation was associated with a significantly greater improvement in ADHD symptoms but not in functional outcome. Parental satisfaction with psychoeducation was high, and satisfaction with pharmacologic treatment was significantly greater in the psychoeducation group. There were no safety concerns.

Conclusion: No significant advantage for parental psychoeducation plus medication over medication alone in terms of time to medication withdrawal was observed. Psychoeducation had inconsistent but interesting effects on other outcomes.

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Neuropsychol Rehabil. 2014 Jul;1-17.

DAILY FUNCTIONING PROFILE OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVE DISORDER: A PILOT STUDY USING AN ECOLOGICAL ASSESSMENT.

Rosenblum S, Frisch C, Deutsh-Castel T, et al.

Children with attention-deficit hyperactivity disorder (ADHD) often present with activities of daily living (ADL) performance deficits. This study aimed to compare the performance characteristics of children with ADHD to those of controls based on the Do-Eat assessment tool, and to establish the tool's validity. Participants were 23 children with ADHD and 24 matched controls, aged 6-9 years. In addition to the Do-Eat, the Children Activity Scale-Parent (ChAS-P) and the Behavioral Rating Inventory of Executive Function (BRIEF) were used to measure sensorimotor abilities and executive function (EF). Significant differences were found in the Do-Eat scores between children with ADHD and controls. Significant moderate correlations were found between the Do-Eat sensorimotor scores, the ChAS-P and the BRIEF scores in the ADHD group. Significant correlations were found between performance on the Do-Eat and the ChAS-P questionnaire scores, verifying the tool's ecological validity. A single discriminant function described primarily by four Do-Eat variables, correctly classified 95.5% of the study participants into their respective study groups, establishing the tool's predictive validity within this population. These preliminary findings indicate that the Do-Eat may serve as a reliable and valid tool that provides insight into the daily functioning characteristics of children with ADHD. However, further research on larger samples is indicated

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Neuropsychopharmacologia Hungarica. 2014;16:91-97.

THE INFLUENCE OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER ON QUALITY OF LIFE: CASE REPORTS.

Gyongyver D, Judit B.

Recently the concept of Quality of Life has gained increasing importance in Psychiatry. Studies focusing on how much attention-deficit hyperactivity disorder (ADHD) - one of the most prevalent psychiatric disorders among children - affects the every day life found that children with ADHD had significantly lower Quality of Life than healthy controls or children with other psychiatric or physical disorders. In the current paper we present the case of two boys with ADHD and their families. These cases demonstrate that adequate treatment of the symptoms of ADHD can improve Quality of Life of the patients and their families, moreover, different life events can worsen the symptoms of ADHD. Professionals should ensure flexible treatment, which conforms to the above described processes.

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Neuropsychopharmacology. 2014 Jul.

DEVIATIONS FROM THE EXPECTABLE ENVIRONMENT IN EARLY CHILDHOOD AND EMERGING PSYCHOPATHOLOGY.

Humphreys KL, Zeanah CH.

Current frameworks for understanding the link between early adverse childhood experiences and later negative life outcomes, including psychopathology, focus on the mediating negative impact on brain and biological systems in the developing child resulting broadly from stress and trauma. While this approach is useful, we argue that the framework could be functionally extended by distinguishing the effects of two different types of negative input, both deviations from the expectable environment in early childhood. Specifically, we review the consequences of inadequate input (e.g., neglect/deprivation) and harmful input (e.g., abuse/trauma) on brain and biological development. We then review evidence on the differential links between each type of abnormal input to four selected domains of psychopathology (indiscriminate social behavior, posttraumatic stress disorder, attention-deficit/hyperactivity disorder, and conduct problems), and

consider potential mechanisms for inadequate and harmful input to lead to these outcomes. We conclude that the careful consideration of the type of deviation from the expected environment, while acknowledging the practical difficulties in assessing this, is likely to lead to clearer understanding of the mechanism of risk for psychopathology, and that tailored approaches to prevention and intervention may be informed by considering the unique consequences of inadequate and harmful input when experienced in early childhood. Neuropsychopharmacology Reviews accepted article preview online, 07 July 2014; doi:10.1038/npp.2014.165

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Neurotoxicol Teratol. 2014 Jul;44:81-88.

PRENATAL TOBACCO EXPOSURE AND RESPONSE INHIBITION IN SCHOOL-AGED CHILDREN: AN EVENT-RELATED POTENTIAL STUDY.

Boucher O, Jacobson JL, Burden MJ, et al.

Prenatal cigarette smoke exposure (PCSE) has been linked to problems in behavioral inhibition and attention deficit hyperactivity disorder in children in several epidemiological studies. We used event-related potentials (ERPs) to examine the effects of PCSE on neural correlates of inhibitory control of behavior. In a prospective longitudinal study on child development in the Canadian Arctic, we assessed 186 Inuit children (mean age=11.3years) on a visual Go/No-go response inhibition paradigm. PCSE was assessed through maternal recall. Potential confounders were documented from a maternal interview, and exposure to neurotoxic environmental contaminants was assessed from umbilical cord and child blood samples. PCSE was not related to behavioral performance on this simple response inhibition task. Nevertheless, this exposure was associated with smaller amplitudes of the N2 and P3 components elicited by No-go stimuli, suggesting an impairment in the neural processes underlying response inhibition. Amplitude of the No-go P3 component was also inversely associated with behavioral measures of externalizing problems and hyperactivity/impulsivity in the classroom. This study is the first to report neurophysiological evidence of impaired response inhibition in school-aged children exposed to tobacco smoke in utero. Effects were found on ERP components associated with conflict processing and inhibition of a prepotent response, indicating neurophysiological deficits that may play a critical role in the attention and behavior problems observed in children with PCSE.

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NeuroToxicology. 2014;44:121-31.

A META-ANALYSIS OF THE EVIDENCE ON THE IMPACT OF PRENATAL AND EARLY INFANCY EXPOSURES TO MERCURY ON AUTISM AND ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN THE CHILDHOOD.

Yoshimasu K, Kiyohara C, Takemura S, et al.

Although a measurable number of epidemiological studies have been conducted to clarify the associations between mercury exposure during embryo or early infancy and later incidences of autism spectrum disorders (ASD) or attention-deficit hyperactivity disorder (ADHD), the conclusion still remains unclear. Meta-analysis was conducted for two major exposure sources; i.e., thimerosal vaccines that contain ethylmercury (clinical exposure), and environmental sources, using relevant literature published before April 2014. While thimerosal exposures did not show any material associations with an increased risk of ASD or ADHD (the summary odds ratio (OR) 0.99, 95% confidence interval (CI) 0.80-1.24 for ASD; OR 0.91, 95% CI 0.70-1.13 for ADHD/ADD), significant associations were observed for environmental exposures in both ASD (OR 1.66, 95% CI 1.14-2.17) and ADHD (OR 1.60, 95% CI 1.10-2.33). The summary ORs were similar after excluding studies not adjusted for confounders. Moderate adverse effects were observed only between environmental inorganic or organic mercury exposures and ASD/ADHD. However, these results should be interpreted with caution since the number of epidemiological studies on this issue was limited and still at an early stage. Further studies focused on subjects with genetic vulnerabilities of developmental disorders are warranted for better understanding of the effects of such environmental exposures.

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Pediatr Neurol. 2014 Jul;51:31-35.

SLEEP DISORDERS IN CHILDREN WITH TOURETTE SYNDROME.

Ghosh D, Rajan PV, Das D, et al.

BACKGROUND: The objective of this study was to determine the frequency, nature, and impact of sleep disorders in children and adolescents with Tourette syndrome and to raise awareness about their possible inclusion as a Tourette syndrome comorbidity.

METHODS: Using a prospective questionnaire, we interviewed 123 patients of age </=21 years with a confirmed diagnosis of Tourette syndrome. Each completed questionnaire was then reviewed in accordance with Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, criteria for categorization to a form of sleep disorder.

RESULTS: Of the 123 patients with Tourette syndrome, 75 (61%) had comorbid attention deficit hyperactivity disorder and 48 (39%) had Tourette without attention deficit hyperactivity disorder. The sleep problems observed included problems in the nature of sleep, abnormal behaviors during sleep, and impact of sleep disturbances on quality of life. Within these cohorts, 31 (65%) of the 48 Tourette-only patients and 48 (64%) of the 75 Tourette + attention deficit hyperactivity disorder patients could fit into some form of Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, coded sleep disorders. Of the 48 Tourette + attention deficit hyperactivity disorder patients with sleep disorders, 36 (75%) had insomnia signs, which could be explained by the co-occurrence of attention deficit hyperactivity disorder and high stimulant use. However, 10 (32%) of the 31 Tourette-only patients with sleep disorders had insomnia irrespective of attention deficit hyperactivity disorder or medication use.

CONCLUSIONS: Sleep problems are common in children with Tourette syndrome irrespective of comorbid attention deficit hyperactivity disorder, justifying their inclusion as a comorbidity of Tourette syndrome.

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Pediatrics. 2014 Jul.

PARENTAL SMOKING DURING PREGNANCY AND ADHD IN CHILDREN: THE DANISH NATIONAL BIRTH COHORT.

Zhu JL, Olsen J, Liew Z, et al.

BACKGROUND: Prenatal maternal smoking has been associated with attention-deficit/hyperactivity disorder (ADHD) in children, but the causal nature of this association is still under scrutiny. We examined the association with maternal smoking and nicotine replacement use during pregnancy, using association with paternal smoking as a marker of potential genetic or social confounding.

METHODS: We included 84 803 singletons who participated in the Danish National Birth Cohort. Information on parental smoking was reported by the mothers during pregnancy. Children with ADHD were identified from the Danish Psychiatric Central Register, the Danish National Patient Register, and the Register of Medicinal Product Statistics by the International Classification of Diseases, 10th Revision diagnosis or medication. We also used hyperactivity/inattention score of the parent-reported Strengths and Difficulties Questionnaire, included in the 7-year follow-up of the National Birth Cohort.

RESULTS: Maternal and paternal smoking during pregnancy were associated with an elevated risk of ADHD defined by hospital diagnosis, medication, and hyperactivity/inattention score, but the association was stronger for maternal smoking than for paternal smoking. Compared with children born to nonsmoking mothers and smoking fathers, children born of smoking mothers and nonsmoking fathers had a higher risk of ADHD (adjusted hazard ratio = 1.26; 95% confidence interval, 1.03 to 1.53). We also saw a higher risk of ADHD in children of mothers who used nicotine replacement during pregnancy.

CONCLUSIONS: Our findings indicate that the association between prenatal maternal smoking and ADHD may overestimate a causal link, but nicotine exposure or related factors may still play a causal role.

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Personality and Individual Differences. 2014 Jul;65:36-41.

THE RELATIONSHIP BETWEEN TRAIT EMOTIONAL INTELLIGENCE AND ADHD SYMPTOMS IN ADOLESCENTS AND YOUNG ADULTS.

Kristensen HA, Parker JDA, Taylor RN, et al.

The present study examined the association between trait emotional intelligence (TEI) and ADHD symptomatology in samples of 1388 adolescents (ages 14–17 years) and 3313 young adults (ages 18–24 years). Consistent with the notion that difficulties in emotion processing and affect regulation are important features of ADHD, TEI was found to be a moderate to strong predictor in both samples. The TEI dimensions of stress management and adaptability uniquely predicted both hyperactivity–impulsive and inattentive symptomatology for both samples. Implications are discussed in terms of the usefulness of the TEI framework for enhancing understanding of the socio-emotional difficulties associated with ADHD symptoms and for informing interventions and coping strategies.

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Personality and Individual Differences. 2014 Jul;64:58-61.

LONGITUDINAL PREDICTION OF THE ONE-YEAR COURSE OF PRESCHOOL ADHD SYMPTOMS: IMPLICATIONS FOR MODELS OF TEMPERAMENT–ADHD ASSOCIATIONS.

Martel MM, Gremillion ML, Roberts BA, et al.

Despite the fact that Attention-Deficit/Hyperactivity Disorder (ADHD) is often conceptualized as an extreme trait, there remains controversy about the best way to understand associations between temperament traits and ADHD. The current study examines longitudinal associations between temperament traits and ADHD during early childhood in order to critically examine vulnerability and spectrum models of trait–ADHD associations. Study participants were 109 children between the ages of 3 and 6 and their primary caregivers and teachers/daycare providers, community-recruited for ADHD-related problems. Primary caregivers completed the Kiddie Disruptive Behavior Disorders Schedule semi-structured diagnostic interview at the initial appointment and one year later. At the initial appointment, primary caregivers completed the Child Behavior Questionnaire as a measure of child temperament traits. Results from the initial time point indicated that high neuroticism and high surgency were associated with inattentive and hyperactive–impulsive ADHD symptoms, and low effortful control was associated with hyperactive–impulsive ADHD symptoms. However, none of these traits predicted the one-year course of ADHD symptoms. Results are more consistent with a spectrum (vs. vulnerability) model of trait–psychopathology associations, suggesting that traits may not influence longitudinal course during early childhood.

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PLoS ONE. 2014;9.

FEEDBACK-RELATED NEGATIVITY IN CHILDREN WITH TWO SUBTYPES OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Gong J, Yuan J, Wang S, et al.

Objective: The current model of ADHD suggests abnormal reward and punishment sensitivity, although differences in ADHD subgroups are unclear. This study aimed to investigate the effect of feedback valence (reward or punishment) and punishment magnitude (small or large) on Feedback-Related Negativity (FRN) and Late Positive Potential (LPP) in two subtypes of ADHD (ADHD-C and ADHD-I) compared to typically developing children (TD) during a children's gambling task.

Methods: Children with ADHD-C (n = 16), children with ADHD-I (n = 15) and typically developing children (n = 15) performed a children's gambling task under three feedback conditions: large losses, small losses and gains. FRN and LPP components in brain potentials were recorded and analyzed.

Results: In TD children and children with ADHD-C, large loss feedback evoked more negative FRN amplitudes than small loss feedback, suggesting that brain sensitivity to the punishment and its magnitude is not impaired in children with ADHD-C. In contrast to these two groups, the FRN effect was absent in children with ADHD-I. The LPP amplitudes were larger in children with ADHD-C in comparison with those with ADHD-I, regardless of feedback valence and magnitude.

Conclusion: Children with ADHD-C exhibit intact brain sensitivity to punishment similar to TD children. In contrast, children with ADHD-I are significantly impaired in neural sensitivity to the feedback stimuli and in particular, to punishment, compared to TD and ADHD-C children. Thus, FRN, rather than LPP, is a reliable index of the difference in reward and punishment sensitivity across different ADHD-subcategories.

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PLoS ONE. 2014;9.

BRAIN VOLUMETRIC CORRELATES OF AUTISM SPECTRUM DISORDER SYMPTOMS IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

O'Dwyer L, Tanner C, Van Dongen EV, et al.

Autism spectrum disorder (ASD) symptoms frequently occur in subjects with attention deficit/hyperactivity disorder (ADHD). While there is evidence that both ADHD and ASD have differential structural correlates, no study to date has investigated these structural correlates within a framework that robustly accounts for the phenotypic overlap between the two disorders. The presence of ASD symptoms was measured by the parent-reported Children's Social and Behavioural Questionnaire (CSBQ) in ADHD subjects (n = 180), their unaffected siblings (n = 118) and healthy controls (n = 146). ADHD symptoms were assessed by a structured interview (K-SADS-PL) and the Conners' ADHD questionnaires. Whole brain T1-weighted MPRAGE images were acquired and the structural MRI correlates of ASD symptom scores were analysed by modelling ASD symptom scores against white matter (WM) and grey matter (GM) volumes using mixed effects models which controlled for ADHD symptom levels. ASD symptoms were significantly elevated in ADHD subjects relative to both controls and unaffected siblings. ASD scores were predicted by the interaction between WM and GM volumes. Increasing ASD score was associated with greater GM volume. Equivocal results from previous structural studies in ADHD and ASD may be due to the fact that comorbidity has not been taken into account in studies to date. The current findings stress the need to account for issues of ASD comorbidity in ADHD.

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PLoS ONE. 2014;9.

A MULTI-METHODOLOGICAL MR RESTING STATE NETWORK ANALYSIS TO ASSESS THE CHANGES IN BRAIN PHYSIOLOGY OF CHILDREN WITH ADHD.

De Celis AB, Hidalgo TS, Dies SP, et al.

The purpose of this work was to highlight the neurological differences between the MR resting state networks of a group of children with ADHD (pre-treatment) and an age-matched healthy group. Results were obtained using different image analysis techniques. A sample of n = 46 children with ages between 6 and 12 years were included in this study (23 per cohort). Resting state image analysis was performed using ReHo, ALFF and ICA techniques. ReHo and ICA represent connectivity analyses calculated with different mathematical approaches. ALFF represents an indirect measurement of brain activity. The ReHo and ICA analyses suggested differences between the two groups, while the ALFF analysis did not. The ReHo and ALFF analyses presented differences with respect to the results previously reported in the literature. ICA analysis showed that the same resting state networks that appear in healthy volunteers of adult age were obtained for both groups. In contrast, these networks were not identical when comparing the healthy and ADHD groups. These differences affected areas for all the networks except the Right Memory Function network. All techniques employed in this study were used to monitor different cerebral regions which participate in the phenomenological characterization of ADHD patients when compared to healthy controls. Results from our three analyses indicated that the cerebellum and mid-frontal lobe bilaterally for ReHo, the executive function regions in ICA, and the precuneus, cuneus and the clacarine fissure for ALFF, were the "hubs" in which the main inter-group differences were found. These results do not just help to explain the physiology underlying the disorder but open the door to future uses of these methodologies to monitor and evaluate patients with ADHD.

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PLoS ONE. 2014;9:e102249.

PREMARKET SAFETY AND EFFICACY STUDIES FOR ADHD MEDICATIONS IN CHILDREN.

Bourgeois FT, Kim JM, Mandl KD.

BACKGROUND: Attention-deficit hyperactivity disorder (ADHD) is a chronic condition and pharmacotherapy is the mainstay of treatment, with a variety of ADHD medications available to patients. However, it is unclear to what extent the long-term safety and efficacy of ADHD drugs have been evaluated prior to their market authorization. We aimed to quantify the number of participants studied and their length of exposure in ADHD drug trials prior to marketing.

METHODS: We identified all ADHD medications approved by the Food and Drug Administration (FDA) and extracted data on clinical trials performed by the sponsor and used by the FDA to evaluate the drug's clinical efficacy and safety. For each ADHD medication, we measured the total number of participants studied and the length of participant exposure and identified any FDA requests for post-marketing trials.

RESULTS: A total of 32 clinical trials were conducted for the approval of 20 ADHD drugs. The median number of participants studied per drug was 75 (IQR 0, 419). Eleven drugs (55%) were approved after <100 participants were studied and 14 (70%) after <300 participants. The median trial length prior to approval was 4 weeks (IQR 2, 9), with 5 (38%) drugs approved after participants were studied <4 weeks and 10 (77%) after <6 months. Six drugs were approved with requests for specific additional post-marketing trials, of which 2 were performed.

CONCLUSIONS: Clinical trials conducted for the approval of many ADHD drugs have not been designed to assess rare adverse events or long-term safety and efficacy. While post-marketing studies can fill in some of the gaps, better assurance is needed that the proper trials are conducted either before or after a new medication is approved.

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Prostaglandins Leukot Essent Fatty Acids. 2014 Jul;91:49-60.

EFFECT OF SUPPLEMENTATION WITH LONG-CHAIN OMEGA-3 POLYUNSATURATED FATTY ACIDS ON BEHAVIOR AND COGNITION IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD): A RANDOMIZED PLACEBO-CONTROLLED INTERVENTION TRIAL.

Widenhorn-Muller K, Schwanda S, Scholz E, et al.

OBJECTIVE: To determine whether supplementation with the long-chain omega-3 polyunsaturated fatty acids eicosapentaenoic (EPA) and docosahexaenoic acid (DHA) affects behavioral symptoms and cognitive impairments in children 6-12 years of age diagnosed with attention-deficit/hyperactivity disorder (ADHD).

STUDY DESIGN: The randomized, double-blind placebo-controlled 16 weeks trial was conducted with 95 children diagnosed with ADHD according to DSM-IV criteria. Behavior was assessed by parents, teachers and investigators using standardized rating scales and questionnaires. Further outcome variables were working memory, speed of information processing and various measures of attention. For a subgroup of 81 participants, erythrocyte membrane fatty acid composition was analyzed before and after the intervention.

RESULTS: Supplementation with the omega-3 fatty acid mix increased EPA and DHA concentrations in erythrocyte membranes and improved working memory function, but had no effect on other cognitive measures and parent- and teacher-rated behavior in the study population. Improved working memory correlated significantly with increased EPA, DHA and decreased AA (arachidonic acid).

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Psychiatr Pol. 2014;48:541-51.

AN INTERACTION BETWEEN A POLYMORPHISM OF THE SEROTONIN TRANSPORTER (5HTT) GENE AND THE CLINICAL PICTURE OF ADOLESCENTS WITH COMBINED TYPE OF ADHD (HYPERKINETIC DISORDER) AND YOUTH DRINKING.

Gorzkowska I, Gorzkowski G, Samochowiec A, et al.

Introduction: The combined type of ADHD and alcohol dependence are two different disorders. Research demonstrate that 45-55% of patients diagnosed with ADHD also suffer from comorbid substance abuse, and 11-55% of patients diagnosed with substance abuse suffer from undiagnosed ADHD. Alcohol is by far

the most widely used psychoactive substance in the European culture. The serotonin transporter (5HHT) gene has been implicated as one of the candidate genes in both disorders in recent molecular genetic research. Aim: The aim of the present study was to seek a common clinical and biological marker for hyperkinetic disorder and youth drinking.
Methods: The study was conducted between 2008 and 2012. The sample consisted of 100 combined type ADHD patients: 51 adolescents youth drinking and 100 individuals without mental disorders or addiction in a population-based group. The 5HHT gene polymorphism was examined using PCR (Polymerase Chain Reaction). Statistical analysis was conducted with STATISTICA.PL software (version 5.0.97) licensed by StatSoft, Inc. USA.
Results: A preferential trend for the "s" short allele of the investigated 5HHT gene polymorphism was observed in all the groups of adolescents compared to the population-based group of adults without alcohol dependence (p=0.01).
Conclusion: Based on the conducted study a provisional conclusion may be drawn that the presence of the short "s" allele of the 5HTT gene polymorphism may be a prognostic factor of impulsivity in ADHD and of predisposition to alcohol dependence.

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Psychiatry Res. 2014.

DIFFERENTIAL PERINATAL RISK FACTORS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BY SUBTYPE.

Park S, Cho S-C, Kim J-W, et al.

We compared the attention-deficit/hyperactivity disorder(ADHD) combined subtype (ADHD-C) to the ADHD inattentive subtype (ADHD-I) in terms of genetic, perinatal, and developmental risk factors as well as clinical and neuropsychological characteristics. A total of 147 children diagnosed with ADHD between the ages of 6 and 15 years participated in this study. The parents of the children completed the structured diagnostic interview, the ADHD Rating Scale-IV, the Children's Behavior Checklist, and structured questionnaires on perinatal risk factors, and the children underwent a neuropsychological test and were genotyped. A total of 502 children without ADHD were recruited from the community as a healthy control group. The ADHD-C children showed more severe externalizing symptoms, showed more deficits in a continuous performance test, and were more likely to have comorbid disorders. Maternal stress during pregnancy, postpartum depression, and changes in the primary caretaker during first 3 years were significantly associated with both ADHD-I and ADHD-C. The ADHD-I group was less likely to have received regular prenatal check-ups and more likely to have had postnatal medical illness than the ADHD-C group. There were no significant differences in the genotype frequencies of the dopamine transporter (DAT1) and the serotonin transporter -linked polymorphic region (5-HTTLPR) polymorphisms between ADHD-I and ADHD-C groups. This study shows that the inattentive subtype of ADHD is different from the combined subtype in many parameters including severity of symptoms, comorbidity, neuropsychological characteristics, and environmental risk factors.

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Psychiatry Res. 2014 Jun 2. pii: S0165-1781(14)00464-8.

EFFICACY OF A MULTIMODAL TREATMENT FOR DISRUPTIVE BEHAVIOR DISORDERS IN CHILDREN AND ADOLESCENTS: FOCUS ON INTERNALIZING PROBLEMS.

Masi G, Milone A, Paciello M, Lenzi F, Muratori P, Manfredi A, Polidori L, Ruglioni L, Lochman JE, Muratori F.

Disruptive Behavior Disorders (DBDs) are among the most common reasons for youth referrals to mental health clinics. Aim of this study is to compare short and medium term efficacy of a multimodal treatment program (MTP), compared to community care (treatment-as-usual, TAU). The sample included 135 youths with DBDs (113 males, age range 9-15 years, mean age 12±2.5 years) were assigned either to a MTP (n=64), or addressed to community care for a TAU (n=71). Outcome measures were the Child Behaviour Checklist (CBCL) and the Children's Global Assessment Scale (C-GAS). All subjects were assessed at the

baseline (T0), after 1-year treatment (T1) and after a 2-year follow-up (T2). Compared with patients receiving TAU, youths in the MTP showed, both at T1 and T2, significantly lower scores on CBCL Externalizing Scale, Internalizing Scale, Anxious/Depressed, Social Problems, and Aggressive Behavior, and higher scores at the C-GAS. Improvement in Internalizing Scales was particularly evident, with a shift from the clinical to the non-clinical range. Rate of use of mental health services and scholastic failure were reduced in the MTP. It is suggested that the improvement of the Internalizing symptoms is a crucial component of the therapeutic process in this MTP.

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Psychol Med. 2014 Jul;1-11.

CORTICAL THICKNESS AND INATTENTION/HYPERACTIVITY SYMPTOMS IN YOUNG CHILDREN: A POPULATION-BASED STUDY.

Mous SE, Muetzel RL, El MH, et al.

BACKGROUND: While many neuroimaging studies have investigated the neurobiological basis of attention deficit hyperactivity disorder (ADHD), few have studied the neurobiology of attention problems in the general population. The ability to pay attention falls along a continuum within the population, with children with ADHD at one extreme of the spectrum and, therefore, a dimensional perspective of evaluating attention problems has an added value to the existing literature. Our goal was to investigate the relationship between cortical thickness and inattention and hyperactivity symptoms in a large population of young children.

METHOD: This study is embedded within the Generation R Study and includes 6- to 8-year-old children (n = 444) with parent-reported attention and hyperactivity measures and high-resolution structural imaging data. We investigated the relationship between cortical thickness across the entire brain and the Child Behavior Checklist Attention Deficit Hyperactivity Problems score.

RESULTS: We found that greater attention problems and hyperactivity were associated with a thinner right and left postcentral gyrus. When correcting for potential confounding factors and multiple testing, these associations remained significant.

CONCLUSIONS: In a large, population-based sample we showed that young (6- to 8-year-old) children who show more attention problems and hyperactivity have a thinner cortex in the region of the right and left postcentral gyrus. The postcentral gyrus, being the primary somatosensory cortex, reaches its peak growth early in development. Therefore, the thinner cortex in this region may reflect either a deviation in cortical maturation or a failure to reach the same peak cortical thickness compared with children without attention or hyperactivity problems.

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Psychol Neurosci. 2014;7:159-62.

A POSSIBLE CORRELATION BETWEEN VESTIBULAR STIMULATION AND AUDITORY COMPREHENSION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Haghshenas S, Hosseini MS, Aminjan AS.

Twenty children, aged 10 to 12 years with attention-deficit/hyperactivity disorder (ADHD), were selected to study the effect of vestibular stimulation on auditory perception and sensitivity using the Integrated Visual and Auditory Continuous Performance Test (IVA CPT; a neuropsychological test that is applied in occupational therapy clinics). The present study examined children based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision. After obtaining guardian and parental consent, the children were enrolled in the study and randomly matched according to age across intervention and control groups. The IVA CPT was applied as a pre-test. The children in the intervention group then received vestibular stimulation during therapy sessions twice per week for 10 weeks. The IVA CPT assessment (post-test) was then applied in both groups. The mean pre- and post-test scores were compared across groups. The statistical analyses revealed a significant difference in improvement in auditory comprehension. In conclusion, the present findings suggest that vestibular training is a reliable and

powerful treatment option for ADHD, especially when combined with other training. Stimulating the sense of balance highlights the important interaction between inhibition and cognition.

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Res Autism Spectr Disord. 2014 Jul;8:881-89.

IMPAIRED SUSTAINED ATTENTION, FOCUSED ATTENTION, AND VIGILANCE IN YOUTHS WITH AUTISTIC DISORDER AND ASPERGER'S DISORDER.

Chien YL, Gau SS-F, Chiu YN, et al.

The study compared the attention-deficit/hyperactivity disorder (ADHD) related clinical symptoms and a wide-ranging attention performance in 216 youths with autistic disorder (autism), 138 youths with Asperger's disorder (AD) and 255 typically-developing youths. The diagnosis of autism and AD were made based on the clinical assessments according to the DSM-IV criteria and confirmed by the Autism Diagnostic Interview-Revised. All the participants were assessed with the Conners' Continuous Performance Test (CCPT) and the questionnaires about ADHD, oppositional, and autistic symptoms. All indices of the CCPT were analyzed based on a recently developed factor structure, including focused attention, cognitive impulsivity, sustained attention, and vigilance. We found that compared with typically-developing youths, youths with autism and AD showed more inattentive, hyperactive/impulsive, and oppositional symptoms, and performed worse in focused attention and sustained attention as assessed by the CCPT. Youths with AD also showed more oppositional symptoms than youths with autism. Moreover, youths with autism had poorer focused attention than youths with AD; but, youths with AD had more impaired sustained attention. Our results validate different manifestations of ADHD-related symptoms and attention performance between youths with autism and youths with AD and suggest intervention for youths with autism spectrum disorders should consider these specific measures.

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Res Dev Disabil. 2014 Jul;35:1658-65.

ASSOCIATION OF DOPAMINE GENE VARIANTS, EMOTION DYSREGULATION AND ADHD IN AUTISM SPECTRUM DISORDER.

Gadow KD, Pinsonneault JK, Perlman G, et al.

The aim of the present study was to evaluate the association of dopaminergic gene variants with emotion dysregulation (EMD) and attention-deficit/hyperactivity disorder (ADHD) symptoms in children with autism spectrum disorder (ASD). Three dopamine transporter gene (SLC6A3/DAT1) polymorphisms (intron8 5/6 VNTR, 3'-UTR 9/10 VNTR, rs27072 in the 3'-UTR) and one dopamine D2 receptor gene (DRD2) variant (rs2283265) were selected for genotyping based on à priori evidence of regulatory activity or, in the case of DAT1 9/10 VNTR, commonly reported associations with ADHD. A sample of 110 children with ASD was assessed with a rigorously validated DSM-IV-referenced rating scale. Global EMD severity (parents' ratings) was associated with DAT1 intron8 (?p² = .063) and rs2283265 (?p² =.044). Findings for DAT1 intron8 were also significant for two EMD subscales, generalized anxiety (?p² = .065) and depression (?p² =.059), and for DRD2 rs2283265, depression (?p² =.053). DRD2 rs2283265 was associated with teachers' global ratings of ADHD (?p² =.052). DAT1 intron8 was associated with parent-rated hyperactivity (?p² =.045) and both DAT1 9/10 VNTR (?p² = .105) and DRD2 rs2283265 (?p 2 =.069) were associated with teacher-rated inattention. These findings suggest that dopaminergic gene polymorphisms may modulate EMD and ADHD symptoms in children with ASD but require replication with larger independent samples.

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Rev Bras Psiquiatr. 2014 Jul;0:0.

ADHD INATTENTIVE SYMPTOMS MEDIATE THE RELATIONSHIP BETWEEN INTELLIGENCE AND ACADEMIC PERFORMANCE IN CHILDREN AGED 6-14.

Costa DD, Paula JJ, Alvim-Soares Junior AM, et al.

Objective: Fluid intelligence and the behavioral problems of attention-deficit/hyperactivity disorder (ADHD) are related to academic performance, but how this association occurs is unclear. This study aimed to assess mediation and moderation models that test possible pathways of influence between these factors.

Methods: Sixty-two children with ADHD and 33 age-matched, typically developing students were evaluated with Raven's Colored Progressive Matrices and the spelling and arithmetic subtests of the Brazilian School Achievement Test. Dimensional ADHD symptomatology was reported by parents.

Results: Our findings suggest that fluid intelligence has a significant impact on academic tests through inattention. The inattentive dimension was the principal behavioral source of influence, also accounting for the association of hyperactive-impulsive manifestations with school achievement. This cognitive-to-behavioral influence path seems to be independent of diagnosis related group, and gender, but lower socioeconomic status might increase its strength.

Conclusion: Fluid intelligence is a relevant factor in the influence of ADHD behavioral symptoms on academic performance, but its impact is indirect. Therefore, early identification of both fluid intelligence and inattentive symptoms is of the utmost importance to prevent impaired academic performance and future difficulties in functioning.

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Rev Psiquiatr Clin. 2014;41:34-39.

LISDEXAMFETAMINE DIMESYLATE IN THE TREATMENT OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER: PHARMACOKINETICS, EFFICACY AND SAFETY IN CHILDREN AND ADOLESCENTS.

Mattos P.

Background: Psychostimulants (methylphenidate and amphetamines) are considered first-line therapy for attention-deficit/hyperactivity disorder (ADHD). Lisdexamfetamine dimesylate (LDX) is a new psychostimulant approved for the treatment of ADHD in Brazil. The pharmacologically active fraction, d-amphetamine, is gradually released by hydrolysis of the LDX prodrug. Objectives: To perform a systematic review of the literature of the efficacy and safety of LDX in the treatment of ADHD in children and adolescents.

Methods: Medline/PubMed searches for "d-amfetamine", "lisdexamfetamine" and "lisdexamfetamine dimesylate" were conducted including articles available from January 2000 to November 2013. Additional references were identified using references listed in those articles. Further data on LDX were requested from its manufacturer.

Results: Thirty-one papers were found related to ADHD treatment in children and adolescents.

Discussion: The therapeutic benefits of LDX in children with ADHD are achieved as early as 1.5 hours after its administration and last for up to 13 hours, with efficacy comparable or superior to that of other available psychostimulants. The literature also reports efficacy in long-term treatment, with safety and tolerability profiles comparable to those of other stimulants used for the treatment of ADHD. Most of the adverse events associated with LDX are considered to be mild or moderate in severity, with the most common being loss of appetite and insomnia.

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Schizophr Res. 2014;157:48-54.

EXECUTIVE ATTENTION IMPAIRMENT IN ADOLESCENTS WITH SCHIZOPHRENIA WHO HAVE USED CANNABIS.

Epstein KA, Kumra S.

Objective: Repeated exposure to cannabis in nonpsychotic adolescents is associated with impairments in executive control of attention, similar to those observed in young adults with first-episode schizophrenia. To assess the impact of recurrent exposure to cannabis on cognitive function, this study characterized

attention performance in both nonpsychotic adolescents and adolescents with early-onset schizophrenia (EOS).
Method: The Attention Network Test, a standard procedure that estimates the functional state of neural networks controlling the efficiency of three different attentional behaviors (alerting, orienting, and executive attention), was administered to four groups of participants: (1) adolescents with EOS and comorbid cannabis use disorder (EOS. +. CUD; n. = 18), (2) "Pure" schizophrenia (EOS; n. = 34), (3) "Pure" cannabis use disorder (CUD; n. = 29), and (4) Healthy controls (HC; n. = 53). Task performance was examined with a 2. null. 2 design (EOS. + versus EOS. - and CUD. + versus CUD. -) using multivariate analysis of covariance. Correlative analyses were conducted between executive attention performance and measures of surface area in the right anterior cingulate cortex.
Results: A significant EOS. null. CUD interaction was observed. In the executive attention network, adolescents with EOS. +. CUD showed reduced efficiency relative to adolescents with pure EOS, whereas no group differences were found between adolescents with pure CUD and HC. Less efficient executive attention was significantly associated with smaller surface area in the right caudal anterior cingulate cortex in EOS. +. CUD.
Conclusions: These preliminary data suggest that the presence of CUD has a moderating effect on attentional performance in adolescents with schizophrenia compared to nonpsychotic adolescents. These deficits could have a role in difficulties with self-regulation and predisposition to substance misuse in this patient group. The anatomic substrate of this cognitive deficit may be related to surface area in the right caudal anterior cingulate cortex.

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Sleep. 2011;34:A276.

CONTRIBUTIONS OF CIRCADIAN TENDENCIES AND BEHAVIORAL PROBLEMS TO SLEEP ONSET INSOMNIA IN CHILDREN WITH ADHD.

Gruber R, Carrier J.

Introduction: Attention-deficit/hyperactivity disorder (ADHD) is characterized by impulsivity/hyperactivity and inattention. It is estimated to occur in 3-7.5% of school-aged children, thus making ADHD one of the most prevalent child psychiatric conditions. Although the presence of Sleep-Onset Insomnia has been noted among 1/3 of children with ADHD, the causes of such sleep issues remain unclear. Within the current literature, both biological and behavioral explanations for sleep problems in this population have been advanced, suggesting different interventional strategies, depending on the pathophysiological mechanism that is in fact at play. The goal of this study was to determine the relative contributions of biological (circadian tendencies) and behavioral (externalizing problems) factors to sleep onset insomnia experienced by children with ADHD.
Methods: 75 children (26 ADHD, 49 Controls), aged 7 to 11 years old (mean age = 8.61, SD = 1.27), participated in the study. Participants were asked to cease medication for the duration of the study and to avoid consuming products containing caffeine (such as chocolate or cola). Sleep was evaluated using polysomnography and the Child Sleep Habits Questionnaire. Externalizing problems were evaluated using the Child Behavioral Checklist and circadian tendency was evaluated using Child Morning-Evening Preference Scale. ADHD was diagnosed using DSMIV criteria.
Results: Multiple Linear Regression Analyses was used to determine the contributions of externalizing problems versus circadian tendencies to sleep onset delay and bedtime resistance. Externalizing problems yielded significant independent contributions only to the explained variance in parental reports of bedtime resistance, whereas an evening circadian tendency contributed both to parental reports of sleep onset delay and to PSG-measured sleep-onset latency.
Conclusion: Externalization and circadian tendency were associated with a different bedtime problems. Thus, circadian phase delay and bedtime refusal may both be common, but are two distinct problems. As such, each may require a different interventional strategy.

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Sleep. 2011;34:A275.

SLEEP DISTURBANCE IN CHILDREN AND ADOLESCENTS WITH ADHD: UNIQUE EFFECTS OF MEDICATION, ADHD SUBTYPE AND COMORBID STATUS.

Helwig JR, Meltzer LJ, Mindell JA, et al.

Introduction: ADHD is estimated to affect 3% to 5% of school-aged individuals, with 11% to 37% reporting sleep disturbance. Disturbed sleep can result in daytime sleepiness and behavioral difficulties that affect cognitive functions in children, including attention and memory, as well as exacerbate symptoms of ADHD. This study aimed to determine the prevalence of ICD-9 sleep disorders, prescribed sleep medication, and complaints of sleep problems as diagnosed by pediatric primary care providers in children and adolescents with ADHD across medication, ADHD subtype, and comorbid status.

Methods: Electronic medical records were reviewed for 3,478 children and 2,403 adolescents. Information was collected regarding ICD-9 sleep diagnoses, medications potentially used to treat sleep disorders, demographic variables, medications commonly used to treat symptoms of ADHD, ICD-9 ADHD subtype, and comorbidity. Reports of sleep problems were also examined in 280 children and 276 adolescents.

Results: Children were more likely to be diagnosed with a sleep disorder if they had ADHD with hyperactivity (ADHD-H; B = 0.554, p<.001) or an externalizing comorbidity (EC; B = 0.407, p<.05); adolescents were more likely to be diagnosed with a sleep disorder if they had an internalizing comorbidity (IC; B = 2.520, p<.01) or EC (B = 0.929, p<.001). Children were more likely to be prescribed a sleep medication if they had ADHD-H (B = 0.925, p<.001), IC (B = 0.975, p<.01), EC (0.848, p<.001), IC and EC (B = 1.547, p<.05), were prescribed a stimulant medication (SM; B = 0.433, p<.001), non-stimulant medication (NM; B = 0.619, p<.05), or SM and NM (B = 0.904, p<.001). Adolescents were more likely to be prescribed a sleep medication if they were also prescribed a SM (B = 0.942, p<.001), SM and NM (B = 1.077, p<.001), diagnosed with an IC (B = 1.291, p<.001), EC (B = 1.035, p<.001), or ADHD-H (B = 0.614, p<.001). Adolescents diagnosed with both an IC and EC (B = 2.515, p<.01) were more likely to report a sleep problem.

Conclusion: This is one of the first studies to highlight the subgroups of children and adolescents with ADHD more likely to exhibit sleep disturbance across a large primary care network. These risk factors and their subsequent effects on the severity of symptoms associated with ADHD must be considered when assessing and treating children and adolescents with ADHD. Future studies should investigate how sleep disturbance is evaluated and treated in this population in the primary care setting.

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Sleep. 2011;34:A273.

QUANTITATIVE ASSESSMENT OF EPILEPTIC FORM DISCHARGES IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Bondugula C, Rao SC, McCarthy V, et al.

Introduction: To identify and quantify the distribution of epileptiform discharges in patients with Attention Deficit Hyperactivity Disorder (ADHD) presenting to a pediatric sleep medicine center for nocturnal video-polysomnography (PSG) because of a complaint of snoring, multiple awakenings, witnessed apneas, daytime sleepiness or restless sleep.

Methods: The PSG of fifty- five children with ADHD (33 male, 22 female and mean age=6.8years) were identified retrospectively and evaluated from January 2008 to June 2010 for epileptiform discharges using scalp electroencephalography (EEG). Forty six patients were on stimulants. Fifty- five non-ADHD patient controls were age, sex, Respiratory Disturbance Index (RDI), and Periodic Limb Movement Index (PLMI) matched. Polysomnographs were studied for epileptiform discharges using the same montages.

Results: ADHD patients had a significant greater likelihood of EDs compared to controls (p= 0.000) specifically, 32 (58.18%) ADHD patients had epileptiform discharges (EDs) with a (range from 3- 984, and mean= 71), and 23 (41.82%) were normal. Nine (16.34%) controls had EDs with a (range from 4- 21 and mean= 10), and 46 (83.66%) were normal. Of the 46 ADHD patients who were on stimulants, 28(60.9%) had EDs with a (range from 3- 984, and mean= 77), and 18(41.86%) had no EDs. Of the 9 ADHD patients who were not on stimulants, 4(44.4%) had EDs with a (range from 8- 97 and mean= 32), and 5 (55.6%) had no EDs, (p=0.46).

Conclusion: Children with ADHD had more epileptiform discharges than age, sex, RDI, and PLMI matched controls. Our findings show that ADHD is associated with epileptiform abnormalities on EEG.

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Sleep. 2012;35:A341.

ALERTNESS AND DRIVING PERFORMANCE IN ADULTS AFFECTED BY ATTENTION DEFICIT DISORDER/HYPERACTIVITY (ADHD).

Philip P, Bioulac S, Capelli A, et al.

Introduction: Attention Deicit Disorder / Hyperactivity (ADHD) is a neurodevelopmental disorder characterized by a triad of symptoms involving hyperactivity, impulsivity and inattention. Several studies in children with ADHD showed a high prevalence of excessive daytime sleepiness. To our knowledge, no study has objectively assessed sleepiness in adults with ADHD. Moreover, it has been shown that adults with ADHD were at risk for driving accidents. The objectives of this study are to quantify objective sleepiness and its impact on driving performance in ADHD adult patients.

Methods: Nocturnal polysomnography was performed to identify potential sleep disorder. The next day patients were submitted to a Maintenance Wakefulness Test (MWT) at 10H, 12H, 14H, 16H to examine their level of daytime sleepiness. After a training of 15 minutes, a driving test of one hour was carried out at 17H on the simulator F2300R (INRETS / Ifsttar-Faros) to evaluate driving performance.

Results: 15 subjects with ADHD were included (age (mean (plus or minus) SE) = 33.3 (plus or minus) 2.6). They were divided into 2 groups according to their level of sleepiness at the MWT: the nullsleepynull group consisted of eight subjects (mean sleep latency (SL) = 23.2 (plus or minus) 1.3 minutes) and the nullalertnull group included 7 subjects (LE = 37 (plus or minus) 1.1 minutes). These two groups differ signiicantly at the MWT (F (1, 13) = 65.8, p <0.001). The nullsleepynull group exhibited more inappropriate line crossings (154.3 (plus or minus) 84) that the nullalertnull group (56.3 (plus or minus) 36.8) (F (1, 13) = 8.1, p <0.05). Performances over time decreased signiicantly in the nullsleepy groupnull when they remained stable in the nullalert groupnull (F (2, 26) = 13.35, p <0.001).

Conclusion: In our sample, half of the patients suffer of excessive daytime sleepiness, which deteriorates signiicantly their driving performance.

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Sleep. 2012;35:A374.

ASSESSING THE IMPACT OF METHYLPHENIDATE ON SLEEP IN CHILDREN WITH ADHD USING POLYSOMNOGRAPHY AND ACTIGRAPHY.

Gendron M, Rusak B, Rajda M, et al.

Introduction: Stimulant medications, such as methylphenidate hydrochloride (MPH), are the most widely used treatment for Attention- Deicit/Hyperactivity Disorder (ADHD). Although MPH can reduce symptoms of ADHD, it can also disrupt children's sleep. Previous studies reported effects of MPH on sleep duration and latency as measured with actigraphy, but results obtained using polysomnography (PSG) have been inconsistent.

Methods: In this study, 30 medication-naive children (mean age=8.2 years, 24 males) who were newly diagnosed with ADHD participated in a placebo-controlled trial of MPH treatment. Data related to sleep quality were obtained using actigraphy recorded every night for four weeks and PSG recorded in a sleep laboratory, once after two weeks of MPH and once after two weeks of placebo treatment.

Results: Results were analyzed using repeated measures MANOVAs comparing MPH to placebo treatment. Results from actigraphy indicated that sleep duration was reduced [F(1,25)=13.18, (rho)<0.01] and sleep latency lengthened signiicantly [F(1,25)=13.46, (rho)<0.01] during MPH treatment relative to placebo, while sleep eficiency, night awakenings, and activity level did not differ between conditions ((rho)>0.05). The PSG results for the same parameters comparing placebo and MPH treatments did not reach statistical signiicance [F(4, 26)=.161, (rho)>0.05]; however, there were trends toward treatment effects on sleep duration, latency, eficiency, and night awakenings. PSG recordings revealed no statistically signiicant differences in sleep architecture between conditions [F(6, 24)=.154, (rho)>0.05].

Conclusion: Although PSG is considered the gold standard for sleep assessment, results from laboratory PSG studies did not match those from actigraphy, which were obtained in the children's usual environment. These results may indicate that PSG recordings in children with ADHD could be affected by interactions among the recording environment, drug treatment, and clinical condition. It is important to establish the relevance of either method by comparing results from each approach to the impacts of MPH on daytime functioning of children undergoing treatment for ADHD.

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Sleep. 2013;36:A375.

SLEEP DISORDERS AND SLEEP QUALITY IN SCHOOL CHILDREN WITH ADHD.

Carlos LM, Morales-Gallardo J, Medellin-Puyou S, et al.

Introduction: Sleep disturbances are common in Attention Deicit Hyperactivity Disorder (ADHD). Up to 70% of parents of children with ADHD report on sleep-related problems in their children, being the most common resistance going to bed, dificulty returning to wakefulness, nocturnal awakenings and daytime sleepiness. This study aimed to compare the quality of sleep and the presence of sleep disorders among school children with ADHD and healthy children.

Methods: We selected a group of 25 school boys with ADHD under pharmacological treatment and without comorbidity and a group of 25 healthy students. Kiddie SADS was used to establish the diagnosis of ADHD and/or absence of other disorders. The sleep quality and sleep disturbances were assessed using the Children's Sleep-Wake Scale, the Pediatric Sleep Questionnaire and Sleep Disorders Scale for Children.

Results: The ADHD group showed signiicantly greater dificulties initiating and maintaining of sleep (12.6(plus or minus)4.5 vs. 9.9(plus or minus)2.7, t=2.4, df 48, p=0.01). They tended to have more symptoms related to disorders the sleep-wake transition (11.2(plus or minus)4.5 vs. 9.1(plus or minus)3.2, t=1.9, df 48, p=0.06) and excessive sleepiness (8.4(plus or minus)3.5 vs. 6.9(plus or minus)2.5, t=1.7, df 48, p=0.09). They also showed more trouble going to bed (21.6(plus or minus)6.8 vs. 25.0(plus or minus)3.7, t= -2.2, df 48, p=0.03), falling asleep (24.4(plus or minus)5.8 vs. 2.7(plus or minus)2.9, t= -2.3, df 48, p=0.02), staying asleep (28.2(plus or minus)6.8 vs. 31.5 (plus or minus)4.2, t= -2.0, df 48, p=0.04), to wake up (17.6(plus or minus)7.2 vs. 21.5(plus or minus)6.3, t = -2.0, df 48, p=0.05) and snoring (0.68 (plus or minus) 1.0 vs. 0.2(plus or minus)0.5, t=2.0, df 48, p=0.04).

Conclusion: Children with ADHD under pharmacological treatment still have sleep problems, such as dificulty initiating and maintaining sleep, daytime sleepiness, and snoring.

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Sleep. 2013;36:A310.

THE RELATIONSHIP BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND SLEEP DISORDERED BREATHING IN PEDIATRIC POPULATIONS: A META-ANALYSIS.

Sedky K, Bennett D, Carvalho K.

Introduction: Some researchers have observed elevated comorbidity among children and adolescents with attention deicit hyperactivity disorder (ADHD) and sleep disordered breathing (SDB). However, others have debated this relationship. The objective of this meta-analysis is to evaluate the extent to which SDB anAd DHD are related.

Methods: PubMed/Medline, PsychInfo and Cochrane data bases were searched using the key words nullattention deicit hyperactivity disordernull or nullADHDnull and nullobstructive sleep apneanull or nullOSAnull or nullsleep disordered breathingnull or nullSDBnull. English language publications through September 2012 were surveyed. A meta-analysis was conducted to assess the relationship between SDB and ADHD.

Results: Eighteen studies satisied the inclusion criteria. This represented 1,113 children in the clinical group (874 diagnosed with SDB who were examined for ADHD symptoms; 239 diagnosed with ADHD who were examined for SDB) and 1,405 in the control-group. Findings indicate that there is a medium relationship between ADHD and SDB (Hedges' g = 0.57, 95% conidence interval: 0.36-0.78; p=0.000001).

Although the use of a high AHI cut-off was associated with lower effect sizes, child age, gender and body mass index did not moderate the relationship.
Conclusion: Patients with ADHD symptomatology should receive SDB screening, as it is possible that their ADHD symptoms are related to SDB. Treatment of SDB coexisting with ADHD aims to decrease clinical symptoms, reduce pharmacotherapy, and promote better health.

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Social Development. 2014 May;23:288-305.
SOCIAL SELF-CONTROL, EXTERNALIZING BEHAVIOR, AND PEER LIKING AMONG CHILDREN WITH ADHD-CT: A MEDIATION MODEL.
Rosen PJ, Vaughn AJ, Epstein JN, et al.
This study investigated the role of externalizing behavior as a mediator of the relation between social self-control and peer liking among children with attention-deficit/hyperactivity disorder-combined type (ADHD-CT). A model was proposed whereby externalizing behavior would fully statistically account for the direct relation of social self-control to peer liking. One hundred seventy-two children ages 7.0–9.9 years with ADHD-CT were rated by their teachers regarding their social self-control and by their parents and teachers regarding their rates of externalizing behavior. Same-sex classmates provided ratings of overall liking. Structural equation modeling was used to assess the proposed model. Results supported the proposed model of externalizing behavior as fully statistically accounting for the relation of social self-control to peer liking. This study demonstrated the crucial role that externalizing behaviors play in the social impairment commonly seen among children with ADHD-CT.

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Trials. 2014;15:269.
DO CHILDREN WITH CEREBRAL PALSY BENEFIT FROM COMPUTERIZED WORKING MEMORY TRAINING? STUDY PROTOCOL FOR A RANDOMIZED CONTROLLED TRIAL.
Lohaugen GC, Beneventi H, Andersen GL, et al.
BACKGROUND: Cerebral palsy (CP) is the most common motor disability in childhood (2 to 3 per 1000 live births), and is frequently accompanied by cognitive impairments and behavioural problems. Children with CP are at increased risk of attention deficit disorder with or without hyperactivity (Attention Deficit Disorder (ADD)/Attention Deficit Hyperactivity Disorder (ADHD)) including working memory deficits. The primary aim of this study is to evaluate if cognitive training may improve working memory in children with CP.
METHODS/DESIGNS: The study is an investigator-blinded, randomized controlled trial with a stepped-wedge design that will include 115 schoolchildren with CP. Eligible for participation are children with CP, aged 7 to 15 years, who are able to follow instructions and handle a computer mouse. Exclusion criteria are the presence of photosensitive epilepsy, Gross Motor Function Classification System (GMFCS) level V (most severe CP) (Phys Ther 80: 974-985, 2000) and severe visual or hearing impairments. Following assessment of eligibility and baseline cognitive assessment the participants will be randomized to either cognitive working memory training or treatment-as-usual ('control group'). The intervention is a computer-based working memory training program consisting of 25 daily sessions to be performed over a 5 to 6-week period at home. A neuropsychological assessment will be performed before and 4 to 6 weeks after completed training. When the latter assessment has been completed in the intervention group, the 'control group' will start on the same training program. Both groups will meet for a final neuropsychological assessment six months after completed training by an examiner unaware of group adherence.
DISCUSSION: There is limited evidence for the effect of most interventions in children with CP, and evidence is completely lacking for interventions aiming to improve deficits in cognition, learning and behaviour. The proposed multicenter study, will bring forth comprehensive information about cognitive, neuropsychological, and daily-life functioning in children with CP aged between 7 and 15 years. In addition, the study will be the first to evaluate the effects of an intervention method to improve working memory in

children with CP. If successful, computer-based working memory training may represent an efficient and cost-effective intervention for this group of children.
TRIAL REGISTRATION: ClinicalTrials.gov Identifier: NCT02119364

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OGGETTO: **CONTINUITÀ TERAPEUTICA PER L'USO DI METILFENIDATO E ATOMOXETINA NEL PAZIENTE CON ADHD AL COMPIMENTO DELLA MAGGIORE ETÀ**

E' con soddisfazione che comunichiamo che nella seduta del 21-23 luglio u.s. la Commissione Tecnico Scientifica dell'Agenzia Italiana del Farmaco ha espresso parere favorevole alla Ns richiesta di inserimento del metilfenidato e dell'atomoxetina nella Lista dei farmaci rimborsabili prevista dalla Legge 648/96. La procedura era iniziata in data 23 gennaio u.s. quando, recependo le aspettative e il disagio di molti pazienti, delle loro famiglie e degli operatori sanitari, abbiamo presentato, formale richiesta supportata da appropriata documentazione.

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dal verbale Esiti Ufficio Ricerca Sperimentazioni Cliniche CTS 21, 22, 23 luglio 2014 pagina 2:

2 Richiesta delucidazioni in merito al parere espresso dalla CTS riguardo all'istanza di inserimento di metilfenidato e atomoxetina per il *"trattamento del disturbo da deficit dell'attenzione e iperattività (ADHD) negli adulti già in trattamento farmacologico prima del compimento dei 18 anni di età"*.

Parere CTS: parere favorevole (lista classica)

http://www.agenziafarmaco.gov.it/it/content/riunione-commissione-tecnico-scientifica-cts-56

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Maurizio Bonati,
Responsabile Dipartimento di Salute Publbica

Silvio Garattini
Direttore

IRCCS Istituto di Ricerche Farmacologiche Mario Negri, Milano

Mother & Child Lab (@MumChild_IRFMN)

29/07/14 16:07
Metilfenidato rimborsato per #ADHD adulto in lista 648/96: @Aifa_ufficiale ha approvato richiesta @MarioNegriIRCCS goo.gl/IzNaST

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http://dx.doi.org/10.4236/ojpsych.2014.43028

Scientific Research

Validation of the Italian Version of the Developmental Disability-Child Global Assessment Scale (DD-CGAS)

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Abstract

***Objective*: The aim of this study is to validate the Italian version of the Developmental Disability-Child Global Assessment Scale (DD-CGAS), a scale developed to assess global functioning in children with Autism Spectrum Disorders (ASDs). *Methods*: Following the validation procedures used for the English version of the scale, inter-rater reliability, temporal stability and convergent validity were assessed in a group of 48 children with ASD and temporal stability in a subset of 42 subjects. *Results*: Inter-rater reliability and temporal stability (ICC) were respectively 0.78 and 0.79; effect size for convergent validity were moderate to large; the pre-post DD-CGAS change had an effect size of 0.59. *Conclusions*: The Italian version of the DD-CGAS is a reliable instrument for measuring global functioning of children with ASD.**

Keywords

Assessment, Autism, Children, Functioning, Pervasive Developmental Disorder, Italian

1. Introduction

The alteration of typical functioning of an individual represents a critical aspect of mental illness: it is funda-

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mental for the diagnosis of most psychiatric disorders, because the mere presence of symptoms—in the absence of impaired functioning—is not sufficient to configure a disease state. The recent tendency, also from a therapeutic point of view, is to consider the impairment of functioning levels to be increasingly important, rather than the presence or intensity of symptoms, as objective evidence and measurement of the treatment's efficacy.

It is particularly important to record treatment effects on functioning level for children with autism spectrum disorders (ASDs) [1]: although there aren't, at present, any curative treatments for autism spectrum disorders' core symptoms [2], evidence suggests that both behavioral and pharmacological treatments can significantly improve adaptive skills and reduce problematic behaviors such as hyperactivity and aggression [3]-[10].

In clinical studies, the assessment of treatment effects of functioning, in children with ASD, is thwarted by the absence of reliable, sensible and easily administered rating tools.

The Children Global Assessment Scale (CGAS) [11] is a modified version of Global Assessment Scale (GAS) for adults [12]: it is a commonly used instrument to get a score of functioning level on child subjects [13].

However, the descriptors used to calculate the score of CGAS aren't easily usable when trying to describe the functioning of a subject with a diagnosis of ASD, because children with ASD usually follow atypical development paths and show severe deficits in specific areas of functioning. Moreover, cognitive functioning changes greatly within the group of subjects with ASD, shifting from severe mental retardation to a superior level, and often—above all—there are differences between intellectual and adaptive abilities, usually with delayed adaptive skills compared to the individual's mental age [14]-[16].

An instrument to assess global functioning in subjects with ASD would need to consider a wide range of functioning levels, with a wide variability, both inter- and intra-individual, and integrate information about multiple domains of functioning.

Although instruments like the Vineland Adaptive Behavior Scales (VABS) [17]-[19], the Assessment of Basic Language and Learning Skills (ABLLS) [20] and the Verbal Behavior Milestones Assessment and Placement Program (VB-MAPP) [21] can be used to assess specific areas of adaptive behavior in children with ASD, their sensibility to the treatment effects wasn't ascertained [22]. Furthermore these tools are lengthy to administer and are limited to specific areas of functioning.

In relation to the high individual variability of functioning among different domains, the assessment tools of global functioning are useful and quicker measures, which provide benefits also from a clinical perspective: strong evidence suggests that instruments of global rating can be more sensitive to change during the acute phases of treatment than other assessment tools with items based on symptoms [23] [24]. In fact, by integrating information on functioning from multiple sources, assessment instruments of global functioning provide a more complete picture than instruments based on specific scales or on a single source of information.

Because of the lack of rating instruments which provide a quantitative measure of global functioning to use in clinical trials with children with developmental disorders, CGAS was modified by adapting the anchor points and the administration procedures to the characteristics of children with developmental disorders, including ASDs.

This work describes the validation of the Italian translation of Developmental Disability-Child Global Assessment Scale (DD-CGAS) and demonstrates the data on inter-rater reliability, temporal stability, convergent validity and sensitivity to changes during treatment, when applied to an Italian population with ASD. This study tends to replicate data obtained in the validation study of the English scale "Developmental Disabilities Modification of the Children's Global Assessment Scale" of Wagner *et al.* [25], following it for basic setup and analysis mode of data and differing from it by number and characteristics of rater and by sample characteristics for total number of subjects and for the group of subjects used to assess the sensibility to change. Another substantial difference from the validation study of the original instrument relates to the other tests used to assess convergent validity and sensitivity to change: the limitation is due to the limited number of instruments validated and available in Italian language.

2. Methods

2.1. Description of DD-CGAS

DD-CGAS is a modified version of CGAS. It is a scale for clinicians which provide a total score of functioning for individuals below 18 years of age with a developmental disability, compared to individuals with typical development of the same age. The score refers to the typical functioning of the child during a certain period of

time, usually the week before the assessment.

The score is based on all available information sources and all functioning domains: self-care, communication, social behavior, school/academic functioning, and it isn't dependent on diagnosis, on cause of dysfunction (for example, cognitive or physical, environmental, behavioral disorders) or on type and severity of symptoms.

We preserved the overall structure of the original GAS and CGAS; therefore, DD-CGAS is a dimensional scale with scores ranging from 1 to 100, where 1 represents the most compromised functioning and 100 the highest level of functioning.

Each decile (for example 1 - 10, 11 - 20) has a descriptive header (for example "Moderate impairment of functioning at least in one area") and examples of behaviors and mode of adaptation which could represent this functioning level (**Appendix A**).

Scores equal to or greater than 70 on DD-CGAS suggest functioning within the normal development in neurotypical children of the same age. Because children with developmental disabilities must have, by definition, a significant alteration of functioning abilities, we will rarely obtain scores higher than 70 within this population. However, children with a mild disability could improve with treatment and placed into a normal range of functioning. Because this is an instrument created for many types of research, and for a wide range of developmental disabilities and control groups, it is a great advantage to have the possibility to capture the full range of functioning.

For the fundamental role of clinical assessment on global evaluation of functioning, we developed a specific procedure to standardize scoring to increase reliability. For this purpose we created a grid (**Appendix B**) to assign a level of impairment (none, soft, moderate, severe, extreme) to the four main domains of functioning (self-care, communication, social behavior and school).

First, the examiner establishes the level of impairment for each domain, considering child's behavior, the stability among different environments (for example home, school and community), the level of environmental adaptation required to support the child and the level of support required.

Afterwards, the examiner selects the range that best describes the level of functioning among different domains (for example "Moderate impairment of functioning in most areas"). The examples in the intervals are used to describe children's functioning, even if no child will be perfectly described by these.

After identifying the most appropriate interval, the evaluator explores the adjacent intervals in order to assign the specific score. For example, if the child fits better at "60 - 51 Moderate impairment of functioning in most areas", but with some similarities to 41 - 50, the evaluator will give a score in the bottom half range (*i.e.* 54 - 51). Vice versa, if the child fits better at 60 - 51, but has strong points in line with the highest category, the evaluator will give a score in the upper half of the category (*i.e.* 60 - 56).

All available sources of information should be used to calculate the score, including direct observation, information by caregiver and results of standardized tests. Whatever the source, the examiner needs a good description of functioning into the examined domains and information from different contexts. Thus the rater integrates all available information into a single index of functioning.

The amount of time required to collect useful information changes according to the situation in which the instrument is used. After collecting all the information, the final score is ready in 5 - 10 minutes. The re-assessment of the same child usually requires less time.

2.2. Translations

The Italian version of DD-CGAS was obtained by a forward-backward process by four clinicians with training and experience in the area of developmental disorders (two specialists in pediatric psychiatry, one community professional educator, one psychologist English mother-tongue).

A translation from English was even done for the clinical vignettes used for the inter-reliability and for temporal stability.

2.3. Inter-Rater Reliability and Temporal Stability

Clinical vignettes and training/reliability procedures for evaluators are were kindly provided by Ann Wagner, Ph.D. of NIH (USA).

The 16 clinical vignettes resulted from 16 clinical cases (concerning a wide range of functioning) of children with ASD. Children described in these clinical cases were aged between 4 to 14 years, included. Nine (56%) of

them were males. IQ ranged between 20 and 98.

Clinical vignettes (averaging 3 - 5 pages in length) held the following information: child's age and gender, wide descriptions of behavior and functioning in the following areas: ability to self-care (feeding, clothing, sleeping, personal hygiene, daily routines), communication (linguistic competencies, social communication, nonverbal communication, reading/writing), social behavior (family, peers) and school functioning (school level, performance and adaptive behavior). Moreover, there was an indication of coherence/incoherence of behavior among different settings, level of necessary environmental adaptation and level of required support.

Gold standard scores were obtained for these clinical cases, for each of them, from the average scores given by the six developers.

Independently, six clinicians assessed the clinical vignettes to evaluate inter-rater reliability. Evaluators had different levels of training and experience with ASD. They had familiarized with DD-CGAS and its scoring, and had discussed and jointly reviewed six vignettes for training purposes. Evaluators were located in two different sites: the Center of Pediatric Neurology in the University of Catania (Italy) and the Service of Pediatric Neurology of ULSS 8 in the Veneto region (Italy).

The examiners didn't know that they would repeat the evaluation after about six months from the first assessment. All examiners performed the re-valuation to measure temporal stability.

2.4. Validity and Sensitivity to Changes

2.4.1. Procedures

DD-CGAS was included among the assessment instruments usually used for monitoring patients with ASD at Center of Child Neurology of University of Catania (Italy) and at integrated clinic for autism of the Service of Child Neurology of ULSS 8, site of Montebelluna (Italy).

Independent evaluators for the study were certified to administer DD-CGAS by the rating of clinical vignettes previously described, through an exchange of emails: for reliability, evaluators independently assessed six clinical cases, to which developers assigned the gold standard score.

An evaluator would be certified only if in 80% of the clinical vignettes' scoring, the difference was not greater than 10 points from the gold standard score. If an evaluator could not be certified with the first six vignettes, he would have another training session available and then would evaluate another group of six clinical cases. If necessary, a third test of four vignettes was further available. Of these evaluators, 5 out of 6 obtained certification within the first test; 1 evaluator obtained the certification at the third test.

DD-CGAS was assessed by an independent evaluator according to the instruction in **Appendixe A** and **Appendixe B**, using all clinical data and tests possessed.

All subjects involved in the study contributed to the score of tests at baseline to assess validity of DD-CGAS. A subgroup of subjects was re-evaluated after an average of six months to assess the sensibility to measure the change of DD-CGAS.

Individuals of subgroups re-assessed in the follow-up underwent a wide range of interventions: pharmacological, behavioral treatment, parent training, psycho-educational and scholastic intervention, psychomotor or no intervention.

2.4.2. Subjects

A total of 48 subjects were involved in the base score to assess the validity of DD-CGAS. All subjects had IQ > 35 or a mental age > 18 months. The average age was 6 years (range 2 - 13 years, SD 3.37 years). 39 subjects (81%) were male. Diagnosis, according to DSM-IV criteria [26], was as follows: autistic disorder, 25 subjects; Pervasive Developmental Disorder, not otherwise specified, 17 subjects; Asperger syndrome, 6 subjects. Baseline scores of DD-CGAS varied from 22 to 74 (mean 57.5).

42 subjects were re-evaluated at follow-up, average age 7 years (range 2.6 - 13.5, SD 2.9). 34 of them were male (80%). Diagnosis was as follows: autistic disorder, 24 subjects; Pervasive Developmental Disorder, not otherwise specified, 14 subjects; Asperger syndrome, 4 subjects. Baseline scores of DD-CGAS varied from 22 to 78 (mean 62.9). **Table 1** shows the subject's features.

2.4.3. Instruments

Vineland Adaptive Behavior Scales-Survey Form (VABS) are a standardized instrument of measure of adaptive functioning based on parent interview. Composite scale represents a summary of the total score with mean 100

Table 1. Subjects features.

	Baseline	Follow-up
N	48	42
Age (years), Mean (SD)	6 (3.37)	7 (2.9)
Gender (% males)	81	80
Diagnosis n (%)		
Autistic Disorder	25 (52)	24 (57)
Asperger Syndrome	6 (13)	4 (10)
PDD-NOS	17 (35)	14 (33)
VABS-Composite, mean (SD)	60 (18.7)[a]	62.9 (17.9)[b]
WPPSI-III/WISC-III, mean (SD)	82.4 (18.9)[c]	83 (24.3)[d]
Leiter-R, mean (SD)	48.3 (16.2)[e]	50.1 (17.9)[f]
PEP3-CVP, mean (SD)	43.6 (22.3)[g]	48.9 (24.2)[h]
PEP3-CP, mean (SD)	7.6 (3.5)[i]	6.7 (2.2)[j]
PEP3-AP, mean (SD)	10.6 (2.7)[i]	12.5 (0.8)[j]
PEP3-CA, mean (SD)	10.4 (2.4)i	10.6 (2.6)[j]
ADOS-A, mean (SD)	2.1 (3.3)[k]	1.7 (0.4)[l]
ADOS-B, mean (SD)	2.5 (4.4)[k]	1.8 (0.3)[l]
DD-CGAS, mean (SD)	57.5 (13.4)	62.9 (11)

[a]$n = 45$; [b]$n = 42$; [c]$n = 12$; [d]$n = 10$; [e]$n = 10$; [f]$n = 9$; [g]$n = 14$; [h]$n = 17$; [i]$n = 37$; [j]$n = 35$; [k]$n = 40$; [l]$n = 38$.

and SD 15. Higher scores indicate a higher adaptive functioning.

WPPSI-III is a clinical instrument of individual assessment evaluating the intelligence of children of ages between 2 years and 6 months and 7 years and 3 months; WISC III assesses intellectual ability of subjects of ages between 6 and 16 years and 11 months; both provide a verbal IQ (VIQ), a performance IQ (PIQ) and a total IQ (TIQ), with mean 100 and SD 15 [27]; exclusively TIQ was used for the study.

The Leiter International Performance Scale-Revised (Leiter-R) [28] is a nonverbal intelligence test for children and teenagers aged between 2 and 20 years. The test provides a composite score with mean 100 and SD 15.

PEP-3, Psychoeducational Profile third edition [29] is an assessment instrument for children with autism spectrum disorder and communication impairments aged between 6 months and 7 years old. The test is divided into 13 subtests: 10 of direct observation and 3 derived from parent questionnaire. In this study the verbal/preverbal cognitive subtest was used to obtain an estimation of cognitive functioning (developmental quotient, DQ) when no information was available from other tools (WPPSI/WISC, Leiter-R) and DQ was the relation between developmental age obtained in the subscale and chronological age × 100. Parent questionnaire gives information about Problem Behavior (PB), Personal Autonomy (PA), Adaptive Behavior (AB). Standard scores were used in the study.

Autism Diagnostic Observation Schedule (ADOS) [30] is an instrument to assess and evaluate autism based on four different modules used in relation to developmental or language levels of the examined subject. In this study, to conform data from different subjects assessed with different modules, it was decided to express the scores of areas A (language and communication) and B (reciprocal social interaction) using the following formula: total score/cut-off score for autism in that area × 100.

2.5. Data Analysis

2.5.1. Inter-Rater Reliability and Temporal Stability

To assess inter-rater reliability the intraclass correlation coefficient (ICC) were calculated on the first scores obtained in the reliability vignettes for six previous examiners. The ICC were even calculated on test-retest scores of reliability vignette to assess temporal stability.

2.5.2. Convergent Validity

Pearson correlation coefficients were used to assess convergent validity between DD-CGAS and other clinical measures for 48 subjects at baseline.

The score at composite scale of VABS, IQ and DQ were used as ordinal variables. Not all correlations were based on the same sample, as some lacked data, whereas different assessment tools were used.

In this study, consistent with Wagner's work, no corrections were made for multiple comparisons, α value fixed at 0.05 and in some correlations analysis the association should be interpreted in terms of effect size. According to the guidelines given by Cohen [31], a correlation 0.10 represents a small effect size, 0.30 a moderate effect size and 0.50 a wide effect size.

2.5.3. Sensitivity to Change

42 out of 48 subjects were reassessed with follow-up after an average of six months. Sensitivity to change in DD-CGAS was assessed correlating changes into DD-CGAS with changes into PB scale of PEP3. To estimate the effect size between baseline and follow-up, the DS pooled was calculated.

3. Results

3.1. Inter-Rater Reliability and Temporal Stability

ICC for 5 examiners for 16 clinical cases was 0.78 (p 0.001). ICC between test and retest had a mean of 0.79 (p 0.001). Therefore statistically, both ICCs were significant.

3.2. Convergent Validity

With α value at 0.05, DD-CGAS resulted in correlation with all the other assessment tools. Correlations between DD-CGAS and the other instruments are in Table 2.

The correlation was significant and positive with IQ obtained in WPPSI/WISC and in Leiter-R (respectively r 0.51, $p < 0.001$ and r 0.40, p 0.003), with DQ obtained in PB subscale of PEP3 ($r -0.52$, $p < 0.001$) and with PB, PA and AB subscales of PEP3 (respectively r 0.28, p 0.010; r 0.27, p 0.013; r 0.28, p 0.010). Correlation was significant and negative with A and B areas of ADOS (for both r −0.35, p 0.006).

3.3. Sensitivity to Change

Correlation between changing scores at DD-CGAS and CP subscale of PEP3 was 0.75 (n 42, p 0.01). The average score of DD-CGAS was 57.5 (SD 13.4) at baseline and 62.9 (SD 11.0) at follow-up (t test for paired samples 5, p 0.001). The average change in DD-CGAS was 4.8 points. The effect size for DD-CGAS was 0.59 (n. 42) and for CP subscale 0.54 (n. 42).

4. Discussion

DD-CGAS is an instrument for clinicians to assess global functioning in children with ASD.

Table 2. Correlations between DD-CGAS and the other instruments.

Tests	r	p	n
VABS-Composite	0.52	<0.001	48
WPPSI-III/WISC-III	0.51	<0.001	12
Leiter-R	0.40	0.003	5
PEP3-CVP	0.52	<0.001	31
PEP3-CP	0.28	0.010	48
PEP3-AP	0.27	0.013	48
PEP3-CA	0.28	0.010	48
ADOS-A	−0.35	0.006	44
ADOS-B	−0.35	0.006	44

It is specifically designed to include a wide range of functioning, with inter- and intra-subject variability changing based on type and grade of impairment. Further, it is accompanied by instructions and a grid to assist the examiner during the rating.

DD-CGAS showed to have a good inter-rater reliability and a good temporal stability in a range of several months, using clinical vignettes.

Reliability was obtained with a diversified group of evaluators, in terms of background and level of competence.

Correlations between DD-CGAS and other measures of functioning and symptoms assessment were moderate [31] [32].

This study was aimed to validate the Italian translation of DD-CGAS repeating data obtained in the validation study of the English version.

Despite differences between the two studies (number and characteristics of raters, sample and type of instruments used) the results obtained in DD-CGAS validation process, in terms of inter-rater reliability, temporal stability, convergent validity and sensitivity to change, substantially overlap the original study, confirming both the quality of translation and the value of the instrument itself.

After adequate training, DD-CGAS was designed to include the typical heterogeneity of ASD. It represents a reliable assessment tool of global functioning: it integrates multiple information sources, it is fast to administer after collecting necessary information and it seems appropriate to be used in clinical studies with children with ASD.

Data used for this study were collected before DSM-5 publication and a comparison with the DSM-5 severity scales could not be made. Despite this, we think that an instrument like DD-CGAS can be useful in the clinical setting for transitioning to the DSM-5, helping to better analyse and separate the constructs of impairment and disorder in order to provide a more appropriate and dimensional evaluation, according to the recent classification system.

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Appendix A

Developmental Disability-Child Global Assessment Scale (DD-CGAS) Versione Italiana

Dopo aver esaminato le prestazioni del soggetto nelle varie aree di funzionamento [a. cura della propria persona, mangiare, vestirsi, dormire; b. comunicazione; c. comportamento sociale; d. prestazioni accademiche] e contesti [casa, scuola e comunità], assegnare un punteggio al suo/a livello globale di funzionamento, per il periodo di tempo specificato, selezionando il numero che ne descrive il comportamento. Utilizzare se necessario i livelli intermedi (es. 35, 58, 62). Valutare il funzionamento attuale indipendentemente dal trattamento o dalla prognosi. Concentrare l'attenzione sull'interferenza funzionale della psicopatologia piuttosto che sui sintomi di per se. Le descrizioni fornite di seguito sono solo illustrative e non sono necessarie per ottenere un particolare punteggio (vedi le istruzioni per i dettegli sull'attribuzione dei punteggi).

Periodo di tempo specificato:

100 - 91 Funzionamento superiore. Sicuro in famiglia, a scuola, con i pari; difficoltà transitorie o preoccupazioni "di ogni giorno" (es, lieve ansia situazionale, occasionalmente arrabiato con i fratelli/sorelle, genitori o pari). Risultati superiori rispetto ai coetanei (es, grandi successi negli Scout). Per bambini in età scolare, buoni risultati accademici. Svolgimento indipendente, in relazione all'età, di attività quotidiane e cura della propria persona.

90 - 81 Funzionamento adeguato in tutte le aree. casa, scuola e pari; brevi disturbi del comportamento o distress emozionale in risposta ad eventi stressanti (es, cambiamenti non previsti nella routine quotidiana o nell'ambiente fisico), ma senza interferenza col funzionamento. Abilità adattive adeguate all'età. Apprende in maniera cooperativa e volenterosa; pratica volentieri ciò che gli viene insegnato.

80 - 71 Lieve compromissione del funzionamento. La maggior parte delle attività della vita quotidiana sono adeguate all'età, ma può aver bisogno di prompt e strutturazione per portarle a termine. Cambiamenti minori nella routine quotidiana o nell'ambiente possono causare problemi comportamentali transitori o distress. Le interazioni sociali possono essere unilaterali e concrete piuttosto che basate sull'intimità. Può apparire immaturo, ma non atipico. Linguaggio generalmente adeguato all'età, ma la conversazione può essere unidirezionale e/o centrata sui propri interessi.

70 - 61 Moderata compromissione del funzionamento in almeno un'area. Deficit sociali apparenti in molte situazioni. Apprende appropriate abilità sociali, ma inflessibilmente e senza capacità di generalizzare. Abilità adattive e/o di autoaccudimento immature nella maggior parte delle aree. Comportamento visibilmente inusuale in alcune situazioni (es., gruppi sociali, setting non strutturati) ma generalmente non distruttivo. Coopera nei training sulle abilità adattive.

60 - 51 Moderata compromissione del funzionamento nella maggior parte delle aree. Necessita di notevole strutturazione e supervisione per le routine quotidiane. Le abilità della vita quotidiana e/o adattive sono non adeguate per l'età, ma è recettivo ad apprendere nuove abilità. Comunica i bisogni, risponde a richieste di base (verbalmente o non verbalmente). Il linguaggio verbale, se presente, è poco flessibile ed in ritardo. I deficit sociali e/o i comportamenti inusuali sono presenti nella maggior parte dei contesti. Possono verificarsi comportamenti distruttivi occasionali.

41 - 50 Elevata compromissione del funzionamento in almeno alcune aree (es., frequenti comportamenti molto distruttivi a scuola) e un certo grado di compromissione nella maggior parte delle aree. Le aperture sociali e/o le risposte sono chiaramente assenti o inappropriate. Le abilità della vita quotidiana sono significativamente in ritardo (es., vestirsi, fare il bagno, mangiare). Presenta una certa ricettività ai tentativi di insegnamento. Comportamenti stereotipati e/o altri comportamenti inusuali persistenti possono essere notati da un osservatore occasionale. Aggressività o comportamento autolesivo occasionale, oppure aggressività/comportamento autolesivo frequente ma lieve (cioè senza danneggiamento dei tessuti).

31 - 40 Elevata compromissione del funzionamento nella maggior parte delle aree. Rudimentali abilità di comunicazione strumentale (non sociale). Comportamenti ripetitivi che interferiscono con il funzionamento adattivo. Marcato ritiro sociale nella maggior parte delle situazioni. Comportamento adattivo significativamente compromesso. Disregolazione emozionale generalizzata e significativa (es., aggressività, comportamento autolesivo) e/o disregolazione funzionale (es., sonno, alimentazione).

21-30 Severa compromissione nella maggior parte delle aree, cioè casa, scuola, in pubblico, con i pari (es., frequente aggressività o comportamento autolesivo; comportamento marcatamente ritirato ed isolato). Richiede

estensivi adattamenti dell'ambiente (es., supervisione 1:1 per il comportamento, chiudere a chiave gli armadi, rimuovere oggetti fragili dalla stanza da letto). Dipendente in tutti gli aspetti della vita quotidiana (es., vestirsi, lavarsi, andare al bagno) in misura maggiore rispetto all'età. Marcato disturbo dei processi regolatori di base (es., dormire, alimentarsi).

11 - 20 Profonda e generalizzata compromissione. Pone in pericolo se stesso o gli altri. Ha bisogno di costante supervisione o di estensivi adattamenti dell'ambiente per evitare che faccia del male a se o agli altri (es., frequentemente violento o autoaggressivo) o per le l'assistenza di base (es., cibarsi, andare al bagno). Non comunica i bisogni di base. Non interagisce con gli altri. Si oppone all'aiuto nella cura di sé (es., farsi vestire).

0 - 10 Ha bisogno di supervision intensiva e costante (es., supporto continuativo al di fuori del proprio ambiente domestico) dovuto a comportamento severamente aggressivo o autolesivo o totale dipendenza nelle abilità di autoaiuto di base. Forte resistenza verso chi fornisce aiuto (es., farsi vestire).

Appendix B

Instructions for Evaluators

Le aree che devono essere considerate nella valutazione includono:

- Il funzionamento globale nei principali domini adattivi
  - Cura della propria persona: mangiare, vestirsi, dormire
  - Comunicazione
  - Comportamento sociale
  - Performance accademiche e l'ambiente
- Coerenza o incoerenza del funzionamento tra i vari ambienti: casa, scuola, comunità
  - Livello di adattamento dell'ambiente necessario
  - Livello di supervisione necessaria

1. Utilizzare la tabella sottostante per organizzare il giudizio sulla compromissione nei quattro domini di funzionamento.

2. Scegliere la voce/categoria che meglio descrive il funzionamento generale (es. "moderata compromissione del funzionamento nella maggior parte delle aree"). Il descrittore dovrebbe rappresentare una buona descrizione del funzionamento generale del bambino, indipendentemente dal fatto che l'origine della compromissione sia cognitiva, comportamentale o altro. Si sta comparando la descrizione del funzionamento adattivo a quello che ci si aspetterebbe da un bambino con sviluppo tipico, indipendentemente dal fatto che la compromissione sia dovuta a disabilita' di sviluppo, disturbi comportamentali, fattori ambientali o altro. E' necessario essere cauti nel non dare troppa importanza ai punteggi standard; la variabilita' nel funzionamento puo' risultare essere la "media" dei punteggi standard. Piuttosto dare maggiore enfasi alla descrizione del funzionamento.

3. Controllare i dettagli della categoria scelta per confermare che corrisponda ad una descrizione generale, ma porre attenzione al fatto che la maggior parte dei bambini non corrisponderà perfettamente a nessuna categoria. Si deve cercare quella che si "adatta meglio".

4. Quando si pensa di aver trovato quella che si adatta meglio, controllare le due categorie adiacenti, per vedere se il bambino ha delle caratteristiche che corrispondono alle categorie superiore o inferiore. Questo serve per aggiustare il punteggio. Per esempio, se il bambino corrisponde meglio alla categoria "60 - 51 Moderata compromissione del funzionamento nella maggior parte delle aree" ma ha alcune somiglianze alla categoria 41 - 50, assegnare il punteggio nella metà inferiore del range (51 - 55). Al contrario, se il bambino corrisponde meglio alla categoria 60 - 51 ma ha alcuni punti di forza corrispondenti alla categoria superiore, assegnare il punteggio nella metà supeiore della categoria (55 - 60).

		Livello di compromissione				
		Nessuno	Lieve	Moderato	Severo	Estremo
Dominio	Cura della propria persona					
	Comunicazione					
	Comportamento sociale					
	Scuola/accademico					

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Beyond interference control impairment in ADHD: Evidence from increased intraindividual variability in the color-stroop test

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The present study investigates intraindividual variability (IIV) in the Color-Stroop test and in a simple reaction time (SRT) task. Performance level and variability in reaction times (RTs)—quantified with different measures such as individual standard deviation (ISD) and coefficient of variation (ICV), as well as ex-Gaussian parameters (*mu, sigma, tau*)—were analyzed in 24 children with attention deficit/hyperactivity disorder (ADHD) and 24 typically developing children (TDC). Children with ADHD and TDC presented equivalent Color-Stroop interference effects when mean RTs were considered, and the two groups did not differ in the SRT task. Interestingly, compared to TDC, children with ADHD were more variable in their responses, showing increased ISD and ICV in the Color-Stroop interference condition and in the SRT task. Moreover, children with ADHD exhibited higher *tau* values—that is, more frequent abnormally long RTs—in the Color-Stroop interference condition than did the TDC, but comparable *tau* values in the SRT, suggesting more variable responses. These results speak in favor of a general deficit in more basic and central processes that only secondarily may affect the efficiency of inhibitory processes in children with ADHD. Overall the present findings confirm the role of IIV as a cornerstone in the ADHD cognitive profile and support the search for fine-grained analysis of performance fluctuations.

Keywords: ADHD; Intraindividual variability; Inhibition; Color-Stroop test; Response time distributions.

Attention deficit/hyperactivity disorder (ADHD) is a complex pervasive developmental disorder, diagnosed in approximately 2%–16% of school-aged children (Rader, McCauley, & Callen, 2009) and characterized by age-inappropriate levels of inattention, hyperactivity,

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and impulsivity (American Psychiatric Association [APA], 2000). Behavioral and cognitive difficulties have been attributed to neuropsychological deficits in executive functions such as attentional regulation, response inhibition, and working memory (Barkley, 1997a; Barkley, Grodzinsky, & DuPaul, 1992; Pennington & Ozonoff, 1996; Sergeant, Geurts, & Oosterlaan, 2002).

Despite the actual debate concerning centrality of inhibition and/or broad executive function processes as a causal model of ADHD (Castellanos, Sonuga-Barkes, Milham, & Tannock, 2006; Scheres et al., 2004; Sergeant, 2005; Sergeant et al., 2002; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), the neurocognitive view of ADHD considers inhibitory processes as a core deficit in ADHD that secondarily disrupts other executive function processes (Barkley, 1997b; Pennington & Ozonoff, 1996). In particular, children with ADHD are supposed to be particularly affected in the different dimensions of inhibition (see de Ribaupierre, Borella, & Delaloye, 2003; Nigg, 2000) such as inhibition of prepotent responses, stopping of ongoing responses, and interference control (Barkley, 1997a).

Among the cognitive paradigms used to quantify interference control deficits in children with ADHD, the Color-Stroop test is one of the most frequently used tests (Barkley et al., 1992; Frazier, Demaree, & Youngstrom, 2004; Hervey, Epstein, & Curry, 2004; Homack & Riccio, 2004; Lansbergen, Kenemans, & van Engeland, 2007; Pocklington & Mayberry, 2006; Schwartz & Verhaeghen, 2008; Van Mourik et al., 2009). It consists of visually presenting the participants with color names displayed in an incongruent color (e.g., the word "red" written in blue). Participants are instructed to name the color in which the word is written as fast and accurately as possible (Cohen, Dunbar, & McClelland, 1990). Complying with the task's instructions implies the ability to inhibit the prepotent reading response—reading the color name—and to favor the appropriate but nondominant naming response—color in which the word is written. The relative decrease in performance (slower response times or decrease in accuracy) associated with naming the color of incongruent color names, as compared to a control condition with neutral features, is referred to as the "Stroop interference effect" and reflects the cognitive effort involved in interference control.

Most of the studies that examined the Color-Stroop test in the context of ADHD literature referred to Golden's (1978) paper version, a variant of the Color-Stroop word test (Stroop, 1935). To date, some meta-analyses have examined the Stroop interference effect in children with ADHD (as examples, see Homack & Riccio, 2004; Van Mourik et al., 2009). Homack and Riccio reported children with ADHD to be more sensitive to interference than typically developing children (TDC), as shown by a large interference effect size. In contrast, the meta-analysis by Van Mourik et al. (2009) showed that children with ADHD are not more vulnerable to interference than TDC. This latter pattern of findings was also confirmed by the recent study by Williams, Strauss, Hultsch, and Tannock (2007).

Therefore, empirical evidence regarding the deficit in interference control in children with ADHD measured by the Color-Stroop test is not a very reliable finding. When these divergent findings are more closely considered, it appears that several methods were used to quantify the Stroop interference effect: the number of words named correctly, the time to complete a given number of stimuli (which obviously includes errors as well), the number of items named in a given time frame (i.e., 45 seconds in Golden's formula), or the response latency per item in milliseconds. Moreover, it is worth mentioning that the majority of studies used a card version in which several trials were presented on the same card and, still more importantly, did not include a baseline control condition (Lansberger et al., 2007). When individual differences in baseline performance are controlled for, by computing a

ratio or a relative ratio, rather than merely considering raw response times or errors in the incongruent condition, children with ADHD no longer appear to present a specific deficit in interference control (for meta-analyses, see Schwartz & Verhaeghen, 2008; Van Mourik et al., 2009). Therefore, it is possible that the deficit highlighted by some authors in the Color-Stroop test for children with ADHD could reflect individual differences in stimuli naming (Tannock, Martinussen, & Frijters, 2000) and be linked to an inappropriate type of measurement (Lansberger et al., 2007), rather than a deficit in interference control.

One of the aims of the present study was thus to assess interference control in children with ADHD and TDC using the Color-Stroop paradigm. In particular, a computerized item-by-item version of this task was used to allow for fine-grained performance analysis of reaction times (RTs); it might help detect behavioral differences in interference control between children with ADHC and TDC children in ways that would not be possible with the most commonly used paper versions. Indeed, recording item-by-item RTs in milliseconds offers an advantage in terms of test sensitivity (Christiansen & Oades, 2009), in particular because it allows examining RTs for correct responses only instead of mixing erroneous and correct responses. Such a procedure also allows mixing trials of the different conditions instead of grouping them by condition. To our knowledge, in all the few studies that used chronometric Color-Stroop tasks, children with ADHD did not appear to be more sensitive to interference than controls (e.g., Albrecht et al., 2008; Carter, Krener, Chaderjian, Northcutt, & Wolfe, 1995; Christiansen & Oades, 2009; Jourdan Moser, Cutini, Weber, & Schroeter, 2009).

Nonetheless, independently of the task version used, those divergent results on the Stroop interference effect in ADHD are based on mean performance levels. As suggested by Nesselroade (1991), individual systematic variations in short-term behavior (that is, moment-to-moment [item-by-item] fluctuations in task performance) provide additional, complementary information that is potentially masked by analyses based on mean performance levels.

There is indeed converging evidence that children with ADHD present a large item-by-item intraindividual variability (IIV), also called "inconsistency," in RTs compared to controls (Borella, Chicherio, Re, Sensini, & Cornoldi, 2011; Castellanos & Tannock, 2002; Kunsti, Oosterlaan, & Stevenson, 2001; Leth-Steensen, Elbaz, & Douglas, 2000; Steger et al., 2001). For instance, Klein, Wendling, Huettner, Ruder, and Peper (2006) showed across a variety of neuropsychological tests—continuous performance test, go/no-go, stop signal, and *n*-back tasks—that IIV reliably contributed to discriminate between children with ADHD and controls. The increased behavioral IIV found in this population is presumably linked to dysfunctions of fronto-striatal-cerebellar circuits and altered dopaminergic modulation (Castellanos & Tannock, 2002; Krain & Castellanos, 2006) and, more generally, to compromised central nervous system integrity (MacDonald, Nyberg, & Bäckman, 2006). As a consequence, increased RT IIV has been hypothesized to be one of the potential markers of underlying neuropsychological deficits related to ADHD (e.g., Castellanos et al., 2006; Borella et al., 2011).

A second aim of the present study was, thus, to examine the patterns of IIV in order to provide information with respect to interference control deficit in ADHD that may potentially be masked by the analyses based on mean RTs (Castellanos et al., 2006). This was possible using a computerized version of the Color-Stroop task, to assess trial-to-trial variability. To our knowledge, only Christiansen and Oades (2009) have analyzed IIV in RTs in the Color-Stroop task. Their results showed no difference in the mean interference effect but significantly greater IIV in children with ADHD compared to TDC.

However, Christiansen and Oades used only a traditional measure of IIV, the individual standard deviation (ISD). The ISD is the measure most widely used to quantify IIV, and it is calculated as the standard deviation across trials of the same task for a given individual. Because it has been shown to be linked to the individual mean level across trials, some researchers used other measures to control for the level of performance, such as the individual coefficient of variation (ICV), which is calculated by dividing the ISD by individual mean (IM). Those indices of IIV assume response times to be normally distributed, whereas RT distributions are often positively skewed. Moreover, a greater proportion of extremely slow responses can lead to a larger size of the tail of the RT distribution and may have a strong influence on the values of the individual mean and ISD (i.e., higher values). Therefore, other researchers have suggested alternative approaches such as fitting ex-Gaussian functions—a convolution of an exponential function and a Gaussian one—to item-by-item RT data to describe more precisely the shape of individual RT distributions (see Ratcliff, 1979).

In fitting the ex-Gaussian distribution, three parameters representing different parts of the curve are obtained: *mu* (μ) and *sigma* (σ) representing the mean and standard deviation of the normal (or Gaussian) component, respectively, as well as *tau* (τ), representing both the mean and standard deviation of the exponential (or ex-Gaussian) component (see Figure 1). In terms of the ex-Gaussian distribution, its mean is given by ($\mu+\tau$) and its variance by ($\sigma^2+\tau^2$).

It has been demonstrated that the ex-Gaussian distribution provides a better statistical fit to RT data than the Gaussian distribution does, and that its parameters may capture important aspects of human cognition (see Heathcote, Popiel, & Mewhort, 1991; Spieler, Balota, & Faust, 1996, 2000). In particular, these parameters might be linked to different processes at play in the task, particularly useful in characterizing the nature of increasingly large performance variability in impaired states and pathological conditions such as ADHD. Leth-Steensen et al. (2000) found that children with ADHD, who were slower (higher mean, IM) and more variable (larger intraindividual standard deviation [ISD]) in their RTs, were highly discrepant from controls in the ex-Gaussian parameter *tau*, but not in *mu* or *sigma*. This pattern served as evidence in support of the hypothesis that children with ADHD demonstrated greater performance variability as a result of abnormally long RTs on some but not all trials, producing a greater positive skew reflected in *tau* in the RT distribution. Additionally, greater values of *tau* combined with similar values of *mu* and *sigma*, further proved to be a more specific performance pattern for identifying children with ADHD than an index of general slowing, reflecting a variety of unspecified difficulties with basic cognitive processes. Indeed, it has been argued that periodic excessively long RTs are a consequence of transient periods of inefficient or nonoptimal processes. These trials have been hypothesized to reflect occasions where children with ADHD demonstrate lapses in attention (see also Douglas, 1999).

While Leth-Steensen et al. (2000) quantified IIV associated with RTs in a relatively simple choice response task (i.e., a discrimination task), which imposes a minimal demand on response control, Hervey et al. (2006) administered another task involving higher demands on response control (i.e., a Go/No-Go task). The authors consistently found children with ADHD to differ from controls with respect to the size of the distribution tail (elevated *tau*). They observed additionally that children with ADHD exhibited larger *sigma* values than controls, which suggests that more variable responses were produced in all trials throughout the task. Further, children with ADHD presented smaller *mu* values, indicating that they, at times, responded more quickly than controls. The divergence in results

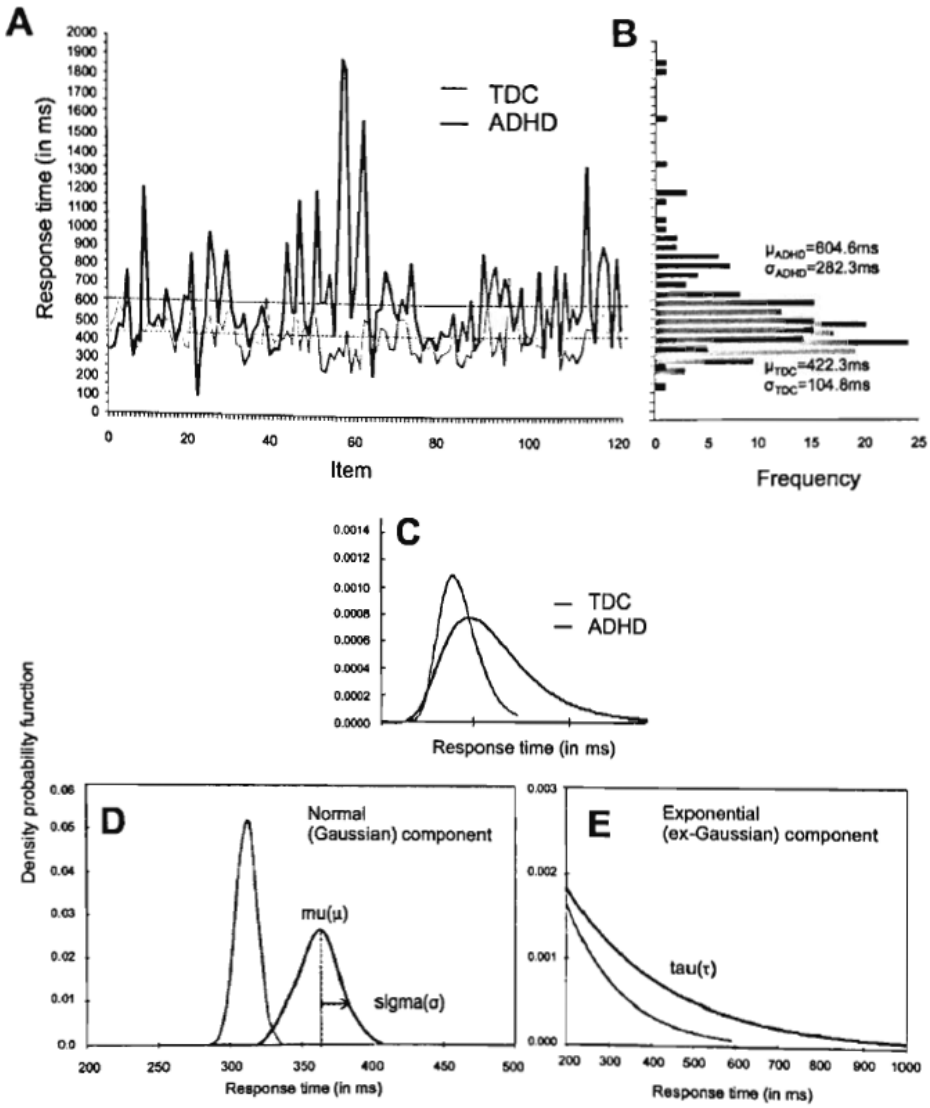

Figure 1 Illustration of the ex-Gaussian distribution: (A) Trajectories of individual responses across 120 items in the SRT (Simple Reaction Time) task from one child with ADHD (dark line) and one TDC (gray line) and (B) their corresponding individual RT distributions. The ex-Gaussian parameters (*mu*, *sigma*, and *tau*) are derived by decomposing (C) each observed RT distribution into (D) its normal (or Gaussian) component and (E) its exponential (or ex-Gaussian) component.

Note. μ = individual mean; σ = individual standard deviation (ISD); TDC = typically developing children; *Mu*(μ) = parameter from the ex-Gaussian analysis reflecting the mean of the Gaussian (or normal) component of the RT distribution; *sigma*(σ) = parameter from the ex-Gaussian analysis reflecting the standard deviation of the Gaussian (or normal) component; *tau*(τ) = parameter from the ex-Gaussian analysis reflecting the mean and the standard deviation of the ex-Gaussian (or exponential) component.

can probably be attributed to differences in the tasks. Indeed, the discrimination task used by Leth-Steensen et al. (2000) seems to produce slower overall response times compared to a Go/No-Go task. Also, the Go/No-Go task with no warning cues and rapid presentation

of stimuli clearly primes impulsive responses. To further determine whether these inconsistencies were due to a difference in the degree of response control required by the tasks used in these two studies, Vaurio, Simmonds, and Mostofsky (2009) presented to children with ADHD and controls two variants of the Go/No-Go task but varying in their complexity (or cognitive demands). The authors observed a higher *tau* value (exponential/ex-Gaussian component) and a higher *sigma* value (the normal/Gaussian component) in children with ADHD as compared to controls, independent of the task version. These results are consistent with those from Hervey et al. (2006) in which a similar Go/No-Go task involving high demands on response control was used.

Overall, these findings suggest that when the task requires relatively little response control, increases in IIV are mainly due to intermittent slow responses. When the requirement for response control is higher, IIV is larger throughout the entire RT distribution (that is in slow as well as in fast responses). This could reflect inefficiency in mechanisms critical to engage a state of preparedness to respond. Therefore, Vaurio et al. (2009) concluded that both impaired response preparation and intermittent lapses in attention contributed to increasing variability in performance in children with ADHD. These findings could not have been detected using conventional RT analyses. The ex-Gaussian approach seems therefore to go above and beyond conventional statistical approaches, which focus on the analyses of central tendency measures.

Despite promising results, only a few other studies applied ex-Gaussian function analyses to RT data of children with ADHD (Buzy, Medoff, & Schweitzer, 2009; Geurts et al., 2008; Hervey et al., 2006; Vaurio et al., 2009); we might therefore further our understanding of inhibitory deficits in children with ADHD by isolating more specifically the IIV associated with RTs.

To our knowledge, the present study is the first one to analyze IIV in children with ADHD in a task that measures more specifically the dimension of interference control (e.g., Nigg, 2000)—that is, the Color-Stroop task. Indeed, the Stop signal and Go/No-Go tasks are the most commonly used in ADHD but refer to a different aspect of inhibition (see Nigg, 2000). These tasks measure the inhibition of a dominant motor response rather than that of a preponderant verbal response as in the Color-Stroop.

In summary, the present study aims to examine IIV in ADHD using a computerized version of the Color-Stroop test. As mentioned previously, not all studies have used a control condition; it is therefore difficult to decide whether potential difficulties in the interference task are really due to a deficit in inhibition or, more simply, to a deficit in a more basic mechanism such as processing speed. It is therefore important to assess whether IIV is larger in an interference condition than in a control one.

Furthermore, to examine the generalizability of IIV in children with ADHD and TDC, it also appeared important to use an independent task that did not involve the same content domain (verbal) as the Color-Stroop task itself. Therefore, a simple reaction times (SRT) task, often used to examine IIV (e.g., Borella et al., 2011), in which participants had simply to react to the appearance of target stimuli and that imposed a minimal demand on response control, was used. The use of both tasks should indeed allow us to determine whether children with ADHD compared to TDC are (a) impaired in interference control processes, as classically found in the literature, or (b) characterized by a deficit in lower and more central mechanisms of information processing such as processing speed, assessed by the SRT task as an independent measure, in which case it could not be considered to be a difficulty specific to the control of interference. Both the mean level and the variability of performance (RTs) will be analyzed. Furthermore, to provide convergent and

complementary results about the role of IIV in interference control in the Color-Stroop test, different indices of IIV in RTs will be considered: the classical indices of ISD and ICV but also the ex-Gaussian parameters *mu, sigma*, and *tau*.

With respect to mean performance level, and in conformity with the meta-analysis by van Mourik, Oosterlaan, and Sergeant (2005), we expected children with ADHD not to differ from TDC. The mean interference effect should also be similar in the two groups. However, children with ADHD should present a larger IIV in the Color-Stroop task, compared to TDC; that is, they should produce slower and more variable responses than TDC, indexed by larger ISD and ICV (e.g., Christiansen & Oades, 2009). With respect to ex-Gaussian analyses (e.g., Hervey et al. 2006; Vaurio et al., 2009), children with ADHD should show higher values of *tau*, reflecting a greater frequency of extremely long RTs, whereas they should not differ from TDC with respect to the *mu* value (mean level of performance); we will examine whether they would also present a larger value for *sigma* (variance). If children with ADHD are more variable than TDC, as we believe and has been assumed in the literature, they should also exhibit higher levels of IIV in the SRT. This would show that processing is altogether less robust in this population; processing robustness has been associated with neural information-processing fidelity (e.g., Li, Huxhold, & Schmiedek, 2004).

METHOD AND MATERIALS

Participants

Twenty-four children with attention deficit/hyperactivity disorder (ADHD) and 24 typically developing children (TDC), aged 9 to 12 years, participated in the study. ADHD participants, all of whom attended normal schools, were recruited through referrals from Italian university-based ADHD clinics. The control group was formed with children who attended the same schools as the ADHD children and came from the same socioeconomic background.

Patients' diagnoses were established by qualified psychiatrists or clinical psychologists following indications in the Diagnostic and Statistical Manual of Mental Disorders, Text Revision (*DSM-IV-TR*; APA, 2000). The diagnosis of children with ADHD was based on the fact that they were beyond the cutoff in rating scales for ADHD disorder, either the ADHD rating scale for teachers (Scala per i Disturbi di Attenzione/Iperattività per Insegnanti -SDAI; Cornoldi, Gardinale, Masi, & Pettenò, 1996) or the Conners' Rating Scale—Revised (Conners, 1997). The SDAI scale is a simple scale, similar in organization and scope to those largely used in other countries (e.g., DuPaul, Power, Anastopoulos, & Reid, 1998). It presents the 18 ADHD symptoms (described by *DSM-IV-TR*), whose frequency and intensity must be rated on 4-point scales from 0 to 3. The scale has been validated and standardized for the Italian population and has shown good reliability ($r = .95$; Marzocchi, Re, & Cornoldi, 2010) and test-retest reliability ($r = .80$; Marzocchi & Cornoldi, 2001). The cutoff for considering a child for a possible diagnosis of ADHD is represented by a mean item rating above 1.5.

In order to be included in the ADHD group, clinical interviews with teachers, children, and their parents had to confirm the presence of at least six symptoms either of inattention or hyperactivity both at school and at home. Furthermore, children had to present weaknesses (scores below the normative mean of at least 1.5 standard deviations) in at least two of a series of neuropsychological tests assessing executive functions (see Sinpia's guidelines, 2006).

Written informed consent was obtained from parents or legal guardians. The patients and controls underwent the same screening and diagnostic procedures, interviews, and psychological testing. We excluded children who presented one or more of the following conditions: (a) their Wechsler Intelligence Scale for Children (WISC) IQ score was below 85; (b) they were receiving medication; (c) they had either a previous diagnosis of a learning disability, or, even if not diagnosed, they were identified by teachers as having severe difficulties either in reading or mathematics; (d) they had a history of neurological disorders, sensory problems, motor impairment, or any developmental psychiatric disorder other than ADHD; and (e) they met the *DSM-IV-TR* criteria for major depression, anxiety, bipolar disorder, a psychotic disorder, or a mood disorder.

Children with ADHD and TDC did not differ in terms of mean age, $F(1, 47) = 0.28$, $p = .60$ (ADHD: 9.50 ± 1.32; TDC: 9.29 ± 1.40), gender distributions, $\chi^2(1) = 1.78$, $p = .18$ (ADHD: 20 male, 4 female; TDC: 16 male, 8 female), and IQ, $F(1, 47) = 0.13$, $p = .72$ (ADHD: 100.04 ± 6.87; TDC: 101.83 ± 6.21).

Color-Stroop Test

The computerized Color-Stroop test was adapted from Spieler et al. (1996) and from Fagot, Dirk, Ghisletta, and de Ribaupierre (2009; see also Ludwig, C., Fagot, D., Chicherio, C., & de Ribaupierre, A, 2011). The experiment was piloted using the E-prime software (E-Prime 1.1; Psychology Software Tools, Pittsburgh, PA). The stimuli consisted of four color names (ROSSO—red; BLU—blue; VERDE—green; GIALLO—yellow) written in red, blue, green, or yellow, depending on the condition either congruent (i.e., the word GREEN printed in green) or incongruent (i.e., the word RED printed in green). Additionally, in the neutral condition, four different stimuli (^^^^; ++++; ****; ’’’’) were presented in red, blue, green, or yellow. Stimuli were presented on a 35 cm (14-inch) video graphics array color computer monitor. All stimuli were presented on a black background. The three experimental conditions were distributed over nine blocks of 24 trials each. The order of the blocks and the order of the trials within a block were first randomized and then identical for all participants. Randomization respected two constraints. First, within a block, no more than three consecutive trials belonged to the same condition. Second, negative priming was controlled for, in that the color word of any given item never matched the color of the succeeding item. In each block, there were eight congruent, eight incongruent, and eight neutral trials. In summary, 72 trials per condition were presented, for a total of 216 items in nine blocks. The task started with nine practice trials (three items per condition), with stimuli and timing identical to those of the experimental blocks. In each trial, the following sequence of events occurred: A white fixation point appeared in the center of the computer screen for 1,000 ms. The stimulus appeared in the center of the screen and remained until the onset of the participants' response. Participants were instructed to name the color of each stimulus as quickly and accurately as possible. Voice onset latency was measured via a voice key interfaced with the computer. Afterward, the screen went blank for 800 ms, following the onset of the participants' response. The experimenter recorded the participants' responses on paper. All participants could take a short break after each block of trials.

Simple Reaction Time Task

The computerized Simple Reaction Time (SRT) task was adapted from Hultsch, MacDonald, Hunter, Levy-Bencheton, and Strauss (2000; see also Ludwig et al., 2011).

The experiment was piloted using the E-Prime software (E-Prime 1.1.; Psychology Software Tools, Pittsburgh, PA). The stimuli consisted of a white cross located in one of five positions corresponding to the points of a five-branch invisible star on the center of the computer screen. Distribution of the stimuli on noncentral locations was meant to prevent anticipatory responses. Stimuli were presented on a 35 cm (14-inch) video graphics array color computer monitor. All stimuli were presented on a black background. The SRT task was presented in five blocks of 24 trials each, for a total of 120 items. The order of the blocks and the order of the trials within a block were first randomized, and then identical for all participants. Randomization respected two constraints. Within a block, no more than two consecutive trials belonged to the same position, and no more than two consecutive trials belonged to the same interstimulus interval. The task started with six practice trials, with stimuli and timing identical to those of the experimental blocks. On each trial, the following sequence of events occurred: a white fixation point appeared in the center of the computer screen and the stimuli remained until the onset of the participants' response. Participants were instructed to react as fast as possible to the apparition of the cross (+) after a fixation point (•) had been presented, by pressing with their dominant hand on a button box. Afterward, the screen went blank for a delay between 500 and 1,700 ms, following the onset of the participants' response. The interstimulus interval varied between 500 and 1,700 ms by increments of 300 ms. Response latency was recorded for each trial via a response box, corresponding to the delay between the apparition of the cross and the participant's response. Participants were given the option of taking a short break every 24 trials (i.e., between blocks of trials).

Tasks Reliability

Reliability estimates were computed on mean correct RTs separately for both children with ADHD and TDC, using the split half method (odd-even) with the Spearman-Brown correction. The Color-Stroop Interference (ADHD: incongruent stimuli, $r = .97$; neutral stimuli, $r = .99$; TDC: incongruent stimuli, $r = .99$; neutral stimuli, $r = .99$) and the Simple Reaction Time (ADHD: $r = .99$; TDC: $r = .97$) tasks provided very good reliability.

Procedure

All tasks were administered individually in one session. After participants were informed of the purpose of the investigation, the SRT task and the Color-Stroop test were administered. The order of the tasks was fixed starting with the SRT and then the Color-Stroop task. On average, the session lasted about one hour.

RESULTS

Design of the Analyses

After examining the reliability of the measures of interest at the group level, analyses were performed to first test the group effect on mean RT performance (a) in the Color-Stroop interference effect, focusing on incongruent and neutral conditions, and (b) in the SRT task. Additionally, as concerns the Color-Stroop test, an index of interference was also computed to control for individual differences in baseline performance: The interference index was based on the relative difference between RTs in the incongruent and RTs in

the "signs" neutral condition, that is: (RTs incongruent – RTs neutral)/RTs neutral (see Borella, Delaloye, Lecerf, Renaud, & de Ribaupierre, 2009). Although mean levels of performance were not the primary outcome of interest, those analyses provide a descriptive context within which group differences in performance variability (i.e., IIV in RTs) can be interpreted.

Second, analyses considering traditional indices to quantify IIV in RTs were conducted for the two tasks. In particular, the (a) intraindividual standard deviations (ISD), (b) intraindividual standard deviations computed for the 25% fastest responses (lower quartile, fast-ISD) and the 25% slowest (highest quartile, slow-ISD), and (c) intraindividual coefficients of variation (ICV) were computed.

Third, and finally, to describe more precisely the shape of the individual RT distribution and to better characterize the nature of increased IIV in children with ADHD, ex-Gaussian parameters were estimated using the statistical package quantile maximum probability estimator (QMPE) (Cousineau, Brown, & Heathcote, 2004; Heathcote, Brown, & Mewhort, 2002). The QMPE package outputs an exit code (e.g., information about convergence properties, Hessian singularity) indicating whether the estimated solution is acceptable. Acceptable exit codes are defined in the QMPE manual (e.g. Cousineau et al., 2004). In the present sample, distributions for ADHD and TDC were acceptable for all experimental conditions and tasks, indicating that ex-Gaussian distributions provide a good fit to the Color-Stroop data. Therefore, we used all estimated ex-Gaussian parameters from cases with acceptable exit codes.

For the Color-Stroop and SRT tasks, only correct response latencies were considered for all analyses. Extremely fast responses—RTs below 150 ms for the SRT task and below 200 ms for the Color-Stroop test—were discarded as implausible (e.g., Fagot et al., 2009). With respect to latencies in the Color-Stroop task, all RTs associated with errors were eliminated to exclude voice-key errors (in which the voice key was triggered by a false start, either stutter or extraneous noise) and intrusion errors (in which the participant responded to the incorrect dimension of the stimulus, such as reading the word instead of naming the color).

Descriptive statistics of mean performance levels and performance variability for the measures of interest are presented in Table 1.

Color-Stroop Interference Effect

To analyze the interference effect, a mixed design 2 × 2 analysis of variance (ANOVA) was conducted on average RTs with Group (children with ADHD, TDC) as the between-subjects factor and Condition (incongruent condition vs. neutral condition) as the repeated measures.

Results demonstrated a nonsignificant main effect of Group, $F(1, 46) = 2.90$, $\eta_p^2 = .06$, $p = .09$. The main effect of Condition (interference effect) was significant, $F(1, 46) = 76.90$, $\eta_p^2 = .63$, $p < .001$, indicating that incongruent stimuli were associated with longer latencies as compared to neutral stimuli. The Group × Condition interaction was not significant, $F(1, 46) = 1.00$, $\eta_p^2 = .02$, $p = .32$.

With respect to the interference index (i.e., relative difference between mean RTs in the incongruent and mean RTs in the neutral conditions), one ANOVA with Group (children with ADHD, TDC) as the between-subjects factor was conducted.

Results showed that the main effect of Group was not significant, $F(1, 46) = 2.50$, $\eta_p^2 = .05$, $p = .12$, indicating that children with ADHD and TDC did not differ.

Table 1 Performance Level and Variability in the Color-Stroop and Simple Reaction Time Tasks for Typical Developing Children (TDC) and Children with ADHD.

	TDC ($n = 24$)	ADHD ($n = 24$)
Color-Stroop Interference task		
IM RT		
Neutral	847.6 ± 51.0	1034.0 ± 72.4
Incongruent	1086.1 ± 79.8	1223.5 ± 69.4
Interference index[a]	0.27 ± 0.03	0.20 ± 0.03
ISD RT		
Neutral	207.5 ± 33.3	398.2 ± 84.8
Incongruent	264.5 ± 37.1	400.0 ± 60.2
ICV RT		
Neutral	0.22 ± 0.02	0.34 ± 0.03
Incongruent	0.23 ± 0.02	0.31 ± 0.02
Simple Reaction Time task		
IM RT	415.1 ± 17.4	437.4 ± 18.0
ISD RT	109.7 ± 8.2	170.8 ± 25.9
ICV RT	0.26 ± 0.01	0.37 ± 0.03

Note. RT = reaction times; IM = individual mean; ISD = individual standard deviation; ICV = individual coefficient of variation. Mean ± standard error.

[a]Index calculated on the basis of response times as follows: ([RT incongruent condition - RT control condition] / RT control condition).

IIV Traditional Indices

Separate mixed-design 2 × 2 ANOVAs were conducted with Group (children with ADHD, TDC) as the between-subjects factor and Condition (incongruent vs. neutral stimuli) as the repeated measures on ISD, fast ISD-slow ISD, and ICV (see Figure 2).

With respect to analyses of ISD, the main effect of Group was significant, $F(1, 46) = 4.20$, $\eta_p^2 = .08$, $p < .05$, indicating that children with ADHD were more variable than TDC (see Table 1). In contrast, the main effect of Condition (or interference) and the Group × Condition interaction were not significant, $F(1, 46) = 2.30$, $\eta_p^2 = .05$, $p = .14$ and $F(1, 46) = 2.10$, $\eta_p^2 = .04$, $p = .16$, respectively.

When interference effect was examined on the fast-ISD, only a main effect of Condition was found, $F(1, 46) = 37.30$, $\eta_p^2 = .45$, $p < .001$: Incongruent stimuli were associated with more variable responses than neutral stimuli for the fastest RTs in both groups, which evidenced an effect of interference. The main effect of Group and the Group × Condition interaction were not reliable (for both, $F < 1$).

Conversely, a significant main effect of Group was found on the slow-ISD, $F(1, 46) = 7.50$, $\eta_p^2 = .14$, $p < .01$, with children with ADHD being more variable in their responses, specifically in the slower tail of the individual RT distributions (see Figure 2) than the controls. The main effect of Condition (interference effect) and the Group × Condition interaction were not reliable (for both, $F < 1$).

Results on ICV showed a significant main effect of Group, $F(1, 46) = 8.70$, $\eta_p^2 = .16$, $p < .01$: Children with ADHD produced more variable responses than did TDC (see Table 1). The main effect of Condition ($F = 1.40$, $\eta_p^2 = .03$, $p = .24$) and the Group × Condition interaction ($F = 2.40$, $\eta_p^2 = .05$, $p = .13$) were not significant.

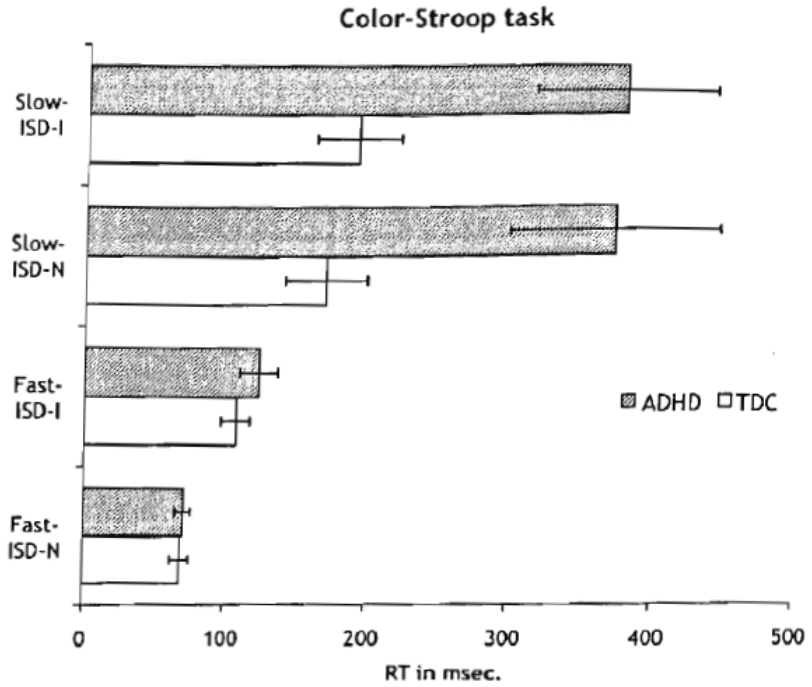

Figure 2 Color-Stroop interference task: Variability of performance for children with ADHD and typically developing children. Error bars represent one standard error.
Note. TDC: typically developing children; ISD: individual standard deviation; Fast-ISD: ISD of the lower quartile for RTs; Slow-ISD: ISD of the upper quartile for RTs; I: incongruent stimuli; N: neutral stimuli. Error bars represent one standard error.

IIV: Ex-Gaussian Analyses

Separate mixed-design 2 × 2 ANOVAs were conducted on *mu*, *sigma*, and *tau* parameters with Group (children with ADHD, TDC) as the between-subjects factor and Condition (incongruent vs. control conditions) as the repeated measures to analyze the interference effect.

Analyses on parameter *mu* revealed a significant main effect of Condition, $F(1, 46) = 91.1$, $\eta_p^2 = .70$, $p < .001$, which indicated higher values in the *mu* parameter that represents central tendency of RT for the Gaussian component of the distribution (i.e., slower mean RTs) for incongruent stimuli as compared to neutral stimuli. The main effect of Group, $F(1, 46) = 3.64$, $\eta_p^2 = .09$, $p = .06$, as well as the Group × Condition interaction, $F(1, 46) = 2.43$, $\eta_p^2 = .03$, $p = .28$, were not significant.

Results for the parameter *sigma* demonstrated a significant main effect of Condition (or interference), $F(1, 46) = 16.18$, $\eta_p^2 = .29$, $p < .001$. Higher values were found for incongruent than for neutral stimuli in the parameter representing the standard deviation for the normal component of the distribution. This indicates overall larger variability for RTs associated with incongruent stimuli as compared to RTs associated with neutral stimuli. The main effect of Group and the Group × Condition interaction were not significant (for both, $F < 1$).

In contrast, as concerns the *tau* parameter, results evidenced a significant main effect of Group, $F(1, 46) = 4.98$, $\eta_p^2 = .11$, $p < .05$, which indicates higher values in the *tau*

parameter representing the mean and standard deviation for the ex-Gaussian component of the distribution for children with ADHD than for TDC (see Figure 3). This means that, as compared to TDC, children with ADHD produced more variable responses specifically in the longer tail of the RT distribution, suggesting a higher frequency of long RTs. The main effect of Condition and the Group × Condition interaction were not significant, respectively, $F(1, 46) = 2.26$, $\eta_p^2 = .03$, $p = .14$, and $F(1, 46) = 2.31$, $\eta_p^2 = .03$, $p = .14$.

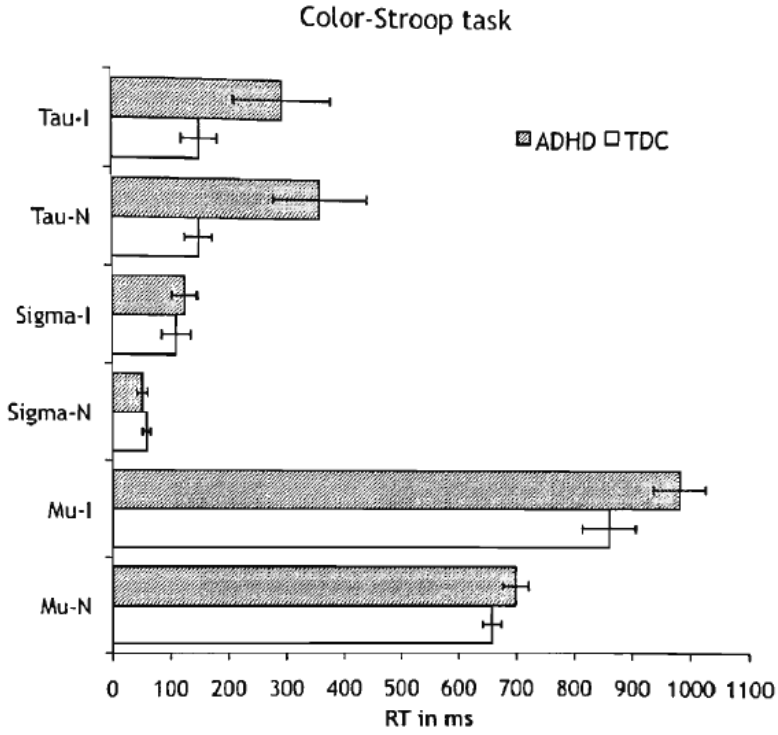

Figure 3 Color-Stroop interference task: Ex-Gaussian parameters from individual RT distributions for children with ADHD and typically developing children. Error bars represent one standard error.
Note. TDC: typically developing children; Mu: mean of the normal component of the individual RT distribution; Sigma: standard deviation of the normal component of the individual RT distribution; Tau: the mean and standard deviation of the exponential component of the RT distribution; I: incongruent stimuli; N: neutral stimuli. Error bars represent one standard error.

SRT Task

The one-way ANOVA conducted to investigate group differences on mean RTs did not show any significant effect ($F < 1$), which indicated that children with ADHD reacted equally fast to the stimuli as compared to TDC (see Table 1).

IIV Traditional Indices

The main effect of Group was significant for ISD, $F(1, 47) = 5.10$, $\eta_p^2 = .10$, $p < .05$, showing that children with ADHD were more variable in their responses than were TDC in the SRT task.

Additionally, the main effect of Group was significant for both fast-ISD, $F(1, 47) = 4.60$, $\eta_p^2 = .09$, $p < .05$, and slow-ISD, $F(1, 47) =. 4.1$, $\eta_p^2 = .08$, $p < .05$, indicating that children with ADHD were globally more variable in their responses (see Figure 4).

The main effect of Group was also significant for ICV, $F(1, 47) = 9.70$, $\eta_p^2 = .18$, $p < .01$, which confirmed that children with ADHD were more variable in their responses than were TDC (see Table 1).

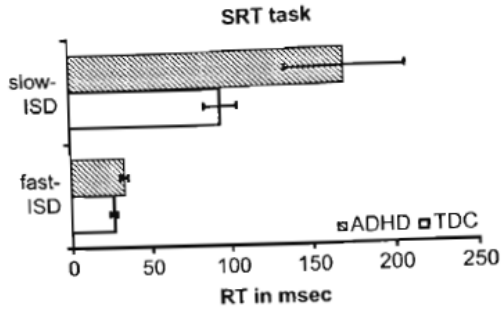

Figure 4 Simple reaction time task: Variability of performance for children with ADHD and typically developing children. Error bars represent one standard error.
Note. SRT task: Simple Reaction Time task, TDC: typically developing children; ISD: individual standard deviation; Fast-ISD: ISD of the lower quartile for RTs; Slow-ISD: ISD of the upper quartile for RTs. Error bars represent one standard error.

IIV: Ex-Gaussian Analyses

One-way ANOVAs were conducted on *mu*, *sigma*, and *tau* parameters in the SRT task. Results showed that the main effect of Group was not significant for the *tau* parameter, $F(1, 47) = 3.2$, $\eta_p^2 = .06$, $p = .08$, and for the *mu* and the *sigma* ones (for both, $F < 1$) (see Figure 5).

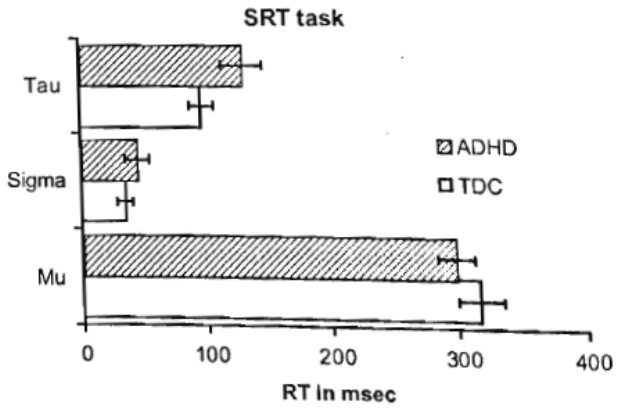

Figure 5 Simple reaction time task: Ex-Gaussian parameters from individual RT distributions for children with ADHD and typically developing children. Error bars represent one standard error.
Note. SRT task: Simple Reaction Time task; TDC: typically developing children; Mu: mean of the normal component of the individual RT distribution; Sigma: standard deviation of the normal component of the individual RT distribution; Tau: the mean and standard deviation of the exponential component of the RT distribution. Error bars represent one standard error.

DISCUSSION

Mixed results are reported in the literature with regard to the deficit of interference control in the Stroop-Color task in children with ADHD as compared to control populations (Homack & Riccio, 2004; Lansberger et al., 2007; Schwartz & Verhaeghen, 2008; Van Mourik et al., 2009). One of the aims of the present study was, therefore, to assess further interference control in children with ADHD and in typically developing children (TDC) in an item-by-item computerized Color-Stroop test. Such a task format allows for a finer grain of analysis than the often-used manual presentation in which items have to be grouped by condition. In particular, this format makes it possible to focus on correct responses only and, more importantly for our present purpose, to study intraindividual variability (IIV) or inconsistency. Study of IIV presents the interest to provide a more complete representation of the distribution of responses than a central tendency such as the mean or the median. Moreover, intraindividual variability has been associated with processing robustness and, when large, has been interpreted to reflect lapses in attentional control.

Our hypothesis, in line with some recent meta-analyses, was that children with ADHD should not be more sensitive to interference when mean performance levels in RTs are considered. In contrast, it was expected that they would exhibit an increased variability in behavioral performance due to dysfunctional regulatory processes producing larger fluctuations in attention or response control (e.g., Tannock, 2003).

To determine whether IIV is specific to a given task and its demands, a classical measure used in the study of IIV, a simple response time task was administered. It was indeed relevant, because the present study aims to select an independent measure of processing speed to better assess the generalizability of IIV in ADHD. Indeed, if increased IIV is a general characteristic of children with ADHD, as we claim, it should show larger fluctuations not only in an interference task such as the Color-Stroop task but also in a task that requires minimal attentional control, such as a simple response time (SRT) task. If, however, increased IIV is specifically due to a deficit in interference control, children with ADHD should exhibit larger fluctuations in the Color-Stroop task only and not in the SRT. It could also be the case, however, that IIV is a general characteristic but varies with the task demands. It would therefore be observed in both types of task but to a greater degree in the interference condition of the Color-Stroop task.

In line with our hypothesis, results showed a similar interference effect in children with ADHD and TDC, as long as the mean performance level was considered. This was true both for the raw RTs, when the incongruent condition was compared to the neutral control one (no Group by Condition interaction in the analysis of variance) and for the interference index, which controls for individual responses in baseline performance. Although contradictory with a number of studies in the field, these results are in line with other studies, which used a computerized version of the Color-Stroop (Alderson, Rapport, & Kofler, 2007; Christiansen & Oades, 2009; Jourdan Moser et al., 2009). Together with a meta-analysis by Van Mourik et al. (2009) and by Schwartz and Verhaeghen (2008), they indicate that group differences in the Color-Stroop interference effect are not as large as suggested by previous studies on ADHD.

It should be noted, however, that the task format may also have played an important role in accounting for these results. The Stroop interference effect, estimated on the basis of RTs, has been shown to be larger in the blocked card-like format than in the item-by-item version in young adults (Kindt, Bierman, & Brosschot, 1996; Salo, Henik, & Robertson, 2001) in typically developing children (Kindt, Bierman, & Brosschot, 1997)

and in older adults (Ludwig, Borella, Tettamanti, & de Ribaupierre, 2010). The grouped format might introduce additional distracting cues, making it more difficult to resist interference. It would therefore be of interest for future studies to compare the control of interference in the two task formats in an ADHD sample to clarify such an issue.

In contrast with the mean level, IIV was larger in children with ADHD than in TDC in the Color-Stroop task: the classical IIV indexes, ISD and ICV, were indeed higher independently of the task condition (or type of stimulus). Analyses performed on the upper and lower quartiles of RTs (rather than on the entire range of RTs) showed that children with ADHD produced more frequent extremely long RTs but comparable fast responses suggesting that children with ADHD suffer from intermittent lapses of attention. They did not seem affected when producing fast responses, which would have attested to an impulsive mode of responses (e.g., anticipations) and to impairments in other aspects of attention. When the ex-Gaussian fitting procedure was used, which is more appropriate to describe the shape of individual RT distributions, children with ADHD were found to exhibit higher *tau* but comparable *mu* and *sigma* values, meaning that the distributions of RTs were more skewed in this group. Furthermore, it should be noted that, as was expected, incongruent stimuli were associated with higher levels of fluctuations than neutral stimuli (Spieler et al., 2000). This result indicates that incongruent stimuli indeed require increasing attentional control to meet the task constraints; this increase was, however, similar for both groups (no interaction). Thus, IIV appears altogether larger in children with ADHD independent of the stimulus condition.

With respect to the SRT, group differences were not significant when mean RTs were considered. In contrast, children with ADHD displayed larger fluctuations than did TDC when classical indices of IIV in RTs were examined (ISD and ICV). Thus, a similar pattern of results was obtained in both the Color-Stroop and the SRT tasks, supporting the hypothesis of a deficit primarily in more basic and central information processing for children with ADHD (Castellanos et al., 2006).

Moreover, in the SRT task, ISDs were larger in children with ADHD than in TDC children for both the 25% slowest and the 25% fastest RTs, which points to an overall higher variability throughout the task. These results could indicate not only that children with ADHD have periodic lapses in attention but also that another mechanism may additionally contribute to increasing IIV, such as an impairment in response preparation as suggested by Vaurio et al. (2009). However, the ex-Gaussian analyses did not reveal significant differences between groups in the SRT task and, as such, do not provide sufficiently strong evidence to definitely support this interpretation of the data.

Of course, we have to acknowledge that the clinical sample size was relatively small. Moreover, we did not investigate ADHD subtypes in the present work. Future studies should thus assess whether IIV interference control is influenced by the ADHD comorbidity, and whether the present results are replicated and can be generalized with other clinical samples. For example, our ADHD group also failed in some executive tasks, and because this failure is not present in all children with ADHD (Willcutt et al., 2005), our group could be particularly impaired. Finally, future studies should also consider assessing reading ability with direct and standardized measures rather than only relying on teachers' ratings.

It is noteworthy that our results are in line with other studies, in particular those using an item-by-item presentation and focusing on the mean performance level in the Color-Stroop task (Christiansen & Oades, 2009; Schwartz & Verhaeghen, 2008; Van Mourik et al., 2009) or on IIV in ADHD (e.g., Castellanos & Tannock, 2002; Williams et al., 2007).

In sum, findings on both mean RTs and IIV clearly do not converge with theories suggesting the existence of a specific deficit, in children with ADHD, in the control of interference in the Color-Stroop test. Interference control may, thus, be a less fundamental characteristic of the disorder than previous empirical work led researchers to believe. Nonetheless, the present data are consistent with difficulties involving a self-regulatory deficit or a failure to allocate adequate effort to meet task demands in children with ADHD, as suggested by Douglas (1999); this deficit leads to some extent to the occurrence of a higher number of attentional lapses during the course of information processing, as shown by IIV indices (Douglas, 1999). Even though Douglas argues, in contrast with the present study, that response inhibition is a fundamental characteristic of children with ADHD, the author also suggests that a broad pattern of variability in performance across a wide range of tasks reflects this dysregulation in ADHD. Our findings provide strong and additional support for considering larger IIV in RTs as a cornerstone in the determination of the cognitive profile of ADHD (Castellanos et al., 2006). Together with other researchers (see Castellanos et al., 2006; Sergeant et al., 2002), we also claim that altered performance in inhibitory tasks, and in particular when interference control is considered, is not due to inhibitory processes only. A complementary interpretation could be in terms of a deficit in processing robustness, which could be associated with neural information-processing fidelity (Li et al., 2004) and linked to the dysfunctions of fronto-striatal-cerebellar circuits, which are responsible for most of the disturbed sensorimotor integration and altered dopaminergic modulation (Castellanos & Tannock, 2002; Krain & Castellanos, 2006) that characterize ADHD.

To conclude, from a clinical point of view, the present results highlight the utility of using a computerized version of the Color-Stroop task, which allows estimating more accurately both the mean performance level and the variability in performance. Both aspects of individual performance should be considered more closely in future research of ADHD before interpreting results in favor of a deficient interference control.

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Efficacy of a multimodal treatment for disruptive behavior disorders in children and adolescents: Focus on internalizing problems

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ABSTRACT

Disruptive Behavior Disorders (DBDs) are among the most common reasons for youth referrals to mental health clinics. Aim of this study is to compare short and medium term efficacy of a multimodal treatment program (MTP), compared to community care (treatment-as-usual, TAU). The sample included 135 youths with DBDs (113 males, age range 9–15 years, mean age 12 ± 2.5 years) were assigned either to a MTP ($n=64$), or addressed to community care for a TAU ($n=71$). Outcome measures were the Child Behaviour Checklist (CBCL) and the Children's Global Assessment Scale (C-GAS). All subjects were assessed at the baseline (T0), after 1-year treatment (T1) and after a 2-year follow-up (T2). Compared with patients receiving TAU, youths in the MTP showed, both at T1 and T2, significantly lower scores on CBCL Externalizing Scale, Internalizing Scale, Anxious/Depressed, Social Problems, and Aggressive Behavior, and higher scores at the C-GAS. Improvement in Internalizing Scales was particularly evident, with a shift from the clinical to the non-clinical range. Rate of use of mental health services and scholastic failure were reduced in the MTP. It is suggested that the improvement of the Internalizing symptoms is a crucial component of the therapeutic process in this MTP.

1. Introduction

Disruptive Behavior Disorders (DBDs), including Oppositional Defiant Disorder (ODD) and Conduct Disorder (CD), are among the most common reasons for youth referrals to mental health clinics (Steiner and Remsing, 2007), and they may be associated with academic failure, persistent maladaptive (impulsive and aggressive) behaviors, and future antisocial outcomes (Pardini and Fite, 2010). Psychosocial maladjustment can be negatively affected by co-occurring internalizing (mood and anxiety) disorders, with related social isolation, low-self esteem, suicidality, self-injury behaviors and substance abuse, although these problems are frequently overshadowed by impulsive aggression (Maughan et al., 2004; Masi et al., 2008). Internalizing comorbidity involves a strong portion of aggressive youths both in community and clinical settings (Boylan et al., 2007; Polier et al., 2012), it is associated with a higher risk of social and school dysfunction (Newcorn et al., 2004; Ezpeleta et al., 2006), with greater persistence of DBD lifetime (Maughan et al., 2004; Nock et al., 2007), and greatly increases the costs for communities (Kolko et al., 2014).

Much progress has been made in identifying evidence-based treatments that decrease aggression (Moffitt et al., 2008). Although psychosocial, psychotherapeutic and familial approaches are usually first-line treatment options, severe behavior disorders may be refractory to such approaches (Kazdin, 2000). Multimodal psychosocial interventions, usually including both youths and parents, have been found to be more effective than interventions delivered only to children (Lochman and Wells, 2002; Pappadopulos et al., 2003; Steiner and Remsing, 2007; Copeland et al., 2009; Kolko et al., 2014; Masi et al., 2013). A cognitive-behavioral therapy (CBT) on youth targets aggressive behaviors and cognitions through behavior management, role playing, social and token reinforcements, and problem solving (Lochman and Wells, 2002; Van Manen et al., 2004). Involvement of parents, aimed at promoting positive parenting practice, significantly increases the effectiveness of interventions

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(Garland et al., 2008; Larsson et al., 2009). Most of the studies have explored efficacy of these interventions in improving severe behavior symptoms, such as hostility and aggression (Kazdin, 2000). Fewer data is available on effects of treatments in improving internalizing symptoms, and their impact on global functioning. In a review article exploring the moderating role of comorbid dimensional symptoms (including those associated with ADHD, anxiety, and depression) on treatment outcomes for ODD/CD children, comorbidity had little or no effect on the treatment of child conduct problems (Ollendick et al., 2008). More specifically, children with and without a comorbid disorder did not differ at the end of treatment in terms of their antisocial behavior, problem behaviors observed in the home, or parent ratings across multiple symptom domains. Results of these studies suggest that comorbidity does not predict negative treatment outcomes for oppositional and conduct problem youth. More recently, Jarrett et al. (2014), in a study designed to evaluate the efficacy of the Coping Power Program (Lochman and Wells, 2004), and to examine how internalizing symptoms predicted change in externalizing problems, reported that greater depressive symptoms, but not anxiety symptoms (as reported by parent or teacher) were associated with a larger reduction in externalizing behaviors problems following a school-based preventative intervention.

Aim of this paper was to explore efficacy of a multimodal, CBT-inspired treatment for patients with DBDs, compared with a community care ("treatment as usual" – TAU), at the end of the treatment (1-year follow-up), and 1 year after the end of the treatment (2-year follow-up). Effects on externalizing and internalizing problems and on psychosocial functioning were separately evaluated.

2. Methods

2.1. Sample

The sample included 135 youths (113 males, age range 9–15 years, mean age 12 ± 2.5 years; 85% Italian, 10% South-American and 5% from Asian and African countries), diagnosed and treated in our Hospital within the period 2005–2011. All the patients were diagnosed according to a clinical interview, the Kiddie Schedule for Affective Disorder and Schizophrenia for School-Age Present Life time Version (K-SADS-PL) (Kaufman et al., 1997), administered to patients and parents by trained child psychiatrists. Furthermore, the Child Behaviour Checklist (CBCL) (Achenbach and Edelbrock, 1983) was completed by parents. To determine IQ, all children were evaluated with the Wechsler Intelligence Scale for Children, 3rd Edition Revised (WISC-III-R) (Wechsler, 1991). Family socio-economic status was evaluated according to Hollingshead (2007). Inclusion criteria were: (1) DSM-IV diagnosis of Conduct Disorder (CD) or Oppositional Defiant Disorder (ODD) according to K-SADS-PL; (2) a Full Scale IQ above 85; and (3) a CBCL Externalizing Scale score above 63.

The patients who met inclusion criteria were assigned either to a Multimodal Treatment Program (MTP) conducted in our hospital ($n=64$), or addressed to community care for a Treatment-As-Usual (TAU) ($n=71$). The sequential allocation in each of the two treatment groups was affected only by the immediate availability of the treatment program of our Hospital. When the treatment was not immediately available, the patients were addressed to the TAU group and followed by the community services, irrespective of their psychosocial or clinical characteristics. No other clinical criteria were used for group assignment. The comparison between the two groups at the baseline showed no statistical differences for socio-demographic variables, including age, gender ratio, ethnicity, socio-economic status according to Hollingshead and Redlich, rate of adoptive children, family type (bi-parental, mono-parental, or custody), and socio-economic status, type of DBD (ODD/CD) and most significant comorbidities (Table 1). Similarly, baseline clinical variables, including all CBCL and C-GAS measures, did not differ between groups, as reported in Table 2.

After 1 year of treatment, the patients in the MTP were followed-up with monthly monitoring visits, while the patients receiving TAU continued the community care. During these 1-hour monthly visits, patients and parents received an unstructured interview exploring behavioral disturbances (including impulsive and aggressive behaviors and substance abuse), social and scholastic functioning, disciplinary measures, and need for further supporting interventions. This information was included in the medical record.

At a 2-year follow-up, the two groups were re-assessed, and parents were also asked, by means of an interview, about further referrals to community mental health services and/or scholastic failure during the follow-up.

The study was approved by the ethical committee of our Hospital. All patients and their families participated voluntarily in the study after written consent was obtained for assessment and treatments procedures.

2.2. Treatment

Multimodal Treatment Program (MTP)

The MTP is a "real world" treatment organized in once-a-week sessions, lasting 1 year, and includes individualized and group support for youths and individual parent training. The duration of each separate session for youth and with parents is two hours. Intervention is conducted by child psychiatrists and psychologists. A social worker helps parents to request welfare benefits or transportation facilities.

During the sessions, an individual and group therapy is focused on teaching children or adolescents to improve self-control, problem-solving skills, and perspective taking. We used the following evidence-based practices to reach these goals: goal setting, modeling, positive reinforcements, anger coping techniques, role-playing and home-works. Structured exercises and group discussions are aimed at improving insight about emotions of self and others, management of rage and temper outbursts. Role playing, videos with group discussion, dramatization, problem solving are used to explore alternatives to increase the insight and improve behavioral dyscontrol. Given the possible role of school failure in worsening the psychosocial adaptation, the children also receive a specific training to improve scholastic achievement, namely their meta-cognitive reading skills, to increase their ability in understanding the text, to develop more effective study strategies and to enhance attention abilities (Masi et al., 2013).

Individual parent training intervention includes defining a selected number of children's behavioral problems (where, when, with whom), and learning techniques to modify parent-youth interaction (for e.g., correct use of prize, punishment and response cost, ignoring and time-out). Parents are trained to monitor conflict situations in which to apply the new parenting practices, to improve predictability and consistency and to increase self-awareness about how to deliver prompts and consequences, and how to manage their child' beliefs, feelings or reactions. In our treatment model, there is not a strict determination in the use of specific evidence-based practices and techniques. However a weekly staff meeting based on case review is used to monitor the adherence of the therapists to the treatment model.

The adherence of the MTP intervention to the model was monitored and measured in the following ways: (a) the therapists attended a official training in cognitive behavioral psychotherapy; (b) the therapists attended case-review meetings with a psychotherapy supervisor; and (c) protocol checklists were completed by the psychotherapist after each session, indicating which objectives were raised and which practices were used. These checklists were reviewed during the weekly supervision sessions, and indicated that over 85% of session objectives were delivered.

Control condition: Treatment as Usual (TAU)

Patients assigned to TAU were treated and followed-up in the community health services. No constraints were set for treatments of this comparison group.

Information about the type and the type of usual-care treatments during the follow-up (1-year and 2 year) were collected with unstructured interviews to patients and parents. According to information available, all the patients received a psycho-educational intervention, with periodic visits (1 or 2 h/week), but only 30 patients received an individual psychotherapy. Parents did not receive therapeutic interventions, but periodic psycho-educational sessions (one or two/month).

2.3. Measures

Two measures were administered at the baseline (T0), after 1 year (at the end of the MTP) (T1), and after 2 years (T2):

- Child Behaviour Checklist (CBCL) (Achenbach and Edelbrock, 1983), a 118-item scale, completed by parents, is one of the most frequently used empirically based instrument for outcome research. Items are scored on a 3-step response scale, and grouped in 8 different syndromes (Withdrawn, Somatic Complaints, Anxious/Depressed, Social Problems, Thought Problems, Attention Problems, Delinquent Behavior and Aggressive Behavior). The CBCL provides a Total Problem Score, two broad-band scores designated as Internalizing Problems (including Withdrawn, Somatic Complaints and Anxious/Depressed syndromes) and Externalizing Problems (including Delinquent Behavior and Aggressive Behavior). A T-score of 63 and above for broadband scales (Total, Externalizing, Internalizing), and of 70 and above for syndrome scales, are considered clinically significant, while a T-score between 61 and 63 for broadband scale and between 65 and 70 for syndrome scales is considered borderline.
- Children's Global Assessment Scale (C-GAS) (Shaffer et al., 1983) is a single-point rating scale designed for use with children from 4 to 16 years of age. It is

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Table 1
Comparison between patients receiving the Multimodal Treatment Program (n = 64) or the Treatment as Usual (n = 71): socio-demographic variables.

	MTP	TAU	P Pearson (χ^2)	Sig
Gender	85.9/14.1% (55/9)	81.7/18.3% (58/13)	$P(1,134)=0.45$	ns
M/F, % (N)				
Age (Mean ± S.D. and range)	12.0±2.4 (range 7–18)	11.0±2.8 (range 6–18)	$P(2,32)=0.13$	ns
Natural children vs	89.1% (57)	91.5% (65)	$P(1,134)=0.24$	ns
adoptive children, % (N)	10.9% (7)	8.5% (6)		
Diagnoses (DSM-IV) % (N)				
DC	20.3% (13)	35.2% (25)	$P(3,694)=0.06$	ns
DOP	79.7% (51)	64.8% (46)		
Comobidity (DSM IV)				
AXIS I				
Mood disoders	45.3% (29)	69.0% (49)	$P(7,751)=0.004$	sig
Anxiety disoders	29.7% (19)	21.1% (15)	$P(4,132)=0.531$	ns
ADHD	20.3% (13)	26.8% (19)	$P(0,774)=0.250$	ns
Eating disorders	0% (0)	1.4% (1)	$P(0,908)=0.526$	ns
Learning disorders	3.1% (2)	12.7% (9)	$P(4,103)=0.004$	sig
AXIS II	6.3% (4)	22.5% (16)	$P(7,640)=0.054$	ns
Socio-economic status	3.1%(2)	0% (0)	$P(4,131)=7.21$	ns
% (N)	31.3%(20)	26.8%(19)		
(CSE Hollingshead)	39.1%(25)	32.4%(23)		
I–II–III–IV–V	25.0%(16)	31.0%(22)		
	1.6%(1)	9.9%(7)		
Family type % (N):			$P(2,133)=1.46$	ns
Custody/Community	3.1% (2)	1.4% (1)		
Biparental	71.9%(46)	80.3%(57)		
Monoparental	25.0% (16)	18.3%(13)		
Ethnicity % (N)				
Caucasian	95.4 % (61)	98.6% (70)	$P(3,485)=0.49$	ns
African	3.0% (2)	1.4% (1)		
South-American	1.6% (1)			

based on a continuum of 1–100, with the higher scores indicating better levels of social and psychological functioning, with increases of 10 points implying the passage to a superior modality of global functioning. Scores above 70 indicate normal functioning. Psychometric properties of CGAS in children and adolescents have been more recently explored (Schorre and Vandvik, 2004).

2.4. Statistical analysis

ANOVA analyses were used to test differences between groups on all selected variables at T0, T1 and T2. Changes over time (T0–T2) for all variables were separately tested for MTP and TAU groups by repeated measure ANCOVA, using time as a within-subject factor and group as a between-subject factor, while controlling for both gender and age. Finally, to test the impact of the different treatments (MTP and TAU) on internalizing and externalizing symptoms and social-psychological functioning at T2, eleven hierarchical regression analyses were conducted. In all regression models age and gender were entered at step 1, the baseline level of symptoms and functioning was entered at step 2, and receiving MTP or TAU was entered at step 3.

3. Results

3.1. Developmental profiles of CBCL in CGAS and MTP and TAU

As reported in Table 2, profile analyses (ANOVAs), conducted at each time, showed no differences between the two treatment groups at the baseline (T0). Compared with patients receiving TAU, youths in the MTP group showed both in T1 and T2 significantly lower scores on CBCL Externalizing Problems and Internalizing Problems. Among the CBCL syndrome scales, Anxious/Depressed, Social Problems, Thought Problems and Aggressive Behavior strongly improved at T1, as well as in T2. Somatic Complaints and Delinquent Behavior differed between MTP and TAU only in T2. C-GAS score in MTP group improved over time from 41.9 ± 6.8 to 51.5 ± 7.7 in T1, compared to a stable score in TAU (from 38.5 ± 7.8 to 39.8 ± 8.7). In T2, C-GAS further improved to 56.7 ± 10.9 in MTP, compared 41.3 ± 10.9 in TAU group.

Based on clinical cut-off scores, in the MTP, but not in the TAU, mean score of Externalizing Scale at T2 improved from the clinical range to the borderline range. Similarly, Internalizing Scale shifted to the normal range in the MTP group, while the externalizing scale score persisted in the clinical range in the TAU group. More specifically, in the MTP group, but not in TAU, a transition from the borderline range to the normal range was evident at T2 for the syndrome scales Withdrawn, Anxious/Depressed, Social Problems, Delinquent Behavior, while Attention Problems and Aggressive Behavior shifted from the clinical range to the normal range. In the TAU group Aggressive Behavior persisted in the clinical range from the baseline to T2, while Anxious/Depressed, Social Problems, Attention Problems and Delinquent Behavior persisted in the borderline range.

Regarding the changes at the end of the treatment and after 1-year follow-up, the repeated results (ANCOVA) showed that C-GAS significantly improved over time [$F(2,156)=4.44$, $p>0.05$]. Moreover, there were several significant interactions between time and group for CGAS [$F(2, 156)=34.81$, $p>0.001$], Somatic Complaints [$F(2, 132)=3.67$, $p>0.05$], Aggressive Behavior [$F(2, 132)=5.98$, $p>0.01$], Delinquent Behavior [$F(2, 132)=2.70$, $p>0.07$] and Externalizing Scale [$F(2, 132)=2.78$, $p>0.07$].

Finally, analyses of covariance indicated significant effect of only gender for Somatic complaints [$F(1,66)=5.01$, $p=0.03$], and for Attention problems [$F(1,66)=5.59$, $p=0.02$]. Girls showed higher scores in Somatic Complaints (C.I.=58.6–66.6) and Attention problems (C.I.=67.6–77.5) than boys (C.I.=56.2–59.2, and C.I.=64.5–68.1, respectively) during time.

3.2. Impact of MTP and TAU treatment on child's emotional/adaptive outcomes

As showed in Table 3, with the only exception of Withdrawn and Delinquent Behavior, all regression models showed that receiving MTP significantly predicted a lower level of child's problems, explaining between 3% and 6% of variance after controlling for

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Table 2
Child Behavior Checklist (CBCL) and Children-Global Assessment Scale (C-GAS) scores across time in patients receiving the Multimodal Treatment Program (MTP) (n=64) and Treatment as Usual (TAU) (n=71).

	MTP		TAU		ANOVA	ANCOVA	
	Mean	Ds	Mean	Ds		Time	Group × Time
Externalizing Problems							
T0	69.73	7.43	71.49	7.25	$F(1,134)=1.93$ ns	$F(2, 132)=0.55$ ns	$F(2,132)=2.78$ +
T1	65.58	7.34	68.58	7.62	$F(1,134)=5.39$*		
T2	63.57	9.34	68.52	9.90	$F(1,69)=4.78$*		
Internalizing Problems							
T0	65.53	7.06	65.59	7.52	$F(1,134)=0.01$ ns	$F(2, 132)=0.91$ ns	$F(2, 132)=1.05$ ns
T1	60.14	8.04	64.62	9.07	$F(1,134)=9.13$**		
T2	59.57	8.94	65.00	8.36	$F(1,69)=6.48$**		
Withdraw							
T0	65.08	9.46	63.34	8.00	$F(1,134)=1.33$ ns		$F(2, 132)=0.57$ ns
T1	60.50	7.67	62.48	8.90	$F(1,134)=1.89$ ns		
T2	60.11	8.83	63.19	9.41	$F(1,69)=1.92$ ns		
Somatic Complaint							
T0	59.03	8.97	58.55	7.50	$F(1,134)=0.11$ ns	$F(2, 132)=0.65$ ns	$F(2,132)=3.67$*
T1	57.00	6.84	59.03	8.23	$F(1,134)=2.39$ ns		
T2	56.75	7.25	60.63	8.07	$F(1,69)=4.39$		
Anxious/Depressed							
T0	65.89	7.67	67.13	8.62	$F(1,134)=1.89$ ns	$F(2, 132)=1.18$ ns	$F(2,132)=0.39$ ns
T1	60.03	7.85	66.85	10.08	$F(1,134)=18.89$		
T2	60.82	7.60	65.63	10.71	$F(1,69)=4.89$*		
Social Problems							
T0	67.22	7.87	67.04	7.87	$F(1,134)=0.01$ ns	$F(2, 132)=0.49$ ns	$F(2,132)=0.85$ ns
T1	61.92	8.21	67.25	9.96	$F(1,134)=11.37$***		
T2	63.39	8.30	67.41	9.68	$F(1,69)=3.45$*		
Thought Problems							
T0	62.02	9.32	65.14	9.37	$F(1,134)=3.74$*	$F(2, 132)=1.63$ ns	$F(2,132)=0.93$ ns
T1	58.36	8.18	63.70	10.10	$F(1,134)=11.26$***		
T2	56.82	7.48	63.15	10.54	$F(1,69)=8.73$**		
Attention Problems							
T0	71.36	9.51	70.37	9.12	$F(1,134)=0.38$ ns	$F(2, 132)=0.35$ ns	$F(2,132)=1.85$ ns
T1	65.23	8.59	68.63	10.39	$F(1,134)=4.23$*		
T2	64.41	8.88	67.41	8.20	$F(1,69)=2.02$ ns		
Aggressive Behavior							
T0	71.67	9.03	74.06	9.77	$F(1,133)=2.14$ ns	$F(2, 132)=0.30$ ns	$F(2,132)=5.98$**
T1	66.81	8.52	71.17	10.00	$F(1,133)=7.34$**		
T2	63.57	10.60	71.00	10.55	$F(1,69)=8.25$**		
Delinquent Behavior							
T0	66.03	8.07	67.90	8.31	$F(1,133)=1.73$ ns	$F(2, 132)=1.75$ ns	$F(2,132)=2.70$+
T1	63.42	7.51	65.20	7.92	$F(1,133)=1.77$ ns		
T2	61.82	9.00	66.04	8.95	$F(1,69)=3.69$*		
CGAS							
T0	41.94	6.84	38.51	7.80	$F(1,134)=3.15$ ns	$F(2, 156)=4.44$ **	$F(2,156)=34.81$***
T1	51.50	7.683	39.80	8.69	$F(1,117)=45.88$***		
T2	56.79	10.86	41.37	10.91	$F(1,82)=39.01$***		

ns = not significant;
+ $p>0.07$.
* $p>0.05$.
** $p>0.01$.
*** $p>0.001$.

gender, age and baseline score. Moreover, receiving MTP explained the 17% of variance in C-GAS at T2.

More specifically, receiving MTP was negatively and significantly correlated with Externalizing Scale score (beta −0.21) and Internalizing Scale score (beta −0.26), and with some syndrome scales, such as Thought Problems (beta −21), Somatic Complaints (beta −0.27) and Aggressive Behavior (beta −0.26). On the contrary, receiving MTP was positively and significantly correlated with positive social-psychological functioning, as assessed by the C-GAS score (beta 0.44).

Finally, baseline CBCL scores predicted higher levels of later Externalizing and Internalizing Scale scores at T2 (explained variance ranging from 9% to 38%). In addition, age was particularly important in explaining Thought and Attention problems, as younger patients were at higher risk for these problems. Gender was more closely related with Attention problems, as females were more at risk than males.

At the end of the 2-year follow-up, parents were asked about the referrals to mental health services and scholastic failure within the follow-up period. Only 10 patients receiving MTP (15.6%) needed further support from health services, compared to 41 (57.7%) from TAU [$F(1,134)=25,4$; $p<0.001$]. Similarly, scholastic failure was reported in 16 patients (25%) from MTP, compared to 41 (57.7%) in TAU [$F(1, 134)=14,79$, $p<0.001$].

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Table 3
Hierarchical regression models.

		Beta 1	Beta 2	Beta 3	R Change	R^2
Externalizing Problems						
Step 1	Age	ns.	ns.	ns.	0.04	
	Gender	ns.	ns.	ns.		
Step 2	Criterion (TD)		0.46***	0.44***	0.20***	
Step 3	Treatment (MTP vs TAU)			−0.21*	0.05*	0.29
Internalizing Problems						
Step 1	Age	ns.	ns.	ns.	0.03	
	Gender	ns.	ns.	ns.		
Step 2	Criterion (TD)		0.35***	0.23**	0.12***	
Step 3	Treatment (MTP vs TAU)			−0.26*	0.05*	0.17
Withdraw						
Step 1	Age	ns.	ns.	ns.	0.00	
	Gender	ns.	ns.	ns.		
Step 2	Criterion (TD)		0.39***	0.39***	0.15***	
Step 3	Treatment (MTP vs TAU)			ns.	0.02	0.18
Somatic Complaint						
Step 1	Age	ns.	ns.	ns.	0.00 (+)	
	Gender	0.25**	ns.	ns.		
Step 2	Criterion (TD)		0.32***	0.31***	0.09**	
Step 3	Treatment (MTP vs TAU)			−0.27*	0.07*	0.19
Anxious/Depressed						
Step 1	Age	ns.	ns.	ns.	0.02	
	Gender	ns.	ns.	ns.		
Step 2	Criterion (TD)		0.51***	0.48***	0.25***	
Step 3	Treatment (MTP vs TAU)			−0.18+	0.03+	0.31
Social Problems						
Step 1	Age	ns.	ns.	ns.	0.07+	
	Gender	0.26*	ns.	0.47***		
Step 2	Criterion (TD)		0.49***	0.47***	0.22***	
Step 3	Treatment (MTP vs TAU)			−0.18+	0.03+	0.32
Thought Problems						
Step 1	Age	−0.27*	−0.28*	−0.24*	0.07+	
	Gender	ns.	ns.	ns.		
Step 2	Criterion (TD)		0.63***	0.59***	0.38***	
Step 3	Treatment (MTP vs TAU)			−0.21*	0.04*	0.49
Attention Problems						
Step 1	Age	−0.25*	−0.24*	−0.21+	0.12**	
	Gender	0.32**	0.24*	0.23*		
Step 2	Criterion (TD)		0.36***	0.38***	0.12**	
Step 3	Treatment (MTP vs TAU)			−0.18+	0.03+	0.27
Aggressive Behavior						
Step 1	Age	−0.23+	−0.20	ns.	0.05*	
	Gender	ns.	ns.	ns.		
Step 2	Criterion (TD)		0.44***	0.41***	0.18***	
Step 3	Treatment (MTP vs TAU)			−0.26*	0.06*	0.30

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Table 3 (continued)

		Beta 1	Beta 2	Beta 3	R Change	R^2
Delinquent Behavior						
Step 1	Age	ns.	ns.	ns.	0.02	
	Gender	ns.	ns.	ns.		
Step 2	Criterion (T0)		0.46	0.44	0.20***	
Step 3	Treatment (MTP vs TAU)			Ns	0.03	
						0.25
CGAS						
Step 1	Age	ns.	ns.	ns.	0.0	
	Gender	ns.	ns.	Ns.		
Step 2	Criterion (T0)		0.70***	0.59***	0.45***	
Step 3	Treatment (MTP vs TAU)			0.44***	0.17***	
						0.65

Legend: ns = not significant;
MTP = 1 and TAU = 0.
Gender = 1 male 2 female.
Criterion (T0) = dependent variable at time 0.
* $p > 0.07$.
** $p > 0.05$.
*** $p > 0.01$.
**** $p > 0.001$.

4. Discussion

Conduct disorders are among the most common psychiatric disorders in children and adolescents. The costs to society are high and impact many public sector agencies, including health services, social, education and criminal justice systems (Knapp et al., 1999; Romeo et al., 2006; Snell et al., 2013), and these costs become even greater when patients grow up (Scott et al., 2001; Colman et al., 2009). Hence, it is crucial to evaluate the efficacy of treatments, in terms of persistence of the disorder, repeated utilization of mental health services, and school- and work-failure (Lochman and Wells, 2004; Bonin et al., 2011; Fonagy et al., 2013). There are many evidence based treatment programs for DBDs (Eyberg et al., 2008) and almost all of these programs are based on Cognitive Behavior practices for reducing externalizing behavior problems in at-risk and clinic-referred youths (Garland et al., 2008). However, not all clinicians agree with the assumption that manualized interventions maximize health gains (Weisz and Kazdin, 2010). Aim of our study is to explore the efficacy of a multimodal, CBT-based treatment involving patients with DBDs and their parents. We used as a comparison a non-specific community care ("treatment as usual"), and we prolonged the assessment period not only to the end of the 1-year treatment, but also to further 1-year follow-up.

The comparison between the two groups at T1 and at T2 revealed a significant treatment effect, with significantly greater improvements in the MTP group, according to both clinicians' and parents' ratings. More specifically, MTP was more effective than TAU in decreasing not only harmful and rule-breaking behaviors, but also internalizing behaviors, and it also improved general social and psychological functioning. Furthermore, based on parents' interviews at the end of the 2-year follow-up, receiving MTP positively affected rates of both further referrals to community mental health services and scholastic failure.

Children-Global Assessment Scale, a reliable measure to evaluate changes in functional impairment over time (i.e., after treatment) (Schorre and Vandvik, 2004), showed a significant improvement only in MTP group. This finding is supported by hierarchical regression, as MTP significantly predicted an improvement of global functioning, evident at the end of treatment (1 year), and persisting 1 year after. Although C-GAS score did not reach the normal range (> 70), it shifted to an upper level (from 41 to 56 in MTP), corresponding to "children with sporadic difficulties or symptoms in some but not in all areas". On the contrary, the TAU group stayed on the same "moderate to severe impairment in most of social functioning areas", corresponding to the baseline level.

CBCL analysis can further specify the C-GAS improvement in the MTP group. The MTP group showed a significant improvement of CBCL Total Externalizing score, at the end of treatment as well as in the post-treatment year, when the Externalizing score moved from the clinical to the borderline range. On the contrary, TAU group presented only a slight improvement, but remaining in the upper level of the clinical range. Among the Externalizing Problems, only in the MTP group Aggressive and Delinquent Behavior improved from the clinical level to the borderline/non-clinical level, with clear prognostic implications, as they are a strong risk factor for school expulsion, school failure and peer rejection (Beauchaine et al., 2005).

The significant improvement in Internalizing Problems is less obvious, and deserves more specific attention. The within and between group analyses show that only in the MTP group, the Internalizing Scale significantly improved from the clinical-borderline to the non-clinical range, particularly evident in Anxious/Depressed and in Social Problems.

How can we explain these results, and namely the persistence of the improvement 1 year after the end of the treatment, with specific

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features of the MTP intervention? A first issue is the involvement of the parents in the treatment program. This is consistent with other studies (Lochman and Wells, 2004; Drugli and Larsson, 2006; Drugli et al., 2007; Larsson et al., 2009), reporting a greater improvement of Externalizing Problems, when a combined child–parent treatment is delivered, to enhance and promote new effective parenting strategies, compared to treatments focused only on patients. Different reasons support a combined youths–parents intervention. Maternal negative/ineffective discipline, lack of warmth, lack of parental monitoring and a father's antisocial personality disorder are frequently associated with DBDs (Dishion et al., 2002; Pfinner et al., 2005). Furthermore, a relation has been noted with maternal distress even when controlling for socioeconomic status (Barry et al., 2005; Peters et al., 2005) and maternal hostile intent attribution (Nelson et al., 2008). Finally, poorer outcomes are often due to low socio-economic status of families (Reyno and McGrath, 2006).

Another component of the treatment which may have affected the result is the attention to the scholastic achievement. We have not included in the outcome measures specific data supporting the effect of the intervention on scholastic results. However, we maintain that an increased attention to a better school functioning, with a specific intervention based on metacognition, study strategies and attention abilities, may decrease the impact of school failure on social and behavioral adaptation.

A crucial issue of our MTP, which may have positively affect the results and their persistence in time, is the particular attention devoted to the Internalizing symptoms of our patients. The clinical relevance of Internalizing symptoms in disruptive youths is still a neglected issue, considering that all the children with DBDs (Stringaris and Goodman, 2009; Pardini and Fite, 2010), and more specifically those with ODD (Nock et al., 2007), have an increased risk for developing internalizing disorders over time. Few studies have documented the role of Internalizing problems in treatments firstly implemented for patients with disruptive behavior disorders (Cornelius et al., 2010; Jacobs et al., 2010). Some studies support the notion that co-occurring anxiety and depression can predict the persistence of externalizing problems in youths following intervention programs for behavior problems (Jarrett et al., 2014) or with DBD (Beauchaine et al., 2005). We suggest that the improvement in the Internalizing domain may be a relevant clinical aim, and at least three aspects of our treatment may be more closely related to this aim: (1) teaching self-control and problem solving to children improves their emotional regulation; (2) facilitating parents' interpretation of their children' behaviors and feelings, and promoting more effective and warm parenting improve affect regulation and self-esteem in children; and (3) working on negative emotionality reduces a common risk factor for both Externalizing and Internalizing problems (Lochman et al., 2011).

Some differences related to gender and age at onset emerged in covariate analysis. While there is a weak influence of gender in Somatic and Social Problems, which lasts in the first step, an important role of female gender is found in the Attention scores, which persists in all three steps of the hierarchical regression. This is in line with the literature assumption that males are more affected by hyperactivity/impulsivity, while females have more frequently disattention than males (Biederman et al., 2002; Wolraich et al., 2005). Clinical and treatment implications request further research, as it may help to implement more tailored and specific treatment strategies.

Our study presents several methodological limitations. Firstly, the raters were not blind to treatment group, and so an experimenter bias may have occurred. Secondly, the allocation of the patients to the treatment groups was not random, but related to immediate availability of the treatment in the Hospital. This method may have introduced a possible assignment bias. However, no differences between groups were identified on demographic and clinical variables; furthermore, we have covaried the comparison in hierarchical regression by age and gender, in order to minimize the effect of the partial lack of randomization. Thirdly, all the patients in the control group did not receive the same treatment. However, TAU is considered a reliable measure of the "normal" prototypical treatments in the community. Finally, our treatment is not manualized (although the most significant features have been explained in the Method section), and it should be compared with a manualized one. However, non-manualized CBT principles and parent training skills are more representative of what occurs in real-world clinical practice.

In summary, the results indicate that MTP group presented a greater improvement than TAU group in the symptomatic and functional domains, in both Externalizing and Internalizing problems. The persistence of the results 1 year after the treatment may suggest that a multimodal treatment may positively affect the impact of DBDs on health services, education and criminal justice systems. This issue should be kept in mind when the costs of the MTP are considered, included its practicality and feasibility in the real-world of managed-care.

The improvement in Internalizing problems is in our opinion an important component of the treatment outcome, and it may further and positively affect outcome, in terms of intensity and stability over time. There is room for further research aimed to explore whether co-occurring symptoms of depression or anxiety may be associated to enhanced changes in externalizing problems following intervention for externalizing problems, and to further explore possible mechanisms of change (Jarrett et al., 2014).

Conflict of interest

Dr. Masi was in the advisory boards for Eli Lilly and Shire, has received research grants from Eli Lilly and Company and Shire, and has been speaker for Eli Lilly, Shire, Lundbeck, and Novartis, and had been consultant for Otsuka. All the other authors do not have conflicts of interest to declare.

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Bipolar Disorder in Children With ADHD: A Clinical Sample Study

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Abstract

Objective: To explore the impact of early-onset bipolar disorder (pediatric bipolar disorder [PBD]) on ADHD. **Method:** We compared ADHD symptom severity, ADHD subtype distribution, and rates of comorbid and familial psychiatric disorders between 49 ADHD children with comorbid PBD and 320 ADHD children without PBD. **Results:** Children with ADHD and PBD showed higher scores in the Hyperactive and Inattentive subscales of the ADHD Rating Scale, than children with ADHD alone. The frequency of combined subtype was significantly higher in ADHD children with PBD, than in those with ADHD alone. ADHD children with PBD showed a higher rate of familial psychiatric disorders than ADHD children without PBD. The rate of conduct disorder was significantly greater in children with PBD and ADHD compared with children with ADHD alone. **Conclusion:** ADHD along with PBD presents with several characteristics that distinguish it from ADHD alone, suggesting that these may be distinct disorders. *(J. of Att. Dis. XXXX; XX(X) XX-XX)*

Keywords

prevalence, bipolar disorder, ADHD, children

Introduction

Pediatric bipolar disorder (PBD) may present differently than bipolar disorder (BD) in adults (Geller & DelBello, 2005; Luby & Belden, 2006; Wolf & Wagner, 2003). Particularly, a marker of juvenile PBD is the high rate of comorbidity with ADHD (Barkley & Murphy, 2006; Biederman et al., 1996; Donfrancesco et al., 2011; Faraone & Biederman, 1997; Galanter & Leibenluft, 2008; Kim & Miklowitz, 2002; Sachs, Baldassano, Truman, & Guille, 2000). This comorbidity often leads to severe impairment, with increased impulsivity, psychotic symptoms, need for hospitalization, and school failure (Wolf & Wagner, 2003). The relationship between PBD and ADHD has received considerable attention in psychiatric research. Elevated rates of PBD–ADHD comorbidity among youth and co-aggregation within families raise the question of whether co-occurring PBD and ADHD represent a more severe subtype of either PBD or ADHD or a unique disorder (Miller, Chang, & Ketter, 2013; Singh, DelBello, Kowatch, & Strakowski, 2006). Rates of PBD in children with ADHD vary widely depending on the sample and which assessment approach is used (Pataki & Carlson, 2013). Specifically, a number of reviewers have pointed out that differences in methodologies influence rates of PBD in ADHD samples and rates of ADHD in PBD samples (Carlson, 2011; Galanter & Leibenluft, 2008; Hassan, Agha, Langley, & Thapar, 2011; Pataki & Carlson, 2013). Serrano, Ezpeleta, and Castro-Fornieles (2013) found that 8% of an ADHD sample met criteria for PBD and 6% for BD–not otherwise specified (BD-NOS).

In the same way, ADHD has been recognized as a prevalent comorbidity in juvenile BD (Sachs et al., 2000; Tamam, Karaku, & Ozpoyraz, 2008). Systematic studies of children and adolescents with a diagnosis of BD show that rates of ADHD range from 57% to 98% (Geller et al., 1995; Kowatch et al., 2005; Tramontina, Schmitz, Polanczyk, & Rohde, 2003), while other study found a prevalence of ADHD of 21.1% in children with BD (Soutullo et al., 2009). These data focus on a bidirectional overlap, even if the percentage of PBD in ADHD children is much lower than the percentage of ADHD in children with BD.

While the rate of ADHD comorbidity in PBD youth appears to be a function of age (Wozniak, 2005), the impact on age of comorbid PBD in ADHD samples is less clear. According to a review article by Wilens et al. (2002),

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children with ADHD are 10 times more likely to develop PBD than age-matched and gender-matched controls. However, ethnic and sociocultural differences are meaningful in the emergence of early-onset PBD (Kennedy, Boydell, van Os, & Murray, 2004).

The overlap of diagnostic criteria between PBD and ADHD (e.g., hyperactivity, impulsivity/aggressiveness, distractibility, irritability, and emotional lability) makes the differential diagnosis difficult (Biederman et al., 1996; Milberger, Biederman, Faraone, Murphy, & Tsuang, 1995; Wozniak, 2005).

The relationship between ADHD and PBD is far from clear; three models have been suggested to explain this overlap: (a) ADHD symptoms can be a prodrome to PBD in some patients, (b) PBD and ADHD are distinct disorders but share an association with emotional dysregulation in children, and (c) PBD may be a severe variant of personality traits in which an underlying dysfunction in affective and cognitive circuitry associated with emotion regulation causes both temperamental difficulties and clinical symptoms (West, Schenkel, & Pavuluri, 2008).

Other studies suggest that PBD with ADHD can be a distinct genetic subtype from PBD or ADHD alone (Biederman et al., 2008; Wozniak, 2005). This issue is not merely nosological as ADHD comorbidity affects several clinical features of PBD and it can be a meaningful predictor of prognosis and treatment (Biederman et al., 1996; Faraone & Biederman, 1997; Masi et al., 2004).

In previous studies, some authors explored the effects of ADHD co-occurrence on PBD phenomenology and treatment by analyzing a sample of children and adolescents with PBD, and stratifying them according to the ADHD comorbidity, that is, presence or absence. According to these findings, ADHD was associated with an earlier onset of PBD (Masi et al., 2007), a chronic course and an irritable mood (Masi et al., 2006), a greater resistance to treatments (Masi et al., 2004), a more frequent diagnosis of BD-NOS (Masi et al., 2007), and a lower rate of lithium response (Masi et al., 2010). In another research study of ADHD (Donfrancesco et al., 2011) in children with PBD spectrum, we found that ADHD children with PBD spectrum, compared with those with ADHD alone, showed a higher rate of combined subtype, higher scores of ADHD Rating Scale, and higher rates of major depression, oppositional defiant disorder (ODD), and conduct disorder (CD).

With these considerations in mind, the main aim of the present study is to expand upon these findings in a larger sample of children with ADHD and PBD rather than those with all bipolar spectrum disorders (e.g., BD-NOS). We hypothesized that youth with ADHD–PBD co-occurrence is associated with (a) a greater severity of ADHD symptoms, (b) a greater rate of combined ADHD subtype, (c) a greater frequency of familial psychiatric disorders, and (d) a higher frequency of other comorbidities than those with ADHD alone.

Method

We studied 369 consecutive drug-naive Caucasian outpatients with ADHD (324 boys and 45 girls, mean age of 8.8 years, $SD = 2.5$), diagnosed at the Clinic for Developmental Neurology and Psychiatry of "S. Pertini Hospital" in Rome, from 2010 to 2013. All participants were in the middle socioeconomic status (SES) level (Hollingshead, 1975), with a mean score of 74.8 ($SD = 13.7$). Parents of participants signed a statement of informed written consent and the privacy policy. In our sample of 369 children with a diagnosis of ADHD, 49 had comorbid PBD (13.28% of the total sample; 46 boys; $M_{age} = 8.54$, $SD = 2.46$; duration of the PBD symptoms: $M = 18.86$ months, $SD = 9.44$) and 320 did not have comorbid PBD (86.72% of the total sample; 278 boys; $M_{age} = 8.80$; $SD = 2.52$). The diagnosis of PBD was defined according to *Diagnostic and Statistical Manual of Mental Disorders* (4th ed., text rev; *DSM-IV-TR*; American Psychiatric Association [APA], 2000) criteria for BD I or BD II, including duration and functional impairment. Bipolar NOS children are excluded. In the group of 49 bipolar participants, 42 were PBD-type 1 and 7 were PBD-type 2. All the children in the ADHD–PBD group showed in the assessment session both ADHD symptoms and mood disorder symptoms. However, the retrospective evaluation confirmed a starting point of bipolar symptomatology, after the onset of ADHD.

Disruptive mood dysregulation disorder (DMDD), according to *DSM* (5th ed.; *DSM-V*; APA, 2013) criteria was not assessed, but the diagnosis of BD was performed following the *DMS-IV-R* criteria.

Regarding the features of BD in our group of children with PBD, the elated mood was more frequent (79.60%) than irritability (65.31%): These data diverge from the data of Wozniak et al. (2005) who found irritability as a cardinal symptom of PBD with a percentage (94%) higher than elated mood (51%). This difference can be explained by cultural features, according to the previous transcultural study (Donfrancesco et al., 2014) about a comparison of PBD in Italy and the United States. Regarding other symptoms of our PBD sample, 61.22% presented grandiosity, 20.41% reported decreased need for sleep, 85.71% were more talkative than usual, 77.55% exhibited racing thoughts, 57.14% showed poor judgment, 65.31% demonstrated increase in goal-directed activity, and none presented psychotic symptoms.

Both children and parents of the samples (ADHD with PBD; ADHD without PBD) participated in three clinical sessions to reconstruct lifetime and medical history and to assess familial psychiatric disorders (only first and second degree siblings are included). They also received a Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL; Kaufman et al., 1997) conducted by an experienced child

psychiatrist (RD). Lifetime comorbid psychiatric disorders were also identified using the K-SADS.

The parents of all participants were also asked to fill out the ADHD Rating Scale Parent Version (ADHD-RS PV) adapted for the Italian population (Marzocchi & Cornoldi, 2000), to explore the severity of ADHD symptomatology. The Wechsler Intelligence Scale for Children–III (WISC-III), Italian version (Orsini & Picone, 2006), was used to estimate the IQ.

Statistical Analysis

Demographic characteristics of children with comorbid ADHD and PBD versus those with ADHD alone were compared using χ^2 analysis for categorical variables and one-way ANOVAs for continuous variables.

One-way ANOVAs were also performed on IQ scores (Total, Performance, and Verbal IQ) and on ADHD Rating Scale scores (Total, Hyperactivity, and Inattention Scales), whereas χ^2 analyses were computed in relation to the distribution of ADHD subtypes, other comorbid diagnoses, including, anxiety disorder, ODD, and CD.

Logistic regressions were used to verify the role of demographic variables, ADHD severity, ADHD subtypes, and the presence of other psychiatric comorbidities on the presence/absence of PBD as a *dummy* variable (respectively codified with 0/1). Specifically, three models were run: The first included, as independent variables, age, sex, IQ, SES, and ADHD Rating Scale PV scores (Total, Hyperactive, and Inattentive scores); the second model included age, sex, IQ, SES, and ADHD subtypes (combined, hyperactive, and inattentive subtypes); the third model included age, sex, IQ, SES, and comorbid lifetime diagnoses (depressive disorders, anxiety disorders, ODD, CD).

Results

No differences in the distribution of sex, age, and SES were found between the ADHD with PBD versus ADHD-alone groups (see Table 1). The first group was composed of 46 boys (93.88%), whereas the second group was composed of 278 boys (86.88%). Mean age of the ADHD group with PBD was 8.54 ($SD = 2.46$), and mean of ADHD group without PBD was 8.80 ($SD = 2.52$).

Moreover, as shown in Table 1, ADHD children with PBD showed higher scores on the Total scale ($F = 9.64$; $p = .00$; effect size = 0.03), Hyperactivity ($F = 20.81$; $p = .00$; effect size = 0.05), and Inattention ($F = 4.25$; $p = .04$; effect size = 0.01) subscales of ADHD Rating Scale than ADHD children without PBD.

Regarding ADHD subtypes distribution, the percentage of combined subtype was significantly higher and the percentage of inattentive subtype was significantly lower in ADHD children with comorbid PBD, compared with children without PBD.

Youth with ADHD and PBD showed higher percentage of lifetime ODD and CD, compared with those with ADHD and without PBD group. Finally, no differences were found in IQ scores between the two groups.

Of the 320 ADHD children without PBD (6.88%), 22 had at least one parent with psychopathology compared with 24 of the 49 ADHD children with PBD (48.98%).

Logistic regressions showed that only high ADHD-RS Hyperactivity score (Cox and Snell Index = .06; $B = 0.17$; $p < .01$) was significantly associated with the presence of PBD in ADHD children, and that only combined subtype was a significant predictor of the presence of PBD (Cox and Snell Index = .02; $B = .76$; $p < .05$). Regarding psychiatric comorbidity, lifetime diagnoses of ODD (Cox and Snell Index = .09; $B = 1.31$; $p < .01$) or CD ($B = 1.03$; $p < .05$) were significantly associated with PBD in ADHD children.

Discussion

The literature strongly suggests that ADHD is associated with very early-onset BD (PBD; Galanter & Leibenluft, 2008; Kim & Miklowitz, 2002). PBD is a crucial issue in current research, as epidemiological studies examining age at onset of the first episode of bipolar illness show that the median age is lower by 4.5 years in participants born in the past 50 years, and that participants with prepubertal onset are significantly higher in the more recent cohorts (Chengappa et al., 2003).

The main aim of the study was to assess the impact of PBD comorbidity in ADHD children. Previous studies reported an overall prevalence of PBD in 0.5% to 30% of ADHD children (Hassan et al., 2011; Tillman & Geller, 2006), but several reviewers have pointed out that differences in methodology influence findings in these rates (Carlson, 2011; Galanter & Leibenluft, 2008; Hassan et al., 2011; Pataki & Carlson, 2013).

In our sample of 369 children, 49 (13.28%) of the participants displayed comorbid PBD. The prevalence of PBD in our sample appears consistent with the literature: Molina et al. (2009) showed rates of 11% to 23% of PBD using lifetime prevalence and the Kiddie-SADS, and Serrano et al. (2013) found an association of 8% for PBD-*DSM* and of 6% for PBD-NOS, resulting in a total comorbidity with PBD of 14%. In a sample of 7- to 13-year-old Turkish children diagnosed with ADHD, Diler, Uguz, Seydaoglu, Erol, and Avci (2007) found that 8.2% had comorbid BD.

According to Donfrancesco et al. (2011), the most prevalent subtype of PBD in ADHD children was the non-cycling disorder.

To clarify the relationship between ADHD and PBD, the two groups were also compared with the following variables: symptoms severity, distribution of ADHD subtypes, other comorbid diagnoses, familial psychiatric disorders. The comorbidity of ADHD and PBD increased the severity of ADHD problems, which is consistent with the results of

Table 1. Comparison Between ADHD Children With and Without PBD on Demographic Data, Cognitive Level, ADHD Symptomatology, and Comorbidity (Lifetime).

	ADHD with PBD	ADHD without PBD		
	n = 49	*n* = 320	χ^2/F	*p*
M; *SD*				
Age (years)	8.54; 2.46	8.80; 2.52	0.45	*ns*
SES	74.96; 17.00	74.82; 13.17	0.00	*ns*
IQ-Total	98.90; 11.83	99.93; 14.55	0.23	*ns*
IQ-Performance	96.63; 12.23	96.84; 14.59	0.01	*ns*
IQ-Verbal	101.88; 12.88	102.44; 14.95	0.06	*ns*
ADHD-RS Total score	40.65; 6.98	35.63; 10.20	9.64	.00
ADHD-RS Hyperactivity subscale	20.69; 3.86	17.48; 4.70	20.81	.00
ADHD-RS Inattentive subscale	19.39; 4.34	17.97; 4.51	4.25	.04
n (%)				
Boys	46 (94)	278 (87)	1.96	*ns*
Combined subtype	33 (67)	152 (48)	6.69	.01
Hyperactive subtype	8 (16)	42 (13)	0.37	*ns*
Inattentive subtype	8 (16)	126 (39)	9.76	.00
Anxiety disorders (generalized and separation anxiety disorders, phobias, panic disorder)	8 (16)	36 (11)	1.04	*ns*
Oppositional defiant disorder	34 (69)	102 (32)	25.52	.00
Conduct disorder	14 (29)	23 (7)	21.54	.00
Familial psychiatric disorders	24 (49)	22 (7)	8.73	.00

Note. PBD = pediatric bipolar disorder; SES = socioeconomic status; ADHD-RS = ADHD Rating Scale.

a previous study (Serrano et al., 2013). Specifically, our findings lead to the hypothesis that ADHD children with PBD are characterized by more disruptive and impulsive behaviors. However, our sample consists of selected outpatients of a specialized center for ADHD, and we could assume that the population which seeks medical attention from a specialized center showed severe symptoms. Further community-based studies are warranted to clarify this controversial topic.

Also consistent with prior studies (Donfrancesco et al., 2011), the combined subtype of ADHD was more frequent in children with PBD comorbidity than in those without PBD comorbidity, whereas the inattentive subtype was less frequent in children with PBD comorbidity.

Moreover, ADHD children with PBD showed higher percentage of other comorbid disorders, than the ADHD-alone group, including ODD and CD. No differences in rates of anxiety disorders were identified. Previous studies indicated that the comorbidity of PBD in ADHD is associated with greater comorbidity with anxiety, disruptive behavior disorders, and a psychopathological profile characterized by increased externalizing problems, anxious/depressed, social problems, and thought problems (Biederman et al., 1996; Diler et al., 2007; Donfrancesco et al., 2011; Mick, Biederman, Pandina, & Faraone, 2003). Recently, Serrano et al. (2013) in a sample of ADHD children with PBD found higher comorbidity with ODD and CD and a psychopathological profile characterized by higher scores on the Child Behavior Checklist (CBCL; Achenbach & Rescorla, 2001) scales of Rule-Breaking Behavior, Externalizing Problems, and Total Problems.

With regard to family history, the analysis revealed a higher number of familial psychiatric disorders in ADHD children with PBD than in children without PBD comorbidity. Data are consistent with previous studies, which revealed that the co-occurrence of psychiatric disorders is more likely in children with ADHD and comorbid disorders, such as oppositional defiant and CD (Pliszka, 2000) and PBD (Donfrancesco et al., 2011).

This study has several limitations. First, we evaluated a clinical and not a community-based sample, which means that only serious cases, that is, those most likely come to the attention of mental health services, were included. Second, the sample was collected in a single city in central Italy. A wider catchment area that included rural areas and was not limited to one city such as Rome would have lent more weight to our findings. Third, familial psychiatric disorders were studied only by an anamnestic method; a direct clinical assessment would be a better way to evaluate the real rates of psychopathology in family members, which in our study are divergent from previous literature.

A consequence of this limitation could be the low rate of parental psychopathology in ADHD without BD children.

In conclusion, the impact of early-onset BD on ADHD further clarifies the clinical relationship between these two diagnoses and their reciprocal influence.

In the assessment of ADHD children, attention must be paid to the identification of the PBD symptoms. Approximately 1 of 10 ADHD children may show this disorder, especially when ADHD symptoms are severe. The presence of PBD in ADHD children should alert clinicians to appropriate therapeutic strategies (pharmacological and psychological) that take into account not only the characteristics of ADHD symptoms but also mood alterations.

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22 MEDICINÆ Sanità 1-7 luglio 2014

Sindrome da deficit di attenzione e iperattività: una patologia nel rebus delle cure

Adhd, sindrome sottotrattata

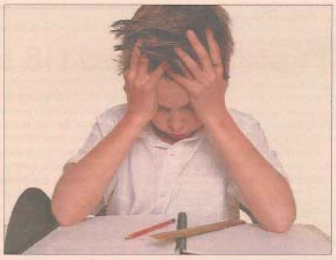
Nei casi più gravi solo 1 bambino su 20 segue un percorso farmacologico

La Sindrome da deficit di attenzione e iperattività, conosciuta come Adhd, colpisce in modo grave almeno l'1% della popolazione pediatrica. Sono pochissimi, però, quelli che riescono ad ottenere una diagnosi corretta, unico strumento che permette loro di accedere agli strumenti dell'integrazione scolastica e a una corretta terapia.

Diagnosticare l'Adhd è in realtà abbastanza semplice. Occorre raccogliere elementi di osservazione del bambino nel clima familiare, nella situazione scolastica, nelle situazioni di gioco. È necessario fare attenzione ai sintomi di disattenzione, iperattività e impulsività, ma nei casi più gravi la diagnosi è immediata. Nella maggior parte dei casi si tratta di maschi, accomunati da una serie di comportamenti peculiari: sono perennemente in attività e faticano a stare fermi, spesso non rispettano le regole e non attendono il proprio turno. Sono tendenzialmente molto impulsivi. Iperattività e vivacità sono sintomi molto comuni nella popolazione, ma la diagnosi di Adhd viene fatta solo quando questi sintomi disturbano realmente il funzionamento cerebrale del bambino. Possono comportare una riduzione del rendimento scolastico in bambini normodotati, oppure un'alterazione della vita sociale che può tradursi nell'isolamento rispetto alla vita di relazione con i coetanei. Per questo per la diagnosi gli aspetti dell'osservazione clinica si integrano con interviste a genitori e insegnanti, che possono riscontrare questo tipo di sintomatologia.

Alla stregua di altri disturbi, come a esempio l'autismo, la diagnosi è esclusivamente clinica e comportamentale: non esiste al momento un marcatore biologico per l'Adhd. Questo però non significa che non ci siano degli elementi di alterazione cerebrale. L'Adhd è un disturbo neurobiologico legato a un ritardo di maturazione di traiettorie di sviluppo di alcuni sistemi cerebrali che riguardano il controllo attentivo, la regolazione emotiva, la regolazione del controllo degli impulsi.

Perché dunque la diagnosi è così difficile? Nei bambini più piccoli generalmente si tende a ignorare il disturbo, ad aspettare che migliori, almeno fino all'età scolare. Arrivati alla prima elementare solitamente si riscontrano alcuni disturbi correlati all'Adhd, cioè i disturbi specifici dell'apprendimento: dislessia, disgrafia ecc. Essi sono però da considerarsi delle vere e proprie comorbilità dell'Adhd. Non è sufficiente diagnosticare la dislessia se il problema è un deficit di attenzione e iperattività, perché in questo caso il solo trattamento logopedico e cognitivo non potrà essere abbastanza sufficiente. In questo senso la scuola e gli insegnanti possono fare la differenza. Sono spesso gli insegnanti a riportare il problema all'attenzione dai genitori, che a questo punto devono rivolgersi al neuropsichiatra infantile.



Alla diagnosi deve quindi seguire immediatamente una presa in carico che, almeno inizialmente, non prevede l'uso di farmaci. È bene avviare la terapia cognitivo-comportamentale, che nei casi lievi può essere risolutiva. Nei casi più gravi è invece necessario avviare una terapia farmacologica, l'unica in grado di riparare alle conseguenze del disturbo e migliorare la qualità di vita del bambino, che può tornare a condurre una vita normale. La prescrizione della terapia farmacologica in Italia è ancora molto bassa, anche in rapporto ad altri Paesi europei. Oggi nei casi gravi di Adhd solo 1 bambino su 20 è trattato dal punto di vista farmacologico. Stando alle correnti linee guida e alle evidenze scientifiche ciò significa che agli altri 19 bambini non sono fornite le cure necessarie a favorire il successo scolastico e prevenire il rischio psicopatologico.

Le conseguenze del mancato riconoscimento e trattamento dell'Adhd possono ripercuotersi pesantemente sulla vita stessa del bambino. Con la crescita infatti - e soprattutto in età adolescenziale - i sintomi possono aggravarsi fino a trasformarsi in condotte antisociali e situazioni di emergenze psichiatriche.

Presso il nostro centro del Policlinico di Tor Vergata, Unità operativa di neuropsichiatria infantile, dedichiamo una parte dei nostri day-hospital alla valutazione del trattamento farmacologico su bambini affetti da Adhd. La prima assunzione del farmaco (metilfenidato a rilascio immediato) è accompagnata da un'attenta attività osservazionale, che comporta la valutazione di attività ludiche e di apprendimento prima e dopo l'assunzione stessa. Nel 70% dei casi notiamo immediati miglioramenti di attenzione, concentrazione e capacità di autocontrollo emotivo dopo appena un'ora dall'assunzione del farmaco. Va infine specificato che entrare in terapia farmacologica non vuole dire prenderla a vita. Nella maggior parte dei casi il trattamento farmacologico può essere sospeso dopo qualche anno, grazie ai miglioramenti ottenuti a scuola e nella vita di relazione.

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CIRCA 3MILA PAZIENTI IN CURA CONTRO I 70MILA CANDIDATI IPOTIZZATI

«Attenzione al rischio d'emergenza psichiatrica»

Adhd è un acronimo di parole inglesi che indicano, in sintesi, Sindrome da deficit di attenzione e iperattività (Attention-deficit/hyperactivity disorder). È un disturbo del comportamento caratterizzato da inattenzione, impulsività e iperattività che rende difficoltoso e in alcuni casi impedisce il normale sviluppo e l'adattamento sociale dei bambini.

È un disturbo descritto nel sistema internazionale di classificazione delle malattie (Icd) dell'Organizzazione mondiale della Sanità e interessa ben l'1% della popolazione pediatrica nella sua forma più grave, quando cioè compromette fortemente la vita del bambino o dell'adolescente. In presenza di questo disturbo e a causa dell'iperattività, della impulsività e della disattenzione, la qualità della vita relazionale del bambino è compromessa non solo in famiglia ma anche a scuola, con gli amichetti, nella squadra di calcio, in piscina...

L'Adhd è stato spesso al centro di forti polemiche, soprattutto perché uno dei possibili trattamenti è rappresentato da un farmaco di cui negli Stati Uniti si è abusato molto. In Italia, però, ciò non è mai accaduto e, più in generale, non esiste una situazione di abuso di psicofarmaci in età infantile.

La cultura del nostro Paese, le norme e i limiti esistenti per la prescrizione sono molto più restrittivi. In Italia si verifica, piuttosto, la situazione opposta: molti bambini che avrebbero bisogno di questo rimedio per la cura dell'Adhd non arrivano ad averlo. Lo dicono i numeri, e sono numeri certi, non stimati, perché da noi ogni bambino o adolescente con Adhd trattato farmacologicamente viene censito in un registro gestito direttamente dall'Istituto Superiore di Sanità.

Se, come abbiamo detto, l'1% della popolazione tra i 6 e i 18 anni presenta una forma grave di Adhd, in Italia circa 70.000 persone, solo poco più di 3.000 ragazzi nel nostro Paese vengono trattati farmacologicamente. Un numero così ridotto, a fronte di una stima di incidenza così elevata, suggerisce che ancora in molti non hanno ottenuto una diagnosi corretta o un trattamento adeguato. In altre parole, non li curiamo o li curiamo male.

Questa incuria comporta, però, rischi elevatissimi: i bambini crescono, diventano adolescenti, e il disturbo può mutare con lo sviluppo e determinare nei ragazzi comportamenti a forte rischio di emergenza psichiatrica: impulsività e aggressività, comportamenti antisociali, uso di sostanze stupefacenti, fughe da casa, ritiro scolastico, forti conflittualità in famiglia, maggior rischio di suicidio. Senza voler fare del terrorismo possiamo sicuramente affermare che si tratta di un possibile destino di molti ragazzi che non hanno avuto la fortuna di ricevere una diagnosi per il proprio disturbo e un trattamento adeguato. Trattamento che, rimarchiamolo, non si traduce automaticamente nella prescrizione di farmaci.

Le linee guida internazionali sostengono, infatti, che il trattamento farmacologico è necessario nelle forme più gravi, in cui il disturbo compromette fortemente la qualità di vita del bambino e dell'adolescente. Nelle forme lievi o al di sotto dei 6 anni d'età sono previsti, invece, interventi di tipo psicoterapico-cognitivo comportamentale per il bambino e un training psico-pedagogico rivolto ai genitori e, se necessario, anche agli insegnanti. La diagnosi è dunque lo strumento fondamentale grazie al quale non solo i bambini possono essere aiutati, ma anche la famiglia e gli insegnanti possono essere guidati e sostenuti.

Dobbiamo imparare a riconoscere e a trattare correttamente questi bambini e ragazzi perché non diventino degli adolescenti con delle implicazioni psichiatriche drammatiche. Il campanello d'allarme può essere lanciato da tutti quei professionisti che, a vario titolo, incontrano il bambino. pediatra di famiglia e insegnanti possono segnalare eventuali comportamenti anomali anche se la diagnosi spetta al neuropsichiatra infantile. È bene tener presente che spesso i bambini e i ragazzi Adhd presentano anche disturbi dell'apprendimento (Dsa) e, in particolare, la dislessia. Ecco che molto spesso questi piccoli pazienti vengono indirizzati a percorsi di tipo riabilitativo, logopedia o psicomotricità. Gli approcci sarebbero corretti se si trattasse solo di un Dsa, ma può essere insufficiente se il problema è un altro. Occorre, perciò, continuare a formare i pediatri, gli insegnanti ma anche i neuropsichiatri infantili in modo da facilitare il riconoscimento di tali disturbi e l'avvio di programmi di cura efficaci.

Stefano Vicari
responsabile del reparto di Neuropsichiatria infantile dell'Ospedale pediatrico Bambino Gesù di Roma

L'epidemiologia

- **1% popolazione pediatrica** soffre di Adhd **in forma grave** (stima 70.000 pazienti italiani tra i 6 e i 18 anni)
- **5% popolazione pediatrica** soffre di Adhd in **forma non grave** (e pertanto non è destinata al trattamento farmacologico)
- **20% popolazione** soffre di **disturbo psichiatrico**
- Assistenza psichiatrica del bambino e dell'adolescente in Italia: **solo 90 posti letto** (Calabria e Umbria non hanno posti letto dedicati alla psichiatria di questa fascia d'età)
- **Il suicidio è la terza causa di morte sotto i 20 anni**. In Italia è **la seconda**, superata solo dagli incidenti stradali che spesso hanno come base una problematica comportamentale

La presa in carico

- In Europa i genitori impiegano in media oltre **due anni** (circa 27 mesi) per ottenere una diagnosi di Adhd per i loro bambini: quasi 2 genitori su 5 (38%) devono rivolgersi a tre o più medici
- Più della metà (**54%**) dei genitori ha dichiarato di sentirsi **frustrata** sia per il numero di visite, sia per i numerosi specialisti consultati
- In Italia la diagnosi viene effettuata dal **neuropsichiatra infantile** o dallo psichiatra nell'adulto
- In Italia, il ministero della Salute e l'Iss coordinano il Registro nazionale Adhd: la prescrizione di una terapia farmacologica è vincolata alla registrazione del paziente nel **Registro nazionale**
- In Italia sono accreditati circa **110 Centri di riferimento** regionali cui spetta trasmettere i dati da immettere nel Registro

Per ricevere la newsletter iscriversi al seguente indirizzo:
http://crc.marionegri.it/bonati/adhdnews/subscribe.html

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza
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"*Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia*".

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