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## **BIBLIOGRAFIA ADHD DICEMBRE 2013**

Acta Clin Croat Suppl. 2012;51:80.

### **VOLUMETRIC CHANGES WITHIN THE FRONTO-STRIATAL REWARD SYSTEM IN ADOLESCENTS AND ADULTS WITH ADHD.**

**Lojowska M, Zwiars M, Von Rhein D, et al.**

**Introduction:** Recently, the focus of research on ADHD has been on the functional deficit within the reward circuit that may account for some of the behavioral manifestations of this disorder. However, the volumetric abnormalities within this circuit across age, in young and adult ADHD patients, have been not investigated yet. Therefore, in this study we examined the age-dependent volumetric changes within reward circuit encompassing the mesial prefrontal cortex (MPFC), orbitofrontal cortex (OFC) and nucleus accumbens (NA), and the correlation between the volumetric outcomes and behavioral symptoms of hyperactivity/impulsivity and inattention.

**Patients and methods:** The structural images of 290 ADHD and control subjects, aged between 8 and 50, were analyzed using voxel-based morphometry. Aligned T1 structural images were bias-corrected, normalized to the standard space, segmented and modulated using the automatic segmentation option in SPM8. A factorial analysis was performed to investigate the cross-sectional GM volumetric differences within the ROIs of MPFC, OFC and NA. Lastly, the correlation analysis between the volumes of the ROIs and behavioral symptoms of hyperactivity and impulsivity was performed.

**Results:** We found a significant decrease in the volume of the MPFC and the OFC in younger but not the adult ADHD subjects, relative to controls. Moreover, there was a significant negative correlation between the volume of the OFC and behavioral symptoms of inattention, controlling for age effect.

**Conclusion:** Our results imply the involvement of the volumetric abnormalities within the reward circuit in the neuropathology of adolescent ADHD and support the hypothesis of delayed brain development in ADHD.

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

Am J Med Genet Part A. 2014;164:141-55.

**ANXIETY, ATTENTION PROBLEMS, HYPERACTIVITY, AND THE ABERRANT BEHAVIOR CHECKLIST IN FRAGILE X SYNDROME.**

***Wheeler A, Raspa M, Bann C, et al.***

Behavior problems are a common challenge for individuals with fragile X syndrome (FXS) and constitute the primary clinical outcome domain in trials testing new FXS medications. However, little is known about the relationship between caregiver-reported behavior problems and co-occurring conditions such as anxiety and attention problems. In this study, 350 caregivers, each with at least one son or daughter with full-mutation FXS, rated one of their children with FXS using the Aberrant Behavior Checklist-Community Version (ABC-C); the Anxiety subscale of the Anxiety, Depression, and Mood Scale; and the Attention/Hyperactivity Items from the Symptom Inventories. In addition to examining family consequences of these behaviors, this study also sought to replicate psychometric findings for the ABC-C in FXS, to provide greater confidence for its use in clinical trials with this population. Psychometric properties and baseline ratings of problem behavior were consistent with other recent studies, further establishing the profile of problem behavior in FXS. Cross-sectional analyses suggest that selected dimensions of problem behavior, anxiety, and hyperactivity are age related; thus, age should serve as an important control in any studies of problem behavior in FXS. Measures of anxiety, attention, and hyperactivity were highly associated with behavior problems, suggesting that these factors at least coincide with problem behavior. However, these problems generally did not add substantially to variance in caregiver burden predicted by elevated behavior problems. The results provide further evidence of the incidence of problem behaviors and co-occurring conditions in FXS and the impact of these behaviors on the family.

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Arch Pediatr. 2013.

**CARDIOVASCULAR RISKS AND MANAGEMENT DURING ATTENTION DEFICIT HYPERACTIVITY DISORDER TREATMENT WITH METHYLPHENIDATE.**

***Bange F, Le Heuzey MF, Acquaviva E, et al.***

Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common of the pediatric neuropsychiatric disorders. Methylphenidate is an important element of therapeutic strategies for ADHD. Clinicians are interested in the safety of methylphenidate. Because this drug raises heart rate and blood pressure, concerns have been raised about its cardiovascular safety. Concerns were based on case reports of sudden cardiac death in methylphenidate users, plausible pharmacological pathways involving well-established stimulant effects on heart rate and blood pressure. Until recently, data were limited to a number of observational studies too small to examine serious cardiac events. In the past two years, large retrospective, population-based cohort studies were performed. These studies did not show any evidence that methylphenidate was associated with an increase in risk of myocardial infarction, sudden cardiac death, or stroke. Treatment of children with methylphenidate is not significantly associated with an increase in the short term or mid-term risk of severe cardiac events. For many, available data now will be seen as reassuring. But gaps persist in the methodical and comprehensive assessments of the safety of methylphenidate. Analyses cannot be generalized to children with long-term use of stimulants. Furthermore, long-term effects of slight increases in heart rate or blood pressure are unknown. Stimulant administration continues to have a detectable adrenergic effect even after years of treatment. In the MTA study, greater cumulative stimulant exposure was associated with a higher heart rate at years 3 and 8. Although less severe, such adverse cardiac events are nonetheless alarming to patients. This adrenergic effect may have clinical implications, especially for individual patients with underlying heart abnormalities and it deserves further investigation. More research is necessary to optimize a safe use of methylphenidate regarding its cardiovascular effects. In light of the controversies surrounding the increase in the number of children being diagnosed with ADHD, the broad use of methylphenidate in these patients, and cardiovascular concerns about it, this article addresses topics of clinical significance. For ease of use by practitioners, the article summarizes the guidelines stated by the European Medicines Agency over the appropriate pretreatment evaluation and cardiovascular assessment. It advocates a thorough history and physical examination before initiating methylphenidate to treat patients with ADHD, with an emphasis on

the identification of risk factors for sudden death. A cardiac sub-specialist consultation is mandatory in case of history or physical examination findings. In other cases, an electrocardiographic screening is recommended in order to check out previously unrecognized heart disease.

Arq Neuro-Psiquiatr. 2013;71:896-901.

**CORRELATION BETWEEN SLEEP DISORDER SCREENING AND EXECUTIVE DYSFUNCTION IN CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER.**

**Zambrano-Sanchez E, Martinez-Cortes JA, Dehesa-Moreno M, et al.**

**Objective:** To compare frequency of sleep disorders (SD) and executive dysfunction (ED) in children with attention deficit-hyperactivity disorder (ADHD) and a control group.

**Method:** We studied 156 children with ADHD with a mean age of 8.5 years, and a control group with 111 children with a mean age of 8.3 years. We utilized the Pediatric Sleep Questionnaire (PSQ) to screen SD and the working memory measurement from the Wechsler intelligence scale for children (WISC-IV) to screen ED.

**Results:** We did not observe an increased frequency of SD in children with ADHD compared with the controls. However, we did identify ED in children with ADHD; additionally a significant correlation was observed between the type of ADHD and SD and among ED, WISC-IV measurements, and type of SD in children with ADHD.

**Conclusion:** An increase of SD frequency in children with ADHD was not observed, but we did identify ED in children with ADHD. Additionally, a correlation among ADHD types, SD, ED, and WISC-IV measurements was observed in children with ADHD.

Asia-Pacific Psychiatry. 2013.

**PREVALENCE AND CONTRIBUTING FACTORS TO ATTENTION DEFICIT HYPERACTIVITY DISORDER: A STUDY OF FIVE- TO FIFTEEN-YEAR-OLD CHILDREN IN ZHABEI DISTRICT, SHANGHAI.**

**Jin W, Du Y, Zhong X, et al.**

**Introduction:** This work aims to understand the features among 5- to 15-year-old children with attention deficit hyperactivity disorder (ADHD) in Zhabei District in Shanghai.

**Methods:** Children with ADHD were studied using general background questionnaire, ADHD symptom rating questionnaire, and cluster-stratified sampling. A total of 9,900 valid questionnaires were utilized in this study. We conducted diagnostic interviews with suspected ADHD children and their parents using the criteria of the Diagnostic and Statistical Manual of Mental Disorders (4th Edition) for ADHD.

**Results:** The prevalence rate of ADHD among the children was 4.6%, of which 2.4%, 0.4%, and 1.8% had ADHD-I ADHD-HI, and ADHD-C types, respectively. The prevalence rates in boys and girls were 6.6% and 2.7% (ratio, 2.41:1), respectively. Significant differences in prevalence rate were found among children with different age groups and ADHD types. Children aged 7-10 years had the highest prevalence rate (6.3%). Externally, residence children had higher prevalence than local residents. Significant differences in prevalence rate were also found among children with parents having different educational and socioeconomic level.

**Discussion:** The prevalence of ADHD-HI was higher than the other two types. The highest prevalence was observed in 7- to 10-year-old children. The influential factors of ADHD prevalence were age, gender, and educational level.

Asian J Psychiatry. 2013;6:483-87.

**ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS REPORTING IN MALAYSIAN ADOLESCENTS: DO ADOLESCENTS, PARENTS AND TEACHERS AGREE WITH EACH OTHER?**

**Wan Salwina WI, Baharudin A, Nik Ruzyanei NJ, et al.**

Attention Deficit Hyperactivity Disorder (ADHD) is a clinical diagnosis relying on persistence of symptoms across different settings. Information are gathered from different informants including adolescents, parents and teachers. In this cross-sectional study involving 410 twelve-year old adolescents, 37 teachers and 367 parents from seven schools in the Federal Territory of Kuala Lumpur, reliability of ADHD symptoms among the various informants were reported. ADHD symptoms (i.e. predominantly hyperactive, predominantly inattentive and combined symptoms) were assessed by adolescents, teachers and parents, using Conners-Wells' Adolescent Self-report Scale (CASS), Conner's Teachers Rating Scale (CTRS) and Conner's Parents Rating Scale (CPRS) respectively. For predominantly hyperactive symptoms, there were statistically significant, weak positive correlations between parents and teachers reporting ( $r= 0.241$ ,  $p<. 0.01$ ). Statistically significant, weak positive correlations were found between adolescents and parents for predominantly inattentive symptoms ( $r= 0.283$ ,  $p<. 0.01$ ). Correlations between adolescents and parents reporting were statistically significant but weak ( $r= 0.294$ ,  $p<. 0.01$ ). Weak correlations exist between the different informants reporting ADHD symptoms among Malaysian adolescents. While multiple informant ratings are required to facilitate the diagnosis of ADHD, effort should be taken to minimize the disagreement in reporting and better utilize the information.

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Australas Psychiatry. 2013;21:499-503.

**CAN A MULTI-DISCIPLINARY ASSESSMENT APPROACH IMPROVE OUTCOMES FOR CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER?**

**Bor W, Heath F, Heussler H, et al.**

**Objective:** Public, consumer and professional views about attention deficit hyperactivity disorder, its assessment and treatment - especially with medication - remain a highly contested domain. Parents in particular express disquiet with services. One response to this tension is a multidisciplinary evaluation. Parental and education perceptions of this process have not been evaluated previously. A community multidisciplinary approach was assessed in terms of diagnostic outcomes and client satisfaction.

**Method:** A comprehensive multidisciplinary structured assessment of the first 50 referred children with severe attentional problems was documented. Demographic and symptom/behavioural profiles, developmental history and indicated multi-disciplinary evaluation were recorded. A team consensus process arrived at diagnostic classification. Post-assessment satisfaction of parents and school staff was surveyed.

**Results:** Thirteen children (26%) were diagnosed with attention deficit hyperactivity disorder and three commenced stimulants. The majority of parents and educators were satisfied with the service.

**Conclusions:** A multidisciplinary assessment clinic for children presenting with attention problems resulted in minimal prescribing. Overall, education staff and parents were satisfied with the service. The model may be a suitable response to the multiple concerns in the community.

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Biol Psychiatry. 2013.

**EFFECTS OF STIMULANTS ON BRAIN FUNCTION IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.**

**Rubia K, Alegria AA, Cubillo AI, et al.**

**Background:** Psychostimulant medication, most commonly the catecholamine agonist methylphenidate, is the most effective treatment for attention-deficit/hyperactivity disorder (ADHD). However, relatively little is known on the mechanisms of action. Acute effects on brain function can elucidate underlying neurocognitive effects. We tested methylphenidate effects relative to placebo in functional magnetic resonance imaging (fMRI) during three disorder-relevant tasks in medication-naïve ADHD adolescents. In

addition, we conducted a systematic review and meta-analysis of the fMRI findings of acute stimulant effects on ADHD brain function.

**Methods:** The fMRI study compared 20 adolescents with ADHD under either placebo or methylphenidate in a randomized controlled trial while performing stop, working memory, and time discrimination tasks. The meta-analysis was conducted searching PubMed, ScienceDirect, Web of Knowledge, Google Scholar, and Scopus databases. Peak coordinates of clusters of significant effects of stimulant medication relative to placebo or off medication were extracted for each study.

**Results:** The fMRI analysis showed that methylphenidate significantly enhanced activation in bilateral inferior frontal cortex (IFC)/insula during inhibition and time discrimination but had no effect on working memory networks. The meta-analysis, including 14 fMRI datasets and 212 children with ADHD, showed that stimulants most consistently enhanced right IFC/insula activation, which also remained for a subgroup analysis of methylphenidate effects alone. A more lenient threshold also revealed increased putamen activation.

**Conclusions:** Psychostimulants most consistently increase right IFC/insula activation, which are key areas of cognitive control and also the most replicated neurocognitive dysfunction in ADHD. These neurocognitive effects may underlie their positive clinical effects.

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BMC Neurol. 2013;13.

**NEUROPSYCHOPATHOLOGICAL COMORBIDITIES IN LEARNING DISORDERS.**

**Margari L, Buttiglione M, Craig F, et al.**

**Background:** Learning Disorders (LD) are complex diseases that affect about 2-10% of the school-age population. We performed neuropsychological and psychopathological evaluation, in order to investigate comorbidity in children with LD.

**Methods:** Our sample consisted of 448 patients from 7 to 16 years of age with a diagnosis of LD, divided in two subgroups: Specific Learning Disorders (SLD), including reading, writing, mathematics disorders, and Learning Disorders Not Otherwise Specified (LD NOS).

**Results:** Comorbidity with neuropsychopathologies was found in 62.2% of the total sample. In the LSD subgroup, ADHD was present in 33%, Anxiety Disorder in 28.8%, Developmental Coordination Disorder in 17.8%, Language Disorder in 11% and Mood Disorder in 9.4% of patients. In LD NOS subgroup, Language Disorder was present in 28.6%, Developmental Coordination Disorder in 27.5%, ADHD in 25.4%, Anxiety Disorder in 16.4%, Mood Disorder in 2.1% of patients. A statistically significant presence was respectively found for Language and Developmental Coordination Disorder comorbidity in LD NOS and for ADHD, mood and anxiety disorder comorbidity in SLD subgroup.

**Conclusions:** The different findings emerging in this study suggested to promote further investigations to better define the difference between SLD and LD NOS, in order to improve specific interventions to reduce the long range consequences.

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BMC Psychiatry. 2013;13.

**ADHD IN GIRLS AND BOYS - GENDER DIFFERENCES IN CO-EXISTING SYMPTOMS AND EXECUTIVE FUNCTION MEASURES.**

**Skogli EW, Teicher MH, Andersen PN, et al.**

**Background:** ADHD is diagnosed and treated more often in males than in females. Research on gender differences suggests that girls may be consistently underidentified and underdiagnosed because of differences in the expression of the disorder among boys and girls. One aim of the present study was to assess in a clinical sample of medication naive boys and girls with ADHD, whether there were significant gender x diagnosis interactions in co-existing symptom severity and executive function (EF) impairment. The second aim was to delineate specific symptom ratings and measures of EF that were most important in distinguishing ADHD from healthy controls (HC) of the same gender.

**Methods:** Thirty-seven females with ADHD, 43 males with ADHD, 18 HC females and 32 HC males between 8 and 17 years were included. Co-existing symptoms were assessed with self-report scales and

parent ratings. EF was assessed with parent ratings of executive skills in everyday situations (BRIEF), and neuropsychological tests. The three measurement domains (co-existing symptoms, BRIEF, neuropsychological EF tests) were investigated using analysis of variance (ANOVA) and random forest classification.

**Results:** ANOVAs revealed only one significant diagnosis x gender interaction, with higher rates of self-reported anxiety symptoms in females with ADHD. Random forest classification indicated that co-existing symptom ratings was substantially better in distinguishing subjects with ADHD from HC in females (93% accuracy) than in males (86% accuracy). The most important distinguishing variable was self-reported anxiety in females, and parent ratings of rule breaking in males. Parent ratings of EF skills were better in distinguishing subjects with ADHD from HC in males (96% accuracy) than in females (92% accuracy). Neuropsychological EF tests had only a modest ability to categorize subjects as ADHD or HC in males (73% accuracy) and females (79% accuracy).

**Conclusions:** Our findings emphasize the combination of self-report and parent rating scales for the identification of different comorbid symptom expression in boys and girls already diagnosed with ADHD. Self-report scales may increase awareness of internalizing problems particularly salient in females with ADHD.

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BMC Psychiatry. 2013;13.

**LONG-TERM EFFECTS OF STIMULANTS ON NEUROCOGNITIVE PERFORMANCE OF TAIWANESE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Tsai CS, Huang YS, Wu CL, et al.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is a common behavioral and neurocognitive disorder in school-age children. Methylphenidate (MPH) is the most frequently prescribed CNS stimulant for ADHD. The aim of this study is to evaluate the changes in intelligence quotient and domains of neurocognitive function after long-term MPH treatment of Taiwanese children with ADHD.

**Methods:** The Wechsler Intelligence Scale (WISC-III) was administrated twice at an interval of at least one year for all 171 subjects (6-12 years) and 47 age- and gender-matched children without ADHD. The ADHD-Rating scale and Clinical Global Impression-Severity (CGI-S) were also used at the time of enrolment, and at 6 months and one year later.

**Results:** Taiwanese children with ADHD had lower Verbal IQ (VIQ) and Full IQ (FIQ) and performed poorly on several subtests of the WISC-III, including Similarities, Vocabulary, and Coding, compared to healthy children without ADHD. After one year of MPH treatment, significant decrements in all scores of the ADHD-Rating scale and CGI-S and increments in several domains of the WISC-III, including FIQ, VIQ, PIQ, Perceptual Organization Index (POI), Picture Completion, Picture Arrangement, Object Assembly, and Digit Span were observed. When the ADHD children under MPH treatment were subdivided into two age groups (6-8 years and 9-12 years), significantly better performance in some subtests and subscales of the WISC-III (such as Similarities, Comprehension, and Object assembly) was found in the 6-8 years age group.

**Conclusions:** Long-term MPH treatment may improve the neurocognitive profiles of the ADHD children, as seen in their performance in several subtests and in the IQ scores on the WISC-III. And this improvement had no correlation with the decrement of ADHD symptoms. Starting stimulant treatment at as young an age as possible is advised due to the greater benefits in the 6-8 years age group, as seen in this study. More research in this area is also needed to confirm these results.

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BMJ (Online). 2013;347.

**AUTHORS' REPLY TO CORTESE.**

**Batstra L, Thomas R, Mitchell G.**

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BMJ (Online). 2013;347.

**ATTENTION, PLEASE.**

**Jackson T.**

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Br J Psychiatry. 2002 Jul;181:43-48.

**PATHWAYS TO CARE IN CHILDREN AT RISK OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER.**

**Sayal K, Taylor E, Beecham J, et al.**

**BACKGROUND:** There is underdiagnosis of and low use of specialist services for attention-deficit hyperactivity disorder (ADHD). **AIMS:** To quantify the filters in the help-seeking pathway through primary care and to investigate factors influencing progress for children at risk of ADHD.

**METHOD:** A total of 127 children (5-11 years old) with pervasive hyperactivity who passed each filter (primary care attendance and general practitioner (GP) recognition of disorder) were compared with those who had not.

**RESULTS:** Primary care attendance was only associated with parental perception of the behaviour as problematic (OR 2.11; 95% CI 1.11-4.03). However, GP recognition was related to both parent and child factors - parental request for referral (OR 20.83; 95% CI 3.05-142.08) and conduct problems (OR 1.48; 95% CI 1.04-2.12). GP non-recognition was the main barrier in the pathway to care; following recognition, most children were referred.

**CONCLUSIONS:** Parents can be regarded as the main gatekeepers for access to specialist services

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Child & Youth Care Forum. 2013 Dec;42:571-84.

**THE ASSOCIATION BETWEEN ATTENTION PROBLEMS AND INTERNALIZING AND EXTERNALIZING PROBLEMS: THE MEDIATING ROLE OF PEER PROBLEMS.**

**Yip VT, Ang RP, Ooi YP, et al.**

**Background:** The high prevalence of attention problems in children warrants concern, as it is a risk factor for internalizing and externalizing problems. There lies a need to understand possible factors that may mediate this link so that interventions may be targeted to alleviate these mediators and interrupt the link between attention problems and negative outcomes.

**Objective:** This study investigated the role of peer problems in the association between attention problems and internalizing problems, and between attention problems and externalizing problems in an Asian sample (N=312).

**Method:** Participants' data were from the archival records of an outpatient child psychiatric clinic.

**Results:** Findings indicated that peer problems was a statistically significant mediator for both associations. Additionally, peer problems was a complete mediator for the association between attention problems and internalizing problems, but a partial mediator for the link between attention problems and externalizing problems.

**Conclusions:** Findings suggest that the association between attention problems and internalizing and externalizing problems occurs via an indirect mediated pathway, through peer problems. These findings provide some preliminary evidence for the design and evaluation of future intervention studies aimed at the peer group level for the amelioration of peer problems in children with attention problems.

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Child Care Health Dev. 2012 Sep;38:611-28.

**DISRUPTIVE BEHAVIOUR DISORDERS: A SYSTEMATIC REVIEW OF ENVIRONMENTAL ANTENATAL AND EARLY YEARS RISK FACTORS.**

**Latimer K, Wilson P, Kemp J, et al.**

Disruptive behaviour disorders (DBDs), including attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD) and conduct disorder (CD) are chronic disorders with significant overlap in aetiology and presentation. An integrative examination of environmental risk factors is lacking.



Six literature searches of web-based bibliographic databases were completed to identify literature on DBDs in general and five disorders in particular: CD, ODD, ADHD, deficits of attention, motor control and perception, and reactive attachment disorder. Searches were filtered to focus on studies including diagnostic assessment, focussing on environmental risk and protective factors in the first 4 years of life. The database searches generated 9806 papers of which 47 were reviewed after filters had been applied. The evidence suggests links between a number of early life risk factors and DBDs, including prenatal cigarette smoking and alcohol use, prenatal viral illness, maternal stress and anxiety, low birthweight, peripartum and early neonatal complications, parental stress and parenting styles in infancy, early deprivation, adoption and separation. Despite the understanding that there is sharing of risk factors between the DBDs, there has been a disproportionate focus on the role of certain risk factors at the expense of others and the field is weakened by difficulties in controlling for all potential confounding variables.

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Child Health Care. 2013;42:311-32.

**THE EFFECTS OF SOCIAL SKILLS TRAINING ON CHILDREN WITH AUTISM SPECTRUM DISORDERS AND DISRUPTIVE BEHAVIOR DISORDERS.**

**Mathews TL, Erkfritz-Gay KN, Knight J, et al.**

Children with autism spectrum disorders (ASD) and disruptive behavior disorders (DBD) have significant difficulties in social interactions. Although social skills training (SST) is often prescribed for children with ASD and DBD, research showing its effectiveness is still emerging. This study examined the effects of SST for children with ASD and DBD. Evaluation measures included the Social Skills Improvement System, direct observation of behaviors during role-play, and social validity ratings. Direct observation data showed that participants successfully acquired the skills during the group, and the skills were maintained 1-month posttreatment. Social validity data revealed the intervention was well-received.

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Clin Trials. 2013;10:949-58.

**METHODOLOGY FOR CONDUCTING THE CHILDREN'S ATTENTION-DEFICIT HYPERACTIVITY DISORDER TELEMENTAL HEALTH TREATMENT STUDY IN MULTIPLE UNDERSERVED COMMUNITIES.**

**Vander Stoep A, Myers K.**

**Background** Children living in nonmetropolitan communities are underserved by evidence-based mental health care and are underrepresented in clinical trials.

**Purpose** In this article, we describe lessons learned in conducting the Childrens Attention-Deficit Hyperactivity Disorder (ADHD) Telemental Health (TMH) Treatment Study (CATTs), a randomized controlled trial testing the effectiveness of TMH in improving outcomes of children with ADHD living in underserved communities.

**Methods** Children were referred by primary care providers (PCPs). The test intervention group received six telepsychiatry sessions with each session followed by an caregiver behavior training session delivered in-person by a local therapist. A secure website was used to support decision making by the telepsychiatrists and to facilitate real-time collaboration between the telepsychiatrists and community therapists. The control group received a single telepsychiatry consultation. Questionnaires tapping ADHD symptoms and other outcomes were administered to parents and teachers online through a secure portal from personal computers.

**Results** A total of 88 PCPs in seven communities referred the 223 children who participated in the trial. Attrition in treatment sessions and research assessments was very low. Lessons learned TMH proved to be a viable means of providing evidence-based pharmacological services to children and training to local therapists. Recruitment was enhanced by offering the control group a telepsychiatry consultation. Sitespecific strategies were needed to meet recruitment targets.

**Conclusions** The CATTs trial used methods designed to optimize inclusion of children living in multiple dispersed and underserved areas. The study will serve as a model for other research projects aiming at reducing geographic disparities in access to quality mental health care.

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Dusunen Adam. 2013;26:286-94.

**INVESTIGATION OF EFFECTS OF ATTENTION DEFICIT AND HYPERACTIVITY DISORDER SUBTYPES ON FAMILY FUNCTIONS.**

**Sebnem Soysal A, Yildirim A, Acar A, et al.**

**Objective:** Attention deficiency and hyperactivity disorder (ADHD) is a mental disorder that seriously affects both the individual and his/her family. The aim of this study is to evaluate family functions of individuals with different subtypes of ADHD who had no significant cognitive and social impairments.

**Methods:** 27 subjects with ADHD-inattentive (ADHD-I) subtype, 18 ADHD-hyperactivity-impulsivity (ADHD-HI) subtype, 32 ADHD-combined (ADHD-C) subtype and 35 control subjects aged 6 to 10 years and their mothers were included in the study. Wechsler Intelligence Scale For Children, Conners Parent And Teacher Rating Scales and Family Assessment Scale (FAS) were used.

**Results:** When the subtests of FAS were evaluated; problem solving scores of ADHD-HI subgroup, communication scores of ADHD-I subgroup, roles scores of ADHD-C subgroup, "showing necessary interest" scores of ADHD-I and ADHD-HI subgroups, and general functioning scores of ADHD-HI subgroups were higher than the other subgroups. ANOVA results of FAS indicated that except the behavior control subtest, there were significant differences for different subtests for all subgroups.

**Discussion:** When assessing the effects of ADHD treatments, not only the child, but also the family and family dynamics should be evaluated. Therefore, the abilities for a better adaptation to social life -such as problem solving, social evaluation and emotional reactions of the individuals with ADHD- will be increased.

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Education & Treatment of Children. 2013 Nov;36:147-67.

**IMPLEMENTATION OF A SINGLE COMPREHENSIVE FUNCTION-BASED INTERVENTION ACROSS MULTIPLE CLASSROOMS FOR A HIGH SCHOOL STUDENT.**

**Whitford DK, Liaupsin CJ, Umbreit J, et al.**

A comprehensive function-based intervention was developed to address the chronic, high levels of off-task behavior by a 15-year-old ninth grade Caucasian male with learning disabilities and ADHD. A descriptive FBA identified that the student's off-task behavior was reinforced by peer attention and task avoidance. Intervention involved the collaborative development of a single, comprehensive intervention that was implemented sequentially across three classes. When implemented, the intervention produced consistently high levels of on-task behavior in each class. Social validity data supported the acceptability of the comprehensive intervention. High levels of treatment integrity showed staff could collaborate and implement a comprehensive intervention. Implications and directions for further research are included.

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Emot Behav Difficulties. 2014;19:59-70.

**IDENTIFYING DEMOGRAPHIC AND LANGUAGE PROFILES OF CHILDREN WITH A PRIMARY DIAGNOSIS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Walsh IP, Scullion M, Burns S, et al.**

As the language presentation of children with attention deficit (hyperactivity) disorder (ADHD) is highly complex, this study aims to delineate the profile of a cohort of 40 children with ADHD, aged between 9 and 12 years, attending a child and adolescent mental health service (CAMHS). Speech and language therapists (SLTs) assessed the children on formal language tests (including tests of verbal comprehension/expression, vocabulary, reading and communication) over three one-hour sessions. Group demographics showed a predominance of males, with a greater number of children presenting with the combined subtype of ADHD over other subtypes (i.e. predominantly inattentive or hyperactive-impulsive

type). The majority of the children also had a secondary psychiatric diagnosis. Test findings revealed some common trends in the overall group's performance, but a general ADHD-specific language profile was not discernible. Almost three-quarters of the study cohort had previously undetected language difficulties, with over 70% of those having both receptive and expressive language difficulties. Just under one-third of the cohort demonstrated reading difficulties. Relatively high correlations were found across performance on measures of verbal comprehension when compared to vocabulary and reading comprehension and expressive language. Most parents reported communication difficulties on completed questionnaires. The range, extent and complexity of the language difficulties of children with ADHD is demonstrated in our findings, with the heterogeneity of this population an obvious feature. Implications for further research and SLT clinical practice are discussed.

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Epilepsy Behav. 2014;31:34-42.

**THE CHILD BEHAVIOR CHECKLIST AND YOUTH SELF-REPORT IN ADOLESCENTS WITH EPILEPSY: TESTING MEASUREMENT INVARIANCE OF THE ATTENTION AND THOUGHT PROBLEMS SUBSCALES.**

**Ferro MA, Boyle MH, Scott JG, et al.**

The objective of this study was to test for the measurement invariance of the Attention and Thought Problems subscales of the Child Behavior Checklist (CBCL) and Youth Self-Report (YSR) in a population-based sample of adolescents with and without epilepsy. Data were obtained from the 14-year follow-up of the Mater University Study of Pregnancy in which 33 adolescents with epilepsy and 1068 healthy controls were included for analysis. Confirmatory factor analysis was used to test for measurement invariance between adolescents with and without epilepsy. Structural equation modeling was used to test for group differences in attention and thought problems as measured with the CBCL and YSR. Measurement invariance was demonstrated for the original CBCL Attention Problems and YSR Thought Problems. After the removal of ambiguous items ("confused" and "daydreams"), measurement invariance was established for the YSR Attention Problems. The original and reduced CBCL Thought Problems were noninvariant. Adolescents with epilepsy had significantly more symptoms of behavioral problems on the CBCL Attention Problems, ( $\beta = 0.51$ ,  $p = 0.002$ ), compared with healthy controls. In contrast, no significant differences were found for the YSR Attention and Thought Problems, ( $\beta = 0.11$ ,  $p = 0.417$  and  $\beta = -0.20$ ,  $p = 0.116$ ), respectively. In this population-based sample of adolescents with epilepsy, the CBCL Attention Problems and YSR Thought Problems appear to be valid measures of behavioral problems, whereas the YSR Attention Problems was valid only after the removal of ambiguous items. Replication of these findings in clinical samples of adolescents with epilepsy that overcome the limitations of the current study is warranted.

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Eur Arch Psychiatry Clin Neurosci. 2013;1-13.

**SPOCK3, A RISK GENE FOR ADULT ADHD AND PERSONALITY DISORDERS.**

**Weber H, Scholz CJ, Jacob CP, et al.**

Attention-deficit/hyperactivity disorder (ADHD) is the most frequent psychiatric disorder in children, where it displays a global prevalence of 5 %. In up to 50 % of the cases, ADHD may persist into adulthood (aADHD), where it is often comorbid with personality disorders. Due to a potentially heritable nature of this comorbidity, we hypothesized that their genetic framework may contain common risk-modifying genes. SPOCK3, a poorly characterized, putatively Ca(2+)-binding extracellular heparan/chondroitin sulfate proteoglycan gene encoded by the human chromosomal region 4q32.3, was found to be associated with polymorphisms among the top ranks in a genome-wide association study (GWAS) on ADHD and a pooled GWAS on personality disorder (PD). We therefore genotyped 48 single nucleotide polymorphisms (SNPs) representative of the SPOCK3 gene region in 1,790 individuals (naADHD=624, nPD=630, ncontrols=536). In this analysis, we found two SNPs to be nominally associated with aADHD (rs7689440, rs897511) and four PD-associated SNPs (rs7689440, rs897511, rs17052671 and rs1485318); the latter even reached marginal significance after rigorous Bonferroni correction. Bioinformatics tools predicted a possible influence of rs1485318 on transcription factor binding, whereas the other candidate SNPs may have effects

on alternative splicing. Our results suggest that SPOCK3 may modify the genetic risk for ADHD and PD; further studies are, however, needed to identify the underlying mechanisms.

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Eur Child Adolesc Psychiatry. 2013;22:S284.

**BEHAVIORAL AND EMOTIONAL PROFILES OF CHILDREN AND ADOLESCENTS WITH ADHD AND COMORBID CONDUCT DISORDER IN SINGAPORE.**

**Tan YL, Weng SJ, Ooi YP, et al.**

**Introduction:** ADHD is commonly associated with comorbid conditions. This study aims to examine the behavioral and emotional profiles of clinically referred children with ADHD, and those with comorbid conduct disorder (CD) using the child behavior checklist (CBCL; Achenbach and Rescola, 2001). We hypothesized that the ADHD + CD group would score higher on the externalizing subscale and total problems score, as measured by the CBCL than ADHD-only group.

**Methods:** One hundred and ninety-six clinically referred children (175 males) in Singapore, aged 7-16 years old (M=10.42, SD=1.77), who were diagnosed either with ADHD only or ADHD + CD were included in this study. As part of their participation, they completed the AQ while their caregivers completed the CBCL. After comparing the CBCL scores between both groups, we proceeded to analyse for a cut-off score on the CBCL scales.

**Results:** As hypothesized, the ADHD + CD group showed more deficits in Total Problems (M=74.59, SD=14.56) on the CBCL scale than the ADHD-only group (M=66.42, SD=11.06),  $t(190) = -4.18, p < 0.01$ , showing a significantly higher cut-off score in the combined group. Similarly, they also showed more Externalizing problems (M=73.05, SD=14.98) than their ADHD-only peers (M=61.16, SD=11.21),  $t(190) = -5.94, p < 0.01$ . In terms of other CBCL subscales, children with ADHD + CD have more Thought and Social problems, than those with ADHD-only. Finally in terms of Internalizing subscales (anxious/depressed, withdrawn/depressed and somatic complaints), there were no statistically significant differences in their Internalizing subscales between groups. We further analyzed for CBCL cut-off scores that can suggest a high likelihood (specificity) of comorbid CD when assessing children with ADHD.

**Conclusions:** The findings indicate that in Singapore, children with ADHD with comorbid CD have significantly higher cut-off on the CBCL in externalizing behaviors, with accompanying thought and social problems than those with ADHD-alone. Internalizing behaviors and attention problems were not shown to differentiate the groups. These results can further help to characterize the behavioral and emotional profiles that distinguish between ADHD only and ADHD with comorbid CD group. The cut-off scores on the CBCL suggest its utility to screen for comorbid CD conditions in ADHD. Clinical implications in relation to these findings will be further discussed.

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Eur Child Adolesc Psychiatry. 2013;22:S212.

**BREAKING DOWN THE BOUNDARIES: COMORBIDITY OF MENTAL AND PHYSICAL DISORDERS.**

**Merikangas K.**

Although there has been substantial information on the associations between mental disorders and specific physical conditions such as anxiety and asthma in both adults and youth, there has been limited information on the broader patterns of associations of these conditions in general population samples. There is substantial impact of mental and physical comorbidity in adults including increased mortality (cancer, COPD, stroke, heart disease), greater health care costs, poorer treatment response, and more functional impairment. The aims of this lecture are to: (1) describe the background and evidence on the patterns and impact of comorbid mental and physical disorders in adults; (2) discuss methodological challenges in investigating mental-physical comorbidity; (3) present patterns of mental-physical comorbidity in community studies of children; and (4) summarize the clinical significance and impact of mental-physical comorbidity in youth. Systematic review of the rates, patterns and impact of physical disorders across international community surveys of mental disorders in children and adolescents revealed that there were few studies that collected sufficient information to yield estimates of comorbidity with the most frequent physical disorders in children including allergies, asthma, headache, and gastrointestinal problems.

Methodologic challenges in studying this association include the lack of comparability of diagnostic assessment of mental and physical disorder, different associations with disorder subtypes, variation in prevalence periods for disorders, and different sample sources for the medical and psychiatric disorder index probands. Specific results of analyses of the patterns and impact of mental and physical disorders in the National Comorbidity Survey Adolescent Supplement, the National Health Examination and Nutrition Survey in the US and the Neurodevelopmental Genomics project at the University of Pennsylvania (R. Gur et al) will be described. Potential explanations for poorer treatment response and outcome of those with this comorbidity include comorbidity as a general marker of severity, primary or secondary inflammatory/immune processes underlying one or both conditions, general sleep and appetite disturbances, poorer health behaviors, increased stress reactivity, and/or poorer compliance with treatment.

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Eur Child Adolesc Psychiatry. 2013;22:S239.

**ATTENTION DEFICIT/HYPERACTIVITY DISORDER AND PSYCHIATRIC COMORBIDITIES: A SYSTEMATIC REVIEW OF LONG-TERM OUTCOMES.**

**Hodgkins P, Caci H, Young S, et al.**

**Introduction:** A characteristic of attention deficit/hyperactivity disorder (ADHD) is a high rate of psychiatric comorbidities, which may result in highly complex presentations for diagnosis, treatment, and assessment of treatment outcomes.

**Objective:** To examine the presence of and control for comorbidities in studies of long-term outcomes of individuals with treated ADHD.

**Methods:** A systematic search of 12 literature databases using Cochrane's guidelines yielded 51 English-language peer-reviewed, primary studies of long-term outcomes ((greater-than or equal to) 2 years) published from 1-1-1980 to 12-31-2011 that assessed treated vs. untreated ADHD. Comorbidities included any psychiatric condition considered by the study authors to be comorbid with ADHD. Treatment included any pharmacological, non-pharmacological, or combination treatment. Outcomes were grouped by common characteristics into nine major domains: academic, antisocial behavior, driving, non-medicinal drug use/addictive behavior, obesity, occupation, services use, self-esteem, and social function outcomes. Outcomes were dichotomized: those reported to improve and reach statistical significance and those that did not.

**Results:** Comorbidities were controlled for either by exclusion, regression/covariance, or separation (comparing ADHD with or without the comorbidity) in 31 studies and not in 20 studies. Comorbidities reported included internalizing and externalizing dimensions and others (eating disorder, learning disorders, low intelligence, pervasive developmental disorders, substance use disorder, tics, and Tourette's). Treatment for ADHD was associated with improvement for 65% of outcomes in studies that controlled for comorbidities (primarily academic, driving, self-esteem, and social function outcomes) and for 55% of outcomes in studies that did not (primarily drug use, obesity, and occupation outcomes). Comparison of different treatment modalities showed similar results: studies in which comorbidities were controlled reported a greater proportion of improved treatment outcomes compared with studies that did not, for both pharmacological and non-pharmacological treatment. For combination treatment, the proportion of improved outcomes was high (82%) when comorbidities were controlled. Only one study of combination treatment did not control for comorbidities, and it reported improved outcomes.

**Conclusions:** Controlling or adjusting for psychiatric conditions comorbid with ADHD may clarify the effects of ADHD-directed treatment on long-term outcomes associated with ADHD.

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Eur Child Adolesc Psychiatry. 2013;22:S124.

**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Banaschewski T.**

Attention-Deficit/Hyperactivity Disorder (ADHD), characterized by a developmentally inappropriate, pervasive and persistent pattern of severe inattention, hyperactivity, and/or impulsivity with an early onset

and associated with substantial functional impairment, is one of the most common mental disorders affecting around 5.3 % of children and adolescents. ADHD symptomatology frequently co-exists with several other types of psychopathology, including oppositional defiant and conduct disorder, emotional lability, anxiety and depression, and persists into adulthood in a substantial number of cases. The disorder has a complex and probably heterogeneous pathogenesis, including multiple genetic and environmental risk factors of mostly small effect size which are acting together to cause a range of underlying neurobiological and neuropsychological alterations. According to various national and international guidelines, multimodal treatment components include psychoeducation, psychological interventions and various pharmacological treatment options. Interventions should be based on a comprehensive assessment and diagnosis, involving the integration of information from different sources, and interventions should be closely monitored for both efficacy and adverse effects. The presentation will summarize the current state of research with a special focus on recent research findings on underlying genetic and environmental risk factors, pathophysiological mechanisms, neurobiological and neuropsychological correlates, associated evidencebased and alternative treatment options and proposed DSM-V changes.

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Eur Child Adolesc Psychiatry. 2013;22:S282-S283.

**ATTENTION DEFICIT HYPERACTIVITY DISORDER AND SLEEP DISTURBANCES.**

**Alda J, Ferreira E, Serrano E, et al.**

**Background:** In clinical practice, the attention deficit hyperactivity disorder (ADHD) is often associated with sleep disturbances, but is core whether these disorders are part of ADHD (primary origin) or secondary to some of its comorbidities or medication.

**Objectives:** (1) To observe the relationship of the symptoms of sleep disturbances and the severity of the ADHD symptoms in patients without treatment for the same, (2) To observe the relationship of the symptoms of sleep disturbances with gender and age.

**Methods:** Preliminary, transversal and descriptive study of a sample of 30 patients of the ADHD Unit in the Psychiatric and Psychology Department of the Hospital Sant Joan de Deu, in Barcelona, diagnosed less than 3 months of ADHD and have never been medicated for it. In addition, participants must have an IQ above 70 and not present comorbid a Pervasive Developmental Disorder or Psychosis. The analysis variables are the symptoms of ADHD as measured by the ADHD-RD-IV version for parents and teachers, and sleep disturbances with an actigraph (ActiLife, Data analysis software ActiLife 6.5.0) measures for a temporary period of 1 week.

**Results:** Naive children diagnosed with ADHD go to sleep on average at 10:56 pm and wake up at 7:40 am, finding that as age increases the children go to sleep later, and it is girls who go to sleep later than boys. That is why the total sleep time is slightly higher in boys with an average of 7:30 h of sleep. As the effectiveness of sleep is concerned, the average is 83.70 %, in next to a sleep latency of 1.9 min on average, and 24.43 awakenings per night, not finding significant differences in gender or age.

**Conclusions:** Children diagnosed with ADHD have a sleep effectively at the limit of what is considered appropriate because of night-time awakenings and conciliation insomnia prevents sleep when it is considered appropriate in relation to their developmental stage.

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Eur Child Adolesc Psychiatry. 2013;22:S274.

**BIOMARKER FOR ADHD IN CHILDREN.**

**Guomundsson OO, Helgadóttir H, Baldursson G, et al.**

**Objective:** Attention deficit hyperactivity disorder (ADHD) is the most common developmental disorder in school-age children. Current diagnostic assessment relies primarily on observations of the child's behaviour, as reported by parents and schoolteachers. By the discovery of an underlying CNS dysfunction in individuals with ADHD, the need for a biomarker screening test became well recognized. Mentis Cura is a research and development company in Iceland, which in collaboration with the National University Hospital, is developing a diagnostic biomarker for ADHD and other developmental disorders. Electroencephalogram

(EEG) measures the electrical activity in the cerebral cortex and is sensitive to metabolic activity in the brain. Several studies show that EEG's may have a role in ADHD diagnosis.

**Methods:** The continuous scalp EEG was recorded in 216 control children and 150 ADHD children age 6-13, while the children rested with their eyes closed. Statistical pattern recognition (SPR) was applied to the data in order to determine which features of the EEG signal best separate the groups.

**Results:** The SPR builds a classifier with an ADHD Index from 0 to 1. The index shows how consistent the EEG is with EEGs of ADHD children or controls in same age. The classifier can separate groups of ADHD children from healthy control groups with the accuracy of 76-92%, depending on age group. The results allowed us to develop an ADHD Classifier, a standardized tool to screen for ADHD with a simple EEG recording.

**Conclusion:** The classifier can serve as a useful screening tool for ADHD. EEG is easy to use, accessible and non-invasive and the recording takes only 5 min. It meets the need for objective diagnosis of neurodevelopmental disorders and has the potential of becoming an instrument measuring the effect of different treatment modalities.

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Eur Child Adolesc Psychiatry. 2013;22:S272.

**BIOMARKER FOR BRAIN MATURATION.**

**Helgadóttir H, ÓGuomundsson O, Baldursson G, et al.**

**Objective:** Mentis Cura is a research and development company in Iceland, which in collaboration with the National University Hospital, is developing a diagnostic classifier for brain maturation in children. The study of brain maturation is an important aspect of the diagnostic evaluation of developmental disorders such as attention deficit hyperactivity disorder (ADHD). Background: EEG (Electroencephalogram) records the electrical activity in the cerebral cortex and is sensitive to metabolic activity in the brain. There are significant changes in power spectral frequencies with development of the cerebral cortex in children. MRI studies have demonstrated difference in brain development of children with ADHD and found a delay rather than a deviance of normal brain maturation. The study of brain development of healthy school children may have a role in the diagnostic of various neuropsychiatric and developmental disorders, including ADHD.

**Methods:** The continuous scalp EEG was recorded in 216 control children and 150 ADHD children age 6-13, while the children rested with their eyes closed. Statistical pattern recognition (SPR) was applied to the data in order to determine which features of the EEG signal change with age.

**Results:** The index results in an EEG age, which is designed to closely correspond to the actual age of a subject with normal development of the cortex and its subsequent metabolic activity. The EEGs of children with and without ADHD were evaluated and the results show a delay in brain maturation measured with quantitative EEG in the ADHD group compared to normal controls. The results allowed us to develop a Brain Maturation Classifier, a standardized tool to monitor the brain developmental in children.

**Conclusion:** The Brain Maturation Classifier can serve as a useful screening tool for differences in development of children. EEG is easy to use, accessible and non-invasive and the recording takes only 5 min. It meets the need for objective diagnosis of neurodevelopmental disorders and has the potential of becoming an instrument measuring the effect of different treatment modalities.

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Eur Child Adolesc Psychiatry. 2013;22:S215-S216.

**BEHAVIORAL PROFILE OF EXECUTIVE DYSFUNCTION IN CHILDREN AND ADOLESCENTS WITH AUTISM SPECTRUM DISORDER.**

**Shahrivar Z, Mahdavi H, Tehrani-Doost M, et al.**

**Background:** A considerable number of studies have tried to explain the behavioral aspects of autism spectrum disorder (ASD) by relating its perseverative features to executive dysfunction; however, the results show inconsistent performances of executive measures in this disorder. In this study, BRIEF was used to compare EF components of a group of Iranian children and adolescents who had ASD with a typically developing (TD) group. The study also evaluated the possible links between executive dysfunction, autistic symptoms and behavioral difficulties

**Methods:** The behavioural profile for EF measured by the Behavior Rating Inventory of Executive Function (BRIEF), was inspected in a 5-16 year old group of otherwise healthy participants with ASD (n=34) recruited from a referral hospital-based child and adolescent psychiatry clinic compared to an age and gender matched normal group (n=36). The childhood autism rating scale (CARS), the Strengths and Difficulties Questionnaire (SDQ), and the Raven Progressive Matrixes (RPM) were used to evaluate related variables.

**Results:** Based on BRIEF results in the ASD group, 88 % had impairment in working memory. The Inhibition scale had the highest mean score (M=71.76), and the organization of materials scale had the least (M=57.03). The sensory abnormalities scales of CARS and EF were correlated negatively. The CARS visual response was correlated with the Metacognition Index ( $r=0.279$ ,  $p=0.036$ ) and the Global Executive Composite ( $r=0.267$ ,  $p=0.043$ ) of BRIEF.

**Conclusions:** A higher dysfunction in inhibition may reflect the developmental variation of EF in children with ASD and possibly a higher cognitive impairment of the group with comorbid ADHD symptomatology. Executive dysfunction related behavioural difficulties in normal individuals may suggest an effect of psychiatric backgrounds on EF profiles.

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Eur Child Adolesc Psychiatry. 2013;22:S264.

**CHARACTERISING COMORBIDITY BETWEEN ADHD AND ASD: A COGNITIVE-ELECTROPHYSIOLOGICAL APPROACH.**

**Tye C, Asherson P, Ashwood K, et al.**

There is substantial behavioural and genetic overlap between attention deficit hyperactivity disorder (ADHD) and autism spectrum disorder (ASD), two common neurodevelopmental disorders that until recently have been treated as separate research fields. In particular both disorders demonstrate attentional and social cognitive deficits, but these have not been directly compared with concurrent electrophysiological recording that is able to capture these fast occurring cognitive events. In order to identify shared and distinct neural markers, systematically assessed groups of 8-13 year old children with ASD (n=19), ADHD (n=18), comorbid ASD + ADHD (n=29) and typically developing (TD) controls (n=26) were compared on performance and underlying brain responses during a cued continuous performance task (CPT- OX) and a face processing task. Results indicate that event-related potential (ERP) indices of response inhibition (NoGo-P3) may be altered specifically in children with ADHD, whereas children with ASD show reduced conflict monitoring (Go vs. NoGo-N2) during the CPT-OX. In addition, children with ASD showed atypical lateralisation of the face-sensitive N170 component and altered gaze processing, while children with ADHD showed similar patterns to TD children during the face processing task. Across these analyses, while it was possible to dissociate ASD-only and ADHD-only on their basis of cognitive-electrophysiological parameters, ASD + ADHD largely show the unique deficits of both disorders, thus supporting an additive co-occurrence. Disentangling phenotypic variation using neurophysiological markers is likely to aid the identification of susceptibility genes and other causal mechanisms underlying the complex aetiology of ADHD and ASD. In addition, elucidating the basis of comorbidity can help to refine classification systems and enhance the assessment of complex cases for more specific treatment strategies.

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Eur Child Adolesc Psychiatry. 2013;22:S285-S286.

**CHARACTERIZING UNMET NEEDS OF CHILDREN AND ADOLESCENTS WITH ADHD IN EUROPE, IN THEIR OWN WORDS: THE ADOLESCENT AND CAREGIVER PERSPECTIVE.**

**Hodgkins P, Sikirica V, Flood E, et al.**

**Objective:** To obtain qualitative feedback from both caregivers of children/adolescents and adolescent patients on unmet needs of pediatric patients with ADHD.

**Methods:** One-on-one interviews with caregivers of pediatric patients aged 6-17 years, and adolescent patients aged 13-17 years, from eight European countries were conducted as part of a concept elicitation phase for a larger survey study. Interviews were conducted by trained interviewers in the subject's native language using an interview guide designed to elicit the impact of ADHD and its treatment on patients'



lives. Interviews were audio-recorded and transcribed in English. A thematic analysis was performed using MAXQDA software, which involved coding key themes related to unmet needs identified in the caregiver/adolescent transcripts.

**Results:** Thirty-eight caregivers of children/adolescents and 28 adolescent patients participated in interviews. The caregiver participants represented 38 pediatric patients aged 6-17 years; 66% were male and 87% were currently on medication. The adolescent participants ranged from 13 to 17 years, 50 % were male, and all were currently on medication. While medication was generally considered helpful, 29 of the 33 (88%) caregivers with children currently on medication reported that their children continued to experience symptoms while on treatment. All adolescents reported experiencing symptoms while on treatment which included being easily distracted, forgetful, restless, impatient, and impulsive. Most (84%) caregivers reported issues at school (e.g. underperformance, disciplinary problems), as did all but one adolescent (e.g. difficulty with schoolwork, being disruptive in class, detention, and difficulty making/maintaining friendships); adolescents reported feeling frustrated with their inability to keep up with school work and connect with peers. Caregivers reported making accommodations for their children (e.g. maintaining a schedule, giving reminders, providing close supervision. ADHD was frequently reported to affect family relationships. Caregivers and adolescents expressed a desire for medication that better controlled symptoms but noted concerns that such a medication might over-subdue them and dampen their energy and personality.

**Conclusions:** Findings suggest that even with treatment, ADHD still may have wide-ranging impacts on children's/adolescents' lives. Further research is needed to explore the magnitude of burden. Nevertheless, comprehensive care plans involving patient/caregiver support systems, counseling and alternative treatments may reduce some of these burdens. This research was funded by Shire Development, LLC.

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Eur Child Adolesc Psychiatry. 2013;22:S251.

**AUDIT OF THE ADHD CLINIC WEXFORD AGAINST NICE GUIDELINES (2008).**

**Kutay D, Moore K, Kilcoyne M.**

**Background:** Attention deficit/hyperactivity disorder (ADHD) is one of the most common disorders in child psychiatric practice. Wexford Child and Adolescent Mental Health Service operates a dedicated multi-disciplinary ADHD clinic. Service Audit is a powerful tool in assessing and improving quality of service. Aims: To assess the performance of the ADHD clinic in Wexford CAMHS against a recognized set of standards.

**Methods:** Retrospective analysis of case notes for all patients diagnosed with ADHD over the period of 1 year. Audit against standards set out in NICE guideline (2008) on ADHD with regard to: - Quality of initial assessment. - Non-pharmacological management. - Initiation of pharmacological therapy. - Follow-up/monitoring during pharmacological therapy.

**Results:** All 49 patients (100%) had a comprehensive diagnostic assessment and met DSM-4 criteria for ADHD. Assessment of comorbid conditions and parental mental health were documented in 80 and 90% respectively. Documented use of different non-pharmacological interventions was low (10-55%). Stimulant medication was prescribed in 29/49 (59%) of patients. Documentation of patient education and physical assessment at time of initiation of pharmacotherapy was undertaken for most parameters (>80%), but was less consistent regarding cardiac history (52%) and cardiac examination (61%). Monitoring of physical parameters at follow-up was documented in the majority of cases (>80%).

**Conclusions:** Wexford ADHD clinic performed well in most areas when audited against standards from the NICE guideline. However, documentation rates of non-pharmacological interventions were low. The audit cannot distinguish whether this was merely a lack of documentation or indeed a lack of intervention. One possible explanation could be the paucity of available resources in this area. Documentation of cardiac history and examination was missing too frequently, bearing in mind the potentially serious cardiac side effects of stimulant medication. Following this audit, a new mandatory assessment form was developed for use in the case notes of all ADHD patients. We expect this will improve service provision and documentation further and facilitate future re-audit.

Eur Child Adolesc Psychiatry. 2013;22:S125-S126.

**THE CHILD HEALTH AND ILLNESS PROFILE AS A MEASURE OF HEALTH-RELATED QUALITY OF LIFE IN STIMULANT-TREATED CHILDREN AND ADOLESCENTS WITH ADHD.**

**Banaschewski T, Soutullo C, Lecendreux M, et al.**

**Introduction:** Optimal management of ADHD aims not only to ameliorate patients' symptoms, but also to improve their health-related quality of life (HRQoL). The Child Health and Illness Profile- Child Edition: Parent Report Form (CHIP-CE:PRF) is a generic (not disease-specific) instrument designed to assess HRQoL in children. The 76 items are grouped into 5 domains and 12 subdomains, and raw scores are standardized to T-scores (mean=50, standard deviation=10), based on US community samples. Published studies have demonstrated the reliability and validity of the CHIP-CE:PRF in children and adolescents with ADHD, but it has not previously been used as an outcome measure for stimulant pharmacotherapy.

**Methods:** Parents of 6 to 17-year-old patients with ADHD completed CHIP-CE:PRF assessments in two recent, consecutive, phase 3 clinical trials of the efficacy and safety of the prodrug lisdexamfetamine dimesylate (LDX). SPD489-325 was a European, 7-week, double-blind, randomized, placebo-controlled study, and included osmotic-release oral system methylphenidate (OROS-MPH) as a reference treatment. Patients from this trial, together with additional US patients, entered a subsequent study, SPD489-326, in which open-label LDX treatment for (greater-than or equal to) 6 months was followed by a 6-week double-blind, placebo-controlled, randomized-withdrawal period. CHIP-CE:PRF data were analysed using an ANCOVA model of the change in domain T-score from study baseline.

**Results:** In study SPD489-325, baseline CHIP-CE:PRF T-scores in all treatment groups were lowest in the Achievement domain (mean in the range 30.1-31.2), followed by Risk Avoidance (31.4-34.7), Satisfaction (34.4-36.2), Resilience (35.5-37.5) and Comfort (43.0-44.5). At endpoint in the LDX group, there were mean improvements compared with placebo of 10.5 points (95 % confidence interval 7.9, 13.0;  $p < 0.001$ ) in Achievement, 9.9 (7.1, 12.7;  $p < 0.001$ ) in Risk Avoidance, 3.8 (1.1, 6.6;  $p < 0.01$ ) in Resilience and 3.5 (0.6, 6.5;  $p < 0.05$ ) in Satisfaction. OROS-MPH treatment effects were also statistically significant in these domains; neither treatment affected Comfort domain T-scores. In study SPD489-326, mean domain T-scores were stable or increased during open-label LDX treatment. In the 6-week randomized-withdrawal period, there was statistically significant deterioration at endpoint in the placebo group only ( $p < 0.05$  compared with baseline, in all domains). These changes were statistically significant compared with LDX in Risk Avoidance, Achievement and Satisfaction ( $p < 0.001$ ).

**Conclusions:** The burden of illness in children and adolescents with ADHD was reflected in baseline CHIP-CE:PRF T-scores (greater-than or equal to) 1 SD below 50 in four of five CHIP-CE:PRF domains. Acute treatment with LDX or OROS-MPH led to improved HRQoL scores in these domains, with the greatest effect seen in the domain with the most profound deficit at baseline (Achievement). These benefits were maintained during long-term LDX treatment, but HRQoL scores declined following treatment withdrawal.

Eur Child Adolesc Psychiatry. 2013;22:S309.

**METHYLPHENIDATE FOR SUICIDE ATTEMPT.**

**Kilicnullonulllu AG, Ipek H, Mutlu C, et al.**

**Introduction:** There are a few reported cases of overdose for suicide attempts with methylphenidate. Majority of these cases fully recovered after supportive therapy<sup>1,2,3</sup>. We present a patient who experienced increased heart rate (HR) and blood pressure (BP) after ingestion of 3,240 mg long acting methylphenidate (Concerta) for suicide attempt.

**Case report:** 14 year old boy with ADHD was using methylphenidate for 3 years. In August, he attempted suicide impulsively after an argument by the ingestion of 60 tablets of Concerta 54 mg. Approximately two hours after ingestion he felt palpitation. He was immediately brought to emergency unit of Bakirkoy SadiKonuk Hospital. In initial evaluation he was conscious and cooperative. His Glasgow Coma Scale Score was 15. His BP was 147/71 mmHg, pulse rate (PR) was 124 beats/min, respiration rate (RR) 20 breaths/min and oxygen saturation of 97 SpO<sub>2</sub>. ECG findings were normal, except for sinus tachycardia. Laboratory tests were normal. Fifty grams of active charcoal was administered in the emergency room. He was observed for 8 h at the emergency unit. His last BP, PR and oxygen saturation were normal.

**Discussion:** The overdose of methylphenidate can be seen only in emergency clinics due to suicide or abuse. Therefore, there are only a few cases of overdose with short acting methylphenidate. Methylphenidate overdose leads to a wide range of clinical manifestations, related with primarily neurologic and cardiovascular system. In this case, approximately 3.2 grams methylphenidate ingestion was much higher than other reported cases<sup>2,3</sup>. In literature the majority of overdoses with methylphenidate was asymptomatic, and treated at home in these age groups. However, overdoses in adolescents occurred with drug abuse or suicide attempt and mostly symptomatic<sup>5</sup>. Although huge amounts of methylphenidate, his general condition and findings were good. Only sinus tachycardia and increased BP was detected. Severe toxicity and deaths has been reported for both intravenous and intraarterial administration of crushed methylphenidate tablets. However we could not find any death case in literature due to unintentional or suicidal ingestion of methylphenidate. Since methylphenidate misused in combination with other drugs, other drugs should be investigated in cases with intoxication <sup>3</sup>. Unintentional or intentional poisoning may increase due to increased prescription. Although no serious neurological or cardiovascular event happened in this case, a supervised stimulant use is needed in child and adolescent population.

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Eur Child Adolesc Psychiatry. 2013;22:S101.

**THE EVOLVING TREATMENT PATTERNS FOR ADHD IN NORDBADEN/GERMANY: A RETROSPECTIVE STUDY BASED UPON ADMINISTRATIVE DATA, YEARS 2003-2009.**

**Banaschewski T, Schwarz O, Goetz-Erik T, et al.**

**Objectives:** To explore the evolving treatment patterns for patients with attention-deficit/hyperactivity disorder (ADHD) in Nordbaden/ Germany, in particular psychostimulant prescriptions in children and adolescents.

**Methods:** The complete claims database of the organization of physicians registered with statutory health insurance [SHI] (Kassenaerztliche Vereinigung, KV) in Nordbaden/Germany was available for analysis, covering the total regional population enrolled in SHI (>2.2 million). The dataset for years 2003-2009 was reorganized as to allow patient-centered evaluation. For calendar year 2009, 21,287 patients with ADHD [nullhyperkinetic disorder null, HKD; ICD-10 codes F90.0 or F90.1] (male, 15,108; female, 6,179; including 5,931 patients or 27.9% [male, 4,582; female, 1,349] with coexisting conduct disorder [HKCD; F90.1 or a combination of F90 and F91]) were available for analysis; of those, 846,677 patients were insured by a vdek member company.

**Results:** Preschool children (age 0-5 years) were prescribed medication in very rare cases (1.6 % in 2009) and after an average lead time of more than 1 year only. Most received some form of nonpharmacological therapy or were left untreated (42 %). In contrast, 41 % of children (age group 6-12 years, continuously increasing from 32% in 2003) and 54 % of adolescents (age group 13-17 years, rate remaining stable since 2006) were prescribed either stimulant (methylphenidate, MPH, or amphetamine) or nonstimulant (atomoxetine) drugs. Males and patients with concomitant conduct disorder were more likely to receive medication treatment. Modified release MPH formulations were more widely used than immediate release MPH. Overall use of medication increased steadily, from 32.2% of ADHD patients in 2003 to 39.9% in 2009, whereas its rate decreased over time in adult patients (declining from 38 % in 2003 to 26% in 2009). Upon identification and individual review of all prescriptions of ADHD medication for members of the control group, no evidence could be found supporting potentially inappropriate use of stimulant medication. Further data on average dosing, therapy duration, switches and augmentation will be presented by age group, gender, severity, and comorbidity status of patients as well as by category of treatment.

**Conclusions:** Treatment patterns were highly age and gender specific. Except for preschoolers, therapeutic management of patients with ADHD relied heavily on drug treatment. No evidence was found for inappropriate prescribing of ADHD medication.

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Eur Child Adolesc Psychiatry. 2013;22:S268.

**IS ADHD RESTRICTIVE SUB-TYPE WHICH IS SPECIFIED BY DSM-V A VALID DIAGNOSIS? HOLISTIC ASSESSMENT WITH EXECUTIVE FUNCTIONS, GENETIC AND MULTIMODAL BRAIN IMAGING METHODS.**

**Suren S, Bacanlı A, Yazici U, et al .**

**Objective:** The aim of this study was to identify differences between DSM V proposed ADHD inattentive subtype (restrictive subtype) and ADHD combined, predominantly inattentive subtypes and healthy controls using three different imaging techniques (fMRI, DTI and ASL) combined with genotyping scores of DAT-1 and DRD4 genes and neurocognitive performance of subjects on a computerized test battery. The three main contributions of this study to the field of ADHD are: (1) combining genetic, neuropsychologic and imaging findings in a well defined sample (2) employing three different imaging techniques (DTI, fMRI and ASL) for ADHD children in the same study sample. 3-comparing genetic, neuropsychologic and imaging aspects of DSM-V proposed ADHD inattentive (restrictive) subtype with other subtypes and controls.

**Method:** The study sample consisted of 201 ADHD patients (101 combined type, 50 Predominantly inattentive subtypes, 50 Restrictive Type) and 100 healthy controls. A semi-structured interview (K-SADS) was conducted with a senior year child psychiatry resident. Subjects were excluded if they meet DSM-IV diagnostic criteria for any psychiatric diagnosis (except ODD), history of medication use, estimated IQ < 80, presence of any neurological or psychiatric disorder. These children were then assessed on a computerized neuropsychologic test battery. Patients were grouped according to the presence of risk alleles at DRD4 locus (7-repeat allele) and DAT1 locus (homozygosity for the 10-repeat allele). 24 cases from each group (ADHD-combined, predominantly inattentive, inattentive, control) were enrolled in imaging study according to their genotyping scores. Multimodal imaging consisted of fMRI, ASL and DTI were performed to 96 patients, who accepted to take part in the study.

**Results:** Our results revealed that, ADHD IA cases were performed worse on psychomotor speed and reaction time subtests of neurocognitive test battery. We also found significantly more DRD4 7 allele carriers in ADHD-IA group. Most interestingly, occipital activation of ADHD restrictive cases significantly differed from ADHD Predominantly Inattentive Subtype on fMRI during go and no-go, and from ADHD Combined on perfusional ASL during go. This overlapping occipital activation difference found in ADHD IA group, which is obtained by two separate imaging techniques, also partially supported by DTI results. ADHD IA group differed from normal controls on Axial Diffusivity including null superior longitudinal fasciculus null.

**Discussion:** These results could be explained as null occipital cortex interacts with the dorsal attentional network to maintain attention and suppress attention to irrelevant stimuli. So we may speculate that, isolated attentional problems which is represented as ADHD IA subtype in DSM V are related to occipital differences that led to psychomotor speed and reaction time problems.

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Eur Child Adolesc Psychiatry. 2013;22:S178.

**MEETING THE MENTAL HEALTH NEEDS OF CHILDREN AND YOUNG PEOPLE WITH INTELLECTUAL DISABILITY.**

**Turk J.**

The mental health needs of children and young people with intellectual disability has been a long neglected field. More recently, increasing attention has been paid to this disadvantaged and often marginalised group, given our greater understanding of the biological, psychological and social contributors to their developmental, emotional and behavioural challenges, and hence corresponding advances in evidence-based treatments and supports. Degree of intellectual disability, and quality of psychosocial environment and upbringing, have long been recognised as critical determinants of likelihood and severity of mental health challenges in this client group. To these, we must now add cause as a crucial variable in determining the natures of challenges faced. Aetiological diagnoses are increasingly possible to make in the fields of developmental medicine, psychology and psychiatry, largely relating to conditions known to have a behavioural phenotype. A behavioural phenotype describes aspects of an individual's psychiatric, psychological and behavioural functioning attributable to an underlying (usually biological) condition which has usually occurred early in development. Behavioural phenotypes often contain common challenging behaviours e.g. self-injury, aggression and sleep disturbance. They also manifest as neuropsychiatric syndromes e.g. autism, ADHD, dementia & schizophrenia. Usually they present as social and communicatory profiles or attentional deficits which characterise the underlying condition but which do not

necessarily fulfil psychiatric diagnostic criteria. Note that behavioural phenotypes can also manifest as relative absence of developmental and/or behavioural difficulties. In addition, there is a potentially confusing conceptual clash between traditional diagnostic clinical categories such as Autism and ADHD, and the characteristic signature profiles of social, communicatory, attentional cognitive and other psychological functions witnessed in individuals with specific underlying genetic variations. This is exemplified by the experiences and vulnerabilities developmentally of individuals with Down Syndrome, Fragile X Syndrome and Smith-Magenis Syndrome to name but a few. The talk aims to increase awareness of the prevalence, nature and presentation of aetiologically-driven conditions in children and young people with and without intellectual disability and why appreciation and knowledge of them is important diagnostically and therapeutically.

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Eur Child Adolesc Psychiatry. 2013;22:S297.

**ATTENTION NETWORK HYPOCONNECTIVITY WITH DEFAULT AND AFFECTIVE NETWORK HYPERCONNECTIVITY IN ADULTS DIAGNOSED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDHOOD.**

**McCarthy H, Skokauskas N, Mulligan A, et al.**

**Context:** The neurobiological underpinnings of attention-deficit/ hyperactivity disorder (ADHD) and particularly those associated with persistence of ADHD into adulthood are not yet well understood. Correlation patterns in spontaneous neural fluctuations at rest are known as resting state functional connectivity and could potentially characterize ADHD-specific connectivity changes.

**Objective:** To determine the specific location of possible ADHD-related resting state functional connectivity differences between adults diagnosed with ADHD in childhood and controls.

**Design:** Using resting state functional magnetic resonance imaging, functional connectivity from attention, affective, default and cognitive control networks involved in the neuropathology of ADHD were calculated and compared between the cases with ADHD and controls. Setting: University, psychiatric service, MRI research centre.

**Participants:** 16 drug-free adults (5 female, 11 male, mean age, 24.5) diagnosed with combined type ADHD in childhood and 16 healthy controls matched for age (mean age, 24.4) gender, handedness and education who were recruited from the community. Main outcome measures: Connectivity data from ventral and dorsal attention, affective, default and cognitive control networks and ADHD symptoms derived from ADHD-specific rating instruments.

**Results:** Adults with ADHD showed significantly decreased resting state functional connectivity within the attention networks and increased resting state functional connectivity within the affective and default mode and the right lateralized cognitive control networks compared to healthy controls ( $p < 0.01$ , FWE whole brain cluster correction). Lower resting state functional connectivity in the ventral and dorsal attention network were significantly correlated with higher ADHD symptoms ( $p < 0.001$ ).

**Conclusions:** These resting state functional connectivity findings might underpin a biological basis for adult ADHD and are functionally related to persistent inattention, disturbance in cognitive control and emotional dysregulation in adults with ADHD.

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Eur Child Adolesc Psychiatry. 2013;22:S202.

**ATTITUDES AND PRACTICES OF HEALTHCARE PROFESSIONALS IN THE MANAGEMENT OF ADHD: A EUROPEAN PILOT SURVEY.**

**McNicholas F, Fitzgerald M.**

**Objectives:** To examine attitudes and practices in the management of attention-deficit/hyperactivity disorder (ADHD) among health professionals across seven European countries

**Methods:** The web-based survey was developed by an international steering committee of ADHD experts and consisted of 64 multiple-choice questions relating to ADHD, covering the following topics: attitudes, diagnosis, referral, treatment and improving care. Clinicians working with ADHD were identified using a medical marketing database (Medical Marketing Service, Inc., IL, USA) and invited via email to participate in the survey. No incentive was offered for participation and the survey was only available in English

**Results:** One hundred and thirty-four clinicians replied to the survey. Results highlighted significant differences by profession and country. In general, ADHD is considered a clinically important and valid disorder (n=111.84%), with biological underpinnings (n=82.62%), continuing into adulthood (n=123.93%) and responsive to treatment. Respondents from France were less likely to be convinced about biological validity (n=4.27%) and those from Italy and France were more likely to be concerned about the risk of under diagnosis (n=9.64% and n=9.60%, respectively). Psychologists were the specialty who most frequently reported not believing in the diagnostic validity of ADHD (n=4.19%). One-third (n=25.35%) of respondents recommended medical tests before prescribing medication, with differences emerging by country (n=2-11, 13-85%), despite the lack of support for such routine assessments in the guidelines.

**Conclusions:** Intriguing country- and profession-specific differences emerged in this study and warrant further exploration.

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Eur Child Adolesc Psychiatry. 2013;22:S188.

**METHYLPHENIDATE TREATMENT IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER: WHAT DO WE KNOW ABOUT THE MECHANISM OF ACTION OF METHYLPHENIDATE?**

**Grunblatt E, Bartl J, Schmid R, et al.**

It is estimated that around 5% of the children and adolescent worldwide suffer from attention-deficit hyperactivity disorder (ADHD). ADHD is one of the most frequent psychiatric disorders occurring at this age group. To date, the most frequent and successful pharmacological treatment in ADHD is the use of stimulants, in particular methylphenidate. Methylphenidate is used in the clinic already over 50 years as therapy for ADHD with very high effect size. Although a great deal of information regarding its effects and side effects was gathered in this period of time, many questions are still open regarding its mechanism of action. In our laboratory, we are currently investigating in vitro as well as in neuronal cell culture its mechanism of action using biochemical, genetic and molecular approaches. We could find that methylphenidate influence the activity of various enzymes involved in monoamine metabolisms. In the cell culture models, we could demonstrate how different concentrations influence proliferation and differentiation of the neurons, as well as the transcription of transporter, receptors and synaptic proteins important for neurotransmission. Furthermore, we did not only investigate the effect of the racemic form given usually for treatment in ADHD, but also investigate the individual effects of each enantiomer: the D-threo- and L-threo-methylphenidate, since it is postulated that the D-threo-methylphenidate predominantly exerts the effects seen in ADHD. The importance of further investigating the mechanism of action of methylphenidate lies on the fact that methylphenidate prescriptions seems to increase in the last century, while still the multiple effects of methylphenidate has not been fully discovered.

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Eur Child Adolesc Psychiatry. 2013;22:S170.

**MENTAL HEALTH PROBLEMS OF CHILDREN AND ADOLESCENTS IN GERMANY. FINDINGS FROM THE BELLA LONGITUDINAL STUDY.**

**Klasen F, Bichmann H, Ravens-Sieberer U.**

**Question:** High prevalence rates of mental health problems in childhood and adolescence are considered one of the biggest global health challenges of the 21st century. The present research reports data on mental health problems and mental health service utilization in Germany.

**Methods:** The sample of the BELLA cohort study is representative for Germany and consists of n=4,000 families with children and adolescents aged 3-17 years. Baseline data was collected from 2003 to 2006 and three follow-up waves were carried out 1, 2 and 4 years after baseline. The data were collected by computer-assisted telephone interview and subsequent questionnaires through parent reporting and, for subjects above the age of 11 years, by additional self-reporting. In order to identify mental health problems the extended version of the Strengths and Difficulties Questionnaire (SDQ) was applied. Further symptoms of anxiety (SCARED), depression (CES-DC), conduct disorder (CBCL), and ADHD (Conners' Scale) were assessed together with other data on child health and wellbeing. A clinical interview (DIPS) was

administered to derive DSM-IV diagnoses (e.g., depressive disorder, anxiety disorders, ADHD, eating disorders, substance disorders)

**Results:** Of all children 21.9 % indicated mental health problems and stability was 50 % at follow-up. Regarding specific mental health problems, anxiety was observed in 10 %, conduct disorder in 7.6 %, depression in 5.4 %, and ADHD in 2.2 % of the 7-17 year-olds 48.5 % of children with reported diagnosed mental health problems received specific treatment. Further results on mental disorders (prevalence, onset, persistence, co-morbidity) are presented

**Conclusions:** Implications for prevention and child mental health services in Germany are discussed.

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Eur Child Adolesc Psychiatry. 2013;22:S125.

**THE FIRST EUROPEAN STUDIES OF LISDEXAMFETAMINE DIMESYLATE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Coghill D, Banaschewski T, Lecendreux M, et al.**

**Introduction:** Lisdexamfetamine dimesylate (LDX) is the first longacting prodrug stimulant for the treatment of attention-deficit/hyperactivity disorder (ADHD). Here we report the primary efficacy and safety results of two European, phase 3 trials of LDX in children and adolescents with ADHD.

**Methods:** In SPD489-325, patients (aged 6-17 years) with ADHD from 48 sites across 10 European countries were randomized (1:1:1) to a once-daily, optimized dose of LDX (30, 50, or 70 mg/day), placebo or osmotic-release oral system methylphenidate (OROSMPH, 18, 36 or 54 mg/day) for 7 weeks. The primary outcome measure was the ADHD Rating Scale version IV (ADHD-RS-IV) total score. Patients who received (greater-than or equal to)4 weeks of double-blind treatment, reached visit 4, and completed the 1-week post-treatment washout in SPD489-325 were assessed for entry into study SPD489- 326; patients from US sites were also evaluated for direct entry. Patients who completed (greater-than or equal to)26 weeks of open-label LDX, and whose responder status was confirmed during a fixed-dose, 2-week period, were randomized (1:1) to continue receiving their optimal dose of LDX, or to switch to placebo, for a 6-week, double-blind, randomized- withdrawal period (RWP). The primary outcome was the percentage of patients meeting treatment failure criteria (C50 % increase in ADHD-RS-IV total score and (greater-than or equal to)2-point increase in Clinical Global Impression-Severity of Illness score, compared with RWP start point). Safety outcomes were assessed in both studies.

**Results:** In SPD489-325, 336 patients were randomized and 196 completed the study. The differences between active drug and placebo in the least squares mean change in ADHD-RS-IV total score (95 % confidence interval [CI]) from baseline to endpoint were statistically significant ( $p < 0.001$ ) for LDX (-18.6 [-21.5, -15.7]) and OROSMPH (-13.0 [-15.9, -10.2]). In SPD489-326, 276 patients were enrolled in the open-label period, 157 were randomized in the RWP and 76 completed the study. During the RWP, significantly fewer patients receiving LDX met treatment failure criteria (15.8 % [95 % CI, 7.6 %, 24.0 %]) compared with those receiving placebo (67.5 % [57.1 %, 78.0 %];  $p < 0.001$ ). Most treatment failures occurred at or before the week 2 visit following randomization (LDX, 6/12; placebo, 39/52). In both studies, the most common treatment-emergent adverse events reported in patients receiving LDX were decreased appetite, headache and decreased weight.

**Conclusions:** LDX produced robust improvements in core symptoms of ADHD in children and adolescents. Continued LDX treatment was associated with maintenance of efficacy compared with placebo. The safety profile of LDX was generally consistent with that of stimulant therapy.

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Eur Child Adolesc Psychiatry. 2013;22:S174.

**COORDINATED OUTPATIENT CARE FOR CHILDREN AND ADOLESCENTS IN GERMANY.**

**Schaff C, Holthusen I, John K.**

In Germany there is an extensive supply of outpatient care for children and adolescents with ADHD by child and adolescent psychiatrists and psychotherapists (CAPP). As, however, prevalence rates of the disorder amongst children and adolescents below the age of 18 range between 2 and 6 percent, supply is not sufficient for providing comprehensive care. The integrated care concept of the CAPP, incorporating

somatic, psychosocial and emotional components of the disorder, should benefit as many ADHD patients as possible. Therefore, over the course of 3 years, CAPP have developed a contract with pediatricians and child and adolescent psychotherapists, which compulsively stipulates cooperation and networking of the three occupational groups. In 2009, this contract was implemented in the German region of Baden-Württemberg with single health insurance funds (BKK and DAK). During the symposium the contents of the contract and the cooperation of the different occupational groups will be introduced. Health care data including patient numbers, numbers of physicians and psychotherapists and data on medication will be presented and discussed against the background of the German health care system. Furthermore, we will present the results of an accompanying intervention study which evaluated the treatment of 224 patients (118 patients in coordinated treatment vs. 110 patients with treatment as usual) over the course of 1 year. Coordinated treatment of children and adolescents with AD(H)D in outpatient services.

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Eur Child Adolesc Psychiatry. 2013;22:S283.

**CORRELATION BETWEEN ADHD AND THE QUALITY OF LIFE ON NAIVE PATIENTS.**

**Alda J, Ferreira E, Cuellar C, et al.**

**Background:** Attention Deficit Hyperactivity Disorder (ADHD) on children and adolescents is a harmful influence on the quality of life of these patients and their families.

**Objective:** Evaluate the quality of life on children and adolescents recently diagnosed with ADHD using the CHIP-CE-PRF Test (child health and illness profile-child edition parent report form).

**Methodology:** A descriptive and retrospective study was conducted on patients admitted in the ADHD Unit of St Joan de Deu Hospital, from January 2009 to December 2012. Inclusion criteria are recent ADHD diagnosis in any of its subtypes (attention, hyperactivity and combined) and has never received pharmacological treatment; have completed the CHIP-CE PRF basal (without pharmacological treatment). This test is divided into 5 subdomains (Satisfaction, Comfort, Risk Avoidance, Resilience and Achievement) values under 40 on each scale are indicative of problems in the quality of life of those children. Descriptive analysis is performed on values of each subscale and a T Student in those areas considered most influenced by this disorder.

**Results:** Results show a sample size of 176 patients, 74 % are male (n=131). The average age is 9.17 (plus or minus) 2.86 ranging from 5 to 17 years old (48.8 % are ADHD combined, n=86). The most affected areas by this disorder are Achievement (74 % present problems in this area) and Satisfaction (50 %). No significant differences were found between achievement in children (<12 years old) and achievement in adolescents ((greater-than or equal to) 12 years old, n=52) (t=0.90, p=0.36). Children with ADHD combined present higher behavioural risk than the rest (t=5.34, p=0.001).

**Conclusion:** Children and adolescents with ADHD present significant problems in some areas of their life, most commonly those related to their academic expectations and their peer group relations.

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Eur Child Adolesc Psychiatry. 2013;22:S267.

**ANALYSIS OF GNAL POLYMORPHISMS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Taner HA, Sener S, Ergun S, et al.**

Dopamine 1 like receptors, dopamine 1 and dopamine 5 receptors, play an important role in the etiopathogenesis of attention deficit hyperactivity disorder (ADHD). These receptors mediate adenylyl cyclase activation by olfactory subunit Galfa(olf) in striatum. Striatum has an essential role in the neurobiology of ADHD. In this study we aimed to investigate two polymorphisms in GNAL which is the gene that codes olfactory subunit of Galfa(olf). The other objectives of the study was to investigate the relationships between GNAL and ADHD types and family history. 100 children aged 6-18 with ADHD and 81 healthy controls were recruited for the study. Children which had IQ score lower than 70 and learning disability were excluded from the study. After detailed clinical evaluations, venous blood samples had collected from children. Genetic analysis were performed with the venous blood samples. rs8095592 and rs3892113 polymorphisms in GNAL were investigated. GG genotype in rs8095592 was significantly higher in the patient group with positive family history. But there was no statistically significant difference between



ADHD and control groups for rs8095592 and rs3892113 polymorphisms. Although these relations were not statistically significant; GG genotype in rs8095592 and TG genotype in rs3892113 were predominantly higher in the children with ADHD, predominantly inattentive type. Conclusion: we found that rs8095592 polymorphism in GNAL could play an important role in ADHD genetics. Having allele A in rs8095591 could be protective for the people who had a family history for ADHD. Further researches that investigate the role of GNAL in ADHD are needed to confirm this result.

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Eur Child Adolesc Psychiatry. 2013;22:S267-S268.

**ADHD IN CHILDREN: GROUP INTERVENTION INCLUDING A SERVICE USER PERSPECTIVE.**

**Mayordomo-Aranda A, De Gracia Dominguez-Barrera M, Emms L, et al.**

**Background:** Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder, whose prevalence varies from 1.5% school-age children in UK (ICD-10) to 3-7% school-age children in USA (DSM-IV-TR). With an onset in childhood, it is characterized by the presence of three main features: hyperactivity, inattention and impulsivity. ADHD treatment includes a comprehensive package of psycho-education, stimulant and non-stimulant medication, parenting and social skills training, school strategies and support groups. The UK National Health System (NHS) is committed to the active involvement of members of the public, patients and users in research, service evaluation and provision of care. This study aimed at presenting the impact of the participation and feed-back of Service User in the provision of a treatment package for children newly diagnosed of ADHD.

**Methods:** This poster presents the treatment package offered to children aged below 13 years old newly diagnosed with ADHD in Hounslow Child and Adolescent Mental Health Service (London, UK) in 2012. It included medication for moderate to severe ADHD, individual psycho-education sessions, school consultations and two different group modalities: a monthly drop-in group and a 6-week group). These groups were run by a Specialist Nurse and a Service User, who is the ADHD Information Service (ADDISS), a UK registered charity which offers information and support for children with ADHD and their families. As the mother of a child with ADHD, she brought her personal experience as a user to the therapeutic process.

**Results:** The Specialist Nurse and the Service User run two group modalities: (i) a monthly drop-in group (1 hour and a half session) and (ii) a 6-week group (2-hours weekly sessions), which covered the following areas: psychoeducation on medication, management of difficult behavior at home and in the school environment, educational statementing at school and management of impact on family life. A detailed description of the groups' content and the Service User's perspective regarding her role in the group and its delivery will be provided.

**Conclusions:** Parenting training and psychoeducation programs, in combination with medication when required, are the first line of treatment for children with ADHD. The NHS and Community Care Act was the first piece of UK legislation to establish a formal requirement for user involvement in Service Planning, back in 1990. Following up from this, in 2000, the Department of Health emphasizes the Government commitment to creating a patient-centre NSH with user needs central to service design and delivery. In this new era, Service Users are not only invited to give input on service planning but also get actively involved in service delivery. Users' views are of value to ensure the usefulness and relevance of provision and their voice can make a difference to the lives of other service users.

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Eur Child Adolesc Psychiatry. 2013;22:S201.

**ADULTS WITH ADHD RECALL A NEGATIVE IMPACT OF THE CONDITION ON THEIR CHILDHOOD: RESULTS OF THE EUROPEAN LIFETIME IMPAIRMENT SURVEY.**

**Fitzgerald M, Asherson P, Caci H, et al.**

This European Lifetime impairment survey was implemented in six EU countries, participants were invited by email to complete the survey online. History of ADHD by healthcare provided was self reported. There was a large variation of individual experiences of ADHD diagnosis and treatment in Europe. N=629 Adults with ADHD, N=736 Adults without ADHD. ADHD was associated with significant impairment with all

aspects of life and behavioural conduct problems are recalled by a greater percentage of adults with ADHD than controls. 48% of adults with ADHD are often quick to become angry and upset at school. This occurred in 18% of those without ADHD. Expulsion at school for 30% of adults with ADHD and 9% of adults without ADHD. I get along with my teachers 56 % of adults with ADHD and 73 % without ADHD. I was able to handle large workloads 44% of adults with ADHD and 61% of adults without ADHD. I fit in with my peers 48 % of adults with ADHD and 65% of adults without ADHD. I had a good relationship with my parent's 48 % of adults with ADHD and 70% of adults without ADHD. I often made mistakes or acted in ways that others saw as inappropriate 56% of adults with ADHD and 2% of adults without ADHD. I was in the bottom of the class 23% of adults with ADHD and 10% of adults without ADHD. Did you ever have a tutor to help you with school work 25 % of adults with ADHD and 9% of adults without ADHD. Did you go out on dates 30% of adults with ADHD and 22% of adults without ADHD. I get along with my friends outside school 63% of adults with ADHD and 77% of adults without ADHD. I was popular outside school 45% of adults with ADHD and 53% of adults without ADHD.

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Eur Child Adolesc Psychiatry. 2013;22:S212-S213.

**DIAGNOSTIC PROBLEMS OF AFFECTIVE PATHOLOGY IN CHILDHOOD.**

**Severnyy A, Iovchuk N.**

The depressions nulljuvenile asthenic insolvency null are most frequent at pubertal age. Main disturbances: inability to concentration, distraction, difficulty of understanding of sense, nullsmall ideational automatism null-nullbreaks null of thoughts, nullshutdowns null of thoughts, parallel, chaotic and intertwining thoughts-up to full nullthoughtlessness null Frustration of thinking are accompanied by the anxiety and fear of nullmind loss null. Disturbances of thinking stick out on against decrease of the activity, the increased intellectual and physical fatigue, decrease in motives and narrowing of interests. Obligate sign are cenestopathies, first of all headache. These conditions are treated as null exhaustion null, nulla syndrome of chronic fatiguenull, etc. For younger school the stupid depression with prevalence of ideational block is characteristic at absence or weak expressiveness of retardation in motive sphere and a poverty of depressive affect. Sharp falling of progress is noted. At the expressed and long character of a stupid depression there is the depressive pseudo-debility imitating mental deficiency. The main criteria for a differentiation of stupid depression from mental deficiency are timely intellectual development at early age, unreasonable loss of ability to education, repeatability of conditions of the nullpseudo- debility null alternating with the periods of normal opportunities of education, gradual deepening of insolvency in study, multiple fragmentary affective symptomatology with daily mood swings, seasonality of intellectual opportunities are. The anxious- depressive syndrome is characterized by feeling of internal intensity, concern, causeless and empty anxiety at which disturbing fears of concrete character from time to time are noted, is frequent with a shade of transitivity. The motive concern, restlessness, aspiration for continuous change of a place, strengthening of psychomotor excitement in evening and night time, sleeplessness are characteristic. Inability to concentration of attention on external events, to perception and assimilation of a training material is expressed. There is difficulty in differential diagnostics a subclinical condition with the hidden anxiety owing to an alexithymia natural to children's age. Aggression and self-aggression manifestations are characteristic. In a pediatric network these conditions are diagnosed by neuropathologists as ADHD. The picture of a hypomaniacal condition is extremely similar to ADHD also Obviously, among children with ADHD diagnosis actually ADHD no more than 1/3, and in other cases is a question of affective disorders.

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Eur Child Adolesc Psychiatry. 2013;22:S299-S300.

**DIFFERENTIAL DIAGNOSIS OF ADHD AND DEPRESSION: SYMPTOMS, PSYCHOSOCIAL FACTORS AND NEUROPSYCHOLOGICAL FUNCTION.**

**Bramham J, Peel R, Curran I, et al.**

ADHD is associated with elevated levels of mood disorders. Differential diagnosis of ADHD, depression, or the comorbid condition, is complicated by similarities in symptoms such as inattention, concentration

problems, irritability and restlessness. The present study aimed to investigate symptoms, psychosocial and neuropsychological features of ADHD and depression in order to facilitate differential diagnosis. The study also aimed to investigate factors associated with the presence of depression in individuals with ADHD. Data were collected from participants with ADHD alone, depression alone, comorbid ADHD and depression, and healthy controls. Groups were compared on current symptoms, retrospective early childhood ADHD symptoms, psychosocial background, and neuropsychological function. The ADHD alone group reported more current impulsive symptoms, but not current inattentive or hyperactive symptoms of ADHD than the depression alone group. However, the ADHD alone group had significantly higher levels of all childhood ADHD symptoms than the depression alone group. There were no differences between the ADHD and depression groups with regard to anxiety symptoms. The ADHD alone group reported more childhood psychosocial problems than the depression alone group. There were no significant differences found between the ADHD alone and depression alone groups on the neuropsychological measures. The comorbid ADHD and depression group reported higher levels of current inattentive symptoms than the ADHD alone group, but the groups did not differ regarding childhood symptoms of ADHD, psychosocial background or neuropsychological function. Therefore, differential diagnosis of ADHD and depression is complex because there are many similarities in presentation.

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Eur Child Adolesc Psychiatry. 2013;1-10.

**DEVELOPMENT OF ICF CORE SETS TO STANDARDIZE ASSESSMENT OF FUNCTIONING AND IMPAIRMENT IN ADHD: THE PATH AHEAD.**

**Bolte S, de Schipper E, Holtmann M, et al.**

In the study of health and quality of life in attention deficit/hyperactivity disorder (ADHD), it is of paramount importance to include assessment of functioning. The International Classification of Functioning, Disability and Health (ICF) provides a comprehensive, universally accepted framework for the description of functioning in relation to health conditions. In this paper, the authors outline the process to develop ICF Core Sets for ADHD. ICF Core Sets are subgroups of ICF categories selected to capture the aspects of functioning that are most likely to be affected in specific disorders. The ICF categories that will be included in the ICF Core Sets for ADHD will be determined at an ICF Core Set Consensus Conference, wherein evidence from four preliminary studies (a systematic review, an expert survey, a patient and caregiver qualitative study, and a clinical cross-sectional study) will be integrated. Comprehensive and Brief ICF Core Sets for ADHD will be developed with the goal of providing useful standards for research and clinical practice, and to generate a common language for the description of functioning in ADHD in different areas of life and across the lifespan.

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Eur Child Adolesc Psychiatry. 2013;22:S231.

**COMPARING THE CLINICAL CHARACTERISTICS OF CHILDREN WITH ADHD VS. ADHD WITH COMORBID BIPOLAR DISORDER.**

**Rao S, Agha S.**

**Background:** A leading source of diagnostic confusion in childhood bipolar disorder is the symptomatic overlap with ADHD. Systematic studies of children and adolescents show that rates of ADHD range from 60 to 90% in paediatric patients with bipolar disorder. The increased rates of ADHD in early onset Bipolar patients and higher rates of ADHD in offspring of Bipolar disorder patients, has led to the concept of ADHD features as a pro-dromal manifestation of Paediatric Bipolar disorder (PBD). If we were to categorize and compare the disorder as two distinct types: (1) ADHD prodrome of PBD and (2) ADHD only, this could facilitate early recognition of the PBD

**Aim:** To undertake a case series examination of the clinical characteristics of ADHD children with and without co-morbid PBD

**Method:** The subjects were selected from a large genetic study of ADHD. Nine children with ADHD and co-morbid PBD were compared with 683 children with ADHD to investigate any differences in clinical characteristics, co-morbidities and family history

**Results:** Children with co-morbid ADHD and PBD had significantly higher severity of inattention and oppositional defiant disorder symptoms. There were no obviously distinguishing features of the children with PBD although 11 % had a family history of bipolar disorder. Statistical testing showed that a significantly higher incidence of Bipolar disorder was found amongst the first and second degree relatives of children in the ADHD and PBD group when compared to children in the ADHD only group

**Conclusions:** Children with co-morbid ADHD and PBD have more severe inattention and oppositional symptoms but do not appear to have distinctive features that distinguished a subtype of ADHD. It is also reported that they have a stronger family history of Bipolar disorder Large scale longitudinal studies are needed to further investigate this overlap.

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Eur Child Adolesc Psychiatry. 2013;22:S219.

**COMPARISON BETWEEN ATTENTION TRAINING AND VISUAL PERCEPTION TRAINING IN CHILDREN WITH ADHD.**

**Lange KW, Fuermaier ABM, Hauser J, et al.**

**Introduction and objective:** Pharmacological treatment of children with attention deficit hyperactivity disorder (ADHD) with drugs such as methylphenidate or atomoxetine has been shown to be effective. However, children with ADHD under medication may still show cognitive impairment including attention deficits. In the present study, attentional functioning in children with ADHD was assessed following an attention training program compared to visual perception training

**Participants and methods:** Thirty-two children with ADHD and 16 healthy children participated in the study. Children with ADHD were randomly assigned to one of two conditions, i.e. an attention training program (n=16) which trained aspects of vigilance, selective attention and divided attention, or a visual perception training (n=16) which trained perceptual skills, such as perception of figure and ground, form constancy and position in space. They were assessed and trained while on ADHD medication. Statistical comparison between groups indicated that the three groups did not differ with regard to sex, age or IQ. The training programs were applied in individual sessions, twice a week, for a period of four consecutive weeks. Healthy children did not receive any training. Alertness, vigilance, selective attention, divided attention and flexibility were assessed prior to and following the interventions

**Results:** Data analysis revealed that the attention training used in the present study led to statistically significant improvements of various aspects of attention, including vigilance, divided attention and flexibility when compared with performance prior to training ( $p < 0.05$ , Wilcoxon test), while the visual perception training had no specific effects

**Conclusion:** The present findings indicate that attention training programs have the potential to improve attention functions in children with ADHD.

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Eur Child Adolesc Psychiatry. 2013;22:S303-S304.

**ASSOCIATION STUDY OF THE SEROTONIN 1B RECEPTOR GENE AND ADHD IN KOREA.**

**Son JW, Cho SC, Kim BN, et al.**

**Objective:** Attention-deficit/hyperactivity disorder (ADHD) is one of the most common childhood psychiatric disorders. The evidences from family, twin, adoption studies suggests that ADHD is a highly heritable disorder. Although many reports have shown the genetic association between ADHD and dopaminergic/noradrenergic system, the number of the reports about the genetic association between ADHD and serotonergic system was relatively low. The aim of this study was to investigate the association between Korean ADHD children and the G861C polymorphism of serotonin 1B receptor (5-HT<sub>1B</sub>)

**Materials and method:** The study sample consisted of 150 Korean ADHD children diagnosed by Kiddie-Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version-Korean Version (K-SADS-PL), both parents of ADHD children, and 150 age/ sex matched normal children. DNA were extracted from the blood of all samples, and genotyping was done. Based on the allele and genotype information, not only the case-control analysis between ADHD and normal children but also the family-based association test among ADHD children and their both parents were performed. Transmission

disequilibrium test(TDT) was used for family-based association test. The results of the clinical rating scales and neuropsychological tests were compared according to the genotype of ADHD children.

**Results:** (1) By case-control analyses, there were statistically significant differences in the genotype frequencies between ADHD >80.7% (genotype with C allele) vs. 19.3 % (genotype without C allele)] and normal children >70.7% (genotype with C allele) vs. 29.3 % (genotype without C allele)] ((chi)<sup>2</sup>=4.07, p=0.044). (2) In family-based association study, TDT failed to detect linkage disequilibrium( LD) between G861C polymorphism and ADHD in whole ADHD families.

**Conclusion:** Those results prove the genetic association between the 5-HTR1B G361C gene polymorphism and Korean ADHD children. And those suggest the possibility of the important interaction between the serotonergic and dopaminergic system in the pathophysiological or the pharmacological treatment mechanism of ADHD.

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Eur Child Adolesc Psychiatry. 2013;22:S216-S217.

**A RANDOMIZED DOUBLE-BLIND STUDY OF ATOMOXETINE VS. PLACEBO FOLLOWED BY AN OPEN LABEL EXTENSION PERIOD OF TREATMENT WITH ATOMOXETINE FOR ADHD SYMPTOMS IN CHILDREN WITH ASD.**

**Harferkamp M, Van Der Meer J.**

**Objective:** The primary objective was to examine whether atomoxetine is superior to placebo in the treatment of symptoms of attention-deficit/hyperactivity disorder (ADHD) in children with a diagnosis of autism spectrum disorder (ASD). Secondary objectives were to assess safety and tolerability of atomoxetine, to analyze whether ADHD symptom improvement was mediated by improvement in response inhibition and interference control, to assess the efficacy of long term treatment with atomoxetine on ADHD symptoms, to assess the course of adverse events, and the short and longer term treatment effects of atomoxetine on ASD symptoms

**Method:** Children aged 6-18 with ASD and ADHD were randomly assigned to a double blind treatment with either atomoxetine or placebo in a 1:1 ratio. After a period of 8 weeks all patients who completed this period were invited to participate in an open-label extension for 20 weeks. Primary outcome measure was the ADHD Rating Scale IV-Parent version: Investigator scored (ADHD-RS-IV P). Some of the secondary outcome measures were inhibitory control (as measured by response inhibition and interference control (Amsterdamse Neuropsychologische Taken (ANT)), the aberrant behavior checklist (ABC) and children's social behavior questionnaire (CSBQ)

**Results:** A treatment effect of atomoxetine was found for ADHD symptoms (ADHD-RS-IV P), hyperactivity (CTRS-R:S and ABC), inappropriate speech, stereotypies (ABC) and fear for changes (CSBQ) in the double blind treatment period. Furthermore, atomoxetine improved response inhibition but not interference control, independent from progress in ADHD-symptomatology. No serious adverse events were reported; reported events (mostly nausea and fatigue) were comparable for atomoxetine and placebo treatment Long-term atomoxetine treatment further reduced ADHD-symptomatology (ADHD-RS-IV P and ABC-hyperactivity), while adverse events overall tended to subside. No beneficial effects of atomoxetine were found on social functioning

**Conclusions:** Atomoxetine improved ADHD-symptomatology in children with ASD, independent from changes in inhibitory control, and was generally well tolerated. Adverse events were similar to those in other studies with ADHD patients without ASD. Continued treatment with atomoxetine further reduced ADHD symptoms. Future studies investigating the long-term efficacy of atomoxetine in children with ASD should be randomized and placebo-controlled.

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Eur Child Adolesc Psychiatry. 2013;22:S123.

**'NOW THAT I LOOK BACK I REALISE THAT...: YOUNG ADULTS' RETROSPECTIVE ACCOUNTS OF MENTAL HEALTH STIGMA EXPERIENCED DURING CHILDHOOD AND ADOLESCENCE.**

**McKeague L, Hennessy E, Heary C, et al.**

**Objectives:** The aim of this study was to investigate stigma from the perspective of young adults who had experienced a mental health problem during childhood or adolescence. An extensive literature suggests

that typically developing children and adolescents hold stigmatising attitudes towards peers with emotional or behavioural problems. Despite this, very little research has focused on how these attitudes are perceived and interpreted by individuals who have themselves experienced a psychiatric disorder. The social identity of youth with mental health problems may be influenced by the stigmatising reactions of others, whereby negative attitudes or discrimination potentially contribute to adverse experiences in the peer group and diminished self-esteem. Therefore, it is imperative that we understand perceived and self-stigma from the point of view of those individuals with lived experience of a mental health problem in childhood or adolescence.

**Method:** In the present study qualitative data were collected from young adults (aged 18-30 years) who had received a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD) or Depression/ Anxiety before the age of 18 (n=15). Young adults provided retrospective accounts of their experiences during their childhood and adolescence. The interview schedule consisted of open-ended questions that focused primarily on functioning within the peer group, experiences in the home and at school, and willingness to disclose information about the mental health problem to others. Interview transcripts were transcribed verbatim and analysed to explore perceptions of peer relations, disclosure decisions, and perceptions of attitudes held by others.

**Results:** Young adults revealed how their experiences and perceptions changed as they became older. Participants reported experiences of peer problems and reluctance to disclose their mental health difficulties to others during their childhood/adolescence. In addition, many of the young people who participated described feelings of difference and felt that there was a lack of understanding among others.

**Conclusions:** Youth with mental health problems experience difficulties in many areas of their lives including school and peer relationships. Young adults who had a mental health problem in childhood/adolescence felt that other people had a limited understanding of the difficulties that they faced.

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Eur Child Adolesc Psychiatry. 2013;22:S293.

**A PRELIMINARY FINDING OF EEG DIFFERENCES OF CHILDREN WITH DISRUPTIVE BEHAVIOUR DISORDERS IN SINGAPORE.**

**Tor HT, Lim-Ashworth NSJ, Rudo-Hutt A, et al.**

**Background:** Many electroencephalography (EEG) studies have underscored that children with attention deficit hyperactivity disorder (ADHD) exhibit brainwave abnormalities. Specifically, they have increased theta (slow wave) and decreased beta (fast wave) brain patterns. These children show elevated theta/beta ratio compared to those in both normal and other clinical populations. Such differences are interpreted to be indicative of a reduction in brain arousal activity to task demands. EEG measures are thus an important clinical tool in aiding the diagnosis and assessment of ADHD. Clinically, ADHD often present with comorbidities and most commonly with conduct disorder (CD). An investigation on how such comorbidities can affect EEG brain wave patterns in ADHD children is of significance.

**Objective:** This study investigated the EEG differences in theta, beta activities and theta/beta ratio using a sample of Asian children in Singapore diagnosed with disruptive behaviour disorders. We hypothesised that these measures will in particular discriminate between those with an ADHD only and those with a comorbid diagnosis of conduct disorder.

**Method:** A total of 105 children aged between 7 and 16 were recruited from a child psychiatric outpatient clinic in Singapore. Participants were included in the study after satisfied the DSM-IV-TR criteria and were assigned into one of the following: (i) ADHD only (n=43), (ii) ADHD + CD (n = 48) and, (iii) CD only (n=14). EEG recording were obtained during a 3-min resting task (with eyes open) using 12 scalp electrodes across 6 regions and 2 hemispheres of the brain. Fourier transformation was performed to provide absolute power for theta and beta bands. Theta and beta values, and theta/beta ratio were then computed.

**Results:** Repeated measures one-way ANOVA was performed. The result indicated that there were no significant differences in theta ( $F(2, 11) = 0.49, p=0.61$ ) and beta ( $F(2, 11) = 0.57, p=0.56$ ) characteristics. Theta/beta ratio ( $F(2, 11) = 0.10, p=0.89$ ) across 6 regions and 2 hemispheres of the brain did not differ across three diagnostic groups either.

**Conclusions:** Contrary to our hypothesis, our preliminary results did not show any significant differences in EEG theta, beta activities and theta/beta ratio between those with only an ADHD diagnosis and those with

a CD comorbidity. Our findings might suggest that these EEG measures do not sufficiently discriminate in our local subsample. It should also be highlighted that the results cannot be extended to children who have secondary ADHD symptom presentation. Data collection is still currently ongoing; this will provide the basis for a more conclusive finding. In addition, due to the complexity of comorbid conditions, it is difficult to elucidate the underlying brain mechanisms and thus a greater need for research aimed at uncovering distinct brain wave patterns of those diagnosed with ADHD and comorbidities.

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Eur Child Adolesc Psychiatry. 2013;22:S244.

**ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN CHILDHOOD AND ADOLESCENCE IS ASSOCIATED WITH REDUCED GRAY MATTER VOLUME IN THE THALAMUS.**

**Tomoda A.**

**Background:** Research has addressed the epidemiology and the increasing prevalence of attention deficit hyperactivity disorder (ADHD). ADHD is reportedly associated with both global and local morphological changes in the brain. Nevertheless, little is known about grey matter volumes (GMV) in patients with ADHD. An objective overall assessment using voxel-based morphometry (VBM) has yet to be reported in paediatric patients with ADHD. The aim of this study was to explore GMV abnormalities in ADHD in childhood and adolescence. Design: Control-matched cohort study.

**Method:** High-resolution T1-weighted MRI datasets were obtained from 39 unmedicated ADHD subjects and 39 healthy controls of equivalent age and socioeconomic status, with no history of trauma or other developmental disorder. We also performed Catechol-Omethyltransferase (COMT) genotyping for each patient.

**Results:** GMV was decreased by 4.6 % in the right thalamus ( $p=0.029$ , corrected) of ADHD subjects. Main effect of COMT genotype and GMV reduction was found in the right thalamus (met/met\val/met\val/val).

**Discussion:** Quantitative genetic studies (i.e., twin and adoption studies) suggest that genetic influences contribute substantially to the development of ADHD. Over the past 15 years, considerable efforts have been made to identify genes involved in the etiology of this disorder resulting in a large and often conflicting literature of candidate gene associations for ADHD. Previously, we have found decreased activation of the nucleus accumbens and thalamus in patients with ADHD during only the low monetary reward condition before MPH treatment by fMRI. Taken together, these results indicate that genetically influenced variations in dopamine transmission modulate the response of brain regions involved in anticipation and reception of rewards.

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Eur Child Adolesc Psychiatry. 2013;22:S275.

**A MUSIC GROUP FOR YOUNG PEOPLE ATTENDING THE LUCENA CLINIC RATHGAR.**

**McDonald J, Codrea A, Gavin B.**

**Background:** Youth mental health is a significant public health concern in Ireland with high rates of youth suicide and self harm. Despite this young people's engagement with mental health services can be poor. A number of recent reports have highlighted the need for creative, youth friendly approaches to promote engagement.

**Aims:** The Lucena Clinic music group was set up as a pilot project to investigate the level of interest in a music group and the feasibility of running such a group in an out-patient Child and Adolescent Mental Health Service, as well as any potential benefits with regards to mental health of the young people attending.

**Methods:** Young people aged fifteen to eighteen attending the Lucena clinic were invited to the group. Invitation was made on the suggestion of key workers. Of fifteen young people invited, five consented to attend eight weekly music sessions. The Strengths and Difficulties questionnaire was completed at baseline and again after 8 weeks along with a study specific feedback questionnaire. Treatment as usual continued alongside the music group.

**Results:** Before and after SDQs revealed a minor mean reduction in scores over the 8 weeks. Feedback from the study specific questionnaire revealed that group was an enjoyable experience for all the young

people attending, with subjective improvements described in mood, motivation, self confidence and social skills.

**Conclusions:** the results of this study suggest that a music group can be a useful adjunct to treatment within a child and adolescent mental health service, providing a youth friendly, non-pathologising intervention which can promote attendance and which may have mental health benefits to the young people attending.

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Eur Child Adolesc Psychiatry. 2013;22:S243.

**ARE THE PERINATAL RISK FACTORS DIFFERENT FOR THE INATTENTIVE AND COMBINED SUBTYPES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?**

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

**Objectives:** To compare the attention-deficit/hyperactivity disorder (ADHD) combined subtype (ADHD-C) to the ADHD inattentive subtype (ADHD-I) in terms of perinatal risk factors and clinical and neuropsychological characteristics.

**Method:** A total of 155 medication-naive 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 (ADHD-RS), the children's behavior checklist (CBCL), and structured questionnaires on perinatal and developmental risk factors, and the children underwent a neuropsychological test. A total of 502 children without ADHD were recruited from the community as a healthy control group.

**Results:** Patients with ADHD-C had higher scores on the ADHD-RS and DBDS, more aggressive behavior, higher externalizing problem scores on the CBCL compared to children in the ADHD-I group and controls ( $p < 0.001$ ). Patients with ADHD-C also had greater numbers of omission errors ( $p = 0.014$ ), commission errors ( $p = 0.005$ ), and higher response time variability ( $p = 0.028$ ) than those with ADHD-I. Severe maternal stress during pregnancy, postpartum depression, and change in primary caretaker were significantly associated with both ADHD-I ( $p = 0.013$ ,  $p < 0.001$ , and  $p = 0.002$ , respectively) and ADHD-C ( $p = 0.027$ ,  $p = 0.003$ , and  $p < 0.001$ , respectively). Advanced maternal age at pregnancy and delayed time to first sentence were significantly associated with only ADHD-I ( $p < 0.001$  and  $p = 0.010$ , respectively), and younger paternal age at pregnancy and rearing by a primary care taker other than the mother were significantly associated with only ADHD-C ( $p = 0.004$  and  $p = 0.012$ , respectively). Non-regular prenatal check-ups ( $p = 0.036$ ) and post-delivery medical illness ( $p = 0.037$ ) were more likely to be associated with ADHD-I than ADHD-C.

**Discussion:** On the level of symptomatology, the ADHD-C group had more externalizing problems than did the ADHD-I group. On the level of neuropsychological function, the most prominent difference between the ADHD-C and ADHD-I groups was in the inhibition deficit (represented by number of commission errors). At the level of perinatal and developmental risk factors, our results suggest that biological environmental factors (chronic and acute problems that usually arise during the gestational and perinatal period) are more likely to be associated with ADHD-I, and psychosocial environmental factors (negative incidents or environments in the early development period) are more likely to be associated with ADHD-C.

**Conclusion:** This study shows that the inattentive subtype of ADHD is different from the combined subtype in many parameters including severity of symptoms, neuropsychological characteristics, and environmental risk factors.

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Eur Child Adolesc Psychiatry. 2013;22:S126.

**ASSESSING ADHD STIMULANT TREATMENT EFFICACY USING THE WEISS FUNCTIONAL IMPAIRMENT RATING SCALE: STRENGTHS AND WEAKNESSES.**

**Soutullo C, Banaschewki T, Lecendreux M, et al.**

**Introduction:** Patients with ADHD encounter a range of day-to-day problems that are characteristic of the disorder, and these represent important potential treatment targets. The Weiss Functional Impairment Ratings Scale-Parent Report (WFIRS-P) was designed specifically for assessment of functional impairment



in children with ADHD. It comprises 50 items, grouped into 6 domains, and parents or guardians use a Likert scale (0-3) to score each item. To date, reported use of WFIRS-P in clinical trials is limited and its psychometric validation has yet to be published. Here, we present WFIRS-P data from two recent, consecutive, phase 3 studies of the efficacy and safety of the prodrug lisdexamfetamine dimesylate (LDX).

**Methods:** SPD489-325 was a European, 7-week, double-blind, randomized, placebo-controlled study, and included osmotic-release oral system methylphenidate (OROS-MPH) as a reference treatment. Patients from this trial, together with additional US patients, entered a subsequent study, SPD489-326, in which open-label LDX treatment for (greater-than or equal to) 6 months was followed by a 6-week double-blind, placebo-controlled randomized-withdrawal period. WFIRS-P data were analysed using an ANCOVA model of the mean change from study baseline in mean domain score or total score.

**Results** In study SPD489-325, mean WFIRS-P total scores at baseline were 1.01 (95 % confidence interval [95 % CI] 0.92, 1.10) for the LDX treatment group, 1.10 (1.01, 1.19) for placebo and 1.07 (0.98, 1.15) for OROS-MPH. At endpoint, there were statistically significant ( $p < 0.001$ ) placebo-adjusted mean improvements in total score of -0.3 (95 % CI -0.4, -0.2) for LDX and -0.2 (-0.3, -0.1) for OROS-MPH. The effects of both drugs were statistically significant in the Learning and School ( $p < 0.001$ ), Family ( $p < 0.001$ ), Social Activities ( $p < 0.001$ ) and Risky Activities ( $p$  (less-than or equal to) 0.01) domains, but only OROS-MPH was significant in Life Skills and Child's Self Concept ( $p < 0.05$ ). In study SPD489-326, mean WFIRS-P scores were stable or decreased during open-label LDX treatment. In the 6-week randomized-withdrawal period, only the placebo group experienced statistically significant deterioration from baseline to endpoint in WFIRS-P total ( $p < 0.001$ ) or domain ( $p < 0.05$ ) scores. These changes were statistically significantly different to those for LDX in the Learning and School, Family, and Risky Activities domains ( $p < 0.01$ ) and in total score ( $p < 0.001$ ).

**Conclusions:** These results indicate that acute treatment with LDX or OROS-MPH is associated with improvement in the day-to-day functioning of children and adolescents with ADHD, as measured using mean WFIRS-P domain or total scores. Continued long-term treatment with LDX was required for maintenance of this benefit, which was at least partially lost in patients whose treatment was withdrawn. The WFIRS-P results complement the symptom-based and generic quality-of-life data from these studies, potentially enabling evaluation of the relationships between different outcome measures during stimulant treatment.

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Eur Child Adolesc Psychiatry. 2013;22:S201.

**ADHD CLINICAL GUIDELINES.**

**McNicholas F.**

Attention deficit hyperactivity disorder is a recognised disorder with international prevalence rates estimated to be 5%, and one of the most common disorders treated in child and adolescent mental health services including Ireland. There have been a number of guidelines produced to aid clinicians in the diagnosis and treatment of ADHD however there are significant differences between countries and disciplines. This symposia will review the guidelines from the American, Canadian and European perspectives, consider the similarities and differences in the context of overall service provision The symposia will present on two European studies along with one Irish. The individual experiences of adults (1,500) with an ADHD diagnosis and treatment from a Europe perspective will be presented, along with the attitudes of Irish Psychiatrists to adult diagnosis. Data from clinicians from 7 different European countries will be presented highlighting intriguing country- and professionspecific differences.

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Eur Child Adolesc Psychiatry. 2013;22:S265.

**A CROSS-SECTIONAL STUDY OF THE HEALTH AND SOCIAL COSTS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN SPAIN: STUDY DESIGN.**

**Mardomingo MJ, Alda JA, Sansebastian J, et al.**

**Background:** The estimated worldwide prevalence of ADHD is 5.3% in childhood and 4.4% in adults. The management of ADHD and its consequences involve high healthcare and social resource use<sup>1</sup>. The overall costs attributed to ADHD in Spain are unknown.

**Objectives:** (1) To describe the direct, indirect, and societal costs of ADHD management; (2) to assess the comparative costs of treating drug responders vs. non-responders in patients <18 years.

**Methods:** Study design is a cross-sectional (1 year retrospective follow up) from a health system (direct costs only) and social (direct and indirect costs) perspective, using concurrent and retrospective data. Patients will be recruited consecutively from 15 participating centres in Spain. Patients aged (greater than or equal to) 6 years with an IQ >70 and a confirmed diagnosis of ADHD will be included after informed consent from the patient or guardian. Any patients with a significant organic disease (excluding asthma), other neurological disorder, severe psychiatric disorder (psychosis, bipolar disorder or pervasive developmental disorder) or depression, or participants in prior clinical trials are not eligible. Treatment responders are defined as those presenting with an ADHD-RS score lower than 18 for (greater than or equal to) 3 months. The sample size needed for objective 2 was calculated to be 147 patients per group ( $\alpha = 0.05$ ,  $\beta = 0.2$ ) to detect a difference of 2,000 (euro) between the cost of responders and non-responders (e.g., 12,000 (euro) vs. 14,000 (euro)), and assuming a standard deviation of 5,000 (euro) and 7,000 (euro) respectively. Data will be collected in one visit, using standardized questionnaires to capture: demographics, social status, parental employment status, working, social relations, disease characteristics (DSM-IV-TR subtype, CGI, CGA, and ADHD IV), service utilization, drug and non-pharmacological treatments, quality of life (EuroQoL-5D) patient's and work productivity (WPAI). A descriptive analysis of the sample will be performed. A univariate analysis will be carried out to explore associations between the costs and the response to treatment and other relevant variables. A multivariate analysis will be performed to obtain adjusted estimates of the association between costs and response. The study has been registered with the Spanish agency of medicines and health products and accepted by the ethics committees of the participating centres. Recruitment has begun.

**Conclusions:** This study in Spain is a novel and innovative approach to the total cost of ADHD, which never has been analyzed before.

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Eur Child Adolesc Psychiatry. 2013;22:S255-S256.

**A MORE EFFICIENT COST EFFECTIVE WAY OF PROVIDING A CHILD PSYCHIATRY ADHD SERVICE IN TIMES OF AUSTERITY?**

**Moore K, Hetherington G, Walsh M.**

**Introduction:** Ongoing difficulty in marrying scarce resources with ever greater clinical need continues apace in healthcare generally and in Child Psychiatry in Ireland particularly. Due to chronic underfunding and economic the service was faced in January 2012 with providing a child psychiatry service to a gross population of 70,000 people with 3 clinical staff (one consultant child and adolescent psychiatrist and 2 clinical nurse specialists-having lost two junior doctors and a psychologist.) The recommended staffing is approximately 25.

**Aim:** To devise a new method of working to allow a continuance of the provision of a quality child psychiatric service to the children of the catchment area despite the dearth in clinical resources.

**Method:** The diagnosis of all patients seen from January 2003 to January 2012 was audited. 30.4% of all referrals were for ADHD. 42.3% of all diagnoses made were of ADHD. As the biggest cohort of patients in terms of numbers was ADHD it was decided to reconfigure the ADHD clinic by instigating a primarily nurse provided ADHD service. Prior to this assessments had involved at least two clinicians; one always being a medical doctor. The 'new' ADHD service was divided into three types: new patient assessments, 'return' clinics and 'intermediate' clinics. New patient assessments were entirely carried out by one clinical nurse specialist. Detailed discussion of the case occurred at team meeting once a week. If there was a clinical need or if patients were to be started on medication, they were seen by the consultant child and adolescent

psychiatrist in the 'intermediate' clinic. Once stabilised on medication patients were reviewed as clinically appropriate by the clinical nurse specialist at the 'review' clinic.

**Results:** From January 2011 to January 2012, there were 42 patients seen for ADHD. On 01/01/2012 there were 21 patients on the ADHD waiting list. From January 2012 until January 2013 38 patients were seen and assessed by the clinical nurse specialist for ADHD. On 1st December 2013 there were 30 patients on the ADHD waiting list.

**Discussion:** The use of a nurse lead ADHD clinic in a rural clinic with very poor resources was an efficient, cost effective way of delivering a service to the 42 % of patients seen with ADHD, freeing the consultant child and adolescent psychiatrist and the other clinical nurse specialist to focus on all the other clinical presentations. We propose the introduction of the next logical step of nurse prescribing in the future.

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Eur Child Adolesc Psychiatry. 2013;22:S240.

**WHEN MOTHER-ADHD CHILD RELATIONSHIP IS IMPAIRED-DIABOLIC CYCLE.**

**Kusmic E, Marsanic VB.**

ADHD is one of the most common behavioural disorders in childhood and adolescence associated with a number of negative outcomes including poor academic performance, and peer and family functioning. The exact aetiological pathways of ADHD are still unknown. ADHD is a multifactorial disorder in which genetic risk factors predominate and various other environmental factors may be involved. Impaired parent-child relationship in children with ADHD is common. Parents may engage in parenting styles and patterns of family functioning which maintain or exacerbate ADHD symptomatology rather than alleviate it. During the year 2012, 22 youths (1 preadolescent girl and 9 preadolescent, 9 early adolescent and 3 late adolescent boys) were admitted for treatment at the Day Hospital of the Psychiatric Hospital for Children and Adolescents, Zagreb, Croatia, reflecting the epidemiology of ADHD which is more prevalent in boys and in childhood. We present a case of a 11 years old boy with ADHD who was referred for treatment in day hospital after his parents divorce. Treatment program included individual, group and family therapy. As mother-child relationship in this case was significantly impaired, family treatment geared to establishing adequate parent-child bonding and communication patterns by educating parents and by skills training programs was undertaken in this case. This case highlights that in order to improve psychosocial functioning of children with ADHD it is important to develop an individually tailored comprehensive treatment plan that involves interventions aimed to reduce stress levels in the family by targeting interactional problems in the family and psychological and behavioral problems of family members.

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Eur Child Adolesc Psychiatry. 2013;22:S242.

**DOES TREATMENT OF ADHD SLEEPING PROBLEMS IMPROVE ATTENTION, HYPERACTIVITY AND IMPULSIVENESS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER?**

**Hvolby A.**

**Introduction:** Sleep difficulties with no explanatory cause can be mistaken for ADHD, and that the kind of symptoms observed in primary sleep disorders can often be mistaken for ADHD as they are very similar to core symptoms of ADHD. These disorders are found to be related to hyperactivity and inattentiveness, and the very treatment of the sleep disorders has reduced or even cured both hyperactivity and inattentiveness. Studies using actigraphy found increased sleep onset latency and increased day-to-day variability in the sleep-wake pattern of children with ADHD compared with children without ADHD.

**Aims:** Based on actigraphic surveillance, sleep diary, ADHD symptom rating (ADHD-RS), functional impairment scale (WFIRS) and daily function (DDODS), this study will evaluate the effect of treating sleep in a sample of 6-13 year-old ADHD children. The sleep latency, number of awakenings and total length of sleep will be measured, as will the possible influence on parent and teacher rated ADHD symptom load and Quality of life. **Methods participants:** A total of 35 children aged 6 years to 13 years are included. All referred to a child and adolescent psychiatric department and diagnosed with ADHD. The diagnostic evaluations is based on face-to-face parent interviews and a clinical assessment, and the hyperkinetic

disorder (ADHD) is diagnosed in accordance with the ICD-10 Classification of Mental and Behavioural Disorder.

**Methods:** To improve sleep we use a ball blanket, which former has shown effect on sleep improvement. The children will sleep with the ball blanket in 8 weeks. Parents are asked to evaluate sleep patterns using sleep questionnaire and sleep diary. Quality of life, using QoL-WFIRS rating scale, daily functional level using DDODS and parents and teachers are asked to evaluate ADHD symptoms before, during and after the child using the Ball Blanket. Actigraph will be used to obtain an objective view of the sleep pattern. Sleep recording will take place in the children's own home and will be obtained in 3 periods of 7 days during the 8 weeks.

**Results:** The study is ongoing. We will present preliminary result from the study, regarding eventual effect on ADHD core symptoms and child and family quality of life by treating ADHD related sleep problems. Our hypotheses is, based on other studies, that prolonged use of a ball blanket in children with ADHD and sleeping difficulties not only will improve their sleep, but also will influence on their ADHD symptoms.

**Clinical relevance:** Provide this study finds impact on treating sleep in children with ADHD on the ADHD core symptoms, the consequence may be more focus on detecting sleep problems in children with ADHD, treating the sleep problem effectively and maybe that way reduce the use of stimulants.

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Eur Child Adolesc Psychiatry. 2013;22:S235.

**TOULOUSE PIERON: UTILITY AS A DIAGNOSTIC TOOL AND COMPARATIVE EVOLUTION OF ADHD TREATMENT.**

**Aparicio T, Ortega A, Galindo E, et al.**

**Introduction:** The ability to maintain an activity or complete a task is one of the usual difficulties in children with ADHD, and improve these aspects one of the goals of treatment. The assessment should include the evolution of objective measurements of changes in the working memory capacity coincident with treatment. This requires reliable and accessible tools from clinical practice.

**Objectives:** Improving the evidence to substantiate the objective assessment of the diagnosis, and the improvements obtained with drug treatments for ADHD in everyday clinical practice. Quantifying changes in working memory capacity coincident with the start drug treatment in cases diagnosed ADHD, measured before the start and after 4-8 weeks.

**Method:** In the present study 40 patients (with a diagnosis of ADHD, and normal mental level that have not yet initiated drug treatment) aged 6 to 17 years Attending our first consultation Center Children and Youth Mental Health referred by their pediatricians or educational institutions (for diagnosis and treatment) suspecting a possible diagnosis of ADHD The consultation will be assessed sustained attention, concentration, resistance to monotony and perceptual speed test by Pieron Toulouse The aim of the study was to study the usefulness of the test as a diagnostic aid measure and to assess the improvement achieved with treatment. In 16 of the 40 cases the study was repeated with TP at 4-8 weeks of starting treatment with methylphenidate.

**Results:** The sample pre-treatment initiation scored an average of 30.3 percentile test, with a mean of 97.26 points. In 16 of the 40 cases the study was repeated after starting treatment with methylphenidate Comparing the observations before and after treatment the yield obtained in the test had increased between 72.4 and 79.8 points with a 95 % confidence.

**Discussion:** The results confirm the untreated TP poor performance in this test, according to the negative impact of ADHD on working memory. Moreover provide a quantified measure both cases gravity as for evaluation, in this aspect of the response to treatment. The significant improvement of the cases after the initiation of treatment may further serve as a reference for quantification of evolution, in this case quantified and objective but should be explored the possibility that the performance in the test is increased from the second exploration.

**Conclusions:** The test is affordable, cost and time, for use in everyday clinical. Adding one more item to evidence-based diagnosis Despite the small sample size, the results suggest the usefulness for the query objectify the quantitative evolution of the patient with drug treatment in their tasks of attention and concentration.

Eur Child Adolesc Psychiatry. 2013;22:S216.

**EFFECT OF OROS METHYLPHENIDATE ON ENCOPIRESIS IN CHILDREN WITH ADHD: A RETROSPECTIVE CHART REVIEW.**

**Yilmaz S, Bilgicnull A, Herguner S.**

Encopresis shows a high rate of comorbidity with attention deficit hyperactivity disorder (ADHD) in childhood. However, the etiologic origin of this relationship and the effect of ADHD agents on encopresis are unclear. In this chart review, we aimed to explore the effect of OROS long-acting methylphenidate (MPH) treatment on encopresis in a group of children with ADHD. We also examined the relationship between clinical variables of ADHD and encopresis. The sample consisted of 21 children (20 boys and 1 girl) with ADHD and coexisting encopresis aged 7-15 years. Clinical characteristics and, baseline (visit 1) and at the end of the second months' (visit 2) Conners' Parent Rating Scale (CPRS) subscale scores of children were recorded. Retrospective clinician determinations were made using the clinical global impressions-severity scale (CGI-S) for encopresis severity and clinical global impressions-improvement scale (CGI-I) for encopresis response. The mean final OROS methylphenidate (MPH) dose was 25.7 (plus or minus) 8.2 mg/day. According to the CGI-I, fourteen children (71.4 %) had much or very much improvement for encopresis at visit 2. All of the CPRS subscale scores decreased significantly over visit 1 through 2. No association was found between the CGI-I score and the changes in any of the CPRS subscale scores between visit 1-2. Baseline oppositional defiant disorder (ODD) and conduct disorder (CD) scores were correlated with CGI-S score ( $r_s=0.70$ ,  $p<0.001$  and  $r_s=0.61$ ,  $p=0.004$ , respectively), whereas no association was found between core ADHD symptoms severity and CGI-S score. With regard to encopresis outcome, baseline CD score was negatively correlated with CGI-I score ( $r_s=-0.51$ ,  $p=0.017$ ) and baseline ODD score was prone to show a correlation with CGI-I score ( $r_s=-0.42$ ,  $p=0.061$ ). These results suggest that coexisting conduct disorder symptoms may be a vulnerability factor for the development of encopresis, and MPH treatment may have positive effect on encopresis course in children with ADHD.

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Eur Child Adolesc Psychiatry. 2013;22:S229.

**EFFECTS OF ATOMOXETINE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AS MEASURED BY NEAR-INFRARED SPECTROSCOPY: A PRELIMINARY STUDY.**

**Ota T, Iida J, Nakanishi Y, et al.**

Neurobiological studies report that prefrontal dysfunction are involved in the pathophysiology of attention-deficit/hyperactivity disorder. Near-infrared spectroscopy is a noninvasive optical tool for studying oxygenation and hemodynamic changes in the cerebral cortex by measuring changes in oxygenated hemoglobin. The aim of the present preliminary study was to evaluate the feasibility of measuring cerebral hemodynamic effects of a clinical dose of atomoxetine by near-infrared spectroscopy in 5 children (3 boys and 2 girls; mean age, 9.0 years) with attention-deficit/hyperactivity disorder. Ethical approval for the present study was obtained through the Nara Medical University. Written informed consent was obtained from all subjects and/or their parents before the study. The relative concentrations of oxyhemoglobin (oxy-Hb) were measured with frontal probes every 0.1 s during the Stroop color-word task, using 24-channel near-infrared spectroscopy machines, in the drug-naive condition and after intake of atomoxetine. At the each condition, we used the ADHD RS-IV-J (Home Version) to evaluate ADHD symptoms of subjects. The total score of ADHD RS-IV-J showed a decreasing trend, from 31.8 before treatment to 26.6 after treatment ( $P=0.053$ ). During the Stroop color-word task, the oxy-Hb changes in the condition after intake of atomoxetine were significantly larger than that in the drug-naive condition at the channel 8 and 21 located at prefrontal cortex. The larger oxy-Hb changes in the condition after treatment might indicate an intensified prefrontal hemodynamic response induced by atomoxetine. Near-infrared spectroscopy is a sensitive tool for measuring pharmacological effects of atomoxetine in children with attention-deficit/hyperactivity disorder.

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**EVALUATION OF A PSYCHOEDUCATION PROGRAMME FOR PARENTS OF CHILDREN AND ADOLESCENTS WITH ADHD: IMMEDIATE AND LONG-TERM EFFECTS USING A BLIND RANDOMIZED CONTROLLED TRIAL.**

**Ferrin M, Moreno-Granados JM, Salcedo-Marin MD, et al.**

Recent guidelines for the diagnosis and treatment of attention deficit hyperactivity disorder (ADHD) have claimed the possible benefits of psychoeducational techniques in the comprehensive management of ADHD. To evaluate the efficacy of a psychoeducation programme for parents of children and adolescents with ADHD in a clinical setting using a blind randomized trial. 81 children/adolescents with ADHD were randomly assigned for their families to receive either a well-structured psychoeducation programme (intervention group, n=44), or a parent counselling and support intervention (control group, n=37). Measures of child ADHD symptoms, psychopathology, quality of life and family stress were taken before and after intervention and after a year follow-up. Parents and evaluators were unaware of the condition received. Compared to the support control group, the psychoeducation group showed ADHD Index and cognitive/inattention levels significantly reduced after the intervention ended (Mann-Whitney U =3.34; p=0.001; Mann-Whitney U=3.47; p= 0.001). An improvement in the pro-social domain was also observed after 1 year follow-up (Mann-Whitney U =-2.37; p=0.018), and clinical global impression found a statistically significant effect for severity over the time. Differences were initially found for the impact of the disorder in the family in different domains, including emotional and social functioning; these differences were no longer significant after alpha correction. No significant differences in quality of life or family stress were found in comparison with the control group. This psychoeducation programme is a valuable treatment for parents/carers of children/adolescents with ADHD, which needs to be considered when evaluating different non-pharmacological treatment options. Psychoeducation and other kind of non-pharmacological approaches need to be regarded not as a substitute, but as a complementary treatment to medications; these approaches might help other very crucial aspects of ADHD including social and familiar outcomes.

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Eur Child Adolesc Psychiatry. 2013;22:S282.

**EVALUATION OF VISUAL MEMORY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-INATTENTIVE TYPE.**

**Tehrani-Doost M, Tabaii RS, Noorian N, et al.**

**Background:** Children with attention-deficit/hyperactivity disorder-inattentive type- have been shown to have some deficits in cognitive functions such as executive functions including working memory. It has been hypothesized that individuals with this type of ADHD have also some impairment in memory functioning. Little is known about this cognitive function in ADHD -inattentive type-. We conducted this study to evaluate visual memory ability in children with ADHD-inattentive type-compared with normal developing children.

**Method:** Twenty children diagnosed with ADHD-inattentive type based on DSM-IV criteria aged between 7 and 11 were compared with 20 normal developing children matched on the age and IQ. They were evaluated using the parent conners rating scale (to evaluate the severity of ADHD symptoms), pattern recognition memory task (PRM) (to evaluate the ability to recognize the patterns seen before), paired associate learning task (PAL) (to assess visual memory and new learning abilities), delayed matching to sample task (DMS) (to evaluate the ability to match the patterns to target seen before), and spatial recognition memory task (SRM) (to assess the recognizing ability of spatial patterns seen before). T test was used to evaluate the difference between the two groups in terms of visual memory variables.

**Results:** In terms of Paired Associate Learning task, children with ADHD -inattentive type- had significantly more errors especially in 8 shapes trials compared to normal developing children (p<0.05). These children performed significantly less trials on this task than that of control group (p<0.05). With regard to pattern recognition memory, spatial recognition memory, and delayed matching to sample, tasks it was found no significant difference between the two groups.

**Conclusion:** Based on the findings of this study it can be concluded that children with ADHD-inattentive type- had no impairment in visual memory ability, but there is some impairment in new learning task which can be related to working memory deficit which have been shown in this group of children.

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Eur Child Adolesc Psychiatry. 2013;22:S301.

**EVALUATING THE EFFECTIVENESS OF PSYCHOSOCIAL BEHAVIOURAL TRAINING INTERVENTIONS FOR CHILDREN WITH SYMPTOMS OF ADHD: A RANDOMISED CONTROLLED TRIAL.**

**Ni Mhaille G, McGilloway S, Leckey Y, et al.**

**Background:** A growing number of children are presenting with attention deficit hyperactive disorder (ADHD) or ADHD-type symptoms and increasing attention has focused on identifying effective forms of treatment. Psychosocial interventions are now recommended as the first-line of treatment for children with ADHD and their families (NICE, 2008).

**Objective:** This study was undertaken to assess the effectiveness of the incredible years basic parent intervention (IYBP) and the incredible years small group Dina programme as an intervention for Irish children (aged 3-7 years) with symptoms of ADHD.

**Methods:** Forty-five children with symptoms of ADHD and their parents were randomly allocated to a Dina child training (CT) plus parent training (PT) intervention group (PT + CT, n = 12), a parent training group (PT, n = 19) or a waiting-list control group (WLC, n = 14). Assessments of child adjustment and parent behaviour and wellbeing were carried out using parent-report measures at baseline and at 6-months post intervention. An intention to treat analysis was carried out to examine post-intervention differences between groups. One-to-one post-intervention interviews were also conducted with a small number of parents (n = 8) who had received the combined intervention, as well as a focus group with Dina programme facilitators (n = 5).

**Results:** The findings highlighted significant differences at 6-month follow-up between the PT group and the WLC group on child hyperactivity and pro-social skills as well as parenting competency. Differences between the PT + CT group and the WLC group at follow-up were largely non-significant. These results suggest that the combined treatment (PT + CT) did not produce any added benefit for child hyperactive/inattentive behaviour post-intervention, although our qualitative findings suggest that the combined programme was viewed very favourably by both parents and children and had led to marked improvements in child behaviour.

**Conclusion:** The findings appear promising for this clinical subgroup of children and their parents, in that a parent-focused intervention led in improvements in ADHD symptoms and behaviour, as well as parent behaviour and wellbeing. However, a low rate of treatment engagement may have contributed to the poorer outcomes in the combined treatment (PT + CT) group, whilst the small sample size may also have reduced the statistical power of the analysis. Nonetheless, the subjective reports of parents indicated improvements in parent and child behaviour as a result of the combined IYBP and small group Dina treatment. Further research is needed to explore the potential of these kinds of programmes in treating children with ADHD symptoms, in both the short and longer term.

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Eur Child Adolesc Psychiatry. 2013;22:S184-S185.

**EFFECT OF COMORBID ATTENTION DEFICIT HYPERACTIVE DISORDER ON THE ONSET OF FIRST DEPRESSIVE EPISODE AND SUICIDE BEHAVIOR IN HUNGARIAN YOUTHS WITH MAJOR DEPRESSIVE DISORDER.**

**Kapornai K, Orosz E, Szabo K, et al.**

**Background and aims:** It is documented, that the comorbid condition of major depressive disorder (MDD) with attention deficit hyperactive disorder (ADHD) leads to more serious impairments and poorer prognosis of MDD. We aimed to explore the effect of ADHD on some specific features (onset, suicidal behavior) of MDD in a sample of depressed Hungarian children. We also investigated the prevalence rates of the different ADHD subtypes in this sample.

**Subjects and methods:** The study sample (N=593) was selected from a larger Hungarian sample of children with MDD in order to evaluate depressed children without ADHD and other externalizing disorder (n=472; 219 boys) and children with comorbid MDD and ADHD (n=121; 101 boys). The mean age of the sample at the assessment was: 11.75 years (sd: 2.02). For the diagnoses, the age of onset of MDD and the suicidal behavior, subjects were assessed by a comprehensive, DSM-IV based semistructured interview (Interview Schedule for Children and Adolescent P, L) as it was administered to the parent and

separately to the youth. To measure the severity of the suicide behavior we created a DSM-IV symptom based suicidal scale (range 0-5).

**Results:** Children in the comorbid group were significantly younger at the first MDD episode (9.61 (plus or minus) 2.25 years) than MDD children (10.78 (plus or minus) 2.25 years;  $p < 0.000$ ). Both girls and boys were also significantly younger in the comorbid group comparing to the girls and boys in the MDD group respectively. The majority of the kids in comorbid group were diagnosed with combined subtype of ADHD ( $n=90$ ). However, there were only 6 patients in the hyperactive/ impulsive type (4.95 %), they were the youngest on average at their first depressive episode (8.15 (plus or minus) 3.03 years). Both girls (2.35 (plus or minus) 1.69) and boys (2.02 (plus or minus) 1.78) showed higher score on the suicidal scale in the comorbid group comparing to the girls (2.14 (plus or minus) 1.92) and boys (1.65 (plus or minus) 1.79) in the MDD group. Still, there was no significant difference between the comorbid and MDD group (2.07 (plus or minus) 1.76 and 1.91 (plus or minus) 1.87 respectively) on the suicidal scale.

**Conclusions:** ADHD not elevated significantly the severity of suicide symptoms in our considerably large depressed sample of Hungarian children. Nevertheless, our results contribute to the literature that is reported the negative effect of ADHD on the onset of major depression in children and adolescent. Moreover, children diagnosed with hyperactive/impulsive subtype of ADHD were the most vulnerable to earlier MDD onset in our sample.

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**THE RISING ADMINISTRATIVE PREVALENCE OF ADHD IN NORDBADEN, GERMANY, AND SPECIALIST INVOLVEMENT IN HEALTH CARE PROVISION.**

**Goetz-Erik T, Schwarz O, Banaschewski T, et al.**

**Objectives:** To determine the prevalence of attention-deficit/hyperactivity disorder (ADHD) in Nordbaden/Germany, to put this data in the context of mental health morbidity, and to assess specialist involvement in health care provision.

**Methods:** The complete claims database of the organization of physicians registered with statutory health insurance [SHI] (Kassenaerztliche Vereinigung, KV) in Nordbaden/Germany was available for analysis, covering the total regional population enrolled in SHI (2.2 million). The dataset for years 2003-2009 was reorganized as to allow patient-centered evaluation.

**Results:** Uncomplicated hyperkinetic disorder (HKD, F90.0) was the number one reason for contacts with health care providers in children (age group 6-12 years, 7.2 %) and adolescents (13-17 years, 3.7 %), reported more than twice as often as the next frequently diagnosed mental health problems, namely various developmental, speech, and adjustment disorders. In preschoolers, speech and developmental problems were diagnosed more frequently than HKD (1.0 %). From 2003 to 2009, the administrative prevalence of ADHD (HKD/F90.0 and hyperkinetic conduct disorder, HKCD/F90.1, combined) increased by 79 %, i.e., from 0.53 % in 2003 to 0.95 % (overall; 6-12 years, 8.0 %; 13-17 years, 4.2 %) in 2009. Notwithstanding lower absolute numbers, ADHD prevalence in adults increased more than fourfold, from 0.04 % (2003) to 0.17 % (2009). Overall, the rate of ADHD patients seen at least once by a CNS specialist (physician) increased from 42.0 % in 2003 to 49.1 % in 2009; the rate of those seen at least twice during the calendar year increased from 26.4 % to 33.2 % (for age group 0-5 years, from 9.1 % to 11.1 %; 6-12 years, from 27.4 % to 33.7 %, 13-17 years, from 30.3 % to 33.1 %, 18+ years, from 26.4 % to 33.2 %). Patients with HKCD were more likely to be seen by CNS specialists than patients with HKD only. Most children (in 2009, 84.4 %) and adolescents (61.0 %) were seen at least once by a pediatrician. The rate of patients seen by psychotherapists remained stable at ~10 %. Within provider groups, health care for patients with ADHD was highly concentrated. Each child and adolescent psychiatrist treated, on average, 231 patients with ADHD.

**Conclusions:** By 2009, ADHD represented the leading mental health related cause of service utilization among children and adolescents in Nordbaden. Despite a moderate increase since 2003, CNS specialist involvement in health care provision for patients with ADHD remains relatively low.

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**THE PREDICTIVE VALIDITY OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE (SDQ) IN PRESCHOOL CHILDREN WITH REGARD TO ADHD DIAGNOSIS IN SCHOOL AGE: A REGISTER BASED STUDY.**

**Rimvall MK, Elberling H, Clemmensen L, et al.**

**Background:** The strengths and difficulties questionnaire (SDQ) is a brief screening instrument for psychopathology in children. This study investigates the predictive validity of the SDQ completed at age 5-6 years with regard to ADHD diagnosed at hospital or treated with central stimulants at age 6-12 years. To our knowledge, this is the first study to investigate screening properties of the SDQ in a longitudinal design with a long follow-up period.

**Methods:** Parents and teachers completed the SDQ for 3501 children of the Copenhagen Child Cohort 2000 (CCC2000) aged 5-6 years. The children were divided into a high-risk and a low-risk group (split at the top10 % percentile) on three subscales (hyperactivity/inattention, conduct, internalizing) and impact score of the SDQ. Data from Danish registers were used to describe mental disorders diagnosed at hospitals and the prescription of central stimulants until age 12 years. These data serve as the outcome measure of this study. Putative early sociodemographic and perinatal risk factors of ADHD will be analyzed, in order to validate the use of register based diagnoses. COX regression analysis was performed and hazard ratios (HR) were calculated and controlled for gender.

**Results:** 2.86 % of all children, who did not have a psychiatric diagnosis in preschool, received an ADHD diagnosis in school age. Approximately three quarters of all ADHD cases were boys. Top10 % scores of impact scores and the hyperactivity/inattention subscale were associated with increased risk of ADHD diagnosis in school age. Risk estimates for hyperactivity/inattention subscale, parents: HR 5.37 (95 % CI: 3.27-8.83), and teachers: HR 3.10 (95 % CI: 1.77-5.42); and for the impact subscale, parents: HR 8.09 (95 % CI: 5.29-12.36), and teachers: HR 10.80 (95 % CI: 6.66-17.49), showed that all subscales significantly predicted ADHD diagnosis in school age. Estimates of sensitivity and positive predictive values (PPV) were low-moderate. Best prediction was found for the impact scores, parents: Sens. 40 % PPV, 15.1 %, teachers: Sens. 62 %, PPV 13.9 % Putative sociodemographic and perinatal risk factors of ADHD were replicated for the ADHD group. Low maternal age, short maternal education, parents not living together at birth, low household income, low birth weight and birth complications were all statistically significantly overrepresented in the ADHD group.

**Conclusion:** High SDQ subscale scores in preschool identify a group of children with increased risk of being diagnosed and/or treated for ADHD in school age.

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**EXECUTIVE FUNCTIONS PROFILE IN CHILDREN AND ADOLESCENTS WITH OR WITHOUT ADHD: BY USING PERFORMANCE-BASED MEASURES AND HOMEWORK AND WORK HABITS (HWH) QUESTIONNAIRE.**

**Yulaf Y, Gumustas F, Imren SG, et al.**

**Objective:** The first purpose of this study was to compare executive functions in children and adolescents with and without attention deficit/hyperactivity disorder (ADHD) using performance-based measures. The second aim was to demonstrate how daily functions of the children and adolescents with ADHD are impaired using the developed questionnaire about homework and work habits (HWH). The final aim was to investigate the relationship between HWH ratings and performance-based measures of executive functions

**Method:** A group of children between the age of 7-17 who met the DSM-IV criteria for the first time for ADHD (n = 60) as the patient group and 7-17 age children and adolescents (n = 60) as the healthy control group were included in this study sample. Parents and teachers of the participations were asked to fill up a form of HWH ratings to evaluate performance based executive functions. Participants completed the Wisconsin Card Sorting, Stroop Color and Word and Trail Making (B) tasks. In addition, HWH questionnaire was given to the children and adolescence and their intelligence level was evaluated with Wechsler Intelligence Scale for Children-Revised.

**Results:** ADHD group participants displayed lower performance in all of the performance-based executive functions measures and lower HWH scores compared to the controls.

**Conclusion:** The low scores in HWH questionnaire were found to be significantly related with performance based executive function tests.

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Eur Child Adolesc Psychiatry. 2013;22:S233.

**EXPERT CONSENSUS FOR THE DIAGNOSIS AND THE TREATMENT OF ADHD IN JAPAN, 3RD STEP: DRUG THERAPY.**

**Makino K.**

**Aims:** The objective of this study was to revise the current guideline for diagnosis and treatment of ADHD in Japan to make more adaptable to present social and clinical situation by investigating the specialists' recommendations and creating expert consensus. This is the 3rd step of all three compositions; diagnosis and assessment, psychosocial therapy, and drug therapy.

**Method:** Eighty-two psychiatrists and pediatricians, who are members of Japanese Association for ADHD, were selected as the experts and asked to answer a series of questions with 513 items of the questionnaire, which is divided into 13 categories: indicators for starting drug therapy in early therapeutic stage, indicators for the introduction of drug therapy after psychosocial therapies become clear not to be effective sufficiently, the recommended duration for the start of drug therapy, the GAF scale for adopting drug therapy, necessary information collected from the patient before drug therapy, necessary information given to the patient before drug therapy, the 1st choice of drug therapy for the ADHD patient without comorbidity, the next strategy of drug therapy for the ADHD patient without comorbidity when 1st medication is not effective sufficiently, the 1st choice of medication for the ADHD patient with anxiety disorders, depression, tic disorders, or ODD/CD, and indicators for the effectiveness of drug therapy. The Delphi method was applied to obtain the consensus.

**Result:** Sixty-seven experts completed two rounds of the questionnaire along Delfi method. Sixty-five of 513 items corresponded to the primary recommendation. For example, the 1st choice of drug therapy for the ADHD patient without comorbidity is, Methylphenidate- OROS or Atomoxetine as a primary recommendation.

**Conclusion:** Though only two drugs, such as Methylphenidate-OROS and Atomoxetine, are officially administered for the ADHD patients, the result of this study offers standards for the drug therapy of ADHD to Japanese clinicians.

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Eur Child Adolesc Psychiatry. 2013;22:S266.

**GENERAL POPULATION KNOWLEDGE (GPK) OF ATTENTION DEFICIT HYPERACTIVITY DISORDER SPANISH SURVEY VS. EXPERTS GROUPS CONSENSUS (EXGC).**

**Soutullo C, Aida JA, Fuentes-Biggi J, et al.**

**Objective:** To compare knowledge among the general Spanish population (GPK) about attention deficit hyperactivity disorder (ADHD) vs. expert groups consensus (ExGC).

**Material and method:** We used a Telephone-administered questionnaire to ask about ADHD (acronym and full name) on a nullspontaneousnull and nullsuggestednull basis (offering hints). Questions were asked related to nullmythsnull, symptoms, treatment, implications and healthcare professionals involved in the disease. Sample was 770 adults (sample precision at national level 3.5) with no personal, familial or professional relationship to ADHD. ExGC: 8 experts (Physicians, nurses, teachers and parents) representing more than 200 ADHD associations. The expert consensus was obtained unanimously (100 % votes).

**Results:** (GPK results/unanimously ExGC). ADHD: Only 4 % of the subjects knew what ADHD means and 50 % thought that the disorder is probably a genetic brain disorder. The general population has not adequate knowledge about ADHD and need more information. All the ExGC knew about ADHD.

**Implications:** Only 13.3 % of the general population considered that ADHD caused academic or learning limitations/ ExGC thought that there is a need for educational system adjustments and more State help to schools and parents. Intervention- Treatment: 39.6 % believed that there was no treatment or healthcare intervention for ADHD/ExGC thought that there is a need for more resources for multimodal therapy and individualization therapy according patients profile (consensus between different ADHD guidelines).

**Conclusions:** The Knowledge among the general population regarding ADHD compared with the experts was much lower about the implications and impairment. There are areas for improvement among the general Spanish population on ADHD knowledge such as the origin of the disease and its management.

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Eur Child Adolesc Psychiatry. 2013;22:S173.

**GUIDED SELF-HELP FOR PARENTS OF CHILDREN WITH ADHD: CONCEPT AND EFFECTIVENESS.**

**Ise E, Kinnen C, Mokros L, et al.**

**Introduction:** Behavioural parent training is an effective treatment for children with attention-deficit/hyperactivity disorder (ADHD) Because practical and psychological obstacles (e.g., travel time, stigma) often prevent families from accessing therapist-led face-toface interventions, there is growing interest in the effects of interventions with minimal therapist contact. The aim of the present study was to evaluate feasibility and effectiveness of a telephone-assisted self-help programme for parents of children with ADHD.

**Method:** This study used a single group, pre-post design. Paediatricians and child psychiatrists informed parents of children with a diagnosis of ADHD about the study. A total of 274 families with children between 6 and 12 years participated. They received eight advice booklets by mail (one booklet every 2 weeks) and 14 weekly telephone consultations (approx. 20 min per contact). The content of the booklets closely follows a self-help book for parents of children with externalizing problem behavior, whose effectiveness as a telephone- assisted self-help intervention has been demonstrated in children with ADHD and/or Oppositional Defiant Behaviour (ODD) and in preschool children with externalizing problem behaviour. 176 families completed the programme (drop-out: N = 101).

**Results and discussion:** Children that participated in the study showed more symptoms of ADHD and had higher SES backgrounds compared with children in an outpatient sample. Children whose parents dropped out of the study differed from those whose parents completed the programme on a number of variables. For example, they were more likely to live in a single-parent household, to have difficulties with peers and to take medication. Intent-to-treat analyses demonstrated significant improvements in parent-reported ADHDrelated child behaviours and significant decreases of behavioural problems (especially with peers). Treatment effects were not influenced by children's medication. These results suggest that telephoneassisted self-help intervention is an effective alternative to more intensive forms of behavioural parent training for children with ADHD.

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**HEALSEEKER: THE EFFECTIVENESS OF A NEWLY DEVELOPED SERIOUS GAME FOR CHILDREN WITH ADHD.**

**Bul K, Franken I, Van der Oord S, et al.**

**Background:** Recent findings demonstrate that educational computer games (Serious Games) can contribute to the multimodal treatment of children with ADHD (Prins et al., 2011). This creates possibilities for the application of Serious Games as an additional intervention to reduce ADHD associated problems and, thereby, improving self management. Children with ADHD often experience difficulties in planning and organisation, time management and maintenance of social relationships. The intervention developed for this study was a Serious Game (called HealSeeker) with a social community that focuses on improving children's skills in the areas of time management, planning and organisation and prosocial behaviour.

**Methods:** From November until March 2012 a pilot study with a randomized pre- post-test design was performed. A total of 42 children with ADHD, aged between 7 and 12 years, participated in this study. More recently an open randomised, controlled, multicenter trial was carried out in the Netherlands and Belgium. A total of 170 children with ADHD, aged between 8 and 12, was randomly assigned to two different conditions: an immediate and a delayed treatment group. Children were asked to play the game three times a week, from week 0-10 for the immediate treatment group and from week 10-20 for the delayed treatment group. Assessments were carried out at baseline and at 10 and 20 weeks.

**Results:** Results of the pilot study yielded promising positive results. Two types of results will be presented: first, the variables that were analysed and are related to children's achievement and behavioural

adaption within the game; secondly, the behavioural questionnaires from parents and teachers and neuropsychological tests administered by the child that were analysed to measure transfer of real-life behaviour change. In addition, preliminary results of the randomized controlled trial will be presented. **Discussion:** Can HealSeeker contribute to the treatment of associated problems of ADHD? Could it complement the current treatment of children with ADHD? These questions will be discussed in the context of the presented results and previous research on HealSeeker.

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**HEALTH UTILITY SCORES IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESPONSE TO STIMULANT TREATMENT.**

**Hodgkins P, Setyawan J, Banaschewski T, et al.**

**Introduction:** The Health Utilities Index-Mark 2 (HUI2) is a generic, preference-based assessment for measuring general health status. The self-administered, proxy-assessed version of HUI2 comprises 15 questions that assess the attributes of sensation, mobility, emotion, cognition, self-care and pain. HUI2 has been used to measure morbidity burdens in patients resulting from a range of disorders but has not previously been applied to patients with attention-deficit/ hyperactivity disorder (ADHD). Further, HUI2 (or similar preference-based instruments) is routinely used to measure treatment benefit (utilities) in economic evaluations for Health Technology Assessment Agencies. The objective of the present study is to quantify the utility gain using HUI2 following treatment with the prodrug stimulant lisdexamfetamine dimesylate (LDX) in children and adolescents with ADHD.

**Methods:** Study SPD489-325 was a 7-week, double-blind, randomized, placebo-controlled study of LDX in patients (6-17 years) with ADHD; osmotic-release oral system methylphenidate (OROS-MPH) was included as a reference treatment. Parents or guardians of patients completed HUI2 assessments at baseline and days 28 and 49. Utility values were estimated for responders and non-responders to therapy (irrespective of treatment) where response was defined as a Clinical Global Impressions-Improvement score of 1 or 2, or reductions in ADHD-Rating Scale-IV score of 25 or 30 %.

**Results:** Of 336 randomized patients in study SPD489-325, 317 were included in the full analysis set (LDX, n=104; placebo, n=106; OROS-MPH, n=107) and 196 patients completed the study. At endpoint and across all treatment groups, mean (SD) HUI2 utility scores were higher for responders than non-responders when response was based on a CGI-I score 1 or 2 (0.896 [0.0990], n=287 vs. 0.838 [0.1421], n=168), a reduction from baseline in ADHD-RS score of (greater-than or equal to)25 % (0.899 [0.0969], n=338 vs. 0.809 [0.1474], n=115) or a reduction from baseline in ADHD-RS score of (greater-than or equal to)30 % (0.902 [0.0938], n=322 vs. 0.814 [0.1477], n=131).

**Conclusions:** This is the first clinical trial to have used HUI2 as an outcome measure for stimulant treatment in patients with ADHD, and provides opportunities to evaluate the relationship between ADHD symptoms and utility scores as well as to perform pharmacoeconomic evaluations using utilities generated within the clinical study. The present results indicate that improvement in the symptoms of ADHD is reflected in higher utility scores. The utility weight estimates obtained in children and adolescents with ADHD using HUI2 were similar to those previously obtained using other health utility instruments (e.g., EQ5D).

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Eur Child Adolesc Psychiatry. 2013;22:S288.

**IDENTIFYING DEMOGRAPHIC AND LANGUAGE PROFILES OF CHILDREN WITH A PRIMARY DIAGNOSIS OF ATTENTION DEFICIT (HYPERACTIVITY) DISORDER.**

**Scullion M, Burns S, Evilly DM, et al.**

**Aims:** As the language and communication presentation of children with ADHD is highly complex, this study aimed to explore the demographic and language profiles of 36 school-aged children with a primary diagnosis of AD(H)D attending a child and adolescent mental health service. A secondary aim was to discern whether the children's language performance on testing bore any relationship to their subtype diagnosis of AD(H)D (i.e. inattentive, hyperactive/impulsive or combined). Profiling these children's skills

may help to elucidate the nature of language functioning in this client group. Demographic variables within this clinic population were also of interest.

**Method:** Thirty-six children aged between 9 and 12 years were assessed on formal language tests in the areas of receptive and expressive language, receptive vocabulary and reading ability. All children were assessed over three 1-hour sessions by a speech-language therapist (SLT) and an SLT student. The profiles of all 36 children were analysed to ascertain (i) demographic variables (ii) whether an overall pattern of language functioning could be identified across the group as a whole and (iii) whether subtype presentation had any bearing on language performance on testing.

**Results:** Demographic variables of this cohort included a predominance of males, a predominance of the combined subtype of AD(H)D and the majority having a secondary clinical diagnosis, including for example Autistic Spectrum Disorder. Analysis revealed some common trends in the overall performance of the group, but a general AD(H)D-specific language profile was not easily discernable. Over 70 % of the sample cohort had language difficulties as assessed on a popular standardized language assessment, with half of these having both receptive and expressive language impairment. A third of the sample showed some levels of reading impairment, while only a fifth of the cohort demonstrated vocabulary comprehension difficulties on testing. There was some correlation between performance on receptive language assessment and performance on a vocabulary comprehension test. Particular AD(H)D subtype performances were not obvious, yet there were some individual profiles that prompted more in-depth consideration of a child's overall presentation, and as related to a diagnosis of AD(H)D in general.

**Discussion and conclusions:** The complexity of the language profiles of children with a primary diagnosis of AD(H)D is played out in our data, with heterogeneity of this clinical population an obvious feature. Male dominance and secondary diagnoses featured heavily among the cohort, the latter confounding any generalisations of AD(H)D-specific language profiles to be made. However, there was enough evidence of patterns of performance to allow us to clinically plan more carefully in designing language assessments and interventions for this client group, within the context of a multidisciplinary team. Implications for further research and practice in this area are discussed.

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Eur Child Adolesc Psychiatry. 2013;22:S175.

#### **INTERDISCIPLINARY COOPERATION IN DECENTRALISED OUTPATIENT CARE STRUCTURES.**

##### **Holthusen I.**

Since April 2009, the contract for quality ensured care for ADHD patients is being implemented with 78 health insurance funds in the region of Baden-Wurtemberg (Germany). Patients have got the opportunity to participate in this special care programme for a maximum of 3 years. Currently, 2,740 patients are registered for participation. A total number of 203 physicians and psychotherapists take part in the programme, amongst them 136 paediatricians, 35 child and adolescent psychiatrists and psychotherapists, 28 child and adolescent psychotherapists and 13 psychotherapists. The participating physicians and psychotherapists have formed 45 interdisciplinary ADHD teams. In order to invigorate cooperation between different specialities participating physicians and psychotherapists join interdisciplinary ADHD teams. A team consists of at least one specialist physician for paediatrics and adolescent medicine, one specialist physician for child and adolescent psychiatry and psychotherapy and one child and adolescent psychotherapist. During the course of the treatment, 558 patients have been unsubscribed because their treatment was terminated or the 3 year period of the programme was completed. 69 patients have so far been unsubscribed due to a negative diagnosis. For the whole course of the care programme, routine data is being collected for purposes of quality insurance and accounting. The first care report was presented 2 years after the initiation of the programme in Mai 2011. It contains structural data as well as sample data on pharmacotherapy within the care programme. The care report showed that ADHD teams had formed in nearly all districts of Baden-Wurtemberg. Care quality was rated positively on the basis of the first analyses. The sample on pharmacotherapy showed that only 26 % (95 %-CI 20-32 %) of patients who had joined the contract received a medicinal therapy.

Eur Child Adolesc Psychiatry. 2013;22:S241.

**THE OVERLAP BETWEEN AUTISM SPECTRUM DISORDERS AND ADHD: ASSESSMENT OF DIAGNOSTIC TOOLS.**

**Mihailescu I, Rad F, Dobrescu I.**

**Background:** Many studies indicate that symptomatology of Attention deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) can co-occur. Although the evidence shows high rates of this phenomenon, both DSM IV-TR and ICD 10 preclude the diagnosis of ADHD in the presence of a pervasive developmental disorder. Until the appearance of DSM V and its change in the relationship between ASD and ADHD, the main effect of the exclusion criteria is a lack of diagnostic tools with implications for the clinical evaluation of this comorbidity.

**Objectives:** The main purpose of the present study was to explore the effectiveness of autism diagnostic observation schedule-generic (ADOS-G) and ADHD-RS (ADHD-Rating Scale) when these disorders co-exist. Using the instruments simultaneously, we aimed to identify the percentage of subjects with significant scores for both disorders and to establish the relationship between ADHD-RS scores and ADOS-G results. Method: We analyzed the ADOS-G (Module 1) and ADHD-RS scores in a clinical sample (n = 100) aged 2-7 years. All of the subjects presented a heterogeneous symptomatology, showing characteristics of both disorders.

**Results:** 86 % of subjects exceeded the cut-off score for an ASD (autism = 64 %, PDD-NOS = 22 %), 55 % met the criteria for ADHD, scoring above 93rd percentile (ADHD-C = 45 %, ADHD-In = 8 %, ADHD-HI = 2 %). Linking the results from both diagnostic instruments we have obtained the following: 52 % had significant scores for both disorders, there was a weak positive correlation between Social-Communication Total score and ADHD-RS Total score ( $r = 0.225$ ,  $p < 0.03$ ) with the same pattern between social/communication score and inattention score. There were statistically significant differences between ASD groups (Autism/PDDNOS) and nonASD group for ADHD-RS Total scores (pt test  $< 0.001$ ) but no difference between Autism and PDD-NOS group. Unexpectedly, there was a significant difference between ADHD-In group and ADHD-C/nonADHD group for their ADOS results ( $p_{MWW} < 0.01$ ), with greater ratings for the first one.

**Conclusion:** The overall findings suggested that using the ADOS-G and ADHD-RS together, could be useful for a proper assessment when symptoms of ASD and ADHD are present. Between ADOS-G results and ADHD-RS scores exists a weak positive correlation. A possible explanation for the unexpected high ADOS-G results in ADHD-In group could be a misinterpretation of the poor eye contact as an impaired attention, but future research is required.

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Eur Child Adolesc Psychiatry. 2013;22:S307-S308.

**INTELLIGENCE AND ADHD: DIAGNOSTICAL IMPLICATIONS IN CLINICAL PRACTISE.**

**Wunsch K, Haessler F, Reis O.**

The prevailing report by BARMER health insurance Germany reports, that roughly 20 % of the insured boys born in 2000 are diagnosed with nullADHDnull. In comparison with the presumed prevalence rates (e.g. Polanczyk et al. 2007) this displays a significant increase which doesn't seem to be evidence-based. We rather see a waxing tendency to sublimate different childish behaviours under this syndrome and thereby loose the proper specifics of it. This consequently challenges the efficiency of therapeutic intervention. The need for specific diagnostics becomes clear when faced with the challenge of singling this syndrome out of the pool of nullcollective diagnosesnull. But mostly the used questionnaires only grasp selected syndromes with subjective incidence and degree of severity and without the possibility to objectify. Psychometric measurements of attention- parameters display a vague link to attitude monitoring and laying down a diagnosis. In our study we searched for variables which offer a better psychometric base of an ADHD- diagnosis, with special focus to individual intellectual skills and situational factors as influence parameters.

**Method:** In our sample (n = 101, age 6-10) a paper-pencil-test was done in each case in a single and a group situation. The length of 21 min and the division into high or low situational diversionary potential seemed adequate to increase the ecological validity of the measurement by simulating school situation. Included were girls and boys with ADHD-diagnosis, compared by a control group. Effects of chronological single and group test order were controlled. The intellectual ability was tested by standard test battery. Test

parameters were measured and compared both intraindividual and in group using single compare tests (t-test) and multivariate testing procedure with attention- parameters as dependent variable.

**Results:** In contrast with middle- and low gifted children the classical attention- parameters of ADHD-children with good or higher intellectual skills normally reach the standard range (percent range between 25 and 75). - ADHD-children with good or higher intellectual skills show specific different concentration profile over time. - For ADHD-children with good or higher intellectual skills the difference between group test and single test seems to be more influenced by situational factors, high potential of diversion decreases the test scores significantly. - Results of multivariate interaction analyses show, that children with ADHD do significantly different react on situational factors, depending by intelligence, ADHD characteristic an interaction of both.

**Conclusion:** The relation of ADHD and attentional performance is moderated by personal (intelligence) and situative (single vs. group, potential of diversion). An exact psychometric ADHD-diagnostic needs different standard test situation and the inclusion if personal intelligence.

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Eur Child Adolesc Psychiatry. 2013;22:S283.

**RELATIONSHIP BETWEEN THE ANXIETY LEVELS AND THE TYPES OF ADHD (COMBINED VS. INATTENTIVE).**

**Alda J, Ferreira E, Garcia C, et al.**

**Introduction:** ADHD shows a profound comorbidity with externalizing and internalizing disorders. Different studies confirm a comorbidity of 20 and 25 % with anxiety disorders.

**Hypothesis:** There is a relationship between the type of ADHD (combined vsvs. inattentive) and the level of anxiety in children. Combined ADHD diagnosis show higher anxiety level than inattentive ADHD.

**Objective:** Specify the percentage of patientswith ADHD and acomorbid anxiety disorder. Analyze the distribution between primary and secondary school. Value the interaction between the subtype of ADHD and the anxiety level.

**Materials and methods:** Descriptive and retrospective study of naive patients from the ADHD Unit of Sant Joan de Deu Hospital who have been attended between August of 2009 and December of 2012. The inclusion criteria are the recent ADHD diagnosis, has never received pharmacological treatment and the application of STAIC Inventory, establishing the age range from 8 to 16. The relationship between anxiety disorder diagnosis and the STAIC scoring is examined. The correlation between ADHD type and STAIC-E/R is valued.

**Results:** Analyzing the sample of 89 patients, 73 % (n=65) are boys and 61.8 % have an Inattentive ADHD diagnosis (n=55). The 30.3 % (n=27) of the patients show a comorbid anxiety disorder. According to the educational level, the 42.3 % (n=22) of primary students and the 13.5 % (n=5) of the secondary students show clinical level of anxiety, there is a significant difference (Chi=8.48, p=0.004) between primary and secondary school. No significant differences were found between the anxiety level measured by STAIC-S/T and the ADHD subtype. There is a correlation between the clinical impression of anxiety and the detection through STAIC Inventory (STAIC-T: r=0.404, p=0.01 and STAIC-S: r=0.292, p=0.01).

**Conclusions:** 1 of 3 children with naive ADHD diagnosis show high anxiety levels, especially for primary school students with a significant difference with secondary school. The STAIC Inventory is a good tool for identifying anxiety levels in ADHD patients. There is no relationship in our sample between the presence of anxiety and the ADHD subtype.

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Eur Child Adolesc Psychiatry. 2013;22:S201-S202.

**REVIEW OF CLINICAL GUIDELINES FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER ACROSS THE LIFESPAN AND THEIR APPLICATION TO AN IRISH CONTEXT.**

**Kavanagh G, Hughes G, McNicholas F, et al.**

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder with international prevalence rates estimated to be 5 %. It is currently the most common disorder treated in child and adolescent mental health services in Ireland. There is a scarcity of data on the prevalence rates of Irish adults with ADHD. Recent studies have indicated that up to 65 % of children and adolescents continue to

exhibit symptoms into adulthood. There have been a number of guidelines produced to aid clinicians in the diagnosis and treatment of ADHD however there are no guidelines available specifically for the Irish population. The objective of this paper is to review the available clinical guidelines for ADHD in children and adults across North America, Canada, Europe and the UK and to adapt these to an Irish context in order to propose a standardised pathway for the assessment, diagnosis and treatment of ADHD across the lifespan. This paper outlines a proposed guideline for Irish clinicians based upon current guidelines and evidence base for the assessment and treatment of ADHD. It will discuss the common co-morbid conditions and recommended treatment options both pharmacological and psychosocial. Guidance on the long term follow up and community supports available in Ireland are included. This paper concludes that formalised guidelines should be devised and implemented to standardise the care of patients with ADHD. Adult ADHD is a particular area that requires further attention with a need for increased recognition and more comprehensive transitions between child and adult psychiatry services.

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Eur Child Adolesc Psychiatry. 2013;22:S258.

**RELATIONSHIP BETWEEN EARLY CHILDHOOD TRAUMA AND ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Martsenkovskiy D, Martsenkovsky I.**

**Aims:** Post traumatic stress disorder (PTSD) and attention deficit hyperactivity disorder (ADHD) at children are becoming an epidemic in our society. Early childhood trauma can have negative, life-long repercussions for children's developing brains if it is not treated properly. Many children experience trauma from emotional, physical or sexual abuse. Others are involved in traumatic events such as natural disasters, and car accidents among other things. Child abuse is generally chronic and usually the effects of this type of trauma are worse and longer lasting than from one time traumatic events. Kids who had been traumatized previously 16 years old are more likely to have attention problems, less frequently symptoms of depression and anxiety. The aim of this trial is to examine how PTSD and ADHD diagnosis are related. More specifically attempt was made to prove that a trauma is a causal factor in a significant number of ADHD cases.

**Methods:** Social services of Kyiv have randomized 120 adolescents in age of 14-17 years, who experienced multiple early childhood traumas. All teenagers had severe disorders of social adaptation, had not attended school, had problems with the police, and had been brought up in socially unsuccessful families. Randomization criteria meet the diagnostic criteria for DSM-IV for PTSD and ADHD. To assess symptoms associated with trauma were used structured Interview- clinician administered PTSD Scale (CAPS) and the self-report Questionnaires-Los Angeles symptom checklist (LASC). ADHD symptoms were assessed using the Conner's rating scales (CRS) to patients, parents and teachers.

**Results:** All randomized children have not suffer from full-blown post traumatic stress disorder (PTSD) as a result of a traumatic experience, they may have attributable symptoms that may cause a flight or flight response of fear in association with movements, noises, or other stimuli-but which may appear to resemble ADD/ ADHD symptoms such as distractibility, inattention, aggression, increased activity, or dissociate behavior. We could not extricate experiences of chronic adverse situations during childhood, also referred to as complex trauma, from ADHD symptomatology. Randomized adolescents experience higher incidences of chronic stress, termed here as environmental trauma, and disruptions in attachment relationships.

**Conclusion:** It is not yet clear is trauma actually a causal factor in ADHD or are post traumatic symptoms merely mimic ADHD symptoms. Two hypotheses may help to explain this relationship: children with ADHD are at higher risk for trauma due to their impulsivity, dangerous behaviors, and parents who may have a genetic predisposition for impairment of their own impulse control; and hyper arousal induced by severe trauma and manifested by hyper vigilance and poor concentration may impair attention to create an ADHD-like syndrome. Either way it seems safe to say that trauma has played a major role in a significant number of ADHD diagnoses



Eur Child Adolesc Psychiatry. 2013;22:S155.

**SEX CHROMOSOME ANOMALIES: 2 CASES WHICH SUGGEST THAT SEX CHROMOSOMES MAY CARRY RISK GENES FOR ADHD AND FOR AUTISM.**

**Mulligan A.**

A case of autism in a girl who was found to have the karyotype 47, XXX is described. A family pedigree shows that a half brother has Asperger's syndrome. It is possible that this family has an X chromosome with risk genes for autism, with more symptoms in the girl with triploidy of the X chromosome than in the boy with one X chromosome. The possibility of an association between triploidy of the X chromosome and autism is proposed. A case of a boy with ADHD who has a major de-novo Y chromosome abnormality consisting of a deletion of the long arm and duplication of the short arm is presented. The possibility that the Y chromosomal abnormality is causing the ADHD syndrome in this boy is discussed. Evidence to support the theory that the sex chromosomes may contain risk genes for ADHD are that (a) ADHD is more common in boys than in girls, (b) the transmission of some genes associated with ADHD may occur preferentially from fathers rather than from mothers, and (c) ADHD is more common in children with XYY syndrome and Turner's syndrome than in other children.

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Eur Child Adolesc Psychiatry. 2013;22:S292.

**SIDE EFFECTS OF PSYCHOPHARMACOLOGY TREATMENT ON ADHD NAIVE PATIENTS.**

**Ferreira E, Alda J, Mesa L, et al.**

**Background:** Attention deficit hyperactivity disorder (ADHD) could have a well-made response to psychopharmacology treatment. Improving the main symptoms of ADHD as attention deficit and hyperactive impulsive behaviour.

**Objective:** Evaluate the most common side effects on patients with ADHD recently diagnosed who start a psychopharmacology treatment for the first time.

**Methods:** Retrospective and descriptive research by reviewing medical records. It is obtained from patients of ADHD Unit of Sant Joan de Deu Hospital during a period of time from January 2009 to December 2011. Representative test amount the following inclusion/ exclusion criteria: patients aged between 5 and 17 years old, recently diagnosed and without previous psychopharmacology treatment (Naive patients). Constants (weight, height, blood pressure, heart rate) should be analysed before starting psychopharmacology treatment and 1 month later. These constants are always measured by the same person from the nurse's department.

**Results:** Data are obtained from representative sample amount of 111 patients, 74.8 % male (n = 83). The average age is 9.21 and DE: 2.65. Weight average is 36.42 (plus or minus) 13.99 kilos (ranging from 17 to 82). Basal height is 1.23 (plus or minus) 0.43 metres, basal BMI is 26.53 (plus or minus) 9.57, heart rate average is 77.5 (plus or minus) 14.1 bpm., SBP blood pressure average is 101.91 (plus or minus) 12.1 mmHg. and DBP blood pressure average is 63.04 (plus or minus) 9.1. Also, 60.6 % of patients receive OROS MPH treatment whereas 29.8 % receive Atomoxetine medication. There is no difference about weight, height, blood pressure (SBP and DBP) and heart rate. Nevertheless, it's observed higher BMI decrease in OROS MPH patients than Atomoxetine. No significant differences were found in others treatments.

**Conclusions:** The results obtained do not demonstrate significant differences on weight, height, heart rate, blood pressure (SBP and DBP) and BMI after 1 month of psychopharmacology treatment. Additionally, psychopharmacology treatments are secure and also, side effects are so improbable.

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Eur Child Adolesc Psychiatry. 2013;22:S156.

**INTRIGUING CLINICAL CASES.**

**McNicholas F.**

This symposium hosts a collection of clinical cases with various diagnostic and management challenges. It hopes to allow participants to refresh their critical diagnostic and therapeutic skills by an in-depth presentation of 4 complex clinical cases, each presenting different diagnostic, and therapeutic approaches.

The discussant will bring an American over view to the presentations thus allowing the participants to consider how their own conceptualisation and treatment plan reflects those of the presenters and discussants from different countries. Presenters: 1. Dr. Therese Thornton, Dublin will introduce the concept of the diagnosis of Pervasive Refusal Syndrome and present a clinical case of an 11 year old girl with severe and protracted symptoms spanning a number of domains. She will give a parent's perspective on the disorder and its management. 2. Dr. Aisling Mulligan, will present two separate cases, each with sex chromosome anomalies and review the evidence to support the theory that the sex chromosomes may contain risk genes for ADHD and autism. 3. Dr. Yulia Zyranova, will present a case study of a 14-year old boy with challenging behaviour in the context of Conduct Disorder and a diagnosis of Early-onset psychosis. She will consider the effectiveness of an individualised, neuro-behavioural approach in a specialised residential setting. 4. Dr. Vincent Guinchat, will present on causes for severe challenging behaviours among hospitalized adolescents with autism. 5. Dr. Elaine Purcell, will provide an overview to the sleep disorders common in all paediatric populations including psychiatric patients; with particular focus on Obstructive Sleep Apnoea, Narcolepsy, Body-Clock Issues and behavioral problems. 6. Dr. David McNamara will present. 1. Discussant. Dr. Dhirk Dhosce, US.

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Eur Child Adolesc Psychiatry. 2013;22:S220-S221.

**SIX YEARS FOLLOW UP OF CHILDREN WITH ATENTION DEFICIT HYPERACTIVITY DISORDER TREATED WITH SUSTAINED RELEASE FORM OF METHYLPHENIDATE.**

**Lakic A, Kesic A.**

**Introduction:** Attentiondeficit hyperactivity disorder (ADHD) is a developmental disorder whose basic events (hyperactivity, impulsiveness and attention deficit) greatly disrupt daily functioning of these children. The recommended access regarding children with ADHD is the combination of two therapeutic modalities: medication (sympathomimetics-psychostimulants and atomoxetine) and behavioral treatment. The therapy of first choice is methylphenidate in sustained release form (MPH-SR).

**Objective:** Evaluation of 6 years follow up the children with ADHD trated with MPH-SR for a more comprehensive assessment of the applied therapy effects.

**Subjects and Methods:** We evaluated 68 children with ADHD(aged 7-15 years). The diagnosis of ADHD was based on DSM TR IV criteria and parental/teachers assessment using the SNAP IV. Patients were treated with 18-36 mg pro die MPH-SR(dose was individualized) All children currently or recently treated were includes Laboratory and paediatric check up were conducted. Neurological check up was conducted of all patients at the time of diagnosis and the time of starting the therapy. Follow up study. Were monitored:side effects, the improvement in clinical symptoms and parental satisfaction All results were statistically analyzed.

**Results:** One patient had serious adverse event expressed as a strong depressive symptoms. In all patient during entire duration of therapy was present a loss of appetite and moderate loss of body weight Three patients presented tics and nervousness as adverse effects Teachers have seen more improvement in the area of reducing hyperactivity while parents, regardless of academic success of children watched as a larger benefit.

**Conclusion:** Side effects of MPH-SR are generally mild. All of the children with ADHD trated with MPH-SR was a statistically significant improvement. Improving school success of children was a protector for better compliance with parent.

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**THE IMPACT OF COORDINATED ADHD TREATMENT IN GERMANY. RESULTS OF AN ACCOMPANYING STUDY.**

**John K, Lange M, Becker K, et al.**

**Introduction:** Children and adolescents with ADHD make up an increasingly large share of child and adolescent psychiatric patients in Germany. To improve and ensure quality of treatment, a contract for quality ensured care has been implemented in the region of Baden- Wuerttemberg (Germany). One of its

goals is to ensure well coordinated, high quality standardized diagnostics and treatment. The aim of this study is to explore if and how the contract for quality ensured care improves outpatient child and adolescent ADHD care.

**Methods:** A naturalistic longitudinal non-randomized intervention study compared two groups (quality ensured care vs. treatment as usual). 25 outpatient clinicians (11 paediatricians, 9 child and adolescent psychiatrists, 5 child and adolescent psychotherapists) recruited 228 patients (118 quality ensured care, 110 treatment as usual). 3 measurements were conducted: Baseline, 3- and 12-months- follow-up. Data were collected by telephone and questionnaire and included standardized measures of quality of life (ILC), strengths and difficulties (SDQ), ADHD symptoms (FBB-ADHD), treatment satisfaction (FBB). Interviews with clinicians about diagnosis and treatment as well as contract implementation and its impact on their practice supplemented patients' data. Summary scores were computed to analyze quality of process and results.

**Results:** The 228 participants (78% male) were between 4 and 17 years of age ( $M=8.7$ ,  $Sd=2.5$ ). 98% were diagnosed with a psychiatric disorder, for 87% the ADHD diagnosis was confirmed 92 % started psychiatric treatment/psychotherapy. There were 157 sets of complete longitudinal data. Patients' symptoms showed significant and clinically relevant improvement in both groups (e.g. SDQ Total Problem score  $d_{baseline-12-month\ as\ follow-up}=0.57/0.56$ ). The summary scores for quality of process and results did not differ significantly between groups. However there were indicators of improved patient satisfaction and more multimodal treatment. Service providers stressed improvements with regards to diagnostics and treatment, multidisciplinary cooperation and financial compensation.

**Discussion:** While the contract for quality ensured care has improved clinicians' multidisciplinary cooperation and compensation, there is no statistical evidence for effects on quality of process and results. Qualitative data however indicated higher patient satisfaction under contract conditions. It is postulated that group differences were overcast by differences in contract implementation and clinicians' ethical aspiration of optimal treatment. Further analysis is required.

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Eur Child Adolesc Psychiatry. 2013;22:S231-S232.

**LONG-TERM ACADEMIC OUTCOMES OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND EFFECTS OF TREATMENT.**

**Hodgkins P, Kahle J, Kewley G, et al.**

**Background:** ADHD is recognized as a serious medical condition of brain dysfunction with long-term sequelae. Although commonly diagnosed in childhood, ADHD may persist into adolescence and adulthood and adversely affect functional outcomes. Academic difficulties are often the reason for a child's initial referral for clinical evaluation and can be a key contributor to future functional outcomes.

**Objective:** Quantify how ADHD affects long-term academic outcomes (both learning information/skills and success within the school environment) and determine if treatment provides benefit.

**Method:** A systematic literature review identified 145 studies with a variety of experimental designs addressing the effects of ADHD on long-term ((greater-than or equal to)2 years) academic outcomes. Academic outcomes were differentiated as either indicators of academic achievement (information and skills learned, measured primarily through standardized achievement scores) or academic performance (success within the school construct such as grades, years of schooling, grade retention, high school graduation, college enrollment). Outcomes were classified as more favourable in one group vs. the other, based on statistical significance reported in each study.

**Results:** In studies comparing untreated individuals with ADHD with non-ADHD controls, 83 % of academic achievement outcomes and 76% of academic performance outcomes were poorer with untreated ADHD. Studies showed both types of outcomes improved with treatment, proportionally more so for achievement outcomes (83%) than performance outcomes (42%). Multimodal treatment was associated with improvement for a higher proportion of outcomes than pharmacological or non-pharmacological treatment alone. Exclusion of low IQ or controlling for IQ did not substantially alter the proportion of outcomes that was poorer with untreated ADHD compared with non-ADHD controls, but did increase the proportion of studies demonstrating improvement associated with treatment. Grade retention policy can vary by country, but no differences were found among world regions in the proportion of poorer grade retention

outcomes for individuals with ADHD. Furthermore, the proportion of studies reporting improvement with treatment was similar between the youngest (<6 years) and oldest ((greater-than or equal to)10 years) ages-of- treatment-initiation groups.

**Conclusions:** Long-term academic outcomes are adversely affected by ADHD, and improvement in both academic performance and achievement measures is associated with treatment, proportionally most often with multimodal treatment.

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Eur Child Adolesc Psychiatry. 2013;22:S100-S101.

**THE MEDICAL COST ATTRIBUTABLE TO ADHD IN NORDBADEN/GERMANY: A STUDY FROM A HEALTH CARE PAYER'S PERSPECTIVE BASED ON CLAIMS DATA.**

**Schlender M, Schwarz O, Goetz-Erik T, et al.**

**Objectives:** To assess the direct medical costs attributable to a diagnosis of attention-deficit/hyperactivity disorder (ADHD), comparing patients to controls in Nordbaden/Germany.

**Methods:** The patient-centered Nordbaden database for years 2003 to 2009, integrating data from Kassenärztliche Vereinigung Baden- Württemberg (KVBaWue, the organization of physicians registered with statutory health insurance, nullSHInull) and a major SHI association (vdek) as to allow patient-centered evaluation, was used to determine health resource utilization and direct medical cost covered by SHI. Patients with a diagnosis of ADHD were compared to a control population matched by age, gender, and type of statutory health insurance (nullSHInull). Here we report on data for years 2006-2009, as nonpharmacological therapy-related cost data were not fully available for earlier years.

**Results:** Average total cost per ADHD patient increased from (euro)897 in 2006 to (euro)1,006 in 2009 (controls, (euro)261 in 2006 and (euro)337 in 2009). Average annual cost per patient correlated positively with age, and female patients were generally more costly than males (in total as well as regarding costs attributable to ADHD). Increasing severity and comorbidity were also associated with higher costs per patient. Physician services constituted the major cost component (on average, overall, (euro)653 per case in 2009), followed by pharmacological therapy ((euro)330 in 2009). Detailed quantitative data will be provided.

**Conclusions:** The average excess cost (from the perspective of German SHI) per ADHD patient (over all age groups and irrespective of gender, compared to matched controls) was (euro)669 per year in 2009. Although any extrapolation from the regional to the national level should be treated with caution, this data from Nordbaden suggests an approximate dimension of annual outpatient treatment costs attributable to ADHD in the magnitude of (roughly) (euro)450 million (for year 2009), from the perspective of Statutory Health Insurance (SHI).

**Discussion:** This compares to total annual expenditures for services (nullLeistungsausgabennull) of the German SHI system of (euro)160 billion in 2009. Of note, the figure (calculated bottom-up using actual microdata, not estimates) is substantially lower than some recently published projections. This discrepancy clearly warrants further investigation, including data sources, their reliability, representativeness, and method of combination, broader research methodology, as well as an examination of vested interests potentially influencing design and presentation of studies.

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Eur Child Adolesc Psychiatry. 2013;22:S302-S303.

**RISK ASSESSMENT USING HEART RATE VARIABILITY DUE TO METHYLPHENIDATE TREATMENT IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Arman AR, Yilmaz S, Carkaxhiu G, et al.**

**Introduction:** Attention deficit hyperactivity disorder (ADHD) is a common neuropsychiatric disorder of the childhood mostly treated with central nervous system stimulants such as methylphenidate (MPH). Risk of sudden cardiac death and serious arrhythmia due to MPH is controversial. The aim of our study was to investigate the effects of MPH treatment on autonomic functions of children by means of heart rate variability (HRV) analysis.

**Method:** Study group included 15 children diagnosed with ADHD (4 girls and 11 boys) between the ages of 7-13 years (mean, SD=9.08 (plus or minus) 1.79 years). The study group consisted of eight combined type, and seven predominantly inattentive type among subgroups of ADHD. Mean scores of the clinical global assessment scale was 68.3 (plus or minus) 8.79 and the mean clinical global impairment- ADHD score was 4.46 (plus or minus) 0.91 in the study group. All children were evaluated by a child and adolescent psychiatrist and a pediatric cardiologist. Cardiac and neurologic diseases affecting the autonomic nervous system were excluded. In addition to a detailed history and physical examination, 12-lead-surface electrocardiogram and 24-hour-ambulatory Holter monitorization were performed prior to MPH treatment. Same evaluations were repeated while the patients were receiving MPH between the dosages of 0.25-1 mg/kg/day (mean (plus or minus) SD=0.6 (plus or minus) 0.21) at the second to fourth week of treatment. HRV parameters including time (SDNN, SDANN, SDNN-i, r-MSSD, pNN50) and frequency domain (LF, HF, LF/HF) indices were calculated and compared in pre and post treatment Holter recordings.

**Results:** None of the patients showed significant rhythm abnormalities during pre, or post treatment Holter recordings. Average heart rate and maximum heart rate were significantly increased after MPH treatment (average HR 88 (plus or minus) 7.3 vs. 92 (plus or minus) 7.1 bpm,  $p=0.022$ ; maximum HR 168.4 (plus or minus) 15.5 vs. 180.5 (plus or minus) 15.0 bpm,  $p=0.031$ ). SDANN values were significantly higher under treatment with MPH (121 (plus or minus) 25.4 vs. 142 (plus or minus) 47 ms.,  $p=0.025$ ). pNN50 values were significantly lower in overall 24 h recordings and especially at the daytime (8 am-10 pm) when children were taking MPH pills (19.7 (plus or minus) 9.9 vs. 14.7 (plus or minus) 7.6,  $p=0.008$ ; 16.6 (plus or minus) 16.9 vs. 8.5 (plus or minus) 4.8  $p=0.011$ , respectively). Statistically significant difference was not found in terms of other HRV parameters.

**Conclusion:** Our study showed a significantly increased heart rate and decreased HRV due to MPH treatment in children with ADHD, suggesting an increased sympathetic tone especially at the daytime. Risk of sudden cardiac death and serious arrhythmia has not been demonstrated.

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Eur Child Adolesc Psychiatry. 2013;22:S200.

**SURVEY EXAMINING THE VIEWS OF ADULT PSYCHIATRY CONSULTANTS AND SENIOR REGISTRARS REGARDING ADHD.**

**Beirne M, McNamara N, O'Keeffe G, et al.**

**Objectives:** Attention Deficit Hyperactivity Disorder (ADHD) has been demonstrated to continue to cause difficulties for patients beyond childhood, although traditionally services for diagnosis, assessment and treatment of ADHD in adulthood have been lacking. The objectives are to explore the views of Adult Psychiatry regarding ADHD prevalence, knowledge base, the most suitable service and the treatment options available and pursued in Ireland.

**Methods:** A questionnaire was constructed based on the stated aims of the study, and was either posted, emailed or handed to 400 Consultants and Senior Registrars throughout the Republic of Ireland between February and December 2011. A total of 92 questionnaires were returned (23 %); one was excluded from analysis due to insufficient information entered by the respondent.

**Results:** Seventy-five per cent of respondents correctly estimated the prevalence rates of Adult ADHD to be under 3 %, but stated it is currently under-diagnosed. (77 %) Seventy-four percent indicated that Adult ADHD should be a diagnostic category in DSM V. Sixty-six percent of respondents were willing to accept referrals of childhood ADHD for ongoing care and a similar number for new ADHD assessments (61 %). Less than half (42 %) surveyed had actually diagnosed ADHD and of these only 33 % felt confident in managing ADHD.

**Conclusions:** Whilst there is a general willingness to offer services for new and existing ADHD cases and a recognition that Adult ADHD is valid and under-diagnosed, the low confidence levels when treating ADHD and the perception of under-diagnosis suggests a role for further training and links between child and adult services.

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Eur Child Adolesc Psychiatry. 2013;22:S246.

**POSSIBLE ASSOCIATION OF THE ALPHA-2A-ADRENERGIC RECEPTOR DRAL POLYMORPHISM WITH METHYLPHENIDATE RESPONSE IN KOREAN CHILDREN WITH ADHD, COMBINED SUBTYPE.**

**Bae JH, Park S, Kim JW, et al.**

**Introduction:** Given the shortage of pharmacogenetic studies on treatment response according to subtype of attention-deficit hyperactivity disorder (ADHD), we investigated the associations between the MspI and Dral polymorphisms of the alpha-2A-adrenergic receptor gene (ADRA2A) and treatment response to methylphenidate according to subtype of ADHD.

**Methods:** We enrolled 115 medication-naive children with ADHD into a open label 8-week trial of methylphenidate. The participants were genotyped and evaluated using the clinical global impression (CGI), ADHD rating scale, and continuous performance test (CPT) pre- and post-treatment.

**Results:** After 8 weeks of methylphenidate treatment, there was no significant association between the MspI or Dral genotypes and the relative frequency of CGI-I 1 or 2 status posttreatment among all subtypes combined. However, among the children with ADHD-C, a significant association was found between the relative frequency of CGI-I 1 or 2 status post-treatment and homozygosity of the C-allele of the ADRA2A Dral polymorphism (OR = 4.45, p = 0.045) after controlling for baseline ARS score, age, gender, and mean dose (mg/kg) of methylphenidate. Among the children with ADHD-I, there was no significant association between the MspI or Dral genotypes and the relative frequency of CGI-I 1 or 2 status posttreatment.

**Discussion:** This study provides evidence for the possible role for the Dral polymorphism of the ADRA2A in the treatment response to MPH in ADHD-C. Dysfunction of alpha-2-adrenergic receptor system, particularly in the frontal region, may cause impairments in response inhibition, which is proposed to be the core deficit in ADHD and to be uniquely linked to ADHD-C. The potential functional significance of the Dral polymorphism is not well understood, but our findings suggest that this polymorphism may affect the expression and function of ADRA2A, thus prevent the function of MPH as improving inhibition deficit, particularly in the subjects with ADHD-C. Further studies should continue to elucidate treatment response according to genetic polymorphisms in homogeneous sample, such as same subtype of ADHD.

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Eur Child Adolesc Psychiatry. 2013;22:S114.

**ESCAP GUIDELINES WORKSHOP ADHD.**

**Banaschewski T, Hohmann S, Taylor E, et al.**

ADHD, a psychiatric disorder characterized by a pervasive pattern of severe inattention, hyperactivity, and/or impulsivity associated with substantial impairment in various functional domains is amongst the most common mental disorders. The clinical presentation is highly variable and may differ according to age, stage of development and the presence of comorbidity. Careful assessment is needed. Evidence based treatment to manage the core symptoms focusses on psychoeducational, behavioural and medication treatments. For many children comorbidity might require additional interventions, which may differ from country to country, depending on therapeutic options. This symposium will centre on two case presentations. Each presenter, an expert in ADHD diagnosis and treatment, will discuss the current approach to evaluation and treatment in his country, reflecting guidelines, standards and/or state of the art practices. Possible moderators and mediators of treatment are also discussed. Four countries are represented: England, Scotland, Italy and Spain. For England and Wales NICE has established a national clinical practice guideline which recommends that pharmacological treatment should only be given as part of a comprehensive treatment plan including psychological, behavioural and educational interventions. The Scottish Intercollegiate Guideline Network (SIGN) have updated their ADHD Guideline recommendations in 2009 based on best available evidence and clinical experience. The SIGN guidelines have now been audited against actual clinical practice on two occasions (2008, 2012) by the NHS in Scotland. Although the Italian guidelines of diagnosis and treatment of ADHD recommend the use of use medication for cases with severe ADHD, psychotherapy and psychosocial intervention is still the main and often only type of treatment in Italy. In Spain, ADHD Guidelines were developed in 2010 by a group of experts. The guidelines were evaluated by a group of independent external reviewers according to the AGREE criteria and considered to have a better score than the AACAP guidelines, and similar to NICE and SIGN. Despite a variety of different clinical traditions and the widespread public controversy about the disorder and

possible overprescription of medication, common European guidelines have been established, alongside with various national guidelines. Similarities and differences in these guidelines will be highlighted and possibilities for continuous development of guidelines in international cooperation will be discussed.

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Eur Child Adolesc Psychiatry. 2013;22:S115.

**EMOTION RECOGNITION AND SOCIAL FUNCTIONING IN CHILDREN WITH ADHD OR AUTISM SPECTRUM DISORDERS.**

**Zuddas A, Carucci S, Peddis C, et al.**

**Background:** Social cognition is a crucial aspect of healthy adjustment. ADHD show poor social skills and impaired interpersonal relationships, which in turn may be a consequence of impaired nonverbal communication. These features could overlap with autism spectrum disorders (ASD) symptoms, such as lack of reciprocity and difficulties in identification of facial expressions.

**Objectives:** (1) To compare the three samples while processing facial emotions and matching emotions using the Amsterdam Neuropsychological Test battery (ANT). (2) To explore, by the Social Responsiveness Scale (SRS), the social functioning of ADHD children compared to ASD and healthy controls (TDC) and investigate the effects of methylphenidate (MPH) on social impairment in the ADHD group.

**Methods:** Facial recognition (FR), identification facial emotion (IFE) and matching facial emotion (MFE) were assessed in 35 ADHD, 32 ASD and 36 TDC aged 6-14 using reaction time (RT) correct (RTC), RT to errors (RTE) and Errors. SRS data were collected from 234 children aged 4-13 and IQ>70 (110 ADHD, 30 ASD and 103 TCD). SRS were re-administered to a group of ADHD (n=38) that underwent on MPH at least for 9-12 months.

**Results:** ADHD children were significantly slower and less accurate than TDCs in both the FR and IFE tasks. A significant main effect for group and task (respectively  $p=0.005$  and  $p<0.0001$ ) and a significant interaction between task and group ( $p=0.039$ ) were found for the FR versus IFE task for both RT and number of errors. Both ASD and ADHD groups compared with the TDC group were slower; the difference in RT between IFE and FR tasks was slower in ADHD compared with TDC group ( $p=0.015$ ). SRS Total and each subscale score in ADHD and ASD were significantly higher than TDC ( $p<0.001$ ) with a significant relationship between Hyperactivity and Autistic Mannerism ( $P<0.001$ ) and between Social Motivation and Age in the ADHD group ( $P=0.05$ ). MPH treatment showed a significant improvement on SRS scores in the ADHD 1 year after.

**Discussion:** This study highlights a significant social impairment in ADHD. The results suggest that specific information processing deficits are present in both ADHD and ASD participants (slower reaction time and larger error rates) especially during face recognition and identification of facial emotions stimuli. ADHD also showed a SRS profile similar to ASD. Significant benefits from MPH on social impairment confirm its utility in treating ADHD as a complex disorder. Recognition of specific social deficit in ADHD may help to consider specific targets for a comprehensive intervention.

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Eur Child Adolesc Psychiatry. 2013;22:S114-S115.

**EMOTIONS, AFFECTIVE STATUS & SOCIAL RESPONSIVENESS IN DIFFERENT PSYCHIATRIC CONDITIONS.**

**Anon.**

ID 425 nullEmotion recognition and social functioning in children with ADHD and ASDnull (Zuddas team, Cagliari) ID 172 nullAlexithymia and attachment in alimentary disordersnull (Balottin team, Pavia) ID 381 nullAffective states and pathology in adolescents with borderline personalitynull (Neri team, Milan) ID 94 nullEmotional control in externalizing and internalizing disordersnull (Cianchetti team, Cagliari) are part of the symposium we have proposed and has been accepted. The symposium aims at dealing with different aspects of emotions, affective status and responsivity to social stimuli in some unrelated psychiatric conditions. It includes 4 reports. The first report is by Alessandro Zuddas et al. (Cagliari) nullEmotion recognition and social functioning in ADHD and ASDnull. Using a questionnaire (Social Responsiveness Scale, Constantino & Gruber 200) and neuropsychological battery (Amsterdam Neuropsychological Test

Battery (De Sonneville 1999, 2005), the authors compare social responsiveness and recognition/matching of facial emotion in children with ASD, ADHD or normal development (ND). Results indicate ADHD children show significant, specific impairment in both social responsiveness and specific emotion recognition compared to ND, although with a milder impairment compared to ASD. The second report is by Umberto Balottin et al. (Pavia) null Alexithymia and attachment in alimentary disorders null. Adolescents affected with anorexia nervosa were evaluated in their ability to identify and describe emotions and in their attachments style; a correlation is found with the affective status evaluated by means of depression and anxiety instruments. Follows a talk by Francesca Neri et al. (Milan) null Affective status and borderline personality disorder (BPD) in adolescence. null BPD inpatients were compared with age and gender matched healthy control subjects. Children's Depression Inventory (CDI) and State-Trait Anxiety Inventory form Y (STAIY) showed increased scores in BPD patients with respect to controls. The results are also discussed in the attempt of dissecting this complex disorder into more meaningful subgroups and of modeling specific traits that could be purposely targeted by dedicated therapeutic strategies. The last talk is by Carlo Cianchetti et al. (Cagliari) null Emotional control in externalizing and internalizing disorders. null Children were asked to indicate their answer mode faced with a number of different situations, for the most frustrating ones (test ICE). Those with externalizing and those with internalizing disorders showed a lower percentage of adaptive responses compared to the controls. Their prevalent responses were concordant with their emotional status. However, a percentage of subjects having externalizing disorders show a high number of internalizing answers.

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Eur Child Adolesc Psychiatry. 2013;22:S295.

**NEW THERAPEUTIC OPTIONS SEEM TO BE EFFECTIVE TREATING PATIENTS SUFFERING FROM ADHD.**

**Niederhofer H.**

**Introduction:** ADHD is a complex disorder which requires biological and psychological therapies. Since the last decades, methylphenidate and atomoxetine are the nearly only biological therapies, with effect sizes of >0.8. Unfortunately, the response rate to these options is about 75 %, i.e. that 25 % require alternative treatments to improve their ADHD symptoms. Recently, biological therapies like, tDCS, rTMS, DBS, BLT as well as pharmacological therapies with e.g. omega 3 fatty acids and zinc were investigated for possible efficacy for ADHD.

**Methods:** This contribution reports advantages and disadvantages as well as effect sizes of those therapies.

**Results:** tDCS, rTMS, DBS, BLT as well as pharmacological therapies with e.g. omega 3 fatty acids and zinc showed some remarkable effect, which is lower than that of methylphenidate and atomoxetine, but exceeds that of placebo.

**Discussion:** tDCS, rTMS, DBS, BLT as well as pharmacological therapies with e.g. omega 3 fatty acids and zinc seem to be somewhat effective treating ADHD patients. Their position as adjunctive therapeutic strategies warrant further research.

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Eur Child Adolesc Psychiatry. 2013;22:S132.

**PSYCHOLOGICAL THERAPIES FOR ADHD: CAN THEY BE MADE TO WORK?**

**Sonuga-Barke E.**

ADHD remains one of the commonest severe disorders of childhood, with serious implications for later mental health. Parenting problems are often present in affected young people. Whether as consequences of the disorder, or as contributions to the origin and course, they need to be addressed by clinical services. Stimulant medication is currently the first line and most efficacious treatment for ADHD. Although it is strikingly effective for many patients in terms of short term symptom control it is limited in a number of other ways: Normalisation of symptoms is rare; long term efficacy remains unclear; some areas of functioning are not improved; side effects are common though rarely severe; translation from RCTs to normal care can be problematic; and many patients and parents do not see medication as being right for them and their family. For all these reasons there is an urgent need to develop effective non-pharmacological treatments to



complement medication approaches. Several psychological approaches are in current use, and are often recommended, but usually with the caveat that further research is necessary. In this talk I will; (A) discuss the strengths and limitations of medication in ADHD treatment; (B) systematically review the evidence for the value of currently available psychological alternatives and highlight the need for more effective approaches; (C) highlight the importance of basing therapeutic innovation in this area on basic ADHD science while at the same time ensuring ecological relevance and; (D) emphasize the value of early intervention. Finally, I will discuss the potential value of the New Forest Parenting Programme. This is an evidence-based science driven treatment for ADHD in preschool children.

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Eur Child Adolesc Psychiatry. 2013;22:S91.

**NEUROPSYCHOLOGICAL AND IMAGING ENDOPHENOTYPES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Gau SSF.**

Attention-deficit/Hyperactivity Disorder (ADHD) is a common earlyonset clinically and genetically heterogeneous neuropsychiatric disorder with executive functions and other neurobiological deficits. This lecture will review the neurocognitive endophenotypes for ADHD and summarize the endophenotype approach to validate ADHD based on studies from my lab using Taiwanese population. Our previous studies have demonstrated that executive functions measured by the Spatial Span, Spatial Working Memory, Intradimensional/Extradimensional Shift, Stocking of Cambridge, and Rapid Visual Information Processing of the CANTAB, visual memory measured by the Delayed Matching to Sample, tau (s) of ex-Gaussian distribution of reaction time, interval timing assessed by the time discrimination and time reproduction dual tasks can be the candidate for cognitive endophenotypes of ADHD; and DAT1 gene associated with ADHD inattentive type, inattention symptoms and executive functions (e.g., spatial working memory). The association of ADHD with neurobiological deficits in the frontostriatal and frontoparietal networks will be presented from our morphometric, functional imaging and diffusion spectrum imaging studies. For example, we found disturbed frontostriatal and cingulum microstructure integrity in ADHD that were correlated with impaired executive functions, attention controls, and ex-Gaussian parameters of reaction time. In addition, the effects of methylphenidate and atomoxetine on the changes of neuropsychological functions and structural and functional connectivity in several relevant networks in ADHD will be presented based on our data on three placebo-controlled or head-to-head randomized clinical trials in child and adult ADHD populations.

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Eur Child Adolesc Psychiatry. 2013;22:S124-S125.

**STIMULANT TREATMENT IN ADHD: FUNCTIONAL, HEALTH-RELATED QUALITY OF LIFE AND HEALTH UTILITY OUTCOME MEASURES.**

**Coghill D, Banaschewski T, Soutullo C, et al.**

Stimulant medications have been used to treat the symptoms of ADHD for over half a century, and their efficacy in clinical trials has been assessed principally using ratings scales based on the symptoms of inattention and hyperactivity-impulsivity listed in the DSM-IV-TR. Yet ADHD affects multiple domains of daily life, including educational achievement and peer or family relations. Evidence of such impairment, usually based on the perceptions of teachers and parents, is required to establish a diagnosis. Optimal treatment should therefore not only reduce symptoms, but also improve day-to-day functioning. This symposium will focus on parent-rated measures of functional impairment, health-related quality of life (HRQoL) and health utility as means of assessing the overall effectiveness of stimulant treatment for ADHD. This approach was taken in two recent international phase 3 trials of the long-acting prodrug lisdexamfetamine dimesylate (LDX), one of which included an extended-release (OROS) methylphenidate reference arm. The four speakers will use results from these studies to evaluate the advantages and disadvantages of the selected instruments, including the issues of proxy assessment, item overlap, psychometric validity and reliability, and sensitivity to treatment. (1) David Coghill will first present an overview of study design, a safety data summary, and the primary efficacy outcomes, which were based on the well-established, investigator-rated ADHD Ratings Scale IV (ADHD-RS-IV) and Clinical Global

Impressions (CGI) instruments. (2) Tobias Banaschewski will describe the Child Health and Illness Profile-Child Edition: Parent Report Form (CHIP-CE:PRF). The raw scores from this generic, paediatric HRQoL instrument are normalised based on a reference population, and its validity and reliability in ADHD have been established. CHIP-CE:PRF has been used in atomoxetine trials, but the results presented are the first data on stimulants in ADHD. (3) Cesar Soutullo will then discuss the strengths and weaknesses of the Weiss Functional Impairment Ratings Scale-Parent Report (WFIRS-P) in the context of study results. Although designed specifically for ADHD in order to improve sensitivity and provide clinically meaningful data, WFIRS-P lacks published psychometric properties and has been used in only two other pharmacological intervention trials. (4) Paul Hodgkins will take a health economist's perspective in his analysis of the data from the Health Utilities Index 2 (HUI-2), a generic, preference-based health status classification and scoring system. He will explore the relationship to other clinical outcomes and briefly discuss how the data help inform reimbursement decisions by health technology assessment agencies. The symposium will conclude with an open discussion of how these results enhance understanding of the influence of psychostimulants on the day-to-day lives of patients with ADHD.

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Eur Child Adolesc Psychiatry. 2013;22:S187-S188.

**METHYLPHENIDATE SIDE-EFFECT PROFILE IS INFLUENCED BY GENETIC VARIATION IN THE ADHD-ASSOCIATED CES1 GENE.**

**Johnson K, Barry E, Cox M, et al.**

A naturalistic, prospective study of the influence of genetic variation on clinical response to stimulant medication in 77 children with ADHD was undertaken. The influence of genetic variation of the CES1 gene coding for carboxylesterase 1A1 (CES1A1), the major enzyme responsible for the first-pass, stereoselective metabolism of methylphenidate was investigated. Parent and teacher-rated questionnaires were collected at baseline when the children were medication naive, and again at 6 weeks whilst they were on medication. Medication dose, prescribed at the discretion of the treating clinician, was recorded at each time-point. Blood and saliva samples were collected for genotyping. Single nucleotide polymorphisms (SNPs) were selected in the coding, non-coding and the 30 flanking region of the CES1 gene. Analyses were conducted using ANCOVA and logistic regression models. None of the CES1 gene variants was associated with the dose of methylphenidate provided or the clinical response recorded at the 6-week time point. An association between two CES1 SNP markers and the occurrence of sadness as a side-effect of short-acting methylphenidate was found. The two associated CES1 markers were in linkage disequilibrium and were significantly associated with ADHD in a larger sample of ADHD trios. The associated CES1 markers were also in linkage disequilibrium with two SNP markers of the noradrenaline transporter gene [SLC6A2]. This is the first study to examine whether genetic variation at the CES1 gene influences methylphenidate treatment response in medication naive children with ADHD. These novel findings indicate new research directions for pharmacogenetic studies of methylphenidate in ADHD.

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Eur Neuropsychopharmacol. 2013.

**BRAIN ALTERATIONS IN ADULT ADHD: EFFECTS OF GENDER, TREATMENT AND COMORBID DEPRESSION.**

**Onnink AMH, Zwiers MP, Hoogman M, et al.**

Children with attention-deficit/hyperactivity disorder (ADHD) have smaller volumes of total brain matter and subcortical regions, but it is unclear whether these represent delayed maturation or persist into adulthood. We performed a structural MRI study in 119 adult ADHD patients and 107 controls and investigated total gray and white matter and volumes of accumbens, caudate, globus pallidus, putamen, thalamus, amygdala and hippocampus. Additionally, we investigated effects of gender, stimulant treatment and history of major depression (MDD). There was no main effect of ADHD on the volumetric measures, nor was any effect observed in a secondary voxel-based morphometry (VBM) analysis of the entire brain. However, in the volumetric analysis a significant gender by diagnosis interaction was found for caudate volume. Male patients showed reduced right caudate volume compared to male controls, and caudate volume correlated with hyperactive/impulsive symptoms. Furthermore, patients using stimulant treatment had a smaller right

hippocampus volume compared to medication-naïve patients and controls. ADHD patients with previous MDD showed smaller hippocampus volume compared to ADHD patients with no MDD. While these data were obtained in a cross-sectional sample and need to be replicated in a longitudinal study, the findings suggest that developmental brain differences in ADHD largely normalize in adulthood. Reduced caudate volume in male patients may point to distinct neurobiological deficits underlying ADHD in the two genders. Smaller hippocampus volume in ADHD patients with previous MDD is consistent with neurobiological alterations observed in MDD.

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Eur Neuropsychopharmacol. 2013.

**THE EFFECT OF A SKIPPED DOSE (PLACEBO) OF METHYLPHENIDATE ON THE LEARNING AND RETENTION OF A MOTOR SKILL IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Fox O, Adi-Japha E, Karni A.**

Individuals with Attention Deficit Hyperactivity Disorder (ADHD) have difficulties in achieving optimal performance in many everyday and academic tasks, deficits attributed to impaired skill acquisition and procedural memory consolidation. We tested the effect of a skipped dose of methylphenidate (MPH) on learning a movement sequence and its subsequent consolidation into procedural memory in adolescents with ADHD. A crossover double-blind design with placebo was used. Sixteen male adolescents, 16-18 years-old, with ADHD and taking MPH formulations on a daily basis, were trained on performing a 5-element sequence of finger-to-thumb opposition movements. Participants took part in two study conditions, 2 months apart. In each condition a different movement sequence was trained and tested. Participants trained on the task either with active medication or placebo on the day of training, crossed-over between study conditions. Learning effects, speed and accuracy, were assessed within-session, during a 24-h memory consolidation phase. Retention was tested by 2 weeks post-training. There were robust gains in performance both within-session and during the 24-h consolidation phase, in both conditions. However, the discontinuation of MPH on the day of training significantly reduced performance speed, with no loss of accuracy. By 2 weeks, post-training performance was comparable. Adolescents with ADHD who are treated daily but skip a dose of MPH show significant slowing of performance relative to their own performance on medication. However, on a background of daily treatment a skipped dose has no deleterious effect on memory consolidation and retention.

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Eur Psychiatry. 2013.

**DAILY LIFE IMPAIRMENTS ASSOCIATED WITH SELF-REPORTED CHILDHOOD/ADOLESCENT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND EXPERIENCES OF DIAGNOSIS AND TREATMENT: RESULTS FROM THE EUROPEAN LIFETIME IMPAIRMENT SURVEY.**

**Caci H, Doepfner M, Asherson P, et al.**

The Lifetime Impairment Survey assessed impairment and symptoms of attention-deficit/hyperactivity disorder (ADHD) in children/adolescents from six European countries. Parents/caregivers of children/adolescents aged < 20 years with ADHD (ADHD group; n = 535) and without ADHD (control group; n = 424) participated in an online survey. History of ADHD diagnosis was self-reported. ADHD and control groups were compared using impairment and symptom scales; higher scores indicate greater impairment. Mean (SD) age at ADHD diagnosis was 7.0 (2.8) years, following consultation of 2.7 (2.6) doctors over 20.4 (23.9) months. Parents/caregivers (64%; 344/535) reported frustration with some aspect of the diagnostic procedure; 74% (222/298) were satisfied with their child's current medication. ADHD had a negative impact on children/adolescents in all aspects of life investigated. The ADHD group had a higher mean (SD) school impairment score (2.7 [0.7]) compared with the control group (2.1 [0.7]; P < 0.001) and were more likely to be in the bottom of their class (P < 0.001). These data provide insights into impairments associated with ADHD in childhood/adolescence, and identify areas for improvement in its management and treatment.

Evid -Based Complement Altern Med. 2013;2013.

**CONCURRENT COMPLEMENTARY AND ALTERNATIVE MEDICINE CAM AND CONVENTIONAL REHABILITATION THERAPY IN THE MANAGEMENT OF CHILDREN WITH DEVELOPMENTAL DISORDERS.**

**Kim SY, Shin YI, Nam SO, et al.**

**Background:** We investigated the concurrent use of conventional rehabilitations and complementary and alternative medicine (CAM) therapies for the long-term management of children with developmental disorders (DDs).

**Methods:** The parents or caregivers of 533 children with DDs (age range, 1-19 years) who visited the rehabilitation centers were surveyed using in depth face-to-face interviews.

**Results:** Of the 533 patients enrolled, 520 completed the questionnaire (97% response rate). A total of 292 (56%) children were receiving multiple therapies, more than two conventional rehabilitations and CAM, at the time of the interview. A total of 249 (48%) children reported lifetime CAM use, 23% used CAM at the time of the interview, and 62% of the patients planned to use CAM therapy in the future. Conventional rehabilitation therapies used at the time of the interview included physical therapy (30%), speech therapy (28%), and occupational therapy (19%), and the CAM therapies included herbal medicine (5%) and acupuncture or moxibustion (3%). The respondents indicated that in the future they planned to use acupuncture or moxibustion (57%), occupational therapy (18%), cognitive behavioral therapy (16%), speech therapy (10%), and physical therapy (8%).

**Conclusion:** Concurrent management as conventional rehabilitations and CAM therapies is widely used by children with DDs.

Expert Rev Pharmacoecon Outcomes Res. 2013;13:791-815.

**ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: AN UPDATE ON MEDICATION ADHERENCE AND PERSISTENCE IN CHILDREN, ADOLESCENTS AND ADULTS.**

**Ahmed R, Aslani P.**

Suboptimal adherence to treatment regimens is a major obstacle to treatment efficacy and positive outcomes for patients. While poor adherence is common across a variety of chronic conditions, an area which presents unique challenges to clinicians and researchers is non-adherence among pediatric populations. These challenges are well illustrated by the management of attention-deficit/ hyperactivity disorder (ADHD), a pervasive pediatric psychiatric condition. The average rates of non-adherence in children and adults ranged between 15 and 87%. Factors predicting increased adherence/persistence included the use of long-acting formulations, younger age, Caucasian background, family structure and the presence and treatment of comorbidities. Decreased adherence/persistence were predicted by multiple daily dosing, family history of ADHD, experiences of adverse effects, stigma and treatment inefficacy. The broad range of non-adherence rates identified reflects the complexities of adherence research in ADHD, and highlights the need for better standardization of adherence/persistence definitions and measurement approaches.

Front Human Neurosci. 2013;7.

**DIFFERENTIAL DIAGNOSIS OF SENSORY MODULATION DISORDER (SMD) AND ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): PARTICIPATION, SENSATION, AND ATTENTION.**

**Yochman A, Alon-Beery O, Sribman A, et al.**

Differential diagnosis between sensory modulation disorder (SMD) and attention deficit hyperactivity disorder (ADHD) is often challenging, since these disorders occur at a high rate of co-morbidity and share several clinical characteristics. Preliminary studies providing evidence that these are distinct disorders have focused solely on body functions, using sophisticated laboratory measurements. Moreover, no studies have compared participation profiles of these populations. This study is the first to compare the profiles of these populations regarding both body functions (attention and sensation) and participation, using measures applicable for clinical use. The study included 19 children with ADHD without SMD and 19 with SMD without ADHD (diagnosed by both pediatric neurologists and occupational therapists), aged 6-9, and

matched by age and gender. All children underwent a broad battery of evaluations: the Evaluation of Sensory Processing, Fabric Prickliness Test (FPT) and Von Frey Test to evaluate sensory processing, and Test of Everyday Attention to evaluate attention components. The Participation in Childhood Occupations Questionnaire was used to evaluate participation. Results support significant group differences in all sensory components, including pain intensity to suprathreshold stimuli and pain after sensation, as well as in tactile, vestibular, taste, and olfactory processing. No differences were found in attention components and participation. This study has both theoretical and clinical importance, inter alia, providing further evidence of two distinct disorders as well as indications of specific clinical instruments that might enable clinicians to implement differential diagnoses. In addition, results accord with other previous statements, which indicate that the clinical diagnosis of children with disabilities may not be a major factor in determining their participation profile.

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Front Human Neurosci. 2013.

**USING ENVIRONMENTAL DISTRACTORS IN THE DIAGNOSIS OF ADHD.**

**Cassuto H, Ben-Simon A, Berger I.**

This study examined the effect of the incorporation of environmental distractors in computerized continuous performance test (CPT) on the ability of the test in distinguishing ADHD from non-ADHD children. It was hypothesized that children with ADHD would display more distractibility than controls while performing CPT as measured by omission errors in the presence of pure visual, pure auditory, and a combination of visual and auditory distracting stimuli. Participants were 663 children aged 7-12 years, of them 345 diagnosed with ADHD and 318 without ADHD. Results showed that ADHD children demonstrated more omission errors than their healthy peers in all CPT conditions (no distractors, pure visual or auditory distractors and combined distractors). However, ADHD and non-ADHD children differed in their reaction to distracting stimuli; while all types of distracting stimuli increased the rate of omission errors in ADHD children, only combined visual and auditory distractors increased it in non-ADHD children. Given the low ecological validity of many CPT, these findings suggest that incorporating distractors in CPT improves the ability to distinguish ADHD from non-ADHD children.

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Indian J Psychiatry. 2013;55:338-42.

**PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN PRIMARY SCHOOL CHILDREN.**

**Venkata JA, Panicker AS.**

**Context:** There is a lacuna of studies on Attention Deficit Hyperactivity Disorder (ADHD) in the Indian context.

**Aims:** (i) To identify the prevalence of ADHD in primary school children, (ii) To identify the gender difference in the prevalence of ADHD, (iii) To compare the distribution of ADHD among different socioeconomic status, (iv) To identify the presence of any co-morbid factors associated with ADHD.

**Settings and Design:** This is a cross sectional study of school aged children selected from four different schools in Coimbatore district.

**Materials and Methods:** Seven hundred seventy children aged between 6 and 11 years were selected from four schools in Coimbatore district after obtaining informed consent from their parents. The presence of ADHD was assessed by using Conner's Abbreviated Rating Scale (CARS) given to parents and teachers. The children identified as having ADHD were assessed for the presence of any co-morbid factors by administering Children's Behavioural Questionnaire (CBQ) to the teachers and Personal Information Questionnaire to the parents. Statistical Analysis: Statistical Product and Service Solutions (SPSS) 10 software, Mean and Standard Deviation, and student's t test were used for statistical analysis.

**Results:** The prevalence of ADHD among primary school children was found to be 11.32%. Prevalence was found to be higher among the males (66.7%) as compared to that of females (33.3%). The prevalence among lower socio-economic group was found to be 16.33% and that among middle socio-economic group was 6.84%. The prevalence was highest in the age group 9 and 10 years.

**Conclusion:** The present study shows a high prevalence of ADHD among primary school children with a higher prevalence among the males than the females.

Int J Eating Disord. 2013.

**BULIMIA NERVOSA PATIENT DIAGNOSED WITH PREVIOUSLY UNSUSPECTED ADHD IN ADULTHOOD: CLINICAL CASE REPORT, LITERATURE REVIEW, AND DIAGNOSTIC CHALLENGES.**

**Ioannidis K, Serfontein J, Muller U.**

There is increasing literature suggesting a link between attention-deficit hyperactivity disorder (ADHD) and eating disorders (EDs), especially bulimia nervosa. ADHD is under-diagnosed in girls and children of high intelligence are typically missed. We identified a case of a 23-year-old woman suffering from severe bulimia nervosa and previously unsuspected ADHD in adulthood; we diagnosed and treated her with extended-release methylphenidate. We performed a literature review on the ADHD and bulimia nervosa comorbidity. We discuss the reasons why her ADHD remained undiagnosed and the difficulties in diagnosing ADHD in patients with EDs. We suggest that identifying comorbid ADHD is crucial for these patients and argue for the use of a structured interview, collateral history and investigation of onset of symptoms to establish a diagnosis of ADHD in adults with bulimia nervosa. Comorbidities and overlap of symptomatology need to be taken into account.

Int J Green Pharm. 2013;7:322-27.

**A COMPARATIVE STUDY ON NALADADI GHRITA IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH KUSHMANDA GHRITA.**

**Gupta K, Mamidi P.**

**Background:** Attention-Deficit/Hyperactivity Disorder (ADHD) is the most commonly diagnosed childhood psychiatric disorder. Children with ADHD have been found to have cognitive deficits, lower IQ, impaired social relationships with in the family and with peers as well as poor study skills and lower academic achievement. ADHD prevalence is estimated to be 5% for the Indian paediatric population. The persistence of these problems highlights the need for effective treatment.

**Objective:** The main objective of the present study was to evaluate the comparative effect of Naladadi Ghrita with Kushmanda Ghrita in reducing the signs and symptoms of ADHD.

**Materials and Methods:** A total of 20 subjects with ADHD satisfying the DSM-IV TR diagnostic criteria were selected and divided in to two groups by following randomisation method. Trial group received Naladadi Ghrita 5 ml twice a day and control group received Kushmanda Ghrita 5 ml twice a day for 1 month. Two assessments were done before and after the treatment. Criterion of assessment was based on the scoring of ADHD Rating Scale. Paired and unpaired 't'- test was used for statistical analysis.

**Results and Conclusion:** Naladadi Ghrita and Kushmanda Ghrita both were effective on ADHD Rating Scale and they provided 35%, 38.68% of relief, respectively ( $P < 0.001$ ). The difference in between the both groups was statistically insignificant ( $P > 0.05$ )

Int J Neuropsychopharmacol. 2014;17:9-21.

**ASSOCIATION BETWEEN THE DAT1 GENE AND SPATIAL WORKING MEMORY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Shang CY, Gau SSF.**

An association between attention deficit hyperactivity disorder (ADHD) and the dopamine transporter gene (DAT1) was reported in clinical samples. This study aimed to explore whether there was an association between DAT1 and spatial working memory (SWM), a promising endophenotype for ADHD. This family-based association sample consisted of 382 probands with DSM-IV ADHD and their family members (n=1298) in Taiwan. The SWM task of the Cambridge Neuropsychological Test Automated Battery (CANTAB) was used to measure SWM of all participants. We screened 15 polymorphisms across the

DAT1 gene, including 14 single nucleotide polymorphisms (SNPs) and the variable number of tandem repeat polymorphism in the 3'-untranslated region. We used the Family-Based Association Test (FBAT) to test the associations of genetic polymorphisms with the SWM measures. In single locus association analyses, two SNPs (rs2617605 and rs37020) were significantly associated with the double errors (adjusted  $p=0.03$  and  $0.03$ , respectively) after adjustment for multiple testing. In haplotype analyses, a haplotype rs403636 (G)/rs463379 (C)/rs393795 (C)/rs37020 (G) was significantly associated with total within-search errors (minimal  $p=0.001$ ), within-search errors in eight boxes (minimal  $p=0.002$ ), total double errors (minimal  $p=0.001$ ) and double errors in eight boxes (minimal  $p=0.004$ ). Our finding of the haplotype rs403636 (G)/rs463379 (C)/rs393795 (C)/rs37020 (G) as a novel genetic marker for spatial working memory suggests that variation in DAT1 may provide insight into the pathways leading from genotype to phenotype of ADHD.

Iran J Pediatr. 2013;23:S67.

#### **TOURETTE SYNDROME AND ITS CO MORBIDITIES.**

**Hemmati S, Amiri N, Sajedi F, et al.**

Tourette is a syndrome with movement disorder most commonly seen in school-age children that isn't rare. Purpose of this study was to identify Tourette and its co morbidities in school-age children in a referral clinic.

**Methods:** 30 children in school-age with Tourette syndrome were studied in Tehran (5 girls and 25 boys). Control group was selected too. K-SADS questionnaire was used and the results analyzed with SPSS.

**Findings:** A clear pattern of co-morbidity was demonstrated with ADHD (Attention Deficit Hyperactivity Disorder), OCD (Obsession Compulsion Disorder) and MDD (Major Depression Disorder). 64% of Tourette group had ADHD, 53.3% had OCD, and MDD was about 56%. These co-morbidities were different in two sexes. At all ages, about 12% of individuals with TS had no reported comorbidities.

**Conclusion:** Tourette demonstrates with vocal and motor tics. It has some co-morbidities with special approach.

Iran J Pediatr. 2013;23:S80.

#### **THE CORRELATION BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AND ASTHMA IN CHILDREN WITH ASTHMA.**

**Sharafkhah M, Yousefi P, Salehi B, et al.**

**Background:** Attention Deficit Hyperactivity Disorder (ADHD) is the most common childhood neurological disorder that affects 5-10% of children of school age. It seems that the disorder is more common among children with asthma. The aim of this study was to investigate ADHD in children with asthma and compare it with a control group in patients referring to Amir Kabir hospital of Arak, Iran.

**Methods:** This case-control study was performed on 100 children with asthma and 100 children without asthma in the age bracket of 5-16 years old. In all patients, Conners questionnaire [based on the diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV)] and a demographic checklist about age, gender, mother's age at the birth, history of maternal disease and smoking by the mother during pregnancy, birth weight and history of major disease in child were filled. The data was analyzed using descriptive and analytical statistics in SPSS15.

**Findings:** Attention deficit was observed in 10 cases (10%) with asthma and 9 controls (9%) ( $P=0.63$ ) that, this difference was not significant between the two groups. Whereas, in the case and control groups 27 (27%) and 7 children (7%) were affected by hyperactivity - impulsive behavior, respectively ( $P=0.002$ ).

**Conclusion:** hyperactivity - impulsive behavior in children with asthma is significantly more common than control group. Thus evaluation and monitoring of ADHD in children with asthma is recommended.

Iranian Journal of Psychiatry and Clinical Psychology. 2013;18:292-97.

**A RANDOMIZED DOUBLE BLIND CROSSOVER STUDY ON THE EFFECTIVENESS OF BUSPIRONE AND METHYLPHENIDATE IN TREATMENT OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS.**

**Shahrbabaki ME, Sabzevari L, Haghdoost A, et al.**

**Objectives:** In this study the efficacy of buspirone was compared with methylphenidate in children and adolescent with attention deficit-hyperactivity disorder (ADHD).

**Methods:** In this randomized double blind clinical trial with crossover design, 40 children and adolescents (6-16 years old) with the diagnosis of ADHD were studied. The samples were selected by conventional method and categorized by blocked randomization into buspirone and methylphenidate groups. This study has two 8-week phases with one week wash-out period. Both medications were prescribed with the dose of 0.5 mg/kg/day. Effectiveness was evaluated using teacher and parents forms of ADHD Rating Scale (ADHD-RS) for both groups. Questionnaires were completed in baseline and every two weeks during the eight-week phase. Medication side effect profile was evaluated. Data were analyzed by repeated measurement ANOVA.

**Results:** At the end of each phase, the scores of attention deficit, hyperactivity and impulsivity had significant decrease in comparison with baseline and previous weeks of study for both drugs and no significant difference was detected between groups. The positive effect of methylphenidate in decreasing the symptoms was detected earlier than buspirone.

**Conclusion:** Buspirone seems to be as effective as methylphenidate in treating ADHD with less side effects.

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J Child Neurol. 2003 Aug;18:517-24.

**HYPERKINETIC SEIZURES IN CHILDREN.**

**Weinstock A, Giglio P, Kerr SL, et al.**

The objective of this study was to delineate the clinical and video-electroencephalographic (EEG) manifestations of children with complex partial seizures with a predominant "hyperkinetic" presentation. Certain types of partial seizures can be difficult to differentiate from nonepileptic seizures because of their intense motor presentation and, at times, lack of alteration of consciousness. Based on a published semiologic seizure classification, this type of seizures can be described as "hyperkinetic," characterized by intense motor activity involving the extremities and trunk. We report five children diagnosed with hyperkinetic seizures by video-EEG monitoring. All patients were referred for video-EEG evaluation because of an initial suspicion of pseudoseizures. Presented in this study is a review of the patients' clinical data, including video-EEG evaluation. There were three boys and two girls; the mean age at presentation was 10 +/- 3 years. In four patients, there was a history of behavioral disorder, with two patients carrying a diagnosis of attention-deficit hyperactivity disorder (ADHD). One girl had significant developmental delay and an abnormal neurologic examination. Brain magnetic resonance imaging was normal in three patients and abnormal in two. The semiology of the seizures consisted of stereotypic intense motor activity, mainly upper extremity flailing and kicking. Screaming and shouting were noted in three cases, and intense fear was present in two patients. The hyperkinetic ictal activity progressed to tonic-clonic seizures in two patients. Seizures occurred out of sleep or on awakening in four patients. The interictal EEG activity was normal in one patient and revealed a continuous generalized slowing and slowing of the posterior dominant rhythm in two patients. One of the latter patients had interictal epileptiform activity in the frontal and midline regions. An intermittent rhythmic slow activity of the left hemisphere with superimposed bifrontal sharp waves was noted in the fifth patient. The ictal EEG revealed profuse superimposed electromyographic (EMG) activity in all patients, making some of the EEG interpretation difficult to analyze, particularly a longitudinal bipolar montage. However, with digital manipulation of the ictal EEG data, such as changes in EEG sensitivity, application of fast frequency filters, and use of different EEG montages, it was possible to discern an ictal EEG pattern or postictal slowing following the diffuse EMG artifact in all patients. On clinical follow-up, adequate seizure control was achieved in three patients. Based on the clinical history, one patient was diagnosed with autosomal dominant nocturnal frontal lobe epilepsy. Diagnosis of hyperkinetic seizures can be difficult because of the similarity of the clinical manifestations with nonepileptic events such



as certain parasomnias and pseudoseizures. Video-EEG is the most effective way of diagnosing this type of seizure.

J Abnorm Psychol. 2013 Nov;122:1179-88.

**NEUROPSYCHOLOGICAL FUNCTIONING AND SEVERITY OF ADHD IN EARLY CHILDHOOD: A FOUR-YEAR CROSS-LAGGED STUDY.**

**Rajendran K, Rindskopf D, O'Neill S, et al.**

Children with attention deficit/hyperactivity disorder (ADHD) have poorer neuropsychological functioning relative to their typically developing peers. However, it is unclear whether early neuropsychological functioning predicts later ADHD severity and/or the latter is longitudinally associated with subsequent neuropsychological functioning; and whether these relations are different in children with and without early symptoms of ADHD. This study aimed to examine the longitudinal associations between ADHD severity and neuropsychological functioning among children at high and low risk of developing ADHD. Hyperactive/Inattentive (H/I; n=140) and Typically developing (TD; n=76) preschoolers (age 3–4 years) were recruited (BL) and followed annually for 3 years (F1, F2, and F3). Teachers rated the children's ADHD severity and impairment using the Behavior Assessment System for Children-2 and the Children's Problem Checklist, respectively. Parent reports of children's ADHD severity were obtained using the Kiddie-Schedule for Affective Disorders and Schizophrenia – Present and Lifetime version. Neuropsychological functioning was assessed using the NEPSY. In the full sample, there were bidirectional longitudinal associations between neuropsychological functioning and ADHD severity between F1 and F3. Among H/I children, neuropsychological functioning at F1 and F2 predicted ADHD severity at F2 and F3, respectively. In contrast, among TD children the only significant relationship observed was that elevated ADHD symptoms at F2 were associated with poorer neuropsychological functioning at F3. Improved neuropsychological functioning may attenuate ADHD symptoms and associated impairment among H/I children during the early school years. Interventions designed to improve neuropsychological functioning among young H/I children may be beneficial in reducing their ADHD severity.

Journal of Attention Disorders. 2013 Oct;17:620-27.

**CHANGE BLINDNESS IN CHILDREN WITH ADHD: A SELECTIVE IMPAIRMENT IN VISUAL SEARCH?**

**Maccari L, Casagrande M, Martella D, et al.**

**Objective:** This study evaluated change blindness and visual search efficiency in children with ADHD in searching for central and marginal changes.

**Method:** A total of 36 drug-naïve children (18 ADHD/18 controls) performed a flicker task that included changes in objects of central or marginal interest. The task required observers to search for a change until they detected it.

**Results:** Children with ADHD performed more slowly and less accurately than did typically developing children, specifically in detecting marginal-interest changes.

**Conclusion:** In contrast to more standard visual search tasks, flicker tasks seem to be more sensitive to highlight focused attention deficits in children diagnosed with ADHD. Concretely, ADHD attentional deficits were more apparent when the task involved serial top-down strategies.

Journal of Attention Disorders. 2013 Oct;17:547-49.

**INTRODUCTION TO THE SPECIAL SECTION ON SLEEP AND ADHD.**

**Miano S.**

This editorial provides an overview of the special issue of Journal of Attention Disorders. Human sleep is considered to be a global phenomenon, orchestrated by central nervous system neuronal networks, and a local phenomenon. The similarity between the spectrum of cognitive consequences of sleep loss and the profile of attention deficit disorder with hyperactivity (ADHD) makes the relationship between sleep and

ADHD an intriguing issue for basic researchers and clinicians on account of its implications in the diagnosis and choice of therapies. With regard to sleep phenotypes, one of the articles examined relationship between ADHD and hypersomnia, hypothesizing that in some cases ADHD may be part of a primary disorder of vigilance, and the core symptoms of ADHD may be an attempt to stay alert, to counteract daytime sleepiness. The growing interest in the distinction of sleep phenotypes associated with ADHD also emerges from another study featured in the present issue. Sleep and wakefulness may be restricted to small groups of neurons, to individual cortical columns, or to larger brain regions. Cognitive impairment and performance deficits induced by sleep deprivation reduced attention and vigilance, decision-making ability, may reflect the occurrence of cortical and subcortical local “islands of sleep” in participants who are behaviorally fully awake.

Journal of Attention Disorders. 2013 Oct;17:608-19.

**ADHD PRESCHOOLERS WITH AND WITHOUT ODD: DO THEY ACT DIFFERENTLY DEPENDING ON DEGREE OF TASK ENGAGEMENT/REWARD?**

**Gopin CB, Berwid O, Marks DJ, et al.**

**Objective:** To examine the impact of reinforcement on reaction time (RT) and RT variability (RT standard deviation [RTSD]) in preschoolers with ADHD with and without oppositional defiant disorder (ODD), and a typically developing (TD) comparison group.

**Method:** Participants were administered a computerized task consisting of two conditions: simple RT (SRT) and reinforced SRT (SRT<sub>r</sub>). Data were analyzed using two-way (Group×Condition) mixed ANOVAs and followed-up using pairwise comparisons.

**Results:** RTs were significantly shorter and less variable during the SRT<sub>r</sub> than the SRT condition. A significant Group x Condition interaction was observed for RTSD ( $F=3.38$ ,  $p<.05$ ); post hoc analyses indicated that the RTSD of the ADHD + ODD group was significantly more variable than that of the TD group during the SRT condition ( $F=4.81$ ,  $p<.05$ ). However, their RTSD was statistically indistinguishable from the other groups during the SRT<sub>r</sub> condition.

**Conclusion:** Preschoolers who are oppositional/defiant and hyperactive are the most responsive to feedback/reward.

J Child Adolesc Psychopharmacol. 2013;23:597-604.

**CLINICAL GAINS FROM INCLUDING BOTH DEXTROAMPHETAMINE AND METHYLPHENIDATE IN STIMULANT TRIALS.**

**Ramtvedt BE, Roinas E, Aabech HS, et al.**

**Objective:** The purpose of this study was to investigate clinical gains from including both dextroamphetamine and methylphenidate in stimulant trials.

**Method:** Thirty-six medication-naive children ages 9-14 years diagnosed with attention-deficit/hyperactivity disorder (ADHD) were enrolled for 6 weeks in a crossover trial, with 2 weeks of methylphenidate, dextroamphetamine, and placebo, in a randomly assigned, counterbalanced sequence. Outcome measures constituted a computer-based continuous performance test combined with a motion tracking system (Qb Test) and an ADHD questionnaire rated by parents and teachers.

**Results:** Group analyses found significant treatment effects of similar size for the two stimulants on both outcome measures. Single-subject analyses revealed that each stimulant produced a favourable response in 26 children; however, an individual child frequently responded qualitatively or quantitatively differently to the two stimulants. By including both stimulants in the trial, the number of favorable responders increased from 26 (72%) to 33 (92%). In children with favorable responses of unequal strength to the two stimulants, a shift from inferior drug to best drug was associated with a 64% mean increase in the overall response strength score, as measured by the ADHD questionnaire.

**Conclusions:** The likelihood of a favorable response and optimal response strength is increased by including both stimulants in the stimulant trial. The study was first registered in clinical trials 28 September 2010. Clinical Trials.gov Identifier: NCT01220440.

J Child Adolesc Psychopharmacol. 2013;23:632-33.

**EFFECTIVENESS OF METHYLPHENIDATE IN THE TREATMENT OF ENCOPIRESIS WHETHER OR NOT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS ARE PRESENT.**

***Yilmaz S, Akca OF.***

J Child Adolesc Psychopharmacol. 2013;23:605-13.

**ATOMOXETINE IMPROVED ATTENTION IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND DYSLEXIA IN A 16 WEEK, ACUTE, RANDOMIZED, DOUBLE-BLIND TRIAL.**

***Wietecha L, Williams D, Shaywitz S, et al.***

**Objective:** The purpose of this study was to evaluate atomoxetine treatment effects in attention-deficit/hyperactivity disorder (ADHD-only), attention-deficit/hyperactivity disorder with comorbid dyslexia (ADHD+D), or dyslexia only on ADHD core symptoms and on sluggish cognitive tempo (SCT), working memory, life performance, and self-concept.

**Methods:** Children and adolescents (10-16 years of age) with ADHD+D (n=124), dyslexia-only (n=58), or ADHD-only (n=27) received atomoxetine (1.0-1.4 mg/kg/day) or placebo (ADHD-only subjects received atomoxetine) in a 16 week, acute, randomized, double-blind trial with a 16 week, open-label extension phase (atomoxetine treatment only). Changes from baseline were assessed to weeks 16 and 32 in ADHD Rating Scale-IV-Parent-Version: Investigator-Administered and Scored (ADHDRS-IV-Parent:Inv); ADHD Rating Scale-IV-Teacher-Version (ADHDRS-IV-Teacher-Version); Life Participation Scale - Child- or Parent-Rated Version (LPS); Kiddie-Sluggish Cognitive Tempo (K-SCT) Interview; Multidimensional Self Concept Scale (MSCS); and Working Memory Test Battery for Children (WMTB-C).

**Results:** At week 16, atomoxetine treatment resulted in significant ( $p < 0.05$ ) improvement from baseline in subjects with ADHD+D versus placebo on ADHDRS-IV-Parent:Inv Total (primary outcome) and subscales, ADHDRS-IV-Teacher-Version Inattentive subscale, K-SCT Interview Parent and Teacher subscales, and WMTB-C Central Executive component scores; in subjects with Dyslexia-only, atomoxetine versus placebo significantly improved K-SCT Youth subscale scores from baseline. At Week 32, atomoxetine-treated ADHD+D subjects significantly improved from baseline on all measures except MSCS Family subscale and WMTB-C Central Executive and Visuo-spatial Sketchpad component scores. The atomoxetine-treated dyslexia-only subjects significantly improved from baseline to week 32 on ADHDRS-IV-Parent:Inv Inattentive subscale, K-SCT Parent and Teacher subscales, and WMTB-C Phonological Loop and Central Executive component scores. The atomoxetine-treated ADHD-only subjects significantly improved from baseline to Week 32 on ADHDRS-Parent:Inv Total and subscales, ADHDRS-IV-Teacher-Version Hyperactive/Impulsive subscale, LPS Self-Control and Total, all K-SCT subscales, and MSCS Academic and Competence subscale scores.

**Conclusions:** Atomoxetine treatment improved ADHD symptoms in subjects with ADHD+D and ADHD-only, but not in subjects with dyslexia-only without ADHD. This is the first study to report significant effects of any medication on SCT. Clinical Trials Registration: This study was registered at: <http://clinicaltrials.gov/ct2/home>, NCT00607919.

J Child Adolesc Psychopharmacol. 2013;23:628-31.

**PHARMACOTHERAPEUTIC CHALLENGES IN THE MANAGEMENT OF ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND CHRONIC TICS IN A SCHOOL AGED CHILD.**

**Sood R, Coffey BJ.**

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Journal of Child and Family Studies. 2013 Oct;22:1000-12.

**PREDICTORS OF RESPONSE AND MECHANISMS OF CHANGE IN AN ORGANIZATIONAL SKILLS INTERVENTION FOR STUDENTS WITH ADHD.**

**Langberg JM, Becker SP, Epstein JN, et al.**

The purpose of the study was to evaluate predictors of response and mechanisms of change for the Homework, Organization, and Planning Skills (HOPS) intervention for middle school students with Attention-Deficit/Hyperactivity Disorder (ADHD). Twenty-three middle school students with ADHD (grades 6–8) received the HOPS intervention implemented by school mental health providers and made significant improvements in parent-rated materials organization and planning skills, impairment due to organizational skills problems, and homework problems. Predictors of response examined included demographic and child characteristics, such as gender, ethnicity, intelligence, ADHD and ODD symptom severity, and ADHD medication use. Mechanisms of change examined included the therapeutic alliance and adoption of the organization and planning skills taught during the HOPS intervention. Participant implementation of the HOPS binder materials organization system and the therapeutic alliance as rated by the student significantly predicted post-intervention outcomes after controlling for pre-intervention severity. Adoption of the binder materials organization system predicted parent-rated improvements in organization, planning, and homework problems above and beyond the impact of the therapeutic alliance. These findings demonstrate the importance of teaching students with ADHD to use a structured binder organization system for organizing and filing homework and classroom materials and for transferring work to and from school.

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Journal of Child Psychology and Psychiatry. 2013 Dec;54:1295-307.

**OFFENDING BEHAVIOURS OF CHILD AND ADOLESCENT FIRESETTERS OVER A 10-YEAR FOLLOW-UP.**

**Lambie I, Ioane J, Randell I, et al.**

**Background:** To assess the postintervention arson recidivism and other offending rates of a group of 182 firesetting children and adolescents referred to the New Zealand Fire Awareness and Intervention Program (FAIP) over a follow-up period of 10 years. To investigate predictors of offending behaviour as well as variables associated with previous involvement in firesetting behaviour and offending severity.

**Method:** Data collected at the time of the FAIP intervention was provided by the New Zealand Fire Service and the offence histories of the sample were accessed from the New Zealand Police database (NIA). Data were analyzed using both descriptive and inferential statistics.

**Results:** Although the arson recidivism rate was low (2%), rates of general offending were high, with 59% of the sample having committed an offence during the follow-up period. Fifteen percent of the sample was classified as severe offenders, 40% as moderate and 4% as minor. Of offenders, 12.6% had been imprisoned during the follow-up period. Offending was predicted by experience of abuse and a previous firesetting behaviour at the time of the FAIP intervention. Living with both parents at the time of intervention decreased the probability of an individual engaging in future offending behaviour. The presence of family stress and a diagnosis of Attention Deficit Disorder or Attention Deficit Hyperactivity Disorder (ADD/ADHD) were associated with previous firesetting behaviour. In addition, involvement with family violence (as a perpetrator, complainant or victim) was associated with more severe offending behaviour.

**Conclusions:** In light of existing research, the findings of this study indicate that many firesetters are at risk for future offending and that identification of high-risk individuals is therefore an important consideration for any organization involved with firesetters. To minimize this risk, there is a need for a collaborative, multiagency approach to firesetting behaviour involving comprehensive risk assessment and appropriate referral for at-risk individuals.

Journal of Child Psychology and Psychiatry. 2013 Dec;54:1284-94.

**COGNITIVE AND BEHAVIORAL INDICATORS OF ADHD SYMPTOMS PRIOR TO SCHOOL AGE.**

**Arnett AB, MacDonald B, Pennington BF.**

**Background:** Previous research on the etiology of ADHD symptoms suggests that neuropsychological differences may be present as early as birth; however, the diagnosis is typically not given until school age. This study aimed to (a) identify early behavioral and cognitive markers of later significant parent and/or teacher ratings of ADHD symptomology, (b) examine sex differences in these predictors, and (c) describe the developmental trajectories of comorbid symptoms in school-aged children.

**Methods:** 1,106 children and at least one parent enrolled in the NICHD Study of Early Child Care and Youth Development were followed from 1 month of age through 6th grade. Effect size calculations, discriminant function analysis, and growth curve analyses were conducted to address the three aims.

**Results:** Children with high- versus low-ADHD symptomology at 3rd grade could be distinguished using cognitive and behavioral measures as early as 15 months (females) and 24 months (males). Sensitivity and specificity were modest at 15, 24, and 26 months. Growth curves revealed significant differences between high- and low-ADHD groups in comorbid symptoms at kindergarten and significantly different slopes for externalizing, social skills, and academic skills ratings across elementary school. There were few gender differences on cognitive and behavioral variables within the high-ADHD group.

**Conclusions:** Cognitive and behavioral markers of ADHD symptoms are present in children prior to entry into formal schooling, but current behavioral screeners are not developmentally sensitive to these differences in infancy and toddlerhood.

Journal of Clinical Child and Adolescent Psychology. 2013 Nov;42:809-19.

**PROSOCIALITY AND NEGATIVE EMOTIONALITY MEDIATE THE ASSOCIATION OF SEROTONIN TRANSPORTER GENOTYPE WITH CHILDHOOD ADHD AND ODD.**

**Brammer WA, Lee SS.**

Although there is evidence that the promoter polymorphism of the serotonin transporter (5-HTTLPR) gene is associated with attention-deficit/hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD), the pathways underlying these associations are largely unknown. Given their theoretical and biological plausibility, we tested whether individual differences in key temperament dimensions (i.e., prosociality, negative emotionality, daring) constituted potential pathways from 5-HTTLPR to ADHD and ODD. Using a well-characterized sample of 194 six to nine-year-old children with and without ADHD, we utilized multiple mediation procedures with bootstrapping to evaluate prosociality, negative emotionality, and daring as independent mediators of 5-HTTLPR with separate parent and teacher ratings of ADHD and ODD. Controlling for ODD, prosociality and negative emotionality significantly mediated the association of 5-HTTLPR and parent-reported ADHD. Similarly, controlling for ADHD, prosociality and negative emotionality each uniquely mediated the association of 5-HTTLPR and parent-reported ODD. For teacher-reported ADHD, prosociality significantly mediated the association of 5-HTTLPR (controlling for ODD) whereas controlling for ODD, negative emotionality significantly mediated the prediction of teacher-reported ODD from 5-HTTLPR. Specifically, the number of 5-HTTLPR long alleles was inversely associated with prosociality and positively associated with negative emotionality; prosociality was inversely associated and negative emotionality was positively associated with ADHD and ODD. We consider the role of

temperament in genetically sensitive designs as well as its potential value in the development and delivery of effective interventions.

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Journal of Clinical Child and Adolescent Psychology. 2013 Nov;42:769-83.

**COGMED WORKING MEMORY TRAINING FOR YOUTH WITH ADHD: A CLOSER EXAMINATION OF EFFICACY UTILIZING EVIDENCE-BASED CRITERIA.**

**Chacko A, Feirsen N, Bedard AC, et al.**

The current review applied the evidence-based treatment criteria espoused by the Society for Clinical Child and Adolescent Psychology (Silverman & Hinshaw, 2008) to specifically evaluate the short-term and longer term efficacy of Cogmed Working Memory Training (CWMT) as a treatment for youth with Attention-Deficit/Hyperactivity Disorder (ADHD). Utilizing a systematic literature search, 7 studies that employed the school-age version of CWMT were identified for this review. The data reviewed herein suggest mixed findings regarding the benefit of CWMT for youth with ADHD. Two randomized controlled studies have demonstrated that CWMT led to improvements in neuropsychological outcomes and parent-rated ADHD symptoms relative to wait-list control and placebo treatment conditions. Another study demonstrated effects of CWMT relative to a placebo condition on an analog observation of behavior during an academic task, although this study did not find an effect of CWMT on parent-rated ADHD. Finally, an additional study utilizing an active comparison control condition did not find incremental benefits of CWMT on parent- or teacher-rated ADHD. Critical issues in interpreting existing studies include lack of alignment between demonstrated outcomes and the hypothesized model of therapeutic benefit of CWMT, issues with equivalence of control conditions, and individual differences that may moderate treatment response. Collectively, the strengths and limitations of the studies reviewed suggest that CWMT is best defined as a Possibly Efficacious Treatment for youth with ADHD. We suggest future directions for research and conclude with clinical implications of our findings for the treatment of youth with ADHD.

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Journal of Clinical Child and Adolescent Psychology. 2013 Nov;42:762-68.

**PERINATAL PROBLEMS AND PSYCHIATRIC COMORBIDITY AMONG CHILDREN WITH ADHD.**

**Owens EB, Hinshaw SP.**

Among two large, independent samples of girls with attention-deficit/hyperactivity disorder (ADHD), we examined associations between specific (maternal gestational smoking and drug use, early labor, low birth weight, and infant breathing problems at birth) and cumulative prenatal and perinatal risk factors and psychiatric comorbidity during childhood. Data from the (a) Multimodal Treatment Study of Children with ADHD, a randomized clinical trial with 579 children aged 7 to 9.9 years with combined-type ADHD, and the (b) Berkeley Girls ADHD Longitudinal Sample, a naturalistic study of 140 girls with ADHD (93 combined-type and 47 inattentive-type) who were first seen when they were 6 to 12 years old, were analyzed separately. In each sample, perinatal risk factors were assessed retrospectively by maternal report, and current childhood psychiatric comorbidity was assessed using maternal report on the Diagnostic Interview Schedule for Children. Consistent findings across these two studies show that infant breathing problems, early labor, and total perinatal problems predicted childhood comorbid depression but not comorbid anxiety or externalizing disorders. These associations remained significant, in both samples, with control of family socioeconomic status (SES) and maternal symptoms of ADHD and depression. Results attenuated slightly with control of the number of child comorbidities plus SES and maternal symptoms. Accumulating evidence suggests that perinatal risk factors are important precursors of childhood psychiatric comorbidity and that the association between these risk factors and detrimental psychiatric outcomes cannot be explained by maternal psychiatric symptoms or SES during childhood.

Journal of Clinical Child and Adolescent Psychology. 2013 Nov;42:749-61.

**CLINICAL USEFULNESS OF OBSERVATIONAL ASSESSMENT IN THE DIAGNOSIS OF DBD AND ADHD IN PRESCHOOLERS.**

**Bunte TL, Laschen S, Schoemaker K, et al.**

The aim of the present study was to investigate the clinical usefulness of an observational tool—the Disruptive Behavior Diagnostic Observation Schedule (DB-DOS)—in the diagnosis of disruptive behavior disorders (DBD) and attention deficit/hyperactivity disorder (ADHD) in preschoolers. We hypothesized that the DB-DOS may help support the presumption of a diagnosis generated by the information from parents and teachers (or other caregivers). Participants were referred preschool children with externalizing behavioral problems (N = 193; 83% male) and typically developing children (N = 58; 71% male). In view of the clinical validity study each child was given a diagnosis of either DBD (N = 40), or ADHD (N = 54) or comorbid (DBD + ADHD; N = 66) based on best-estimate diagnosis. The DB-DOS demonstrated good interrater and test–retest reliability for DBD and ADHD symptom scores. Confirmatory factor analysis demonstrated an excellent fit of the DB-DOS multidomain model of DBD symptom scores and a satisfactory fit of ADHD symptom scores. The DB-DOS demonstrated good convergent validity, moderate divergent validity, and good clinical validity on a diagnostic group level for DBD and ADHD symptom scores. The Receiver Operating Characteristic curve analyses revealed that for DBD the sensitivity and specificity are moderate and for ADHD good to excellent. The presumption of a diagnosis based on information from parents, teachers, and cognitive assessment was supported by the DB-DOS in 60% for DBD and 75% for ADHD. The DB-DOS can be used to help support a presumption of a DBD and/or ADHD diagnosis in preschool children.

Journal of Clinical Child and Adolescent Psychology. 2013 Nov;42:796-808.

**DISTINCTIONS BETWEEN SLUGGISH COGNITIVE TEMPO, ADHD-IN, AND DEPRESSION SYMPTOM DIMENSIONS IN SPANISH FIRST-GRADE CHILDREN.**

**Burns GL, Servera M, del Mar Bernad M, et al.**

The objective of this study was to evaluate the validity of a new parent rating scale of Sluggish Cognitive Tempo (SCT). SCT was defined with 10 symptom domains—daydreams; attention fluctuates; absentminded; loses train of thought; easily confused; seems drowsy; thinking is slow; slow-moving; low initiative; and easily bored, needs stimulation—with each domain represented by multiple examples. Mothers' and fathers' ratings of SCT, ADHD-IN, ADHD-HI, oppositional defiant disorder (ODD), and depression symptoms along with ratings of academic and social impairment were obtained for a sample of 802 Spanish first-grade children (54% boys). SCT Symptom Domains 4 to 8 showed substantial loadings on the SCT factor (i.e., convergent validity) and substantially higher loadings on the SCT factor than the ADHD-IN factor (i.e., discriminant validity). This 5-domain measure of SCT showed good interrater and test–retest reliability for a 6-week interval. Higher scores on the 5-domain measure of SCT predicted higher levels of academic and social impairment even after controlling for ADHD-IN and depression. In contrast, higher levels of SCT were not uniquely related (or uniquely negatively related) to ADHD-HI and ODD, whereas ADHD-IN and depression were uniquely positively related to ADHD-HI and ODD. The new measure of SCT more clearly establishes that SCT, ADHD-IN, and depression represent independent symptom dimensions, thus providing a measurement tool to help determine if SCT and ADHD-IN dimensions have unique biological correlates and if SCT and ADHD meet the criteria for different disorders.

J Clin Psychopharmacol. 2013.

**EFFECTS OF SWITCHING TO ONCE-DAILY MODIFIED-RELEASE METHYLPHENIDATE FROM PREVIOUS TREATMENT WITH OTHER PSYCHOSTIMULANTS IN CHILDREN AND ADOLESCENTS WITH ADHD: AN OBSERVATIONAL STUDY WITH CLINICIAN, PARENT, AND TEACHER EVALUATIONS.**

**Frolich J, Breuer D, Gortz-Dorten A, et al.**

J Cogn Neurosci. 2014;26:54-62.

**POLYMORPHISMS IN THE DOPAMINE RECEPTOR 2 GENE REGION INFLUENCE IMPROVEMENTS DURING WORKING MEMORY TRAINING IN CHILDREN AND ADOLESCENTS.**

**Soderqvist S, Matsson H, Peyrard-Janvid M, et al.**

Studying the effects of cognitive training can lead to finding better treatments, but it can also be a tool for investigating factors important for brain plasticity and acquisition of cognitive skills. In this study, we investigated how single-nucleotide polymorphisms (SNPs) and ratings of intrinsic motivation were associated to interindividual differences in improvement during working memory training. The study included 256 children aged 7-19 years who were genotyped for 13 SNPs within or near eight candidate genes previously implicated in learning: COMT, SLC6A3 (DAT1), DRD4, DRD2, PPP1R1B (DARPP32), MAOA, LMX1A, and BDNF. Ratings on the intrinsic motivation inventory were also available for 156 of these children. All participants performed at least 20 sessions of working memory training, and performance during the training was logged and used as the outcome variable. We found that two SNPs, rs1800497 and rs2283265, located near and within the dopamine receptor 2 (DRD2) gene, respectively, were significantly associated with improvements during training ( $p < .003$  and  $p < .0004$ , respectively). Scores from a questionnaire regarding intrinsic motivation did not correlate with training outcome. However, we observed both the main effect of genotype at those two loci as well as the interaction between genotypes and ratings of intrinsic motivation (perceived competence). Both SNPs have previously been shown to affect DRD2 receptor density primarily in the BG. Our results suggest that genetic variation is accounting for some interindividual differences in how children acquire cognitive skills and that part of this effect is also seen on intrinsic motivation. Moreover, they suggest that dopamine D2 transmission in the BG is a key factor for cognitive plasticity.

J Consult Clin Psychol. 2013;81:988-98.

**PARENTAL ADHD SYMPTOMS AND SELF-REPORTS OF POSITIVE PARENTING.**

**Lui JHL, Johnston C, Lee CM, et al.**

**Objective:** In 2 studies, we tested whether parental attention-deficit/ hyperactivity disorder (ADHD) symptoms are associated with self-reports of more positive parenting, even after accounting for observed positive parenting behaviors.

**Method:** In Study 1, 96 mothers with sons 8-11 years of age participated; 44% of the boys were diagnosed with ADHD. The majority of mothers and sons were European Caucasian. In Study 2, 48 parents (24 mother-father pairs) with children 6-12 years of age participated. All children in Study 2 were diagnosed with ADHD, and 75% of the children were boys. More than 90% of the families were Caucasian. In both studies, parents self-reported on their positive parenting, and positive parenting was observed in parent-child interactions.

**Results:** In models including relevant demographic variables, other parental psychopathologies, and both inattentive and hyperactive/impulsive symptoms, parents with higher levels of hyperactive/impulsive symptoms self-reported engaging in significantly more positive parenting behaviors than were observed. Parental inattentive symptoms were not uniquely associated with self-reports of positive parenting. This pattern was found for both mothers and fathers, and across families with and without children diagnosed with ADHD.

**Conclusions:** Results suggest that high levels of parental ADHD symptoms may be associated with over-estimation of positive parenting behaviors. Reasons for the distinction between the types of ADHD symptoms associated with higher self-reports of positive parenting and the clinical implications of the findings are discussed.



J Dermatol Treat. 2014;25:115-18.

**INCREASED FREQUENCY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN ACNE VERSUS DERMATOLOGIC CONTROLS: ANALYSIS OF AN EPIDEMIOLOGIC DATABASE FROM THE US.**

**Gupta MA, Gupta AK, Vujcic B.**

**Introduction:** Acne can be associated with psychiatric morbidity and suicide, which have sometimes been considered an adverse reaction to some acne therapies such as isotretinoin. A recent population-based study reports that suicide in acne is related to the psychosocial burden of substantial acne, rather than medication effects. As suicidality is not always directly related to acne severity, factors other than acne's direct psychosocial burden also likely contribute to the suicide risk. Attention Deficit Hyperactivity Disorder (ADHD) is a disorder of childhood and adolescence that is associated with increased suicidality. We examined the frequency of ADHD in acne versus all other dermatology-related patient visits, after controlling for age and other factors.

**Methods:** Retrospective cross-sectional study of epidemiologic databases (NAMCS and NHAMCS) representing 55 825 dermatology outpatient visits from 1995 to 2009.

**Results:** In comparison to other dermatologic disorders, acne was over two times more likely to be associated with ADHD (odds ratio = 2.34, 95%CI 1.06-5.14) after controlling for the possible confounding effects of age, sex, stimulant medications, comorbid anxiety or depressive disorders, and atopic dermatitis, a condition previously associated with ADHD.

**Discussion:** Our preliminary findings suggest a significant association of acne with ADHD, which could contribute to the increased psychological morbidity and suicidality in some acne patients.

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Journal of Emotional and Behavioral Disorders. 2013 Dec;21:227-39.

**THE INCREMENTAL UTILITY OF BEHAVIORAL RATING SCALES AND A STRUCTURED DIAGNOSTIC INTERVIEW IN THE ASSESSMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Vaughn AJ, Hoza B.**

The current study examined the incremental utility of rating scales, a structured diagnostic interview, and multiple informants in a comprehensive assessment of attention-deficit/ hyperactivity disorder (ADHD). The sample included 185 children with ADHD ( $M_{\text{age}} = 9.22$ ,  $SD = 0.95$ ) and 82 children without ADHD ( $M_{\text{age}} = 9.24$ ,  $SD = 0.88$ ). Logistic regressions were used to examine the incremental contribution of each method within an assessment of ADHD. Results indicated that information collected from a structured diagnostic interview was unable to significantly improve a prediction model including parent and teacher ratings ( $\Delta R^2 = 0.01$ ,  $p = .64$ ). Teacher ratings on symptom-based scales resulted in significant model improvement beyond parent ratings alone ( $\Delta R^2 = 0.48$ ,  $p < .001$ ). Exploratory analyses indicated that using behavioral rating scales correctly classified all participants by diagnosis. Clinical implications are highlighted, and future research directions are discussed.

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J Nepal Paediatr Soc. 2013;33:172-76.

**ASSESSMENT OF MENTAL HEALTH PROBLEMS OF SCHOOL CHILDREN AGED 11-17 YEARS USING SELF REPORT STRENGTH AND DIFFICULTY QUESTIONNAIRE (SDQ).**

**Rimal HS, Pokharel A.**

**Introduction:** It is now recognized that psychological disorders, among children and adolescents have high prevalence rate. Currently, there is limited data on the prevalence of mental health problems among adolescents especially in the developing country like Nepal. The objective of this study was to investigate the prevalence of mental health issues among school children aged 11-17 years.

**Materials and Methods:** The self rated version of Strength and Difficulty Questionnaire (SDQ-YR1) were given to the students and answers were collected and the data was analyzed using SPSS version 16.1. The questions were in the Likert scale 0(not true), 1(somewhat true) and 2(certainly true). The data collected also included parent's educational and occupational status.

**Results:** A total of 159 students participated in the study after receiving well informed consent from the parents. There were 96(60%) boys and 63 (40%) girls' participants in the study. Among all the participants

in this study 18.6% had a total-Strength and Difficulty Questionnaire (SDQ) score that can be classified as abnormal by published cutoffs. The emotional problems (24.5%) and peer relationship problem (22%) were the two common problems screened as an abnormal SDQ score. Girls were significantly more likely to have emotional problems than boys ( $p$  value  $<0.05$ ) where as boys were significantly more likely to have Hyperactivity/inattention score in SDQ than girls ( $p$  value  $<0.05$ ). Gender difference was also significant statistically as girls had higher abnormal total SDQ score than boys ( $p$  value  $< 0.05$ ).

**Conclusion:** There is high prevalence of mental health issues in children but a study in large sample is recommended.

Journal of Neurological Sciences. 2013;30:182.

**EFFECT OF MEDICATION ON AUDITORY PROCESSING DISORDER AND ATTENTION DEFICIT DISORDER.**

**Oztekin C, Kocnullak O, Yalcnnullinkaya F.**

**Objective:** Attention deficit, hyperactivity and difficulty in listening are symptoms that can be seen in both Attention Deficit and Hyperactivity Disorder (ADHD), and Central Auditory Processing Disorder (CAPD). While ADHD is treated with medication, the only remedy for CAPD is central training. This study aims to create an awareness for the necessity of considering the possibility of CAPD together with the diagnosis of ADHD if a child has problems in attention and learning through listening.

**Material and Methods:** The study was conducted with 2 elementary school children (1 male, 1 female) aged 7 and 9, who did not show progress through ADHD treatment and had normal bilateral auditory functioning. Their central auditory processing functions were compared to the same age, same gender children in the control group.

**Results:** Processing difference was found between right and left hemispheres in both cases. For the given cases, both children had lower left hemisphere performance when compared with their right hemispheres. These findings imply that although ADHD and CAPD have similar behavioral problems, the nature and the treatment of the two disorders are different.

**Conclusion:** In this study the given cases who were being treated for ADHD did not show the expected progress since the nature of their disorder was caused by CAPD as well, rather than being pure ADHD. In order to achieve progress, attention, listening, language and speaking training were added to the treatment plan together with the evaluation of central auditory processing functions.

J Neurosci Methods. 2014;222:62-68.

**THE EFFECT OF ENVIRONMENTAL DISTRACTORS INCORPORATION INTO A CPT ON SUSTAINED ATTENTION AND ADHD DIAGNOSIS AMONG ADOLESCENTS.**

**Berger I, Cassuto H.**

**Background:** Diagnosis of ADHD in adolescents involves specific challenges. Conventional CPT's may fail to consistently distinguish ADHD from non-ADHD due to insufficient cognitive demands. The aim of this study was to explore whether the incorporation of environmental distractors into a CPT would increase its ability to distinguish ADHD from non-ADHD adolescents.

**New method:** Using the rate of omission errors as a measure of difficulty in sustained attention, this study examined whether ADHD adolescents are more distracted than controls and which type of distractors is more effective in terms of ADHD diagnosis. The study employed the MOXO-CPT version which includes visual and auditory stimuli serving as distractors. Participants were 176 adolescents aged 13-18 years, 133 diagnosed with ADHD and 43 without ADHD.

**Results and comparison with existing methods:** Results showed that ADHD adolescents produced significantly more omission errors in the presence of pure visual distractors and the combination of visual and auditory distractors than in no-distractors conditions. Distracting stimuli had no effect on CPT performance of non-ADHD adolescents. ROC analysis further demonstrated that the mere presence of distractors improved the utility of the test.

**Conclusions:** This study provides evidence that incorporation of environmental distractors into a CPT is useful in term of ADHD diagnosis. ADHD adolescents were more distracted than controls by all types of

environmental distractors. ADHD adolescents were more distracted by pure visual distractors and by the combination of distractors than by pure auditory ones.

J Pharmacokinet Pharmacodyn. 2013;40:S53.

**A DOSE ADAPTATION APPROACH OF METHYLPHENIDATE FOR CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).**

**Bonnefois G, Barriere O, Li J, et al.**

**Objectives:** Attention deficit hyperactivity disorder (ADHD) is a serious neuro-behavioral disorder that affects up to 12 % of children worldwide. Stimulant medications have been used for about 50 years, with methylphenidate (MPH) as the main agent. A variety of oral formulations are made available under immediate, to circumvent known limitations of immediate release, while keeping its advantages [1]. Indeed, immediate release formulations have shown problems in terms of effectiveness duration, patient compliance and issues of privacy and inconvenience caused by frequent administration outside home. In the current practice, three levels of doses, from high to medium to low, are prescribed, in alignment with the observed therapeutic effect. In this study, we propose a computational strategy of dose adaptation using a Population pharmacokinetic (Pop-PK) approach to identify the most efficient PK profile of immediate release MPH.

**Methods:** Inspired by these practical problems, we will apply our recently developed methodology to investigate the best dosing regimen of MPH using a grid search for best dose and time schedules. With the aim to reduce the considerable constraints related to the MPH use, we will base our work on a reported Pop-PK model [2] to investigate the use of PK as informative surrogate to enhance the predictability of therapeutic effect, using clinical data for doses and reported effect scales.

**Results:** The developed computational algorithm was applied to delineate drug regimens in terms of their efficacy without recourse to direct blood sampling.

**Conclusions:** The generated methodology and knowledge can be translated to help designing new drug formulation and used to develop educational tools.

J Am Acad Child Adolesc Psychiatry. 2013;52:1243-44.

**HERE AND THERE/GLOBAL BURDEN OF DISEASE.**

**Kieling C.**

J Am Acad Child Adolesc Psychiatry. 2013;52:1281-93.

**CALLOUS-UNEMOTIONAL TRAITS, PROACTIVE AGGRESSION, AND TREATMENT OUTCOMES OF AGGRESSIVE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Blader JC, Pliszka SR, Kafantaris V, et al.**

**Objective:** Stimulant treatment improves impulse control among children with attention-deficit/hyperactivity disorder (ADHD). Decreased aggression often accompanies stimulant pharmacotherapy, suggesting that impulsiveness is integral to aggressive behavior in these children. However, children with high callous-unemotional (CU) traits and proactive aggression may benefit less from ADHD pharmacotherapy, because their aggressive behavior seems more purposeful and deliberate. This study's objective was to determine whether pretreatment CU traits and proactive aggression affect treatment outcomes among aggressive children with ADHD receiving stimulant monotherapy.

**Method:** We implemented a stimulant optimization protocol with 160 children 6 to 13 years of age (mean [SD] age of 9.31 [2.02] years; 78.75% male) with ADHD, oppositional defiant or conduct disorder, and significant aggressive behavior. Family-focused behavioral intervention was provided concurrently. The primary outcome was the Retrospective Modified Overt Aggression Scale. The Antisocial Process Screening Device and the Aggression Scale, also completed by parents, measured CU traits and proactive

aggression, respectively. Analyses examined moderating effects of CU traits and proactive aggression on outcomes.

**Results:** In all, 82 children (51%) experienced remission of aggressive behavior. Neither CU traits nor proactive aggression predicted remission (CU traits: odds ratio [OR] =0.94, 95% CI =0.80-1.11; proactive aggression, OR=1.05, 95% CI=0.86-1.29). Children whose overall aggression remitted showed decreases in CU traits (effect size =-0.379, 95% CI=-0.60 to -0.16) and proactive aggression (effect size =-0.463, 95% CI=-0.69 to -0.23).

**Conclusions:** Findings suggest that pretreatment CU traits and proactive aggression do not forecast worse outcomes for aggressive children with ADHD receiving optimized stimulant pharmacotherapy. With such treatment, CU traits and proactive aggression may decline alongside other behavioral improvements. Clinical trial registration information - Medication Strategies for Treating Aggressive Behavior in Youth With Attention Deficit Hyperactivity Disorder; <http://clinicaltrials.gov/>; NCT00228046; and Effectiveness of Combined Medication Treatment for Aggression in Children With Attention Deficit With Hyperactivity Disorder (The SPICY Study); <http://clinicaltrials.gov/>; NCT00794625.

J Am Acad Child Adolesc Psychiatry. 2014;53:34-46.

**TRENDS IN THE PARENT-REPORT OF HEALTH CARE PROVIDER-DIAGNOSED AND MEDICATED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: UNITED STATES, 2003-2011 .**

**Visser SN, Danielson ML, Bitsko RH, et al.**

**Objective:** Data from the 2003 and 2007 National Survey of Children's Health (NSCH) reflect the increasing prevalence of parent-reported attention-deficit/hyperactivity disorder (ADHD) diagnosis and treatment by health care providers. This report updates these prevalence estimates for 2011 and describes temporal trends.

**Method:** Weighted analyses were conducted with 2011 NSCH data to estimate prevalence of parent-reported ADHD diagnosis, current ADHD, current medication treatment, ADHD severity, and mean age of diagnosis for U.S. children/adolescents aged 4 to 17 years and among demographic subgroups. A history of ADHD diagnosis (2003-2011), as well as current ADHD and medication treatment prevalence (2007-2011), were compared using prevalence ratios and 95% confidence intervals.

**Results:** In 2011, 11% of children/adolescents aged 4 to 17 years had ever received an ADHD diagnosis (6.4 million children). Among those with a history of ADHD diagnosis, 83% were reported as currently having ADHD (8.8%); 69% of children with current ADHD were taking medication for ADHD (6.1%, 3.5 million children). A parent-reported history of ADHD increased by 42% from 2003 to 2011. Prevalence of a history of ADHD, current ADHD, medicated ADHD, and moderate/severe ADHD increased significantly from 2007 estimates. Prevalence of medicated ADHD increased by 28% from 2007 to 2011.

**Conclusions:** Approximately 2 million more U.S. children/adolescents aged 4 to 17 years had been diagnosed with ADHD in 2011, compared to 2003. More than two-thirds of those with current ADHD were taking medication for treatment in 2011. This suggests an increasing burden of ADHD on the U.S. health care system. Efforts to further understand ADHD diagnostic and treatment patterns are warranted.

J Am Acad Child Adolesc Psychiatry. 2014;53:47-60.

**WHAT DOES RISPERIDONE ADD TO PARENT TRAINING AND STIMULANT FOR SEVERE AGGRESSION IN CHILD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER?**

**Aman MG, Bukstein OG, Gadow KD, et al.**

**Objective:** Although combination pharmacotherapy is common in child and adolescent psychiatry, there has been little research evaluating it. The value of adding risperidone to concurrent psychostimulant and parent training (PT) in behavior management for children with severe aggression was tested.

**Method:** One hundred sixty-eight children 6 to 12 years old (mean age 8.89 (plus or minus) 2.01 years) with severe physical aggression were randomized to a 9-week trial of PT, stimulant (STIM), and placebo (Basic treatment; n=84) or PT, STIM, and risperidone (Augmented treatment; n=84). All had diagnoses of attention-deficit/hyperactivity disorder and oppositional-defiant disorder (n=124) or conduct disorder (n=44).

Children received psychostimulant (usually Osmotic Release Oral System methylphenidate) for 3 weeks, titrated for optimal effect, while parents received PT. If there was room for improvement at the end of week 3, placebo or risperidone was added. Assessments included parent ratings on the Nisonger Child Behavior Rating Form (Disruptive-Total subscale was the primary outcome) and Antisocial Behavior Scale; blinded clinicians rated change on the Clinical Global Impressions scale.

**Results:** Compared with Basic treatment (PT+STIM [44.8 (plus or minus) 14.6 mg/day] + placebo [1.88 mg/day (plus or minus) 0.72]), Augmented treatment (PT+STIM [46.1 (plus or minus) 16.8 mg/day] + risperidone [1.65 mg/day (plus or minus) 0.75]) showed statistically significant improvement on the Nisonger Child Behavior Rating Form Disruptive-Total subscale (treatment-by-time interaction,  $p=.0016$ ), the Nisonger Child Behavior Rating Form Social Competence subscale ( $p=.0049$ ), and Antisocial Behavior Scale Reactive Aggression subscale ( $p=.01$ ). Clinical Global Impressions scores were substantially improved for the 2 groups but did not discriminate between treatments (Clinical Global Impressions-Improvement score (less-than or equal to) 2, 70% for Basic treatment versus 79% for Augmented treatment). Prolactin elevations and gastrointestinal upset occurred more with Augmented treatment; other adverse events differed modestly from Basic treatment; weight gain in the Augmented treatment group was minor.

**Conclusions:** Risperidone provided moderate but variable improvement in aggressive and other seriously disruptive child behaviors when added to PT and optimized stimulant treatment.

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J Can Acad Child Adolesc Psychiatry. 2013;22:317-23.

**ADHERENCE TO PSYCHOSTIMULANT MEDICATION IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: THE ROLE OF ATTITUDES.**

**Hebert J, Polotskaia A, Joober R, et al.**

**Objective:** To investigate how attitudes towards psychostimulant medication influence the adherence to psychostimulant treatment in children with Attention-Deficit/Hyperactivity Disorder (ADHD).

**Method:** Thirty-three children with ADHD were prospectively recruited to take part in this study. The children and their parents filled questionnaires at both baseline and at a three-month follow-up to assess the severity of ADHD symptoms in the child and attitudes towards psychostimulant medication. Adherence to medication was assessed through standardized interviews of parents.

**Results:** Parental perceived psychosocial benefits of psychostimulant medication at the three-month follow-up were found to be positive predictors of adherence to medication. Parental perceived psychosocial benefits of medication at the three-month follow-up was in turn predicted by parental medication acceptability at three months and child's perceived psychosocial benefits of medication at three-months.

**Conclusion:** Improving parents' awareness of psychosocial benefits of psychostimulant medication may increase adherence to psychostimulant medication in children with ADHD. Age of the child and severity of symptoms did not significantly affect medication adherence.

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J Neurol Sci. 2013.

**DAYTIME DYSFUNCTION IN CHILDREN WITH RESTLESS LEGS SYNDROME.**

**Furudate N, Komada Y, Kobayashi M, et al.**

We investigated daytime dysfunction in children with restless legs syndrome (RLS) and the effects of treatment primarily with iron supplements on RLS symptoms and daytime dysfunction. We recruited 25 children with RLS (male:female = 6:19, mean age at study onset: 12.3 years) for this prospective study, assessing their demographics, symptomatic characteristics, serum ferritin levels, and daytime functioning using the ADHD Rating Scale IV (ADHD-RS-IV), the Pediatric Symptom Checklist (PSC), and the Pediatric Quality of Life Inventory (PedsQL(trademark)). Children with RLS were compared with 28 controls (male:female = 10:18, mean age: 13.2 years) on these measures, pre- and post-treatment. Before treatment, ADHD-RS-IV (all  $ps < 0.05$ ) and PSC scores ( $p < 0.05$ ) were significantly higher and PedsQL(trademark) scores (all  $ps < 0.05$ ) significantly lower in the RLS group than in the control group. Eight and one of the RLS group had abnormally high PSC and ADHD-RS-IV scores, respectively.

Following treatment, participants' daytime function had improved to levels similar to those of controls. Sixteen out of twenty-three cases were successfully treated primarily with iron supplement. Some children with RLS have daytime dysfunction; however, this can be treated with iron supplements.

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J Voice. 2013;27:787.

**CLINICAL AND ACOUSTIC VOCAL PROFILE IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**García-Real T, Díaz-Roman TM, García-Martínez V, et al.**

**Purpose:** The objective of this study was to evaluate the presence of etiologic factors, symptoms, and vocal acoustic alterations related to vocal hyperfunction in children with attention deficit hyperactivity disorder (ADHD).

**Method:** In 23 children with ADHD and 28 control children, vocal acoustic exploration was performed to analyze the F0, jitter %, and voice turbulence index for the sustained vowels /a/ and /i/ and the average tone and intensity and tonal modulation in tests of continuous speech. The children's parents completed a specific questionnaire aimed at detecting etiologic factors and vocal symptoms.

**Results:** Children with ADHD displayed more vocal symptoms (hoarseness, neck strain, and shortness of breath while talking) and more etiologic factors (they shouted more, spoke louder and faster, and became angry more easily) than did children in the Control group. Likewise, children in the ADHD group exhibited a greater % jitter and a lower average intensity in the continuous speech tests.

**Conclusions:** These results indicate that children with ADHD display greater vocal hyperfunction as compared with children in the Control group and suggest a higher risk of developing dysphonia. The results of this study could be useful for designing vocal programs focusing on vocal education and hygiene to prevent and decrease vocal risks and on promoting vocal health in children with ADHD.

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Klin Psikofarmakol Bul. 2013;23:S53-S54.

**RESISTANCE AND RESOLUTIONS IN ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Semerci ZB.**

As in children and adolescents, medicinal treatment is the first choice in the treatment of adult Attention Deficit Hyperactivity Disorder (ADHD). However, in adults, the rate of success of medicinal treatment is 50% or less. The reason for this is that whilst medicinal treatment is effective for main symptoms (attention deficit, restlessness, impulsivity), it is not very effective for functional symptoms (time management, organization, planning etc.). For the same reason, the rate of continuation of treatment is also lower for adults. The patient who thinks that treatment is not delivering the expected results will not continue treatment. To prevent this, before commencing with medicinal treatment, the symptoms for which the treatment may be effective are described and possible treatment methods for other issues are explained. Another reason for the decrease of patients' compliance with treatment is the symptoms of the illness itself, such as lack of concentration, forgetfulness. Because of their habits, groups who suffer from more substantial attention deficit, obtain less benefit from medicines. In adult patients, other treatments are therefore applied besides medicinal treatment. These other treatments may be listed as follows: psychotherapy, cognitive behavioral treatment, family treatment, consultancy on the issue of Attention Deficit Hyperactivity Disorder, education oriented on self control. For the large part of patients, treatment of adult Attention Deficit Hyperactivity Disorder is started with stimulants or Atomoxetine. If there is no response through the appropriate dose of medicine, a different medicine is tried. In the event of cardiac side-effects, tic disorders, mood dysregulation, medicine is not continued. For some side-effects, the decrease of dosage of medicine or the addition of other medicine will solve the problem. If the problem is not resolved despite this, another group of medicines will be reverted to. Despite all available medicines, some patients will not respond to treatment or symptoms will worsen. It is necessary in such situations to alter the dosage of medicine. Depending on the condition of the patient and the symptoms, the dosage will either be decreased or increased. Another manner of changing effectiveness is the alteration of the moment of administration of medicine. If there is no improvement despite this, the most correct thing to do is to revert to another group of medicines and cognitive behavioral treatment, giving the patient individual,

guiding, support. If side effects are the reason for the lack of effectiveness of treatment, the relation between these side effects and the medicine is evaluated. Sometimes, altering the moment of administration of medicine can decrease the side effects. If not, the medicine should be changed and therapies must be added. If symptoms reoccur during treatment, altering the moment of the administration of medicine, the frequency of the administration of medicine, may resolve the problem. If not, it is necessary to alter treatment. In approximately one fourth of adult Attention Deficit Hyperactivity Disorder patients, one or more additional disorders are manifest. Anxiety disorders, depression and anti-social personality disorders are most frequently to be seen. In treatment, the response to stimulants is good. In about only 30% of patients is an adequate response not achieved or is no use made because of side effects. If serious mental problems arise during treatment, irrespective of the medicine, the effectiveness of treatment will decrease. In these situations, a careful evaluation must be made as to whether or not an additional disorder is manifest. Because if the problem is related to the other illness, the alteration of the dose of medicine or the medicine will not resolve the problem. Two important groups are to be observed in relation to the medicinal treatment of adult ADHD patients. The first group is the group, which encounters difficulties in treatment because of additional disorders, intolerable side effects; the other is the group, which shows no response to any medicinal treatment. The resistant group which does not respond to treatment more often regards patients who have other mental problems besides ADHD. In these situations, with the discontinuation of medicine, the application of other treatments comes to the fore. Furthermore, problems in the cure of functionally oriented symptoms, despite the cure of main symptoms in those who benefit from treatment, are also a reality. For this reason, in the treatment of adult ADHD, extra-medicinal treatments become more important. Cognitive behavioral therapy, individual therapy support and giving guidance to the patient with regards to ADHD are the most applied and advised psychological treatment methods.

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Klin Psikofarmakol Bul. 2013;23:S197.

**POSSIBLE PRENATAL AND GENETIC FACTORS IN THE ETIOLOGY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: A TURKISH REFERRED SAMPLE.**

***Bilgec SB, Tanidir C, Kurban S, et al.***

**Objective:** This study aimed to investigate the prenatal problems in children with attention deficit hyperactivity disorder (ADHD) and the smoking habits, substance or alcohol abuse and history of psychiatric disorders and criminal offence in the parents of these children.

**Methods:** Eighty-nine children aged between 6 to 12 years, with a diagnosis of ADHD and no comorbid psychiatric disorder or chronic medical disease and their parents were included in the study. ADHD diagnosis was made according to DSM-IV criteria. Assessment of prenatal problems and parents was made by interviewing with both parents and using a form prepared by the authors.

**Results:** In the history of the children with ADHD, 18 mothers had a threatened miscarriage, 13 had used medication and 19 were smoking during their pregnancy. Eight mothers had medical diseases due to pregnancy. %76.4 of the fathers and %39.3 of the mothers had a history of smoking, %13.5 of the fathers was consuming alcohol regularly and %7.9 were using various psychoactive drugs. Twenty-nine mothers and 12 fathers had psychiatric treatment history. Nine fathers had a history of criminal offence.

**Conclusion:** The high rate of prenatal problems and high rate of psychopathology in the parents found in this study is striking because the children included in this study had no comorbid conduct disorder or chronic medical disease other than ADHD. So this study is important to highlight the etiology of ADHD and emphasize the importance of preventing smoking during pregnancy and decreasing maternal morbidity.

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**ATTENTION DEFICIT HYPERACTIVITY DISORDER AT SCHOOLS IN SFAX, TUNISIA.**

**Khemakhem K, Ayadi H, Cherif L, et al.**

**Introduction:** Attention deficit hyperactivity disorder (ADHD) is the most common neurobehavioral disorder among school children. It may persist into adulthood and affect performance in the academic, social and familial spheres. The prevalence rate is a controversial matter.

**Objective:** The aim of this research was to determinate the prevalence of ADHD and its distribution according to subtypes, gender and age in school children from Sfax, Tunisia.

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Klin Psikofarmakol Bul. 2013;23:S89-S90.

**TREATMENT OF CHILDREN WITH AUTISM SPECTRUM DISORDERS AND CO-EXISTING ATTENTION DEFICIT HYPERACTIVITY DISORDER, WITH ATOMOXETINE: A RETROSPECTIVE STUDY.**

**Kilincaslan A, Mutluer T, Pasabeyoglu B, et al.**

**Objective:** The present study examined the effects of atomoxetine (ATX) on attention deficit/hyperactivity disorder (ADHD) symptoms and autistic features in children with autistic spectrum disorders (ASD).

**Method:** The files of children with confirmed ASD and ADHD, who had been on ATX treatment, were examined. Forty-two individuals (33 males and 9 females, age range 6-17 years, mean: 10.0)±3.5) were selected. Thirty-three of the children have already been taking other psychotropic medications, which were not changed during the ATX treatment. All patient files provided information about severity of symptoms, improvement in clinical features and observed side effects using the Clinical Global Impressions-improvement scale (CGI-I), DSM-IV based ADHD rating scale (ADHDRS-IV), Aberrant Behavior Checklist and Barkley Stimulant Side Effect Rating Scales at baseline, in week 4 and week 12. Autistic symptoms were rated via the Childhood Autism Rating Scale. ATX was started with a dose of 0.3-0.5 mg/kg/ day, titrated slowly to 1-1.2 mg/kg/day in 4 weeks, and the dose was adjusted to 1-1.4 mg/kg/day according to clinical opinion.

**Results:** ATX was well tolerated with the exception of 6 patients (14%), who stopped medication after the 4th week visit. Among these subjects efficacy data were treated by using the last observation carried forward model. Twenty-two subjects (52.4%) were considered responders to treatment with a CGI-improvement of null/very much improved/null or null/much improved/null. On the parent rated ADHDRS-IV, there was significant reduction from baseline to week 4 and from week 4 to week 12 in inattention, hyperactivity and impulsivity. Fifty percent, 42.9% and 50% of the patients showed  $\geq 25\%$  improvement in inattention, hyperactivity and impulsivity by week 12, respectively. Decrease was significant in the hyperactivity and social withdrawal subscales of the parent reported ABC and 52.4% and 45.2% of the patients showed  $\geq 25\%$  improvement, respectively. No significant change was reported for stereotypic, self-mutilative and other problem behaviours. Responders (n=22) were not significantly different from non-responders (n=20) in terms of age, gender, ASD type, intellectual and language level, baseline CGI severity, level of autistic symptoms and presence of epilepsy. The most common side effects were irritability, decrease in appetite, drowsiness, sleep problems, moodiness. Six patients stopped taking medications due to lack of efficacy, increased motor activity and talkativeness, irritability, temper outbursts and increased blood pressure.

**Conclusions:** ATX appears to be safe and effective for the core symptoms of ADHD as well as withdrawal in children with ASD. None of those clinical and demographic parameters helped to predict the responders in our sample.

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Klin Psikofarmakol Bul. 2013;23:S148.

**AGITATION ASSOCIATED WITH METHYLPHENIDATE IN A CHILD: A CASE REPORT.**

**Sogutlu L, Karacetin G.**

Agitation is a severe anxiety associated with motor restlessness. This physical and mental motor overactivity is usually nonproductive and is associated with a feeling of inner turmoil. Stimulants are the first choice in the treatment of attention deficit hyperactivity disorder (ADHD). In this report, a case of a 12 years



old boy who developed acute psychomotor agitation and irritability with methylphenidate 27mg/day (0.5mg/kg) treatment for ADHD is presented. According to our knowledge, this is the first report of psychomotor agitation related to methylphenidate use in the literature (except overdose).

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Klin Psikofarmakol Bul. 2013;23:S32-S33.

**ADHD: PERSPECTIVE FROM IMPULSE.**

***Karahmet E.***

Attention-deficit/hyperactivity disorder (ADHD) is characterized by impulsive behavior, increased behavioral problems, social adaptation problems. Impulsivity, broadly defined as action without foresight, is a component of numerous psychiatric illnesses. Both the attentional and impulse control deficits can be illustrated by ADHD patients performance of the CPT. ADHD subjects make more errors of omission indicative of poor attentional ability. ADHD subjects have slower and more variable reaction times, and make more errors of omission indicative of poor attentional ability and similarly fail to cancel their null go null response on the null no-go null trials in go/no-go task. Furthermore, it has also been reported that ADHD children make more errors of commission on a choice reaction time version of the task (i.e. choose the wrong response on the go trials), and omit more trials (i.e. do not respond at all). ADHD patients also choose more impulsively in delay-discounting tasks, preferring the smaller but more immediate rewards to the larger more delayed rewards. However, if the selection of a smaller immediate reward does not reduce the total length of the time the subject spends engaged in the experimental task, it has been reported that ADHD patients are able to wait for rewards. It has been suggested that this pattern of impulsive choice is indicative of enhanced motivation to escape or avoid delay, and that the inattentive, overactive and impulsive behaviors in which ADHD patients engage are functional expressions of delay-aversion. Inhibition controlled the weakness and increased impulsive choices are core symptoms of ADHD.

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Klin Psikofarmakol Bul. 2013;23:S50-S51.

**FRONTIERS BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND BIPOLAR DISORDER.**

***Pekcanlar-Akay A.***

This presentation aimed to describe and discuss the comorbidity between pediatric bipolar disorder (BD) and attention deficit hyperactivity disorder (ADHD) and difficulties in management in terms of discrimination. These two conditions would be distinct and unrelated; these conditions may be manifestations of the same disorder. There may be a complex relationship between these two extremes. ADHD comorbidity has become a popular discussion topic in academic circles and many journals for children and youths with BD. Studies report presence of comorbid ADHD in as much as 98% of children with BD. Irritability is a common and disabling symptom in pediatric BD, and the presence of irritability and motor disinhibition in both pediatric BD and ADHD has been one cause of the diagnostic confusion between these two illnesses. A discussion of how none overlapping with ADHD Diagnostic and Statistical Manual of Mental Disorders (4th ed.) mania symptoms can be useful in the differential diagnosis of irritability is also provided. Five symptoms (i.e., elation, grandiosity, flight of ideas/racing thoughts, decreased need for sleep, and hypersexuality) provided the best discrimination of BD subjects from ADHD. Irritability, hyperactivity, accelerated speech, and distractibility were very frequent in both BD and ADHD groups and therefore were not useful for differential diagnosis. High levels of irritability and aggression, along with presence of high levels of mania non-specific mood dysregulations, are reported by numerous studies to be a result of presence of comorbid ADHD. This supports the notion that there may be a subtype of BD/ADHD disorder which presents in early childhood and which has BD features different to those of classical adult onset BD. ADHD has become the biggest focus in the controversy about whether hyperactive, inattentive, emotionally labile children are really manic or really 'just ADHD'. However, the history of 'the hyperactive child' syndrome reveals that it was initially designated with emotional lability, sleep disturbance, and variation in behavior. In conclusion; recent studies showing substantial comorbidity between ADHD and Bipolar Disorder in childhood are consistent. Comorbid ADHD and Bipolar Disorder may be a separate subtype of ADHD or Bipolar Disorder, similar to the situation with hyperkinetic conduct

disorder which is recognized as a subtype of hyperkinetic disorders within ICD 10. The similarity between symptoms of ADHD and Bipolar Disorder supports the notion of a relationship between the symptoms. However, it is also possible that it is simply an artifact of the diagnostic systems.

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**FRONTAL LOBE SYNDROME OR ATTENTION DEFICIT HYPERACTIVITY DISORDER? DIAGNOSIS OF IMPULSIVITY AND HYPERACTIVITY SYMPTOMS AFTER TRAUMATIC BRAIN INJURY AND ITS TREATMENT.**

**Gurbuz HGA, Poyraz BC.**

We present a case that was brought by parents after the brain damage and we aimed to present the path we followed during the treatment. A 22-year-old male had a car accident that caused multiple brain damage and compelled him to stay in an intensive care unit. In his history, he was taken to child and adolescent psychiatry clinic and was diagnosed by attention deficit hyperactivity disorder (ADHD) due to his hyperactivity, risky behavior, difficulty in attention and concentration. After six years of methylphenidate treatment, the patient's symptoms had decreased and the family considered him as nullnormalnull. However his parents stated that the patient had regressed to his childhood state after the accident. After traumatic brain injury, several cognitive and behavioral damages can occur. The great majority of individuals with a mild injury report cognitive, somatic and emotional problems. Although the majority of individuals report improvement after several weeks of the injury, some individuals may have persistent symptoms that could be attributed to the injury. The pharmacotherapy for treating psychiatric symptoms after brain injury has not been defined clearly. Aripiprazole, a new generation antipsychotic, is a promising alternative for the treatment of conduct problems and mood instabilities, with its cognitive recovery effect.

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Klin Psikofarmakol Bul. 2013;23:S82.

**THE RELATIONS BETWEEN VITAMIN B12, FOLATE AND FERRITIN LEVELS AND CLINICAL FEATURES OF TURKISH CHILDREN AND ADOLESCENTS WITH ADHD AND ADHD-NOS: A PRELIMINARY STUDY.**

**Demir N, Topal Z, Tufan E.**

**Objective:** It is thought that some psychiatric symptoms may have a relevance with the importance of roles played by vitamin B12 and folate in carbon transfer metabolism (i.e. methylation), required for production of serotonin, dopamine, other monoamine neurotransmitters and catecholamines. Also, methylenetetrahydrofolate reductase (MTHFR) is thought to act directly on dopamine neurons to prevent oxidative damage. Dopamine, itself stimulates methylation of phospholipids in the neuronal membrane and this reaction depends on single carbon folate pathway, thereby underlining the importance of the relationship between dopaminergic neurotransmission and single carbon metabolism. Basal ganglia may especially be vulnerable to deficiencies of vitamin B12 as well as folates and those structures are thought to play a role in Attention-Deficit/Hyperactivity Disorder (ADHD).

**Methods:** This cross-sectional, retrospective study was conducted at the outpatient clinics of Child and Adolescent Psychiatry in the Faculty of Medicine of Abant İzzet Baysal University.. The records of 6074 patients who applied to the study center in between January 2012 and January 2013 were screened for their presenting complaints and those applying for nullinattentionnull and nullhyperactivitynull were recorded. It was found that 332 patients were referred for those two complaints and with initial diagnosis of ADHD or ADHD-NOS. To be eligible for ADHD or ADHD-NOS, the patients should be diagnosed with semi-structured interviews. MR should be ruled out with Wechsler Intelligence Scale for Children (Revised) or clinical interviews. Patients who were diagnosed in interview to have ADHD according to DSM-IV-TR criteria formed the ADHD group. The ADHD-NOS group was consisting of children and adolescents, who fulfilled ADHD criteria according to symptom counts and dysfunction while reporting an age of onset of 7 or more years or those who did not fulfill the DSM-IV-TR criteria.

**Results:** It was found that patients diagnosed to have ADHD and ADHD-NOS predisposed to differ in terms of age and TSH concentrations (both being lower in ADHD-NOS), although the differences did not reach significance. In the second step of the analyses, it was found that among the whole sample, IBC correlated negatively with baseline scores on the Turgay-DSM-IV-Based Scale for Disruptive Behavior

Disorders (Rho=- 0.59, p=0.03) while Folate levels leaned to correlate negatively with baseline scores on Child Depression Inventory (Rho= -0.43, p=0.06) although not reaching significance. Interestingly, baseline folate levels correlated positively with scores on Scale for Anxiety and Related Disorders (Rho=0.44, p=0.03).

**Conclusion:** Subtle abnormalities of folate, Vitamin B12 and iron metabolism may correlate with clinical features both among patients with ADHD and ADHD-NOS. Our results should be supported with future studies

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Klin Psikofarmakol Bul. 2013;23:S157.

**THE RELATIONSHIP BETWEEN TRAUMATIC ORTHOPEDIC INJURIES AND ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS IN CHILDREN.**

**Gokcen C, Isik M, Karayagmurlu A, et al.**

**Objective:** Traumatic injury is one of the significant causes of orthopedics outpatient clinic visits in children. Attention deficit hyperactivity disorder (ADHD) has been identified as a potential risk factor that may have contributed to the incidence of unintentional injuries. The aim of this study was to evaluate the relationship between traumatic orthopedic injuries and prevalence of ADHD symptoms in children.

**Methods:** A prospective study was conducted between September 2012 and June 2013. Ninety two pediatric patients were admitted to orthopedic outpatient clinic of a university hospital. Patients aged 4-18 years were included in the study group. Control group consisted of sixty children who were similar to patient group by age and gender. The Conner Parent Rating Scale (CPRS) and Turgay's DSM-IV based ADHD and disruptive behavior disorders screening scale (T-DSM-IV-Scale) were used to investigate ADHD symptoms.

**Results:** Both CPRS and T-DSM-IV-Scale impulsivity/hyperactivity subscale scores were significantly higher in the study group than the controls ( $p < 0.05$ ). Furthermore, the analysis held within the study group showed that all the subscale scores of both scales in the subgroup with history of repetitive injuries were significantly higher than the subgroup without history of repetitive injuries ( $p < 0.05$ ).

**Conclusions:** In this study, the ADHD symptoms were higher in patients, who admitted to orthopedics outpatient clinic for traumatic injuries. For this reason, psychiatric evaluation of patients, who were admitted to clinics with similar injuries especially to those, who has history of repetitive injuries should be made to consider ADHD.

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Klin Psikofarmakol Bul. 2013;23:S34-S35.

**FROM THE PERSPECTIVE OF IMPULSE CONTROL DISORDERS: ADULT ADHD AND COMORBIDITIES.**

**Tatar ZB.**

This presentation shall discuss on the concept of impulsivity in Attention Deficit Hyperactivity Disorder (ADHD), neurobiology of impulsivity in ADHD and disorders significant for differential diagnosis and comorbidity in adult ADHD due to the impulsivity symptom. A literature review shall be made in light of the concepts of impulsivity and impulse control disorder, impulsivity in and neurobiology of adult ADHD, differential diagnosis and comorbidity with other psychiatric disorders with impulsivity symptoms. ADHD is a chronic, developmental psychiatric disorder which begins in early childhood, with continuing basic symptoms of which are inattention, hyperactivity and impulsivity, throughout adulthood as well. In DSM-V, 18 symptoms are listed for attention deficit and hyperactivity/impulsivity areas just as in DSM-IV, and meeting of minimum six symptoms in one area is required for an ADHD diagnosis. Among these symptoms, those stating as nullUsually replies before the question is completednull, nullUsually experiences difficulty as to waiting for his/her turnnull and nullUsually interrupts other people's speeches or interferes in what they are doingnull point out to impulsivity symptoms. There are 3 subtypes of ADHD: predominantly Inattentive, predominantly Hyperactive-Impulsive, or the two Combined. Combined subtype is the most frequently observed during childhood, where hyperactivity and impulsivity symptoms are reported to be significantly decreased compared to attention deficit during adolescence and young adulthood. Executive functions such as sustaining concentration and attention, perseveration, resistance to

interfering impacts, ability to change categories, sustaining goal oriented behavior, ability to suppress/inhibit the tendency to react which is inconvenient for the moment are known to be impaired in children and adults with ADHD as compared to the healthy population. Executive function disorders lead to impulsive behavior and indifferent attitudes lacking empathy. Executive functions are defined as the functions of frontal area. Dorsolateral prefrontal cortex (DLPFC) is responsible for attention, working memory, planning, organization of a task, functions related to processing new information, whereas orbitofrontal cortex (OFC) ensures regulation of emotional stimuli and inhibitor control. In DLPFC, the damage leads to apathy, lack of motivation, disinterest, insufficiency in planning and behavioral flexibility, where in OFC, it leads to symptoms such as socially inappropriate behavior, increase in motor activities, being inconsiderate to others, being affected by environmental stimulants and removal of sexual inhibition. In many cases where orbitofrontal lesions are involved, impulsive and antisocial behaviors are observed. It has been reported that OFC dysfunction can exist in predominantly hyperactive-impulsive subtype of ADHD, and DLPFC dysfunction in predominantly inattentive subtype of ADHD. Although impulsiveness can be observed in anybody, whether a DSM-V axis I or II diagnosis exists, it is likely to be more frequently observed in people associated with specific psychiatric diagnosis such as ADHD, substance addiction, personality disorders, etc. The relation between these disorders and impulsivity can be related with behavioral inhibition deficit, which is partially a part of the foregoing disorders. Impulsivity can be described as a process including a rapid action without a conscious judgment, acting without adequate consideration and a tendency to act with less common sense despite the existence of a normal intelligence level. Impulse control disorder is a class of psychiatric disorders characterized by impulsivity - failure to resist a temptation, urge or impulse that may harm oneself or others. ADHD differential diagnosis together with bipolar disorder, substance abuse, behavioral addictions, cluster B personality disorders, where impulsivity appears as a symptom, as well as impulse control disorder is significant. Comorbid cases with these disorders can lead to overlook an ADHD diagnosis. Lifetime expansion of bipolar disorder type II & I have been found to be 10% in people in both genders who has an adult ADHD. Bipolar disorder and ADHD can demonstrate similar symptoms such as hyperactivity, inattention, emotional lability, impulsivity etc. Symptoms such as excessive spending, deliriums and other psychotic symptoms, grandiosity, acceleration in thinking and decrease in sleep need assist differentiation of mania or hypomania cases from ADHD. There exist evidence as to increase of borderline personality disorders in adults with ADHD and existence of ADHD as a co-diagnosis in the subgroup of people with borderline personality disorder. Borderline personality disorder is characterized with impulsivity, mood lability and hostility such as in ADHD, however, these symptoms are episodic, shorter and less serious in persons with ADHD. Moreover, ADHD is not characterized with dichotomic thoughts, fears of abandonment and self mutilating behavior as in borderline personality disorder. Anti-social personality disorder can be seen with a frequency of 10-23%. Hyperactive-impulsive and combined ADHD types can be associated with aggression, committing crimes, being opponent-opposing, and anti social behavior. Antisocial personality disorder shares the impulsivity and effective liability symptoms with ADHD. Behaviors observed in antisocial personality disorder such as a history of arrest, lack of empathy and lack of prick of conscience might be of help to distinguish between the two disorders. ADHD double folds substance addiction risks compared to society in general. Co-diagnosis of substance addiction in ADHD is 40-50% whereas co-diagnosis of ADHD in substance addicts remains at 15-25% level. Higher ADHD symptoms have been detected in adolescents with internet addiction. There are studies available showing associations between pathological gambling and childhood ADHD symptoms as well as adult ADHD symptoms. In such a study, an ADHD history was found in 25% of people who have pathological gambling and at-risk gambling and people with an ADHD history have more serious gambling problems, higher level of gambling-related cognitions, more frequent psychiatric comorbidity and increased suicide risks. It was shown that higher impulsivity proposes a risk factor for ADHD comorbidity. Higher ADHD symptoms were reported in people with compulsive buying disorder as compared to control group. Frequent association with other psychiatric disorders might lead to overlook ADHD. Being aware of the comorbid conditions with psychiatric disorders with which it shares similar symptoms such as impulsivity and differential diagnosis against these disorders are significant factors for efficient treatment of these so called disorders.

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Klin Psikofarmakol Bul. 2013;23:S72.

**INVESTIGATION OF IRON DEFICIENCY, THYROID FUNCTION ABNORMALITIES AND DEFICIENCY OF FOLATE AND VITAMIN B12 IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Torun YT, Taner YI, Sener S, et al.**

**Objective:** Attention deficit hyperactivity disorder (ADHD) is a commonly diagnosed psychiatric disorder in the childhood and it has been suggested that both environmental and genetic factors take place in the etiology. Therefore, it is important to determine metabolic and endocrine abnormalities that accompanies with ADHD in order to understand the pathophysiology of ADHD and in order to develop new treatment strategies. The aims of this study were to evaluate serum TSH, vitamin B12, folate abnormalities and iron deficiency in children with ADHD and investigate the association between iron deficiency and subtypes of ADHD.

**Methods:** Patients who applied to Gazi University Medicine Faculty Child and Adolescent Psychiatry Out-Patient Clinic diagnosed with ADHD as per DSM-IV-TR diagnoses criteria between time period May 2012-Feb 2013 were involved in this study. Records and laboratory results of patients were retrospectively collected and evaluated.

**Results:** This study included 199 children age between of 6-16 years (mean age 9.43)±2.2) with ADHD whose 87.2% were boys (n=174) and 12.6% of children (n=25) were girls. 80.9% of children (n=161) were combined type ADHD while 19.1% of children (n=38) were predominantly inattentive type. 52.8% of children (n=105) had iron deficiency while 2.5% of children (n=5) had subclinical hypothyroidism and 3% of children (n=6) had vitamin B12 deficiency. It was determined that 59% of children with combined type ADHD had iron deficiency while in children with predominantly inattentive type rate was 26.3%. There was statistically significant relation between iron deficiency and subtypes of ADHD ( $p<0.001$ ).

**Conclusion:** Iron deficiency and thyroid function abnormalities which are known to have important roles on neurocognitive functions are frequently accompanies with ADHD in childhood. In addition, accompanying iron deficiency affects the clinical status of the ADHD. In recent literature several studies published about the relationship between iron deficiency and subtypes of ADHD but results are inconsistent. According to results of this study, iron deficiency is more frequent in children with combined type ADHD with respect to predominantly inattentive type; it is suggested that iron metabolism considered to have more important effects on symptoms related with hyperactivity and impulsivity.

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Klin Psikofarmakol Bul. 2013;23:S106.

**AUTISTIC SPECTRUM SYMPTOMS IN SUBTYPES OF ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Ayaz AB, Imren SG, Gumustas F, et al.**

**Objective:** Some children suffering attention deficit/hyperactivity disorder (ADHD) have similar social interaction and communication problems as those diagnosed to have autistic spectrum disorders (ASDs). This study aimed to compare autism spectrum symptoms in children according to ADHD subtypes and children without ADHD.

**Method:** ADHD and comorbid diagnoses were made using the Schedule for Affective Disorders and Schizophrenia for School-Age Children. The Social Responsiveness Scale (SRS), Childhood Behavior Checklist (CBCL), and ADHD Rating Scale (ADHD-RS) were used to evaluate symptoms.

**Results:** This study included 387 children: 238 in the ADHD group and 149 in the control group. Among those in the ADHD group, 28.6% were diagnosed to have ADHD inattentive subtype, 13.0% to be ADHD hyperactive/impulsive subtype, and 58.4% ADHD combined subtype. All the ADHD patients had higher SRS total and subscale scores than the control group ( $p<0.001$ ). The SRS total and the social subscale scores were higher in the ADHD combined subtype than in the ADHD H/I subtype ( $p<0.05$ ). After controlling for age, gender, and CBCL social withdrawal score, the difference in autism spectrum symptoms between the three ADHD subtypes was not significant. Assessment of the relationship between the ADHD-RS subscale scores and the SRS total and subscale scores based on Pearson's correlation analysis showed that there was not a significant correlation between ADHD-RS subscale scores and any SRS score in any of the three ADHD subtypes.

**Conclusion:** The present study's findings show that social withdrawal symptoms in those with ADHD might have effects on ASSs. However, no significant differences were found in ASSs between the ADHD

subtypes when this effect was removed, all ADHD subtypes had a similar risk of ASSs, and ASSs might be accompanied by ADHD regardless of the symptoms of ADHD. To our own clinical experience, children with a combination of ADHD symptoms and ASSs are generally much more difficult to treat than children with ADHD alone. The present findings indicate the importance of evaluating ASSs, planning, and implementing treatment modalities such as early social skill training and interpersonal psychotherapy oriented for ASSs regardless of ADHD subtypes in all children with ADHD.

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Klin Psikofarmakol Bul. 2013;23:S19-S20.

**THE IMPORTANCE OF THERAPEUTIC DRUG MONITORING IN CHILD AND ADOLESCENT PSYCHIATRY.**

**Yorbik O.**

**Objective:** Drug treatment of children and adolescent is disadvantaged by lack of evidenced based efficacy and safety for many indications. For that reason, many psychoactive drugs in children and adolescent are not approved for use until now. Because pharmacokinetics and pharmacodynamics properties of children and adolescent are different from adults, and these properties change during development, therapeutic drug monitoring (TDM) is recommended in these groups. However, there is still lack of sufficient studies to illustrate age and indication specific therapeutic ranges of serum or plasma concentrations in these groups. The aim of this study is to investigate relationship between doses of various psychoactive drugs and plasma concentrations in children and adolescents with attention deficit hyperactivity disorder ADHD, and to review TDM in the literature.

**Materials and Methods:** The literature on TDM in children and adolescent with psychiatric disorders was reviewed. The study group was consisted of children and adolescents with ADHD. Plasma methylphenidate and other psychoactive drug concentrations of children and adolescents with ADHD were determined by using high-pressure liquid chromatography coupled to mass spectrometry (LC-MS/MS). The relationship between drug dose and plasma drug concentration of children and adolescents was determined by using Pearson correlation test. The effect of other drugs on methylphenidate plasma level was also tested. In addition, the effect of age, sex, and body mass index on plasma concentration of drugs at usual therapeutic doses was investigated.

**Results:** TDM may be a valuable tool for qualification of serum or plasma concentrations of drugs for optimal dose, and to illustrate uncertain drug adherence, non-response at therapeutic doses, tolerability problems, and drug-drug interactions. Because drug treatments of psychiatric disorders take a long time, TDM may ensure lower risk for toxicity and cost effective treatment. According to Arbeitsgemeinschaft für Neuropsychopharmakologie und Pharmakopsychiatrie (AGNP) Consensus Guidelines, TDM is strongly recommended for the typical antipsychotics (e.g. haloperidol, perphenazine and fluphenazine), atypical antipsychotics (e.g. amisulpride, clozapine, olanzapine, and risperidone), mood stabilizing or antimanic drugs (e.g. lithium, valproic acid, and carbamazepine), and most tricyclic antidepressants. Typical indications for measuring plasma concentrations of psychoactive drugs may include dose optimization after initial prescription or after dose change, drugs that TDM is mandatory for safety reasons (e.g. lithium), suspected complete or partial non-adherence (non-compliance) to medication, lack of clinical improvement under recommended doses, adverse effects and clinical improvement under recommended doses, combination treatment with a drug known for its interaction potential or suspected drug interaction, relapse prevention under maintenance treatment, recurrence under adequate doses, presence of a genetic particularity concerning drug metabolism (genetic deficiency, gene multiplication), pregnant or breast feeding patients, children and adolescents patients, elderly patients, individuals with intellectual disabilities, patients with pharmacokinetically relevant comorbidities (hepatic or renal insufficiency, cardiovascular disease), forensic patients, problems occurring after switching from an original preparation to a generic form (and vice versa), and TDM in pharmacovigilance programs (Hiemke et al 2011).

**Conclusions:** Limited studies are investigated relationship between clinical doses and plasma levels of psychoactive drugs in children and adolescents with psychiatric disorders. More studies are needed to use evidence based usage of TDM in children and adolescents with psychiatric disorders.

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Klin Psikofarmakol Bul. 2013;23:S183-S184.

**IS IT ADHD OR BIPOLAR DISORDERS? A CASE REPORT.**

**Aydemir H, Oztop DB, Uytun MC, et al.**

Bipolar disorder (BD) is a relatively rare disease in childhood and adolescence. There is increasing recognition about bipolar disorder in childhood and adolescence because of poor therapeutic outcome and serious disruption of the development and emotional growth of the youth. The prevalence of bipolar disorder in prepubertal children has not been explored, however the prevalence in adolescence has been estimated to be approximately 1%. Bipolar disorder symptoms in children differ from symptoms in late adolescence and adulthood and this situation makes the diagnosis of BD complicated. The symptom overlap between ADHD and BD can create diagnostic problems and associate with poor prognosis. Early-onset bipolar disorder is a serious psychiatric disorder associated with social and academic difficulties, family dysfunctioning, relational difficulties with peers and suicidality. We have presented this case that we have considered to be early-onset bipolar disorder with ADHD. A 13-year-old male patient, with 7 years old symptoms such as, irritability, hyperactivity, inattendance to his school went under psychiatric examination and psychological testing and was diagnosed to have ADHD and mild mental retardation. Atomoxetine and risperidone treatment were prescribed. Then, the patient reported hearing of a sound, chuckles, delusions. These symptoms were associating with psychotic process. The patient was observed to have a constant religious ritual compulsion and talkativeness. Atypical Affective Disorder and Bipolar Affective Disorder were concluded and Sodium Valproate treatment was started. Patient's symptoms partially reduced. It is rather difficult to identify BD in childhood and early adolescence. It is proposed that the reason of this difficulty is that BD is defined as non-cyclic or excessively rapid-cycling in this period and that it has common symptoms with ADHD like hyperactivity, distractibility or short duration of attention. The ADHD diagnosis made in our patients seems to be confirmatory for the difficulty in differential diagnosis of both disorders. All these opinions raise the debate whether the symptoms before the age of 7 years are the symptoms-related to ADHD or premising symptoms of bipolar disorder in our patient diagnosed as bipolar affective disorder. It has been proposed that childhood onset mania is a complex, continuous, rapid-cycling affective disorder which progresses with severe uneasiness and aggressive temperament crisis. Anger and uneasiness can be defined as prodromal symptoms in early-onset bipolar disorder. In our case, the main complaints were anger and aggressive temperament features when the parents presented to our clinic. Carlson suggested that uneasiness and emotional instability are detected in manic children younger than 9 years of age, while paranoia and grandiose delusions, euphoria and emotional surges in manic children older than 9 years of age. In fact, our patient also had grandiose delusion and paranoia. Bipolar affective disorder before puberty comprises an atypical clinical manifestation that progresses with short mania episodes as well as behavior and impulse control problems. The schizophrenia-like symptomatology should not mislead clinician and correct diagnosis should be made based on either personal or family history.

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Klin Psikofarmakol Bul. 2013;23:S179.

**EVALUATION OF THE EFFECTS OF TREATMENT OF ADHD ON IMPAIRMENT OF FUNCTIONING.**

**Gundogdu OY, Memik NC, Tarakcioglu MC, et al.**

**Objective:** Attention deficit hyperactivity disorder (ADHD) is one of the neurobehavioral disorders that begins in early childhood and adversely affect the functions of daily life in many ways . Symptoms and functional decline created by ADHD are interrelated but different. In diagnosis and treatment it is recommended to evaluate the functional impairments as well as symptoms. . In follow-up studies of ADHD treatment, the scales that measure symptom severity and number generally evaluate treatment response rates, but the scales, which measure functional impairment, have not been used yet. In this study, it is aimed to evaluate the level of functional impairment in children and adolescents with diagnosed ADHD by using Weiss Functional Impairment Rating Scale - Parent Report (WFIRS-P) after a one-year treatment and follow-up and to investigate the factors, which play role in improvement of functional impairments.

**Method:** Two hundred and forty-nine children and adolescents from 1st to 8th classes, who applied to the clinic between September 2011 and June 2012, were recruited.. Those patients were diagnosed for the first time as ADHD by Clinical interview based on DSM-IV criteria and the Schedule for Affective Disorders and Schizophrenia for School Age Children Present and Lifetime Version-Turkish Version (SADS-PL-T).

Sociodemographic characteristics were evaluated by using a sociodemographic questionnaire that was prepared by the researchers. WFIRS-P and the clinical global impression scale (CGI) were administered to the parents. By the end of one year follow-up 54 children and adolescents, who were regular on interviews and drug treatment were identified. Those children and adolescents were evaluated again with WFIRS-P and CGI applied by researchers. Rates of improvement in functional impairments, treatment options playing role in improvement and demographic characteristics are compared with the initial data by using statistical methods.

**Results:** Between regularly followed up 54 children and 195 children who were not regular, there were no significant difference found in terms of age, gender, in WFIRS-P and CGI total and subscale scores. Children's that were followed up regularly had subtype distribution of diagnosis as %87 combined, %11 attention deficit, %1,9 hyperactive impulsive type. %74 of children who did not continue to follow up were found to be combined, %17,9 attention deficit, %7,2 hyperactive impulsive type. 75.9% of children who continued to follow up were given psychostimulant (14.8% of atomoxetine, 9.3% of psychostimulant + atomoxetine) treatment. CGI average scores, WFIRS-P family, school, life skills and social interaction and the total score's average in children who continued to follow up revealed a statistically significant improvement from baseline. Among the subtypes of ADHD there was no significant difference found in terms of improvement in CGI and WFIRS-P scores. In the same way, drugs groups in terms of improvement in CGI and WFIRS-P scores were not significantly different.

**Conclusion:** Regular monitoring in ADHD with versatile treatment programs provides a significant improvement in symptom severity as well as functioning. In addition to the symptoms of the ADHD, diagnosis and treatment of the ADHD, the evaluation of the functional impairment and quality of life concepts is thought to be important in dealing with ADHD as a whole.

Med Hypotheses. 2014;82:111-16.

**ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) AS A PYRIDOXINE-DEPENDENT CONDITION: URINARY DIAGNOSTIC BIOMARKERS.**

**Dolina S, Margalit D, Malitsky S, et al.**

The data obtained in children with different forms of epilepsy allowed us to consider epilepsy as an inborn error of pyridoxine (vitamin B6) metabolism (Dolina et al., 2012). Mutual interconnections between ADHD and epilepsy indicate that such an approach is reasonable for ADHD. To check such an assumption we analyzed in ADHD patients the same parameters of pyridoxal phosphate (PLP)-dependent tryptophan (TRP) degradation, which were analyzed in epileptic children. The level of TRP and concentrations of compounds formed or metabolized by TRP degradation, the ratios between some of them, and the level of 4-pyridoxic acid were HPLC detected in ADHD children and healthy controls. The data obtained, including low values of 4PA/TRP, IND/TRP and IND/KYN ratios, have evidenced dramatically impaired activity of pyridoxine-dependent enzymes in ADHD patients. Ritalin treatment did not change the general pattern of TRP degradation, but still created a kind of balance between some of detected metabolites. However, the 4PA/TRP, IND/TRP and IND/KYN ratios remained as low as in untreated patients, keeping the importance of diagnostic markers. Almost identical parameters of TRP degradation in untreated ADHD and epileptic patients allow to assume that inborn disorders of vitamin B6 metabolism are the common biochemical background of both diseases. The disturbed activity of PLP dependent enzymes apparently forms those profound disturbances of neurotransmitter systems, which are inherent in ADHD: low concentrations of monoamines and disordered amino acid metabolism. If vitamin B6 disorders are the core biochemical disturbances inherent in ADHD, then the long-term pyridoxine treatment is pathogenetically based replacement therapy of the disease. According to our data, multi-year pyridoxine treatment normalizes completely the pattern of ADHD behavior, without causing any serious side effects.



Neuropsychiatr Dis Treat. 2013;9:1791-99.

**PSYCHIATRIC COMORBIDITY DISTRIBUTION AND DIVERSITIES IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A STUDY FROM TURKEY.**

**Yucwe M, Zoroglu SS, Ceylan MF, et al.**

**Objective:** We aimed to determine distribution and diversities of psychiatric comorbidities in children and adolescents with attention deficit/hyperactivity disorder (ADHD) in terms of age groups, sex, and ADHD subtype.

**Materials and methods:** The sample included 6-18 year old children and adolescents from Turkey (N=108; 83 boys, 25 girls) diagnosed with ADHD. All comorbid diagnoses were determined based on the Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime Version assessment.

**Results:** 96.3% of the cases were found to have at least one psychiatric comorbid diagnosis. The most frequent psychiatric comorbid disorder was oppositional defiant disorder (69.4%) followed by anxiety disorders (49%) and elimination disorders (27.8%). Disruptive behavior disorders were more common in ADHD-combined type. Depression and anxiety disorders were more common in girls. Separation anxiety disorder and elimination disorder were more common in children, whereas depression, bipolar disorder, obsessive-compulsive disorder, and social phobia were more common in the adolescents.

**Conclusion:** According to our results, when a diagnostic tool was used to assess the presence of comorbid psychiatric disorders in children and adolescents diagnosed with ADHD, almost all cases had at least one comorbid diagnosis. Therefore, especially in the clinical sample, ADHD cases should not be solely interpreted with ADHD symptom domains, instead they should be investigated properly in terms of accompanying psychiatric disorders.

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Neuropsychiatr Dis Treat. 2014;10:1-12.

**ANALYSIS OF INDIVIDUAL ITEMS ON THE ATTENTION DEFICIT/HYPERACTIVITY DISORDER SYMPTOM RATING SCALE IN CHILDREN AND ADULTS: THE EFFECTS OF AGE AND SEX IN PIVOTAL TRIALS OF LISDEXAMFETAMINE DIMESYLATE.**

**Weisler RH, Adler LA, Kollins SH, et al.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) symptom presentation across age and sex has not been fully elucidated. The present post hoc analyses qualitatively explored the baseline levels of ADHD symptomatology across subgroups in two clinical trials of children and adults with ADHD to elucidate differences in participant presentation. The response to treatment was examined to determine patterns of response among items of the ADHD Rating Scale IV.

**Methods:** Exploratory post hoc analyses of ADHD Rating Scale IV item scores were conducted on data from two 4-week placebo-controlled trials in children (6-12 years) and in adults (18-55 years) with ADHD. Baseline and endpoint mean item scores were determined for subgroups defined by age (6-9, 10-12, 18-39, and 40-55 years) and sex.

**Results:** The baseline mean item scores were generally numerically similar for all age-by-sex subgroups. The inattention (IA) items were numerically higher than hyperactivity/impulsivity (H/I) items among older children and adults. The endpoint mean item scores were numerically lower after lisdexamfetamine dimesylate treatment for IA and H/I items in all subgroups.

**Conclusion:** These results suggest that regardless of age or sex, baseline IA and H/I symptom profiles were comparable; however, IA vs H/I symptoms were more severe in older participants. In all age-by-sex subgroups, IA and H/I symptoms appeared to decrease after active treatment.

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Neuropsychiatry. 2013;3:587-600.

**PHYSICIAN-REPORTED TREATMENT OUTCOMES FOR ADHD AMONG CHILDREN AND ADOLESCENTS IN EUROPE.**

**Setyawan J, Fridman M, Hodgkins P, et al.**

**Aims:** The aim of this study was to describe associations between physician-reported patient characteristics, treatment modalities and assessed outcomes in children diagnosed with ADHD in six countries.

**Methods:** Clinical records of ADHD patients were retrospectively reviewed by treating physicians. Patients had optimal treatment success (OTS) if the physician assessed them as having complete symptom control and was highly satisfied with treatment.

**Results:** Out of the 708 patients, 505 (71.3%) were treatment adherent. OTS was reported in 28.1% of patients (33.7% adherent and 14.3% nonadherent;  $p < 0.0001$ ). Among adherent patients, there was no association between treatment type and OTS. Multivariate logistic regression models suggest that patients achieving OTS were more likely to have fewer comorbidities and lower reported impairment levels for ADHD-associated symptoms/behaviors.

**Conclusion:** Overall, OTS was low. Among adherent patients, those with more comorbidities/greater ADHD impairment achieved lower OTS. There was no difference between treatment modalities, suggesting that opportunities exist to develop improved ADHD treatments.

Paediatr Perinat Epidemiol. 2013.

**PERFLUOROCTANOATE EXPOSURE IN A HIGHLY EXPOSED COMMUNITY AND PARENT AND TEACHER REPORTS OF BEHAVIOUR IN 6-12-YEAR-OLD CHILDREN.**

**Stein CR, Savitz DA, Bellinger DC.**

**Background:** In toxicology studies, perfluorinated compounds affect fetal growth, development, viability, and postnatal growth. There are limited epidemiologic studies on child development.

**Methods:** We recruited and evaluated 321 children who participated in the C8 Health Project, a 2005-06 survey in a mid-Ohio Valley community highly exposed to perfluorooctanoate (PFOA) through contaminated drinking water. We examined associations between measured childhood PFOA serum concentration and mother and teacher reports of executive function (Behaviour Rating Inventory of Executive Function), attention deficit hyperactivity disorder (ADHD)-like behaviour (Conner's ADHD Diagnostic and Statistical Manual of Mental Disorders IV Scales), and behavioural problems (Behaviour Assessment System for Children) assessed 3 to 4 years later at ages 6-12 years.

**Results:** Overall, neither reports from mothers nor teachers provided clear associations between exposure and child behaviour. Mother reports, however, did suggest favourable associations between exposure and behaviour among boys and adverse associations among girls. On the composite scale from the Behaviour Rating Inventory of Executive Function ( $n=318$ ), PFOA exposure had a favourable association among boys (highest vs. lowest quartile ( $\beta$ )=-6.39; 95% confidence interval [CI] -11.43, -1.35) and an adverse association among girls (highest vs. lowest quartile ( $\beta$ )=4.42; 95% CI -0.03, 8.87; interaction  $P=0.01$ ). Teacher reports ( $n=189$ ) replicated some, but not all of the sex interactions observed in mothers' reports.

**Conclusions:** Aggregate results did not suggest adverse effects of PFOA on behaviour, but sex-specific results raise the possibility of differing patterns by sex. Results are not consistent between mothers' and teachers' reports. Effect modification by sex may warrant further investigation.

Pediatr Pol. 2013.

**SELECTED DETERMINANTS OF CHRONIC FATIGUE IN MOTHERS OF CHILDREN WITH ADHD.**

**Basinska MA, Kielnik J, Grzankowska I.**

**Preface:** Fatigue can be treated as a psychosomatic occurrence. It is felt individually and in varying degrees of intensity. If it takes a chronic form, it is considered as a pathological condition of the body. It is caused by a long-term effort or a significant psychological burden felt by e.g. parents, especially by mothers of children with ADHD.

**Purpose:** The main aim of this study was to examine whether high everyday life fatigue, low resilience and social support determine chronic fatigue in mothers of children with ADHD.

**Material and method:** The group of 41 mothers of children with ADHD and a control group of 39 mothers of healthy children were examined. The Questionnaire Fatigue of Everyday Life (KZZC) by J. Urbanska, Chronic Fatigue Scale (FAS) by H.J. Michielsen et al. and The Scale to Measure of Resilience (SPP-25) by N. Oginska-Bulik and Z. Juczynski were used in the study.

**Results:** The results indicate that high everyday life fatigue and low resilience allow to predict the occurrence of chronic fatigue in mothers of children with ADHD. The study revealed significant differences between mothers of sick children and mothers of healthy children at the level of perceived chronic fatigue; yet showed no differences at the level of everyday life fatigue, except for social fatigue. The smaller the fatigue experienced by the mother, the greater the support received from the relatives.

**Conclusions:** Child's ADHD disorder is in mother's life a heavy burden in everyday functioning, which is associated with the gradual depletion of the body and the possibility of a pathological form of fatigue - chronic fatigue. An element that protects the mother against fatigue is support of people living with the mother and the sick child.

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Pediatrics. 2013;132:e1649-e1658.

**ACETYLCHOLINESTERASE ACTIVITY AND NEURODEVELOPMENT IN BOYS AND GIRLS.**

**Suarez-Lopez JR, Himes JH, Jacobs J, et al.**

**Background:** Organophosphate exposures can affect children's neurodevelopment, possibly due to neurotoxicity induced by acetylcholinesterase (AChE) inhibition, and may affect boys more than girls. We tested the hypothesis that lower AChE activity is associated with lower neurobehavioral development among children living in Ecuadorian floricultural communities.

**Methods:** In 2008, we examined 307 children (age: 4-9 years; 52% male) and quantified AChE activity and neurodevelopment in 5 domains: Attention/executive functioning, language, memory/learning, visuospatial processing, and sensorimotor (NEPSY-II test). Associations were adjusted for demographic and socioeconomic characteristics and height-for-age, flower worker cohabitation, and hemoglobin concentration.

**Results:** Mean (plus or minus) standard deviation AChE activity was 3.14 (plus or minus) 0.49 U/mL (similar for both genders). The range of scores among neurodevelopment subtests was 5.9 to 10.7 U (standard deviation: 2.6-4.9 U). Girls had a greater mean attention/executive functioning domain score than boys. In boys only, there were increased odds ratios of low (<9th percentile) neurodevelopment among those in the lowest tertile versus the highest tertile of AChE activity (odds ratios: Total neurodevelopment: 5.14 [95% confidence interval (CI): 0.84 to 31.48]; attention/executive functioning domain: 4.55 [95% CI: 1.19 to 17.38], memory/learning domain: 6.03 [95% CI: 1.17 to 31.05]) after adjustment for socioeconomic and demographic factors, height-for-age, and hemoglobin. Within these domains, attention, inhibition and long-term memory subtests were most affected.

**Conclusion:** Low AChE activity was associated with deficits in neurodevelopment, particularly in attention, inhibition, and memory in boys but not in girls. These critical cognitive skills affect learning and academic performance. Added precautions regarding secondary occupational pesticide exposure would be prudent.

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Pediatrics. 2013;132:1081-89.

**MEDIA USE AND SLEEP AMONG BOYS WITH AUTISM SPECTRUM DISORDER, ADHD, OR TYPICAL DEVELOPMENT.**

**Engelhardt CR, Mazurek MO, Sohl K.**

**Objective:** The current study examined the relationships between media use (television, computer, and video games) and sleep among boys with autism spectrum disorder (ASD) compared with those with attention deficit/hyperactivity disorder (ADHD) or with typical development (TD).

**Methods:** Participants included parents of boys with ASD (n=49), ADHD (n=38), or TD (n=41) (ages 8-17 years). Questionnaires assessed daily hours of media use, bedroom access to media, and average sleep hours per night.

**Results:** Bedroom media access was associated with less time spent sleeping per night, irrespective of diagnostic group. Bedroom access to a television or a computer was more strongly associated with reduced sleep among boys with ASD compared with boys with ADHD or TD. Multivariate models showed that, in addition to bedroom access, the amount of time spent playing video games was uniquely associated with less sleep among boys with ASD. In the ASD group only, the relationship between bedroom access to video games and reduced sleep was mediated by hours of video game play.

**Conclusions:** The current results suggest that media-related variables may be an important consideration in understanding sleep disturbances in children with ASD. Further research is needed to better characterize the processes by which media use may affect sleep among individuals with ASD. Overall, the current findings suggest that screen-based media time and bedroom media access should be routinely assessed and may be important intervention targets when addressing sleep problems in children with ASD.

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Pediatrics. 2013;132:e1210-e1215.

**ASSOCIATION OF CONSTIPATION AND FECAL INCONTINENCE WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Mckeown C, Hisle-Gorman E, Eide M, et al.**

**Objective:** Functional constipation and fecal incontinence are common childhood gastrointestinal conditions. Both conditions may be associated with behavioral problems. Attention-deficit/hyperactivity disorder (ADHD) is the most common behavioral disorder of childhood, characterized by shortened attention span and hyperactivity. We hypothesize that a diagnosis of ADHD increases the risk for functional constipation and fecal incontinence.

**Methods:** A retrospective cohort study of children was performed by using the military health system database. Children of active-duty military personnel, aged 4 to 12 years, from October 2005 to September 2007, were included. ADHD, constipation, and fecal incontinence were identified by International Classification of Diseases, Ninth Revision, Clinical Modification diagnostic codes. Relative risks and adjusted incidence rate ratios (IRRs) were calculated. A subgroup analysis of subjects receiving medical therapy was performed.

**Results:** There were 742 939 children identified in the study, 32 773 (4.4%) of whom had ADHD. Children with ADHD had an increased prevalence of constipation (4.1% of children with ADHD vs 1.5% children without ADHD;  $P = .001$ ) and fecal incontinence (0.9% of children with ADHD vs 0.15% of children without ADHD;  $P = .0001$ ). Children with ADHD had more visits than those without ADHD for both constipation (IRR 3.39; 95% confidence interval 2.59-4.43) and fecal incontinence (IRR 7.74; 95% confidence interval 5.01-11.98). Children with ADHD receiving medicinal therapy did not differ significantly from children with ADHD not receiving medicinal therapy on rates of constipation visits ( $P = .57$ ) or fecal incontinence visits ( $P = .32$ ).

**Conclusions:** Children with ADHD are significantly more likely to have constipation and fecal incontinence. Medical therapy for ADHD does not impact visit rates for defecation disorders.

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Pharmacoepidemiol Drug Saf. 2013;22:167.

**RELATION BETWEEN THE PREVALENCE OF ATTENTION DEFICIT AND HYPERACTIVITY DISORDERS (ADHD) AND AUTISM SPECTRUM DISORDERS (ASD), AND MATERNAL DEPRESSION AND ANTIDEPRESSANT USE DURING PREGNANCY.**

**Berard A, Sheehy O, Boukris T.**

**Background:** Although the impact of gestational use of antidepressant on children's overall cognitive development remains controversial, a recent study has shown an association between antidepressant use during pregnancy and the risk of ASD. Given that ADHD and ASD are two entities sharing similar features, this finding could potentially have great implications.

**Objectives:** To compare annual trends in the prevalence of maternal depression and antidepressant use during pregnancy, ADHD and ASD over time.

**Methods:** This study was performed within the Quebec Pregnancy Registry which includes data on all pregnancies/ children in Quebec from 1998 to 2009. Women are followed from the date of entry in the Registry (beginning of pregnancy) until the end of pregnancy; children are followed from birth until 12/31/2009. A child was defined as having ADHD or ASD if he had 1 diagnosis made by a psychiatrist or developmental pediatrician, or at least two diagnoses made by other physicians. Maternal depression was identified using validated ICD9/ICD10 codes, and exposure to antidepressants during pregnancy was defined as having filled at least one prescription between the first day and the end of pregnancy.

**Results:** Of 157,802 pregnancies and 159,067 children comprised the study population. Between 1998 and 2009, diagnosed maternal depression during pregnancy significantly increased ( $p = 0.04$ ) from

48.4/1000 pregnancies in 1998 to 54/1000 pregnancies in 2009. Gestational use of antidepressants more than doubled during the same period: 21.8/1000 pregnancies in 1998 to 43/1000 pregnancies in 2009 ( $p=0.01$ ). In parallel, the prevalence of diagnosed ADHD increased from 0.53/1000 livebirths in 1998 to 15.8/1000 livebirths in 2009 ( $p=0.01$ ), and a similar trend was observed for ASD (0.12/1000 births in 1999 and 1.52/1000 births in 2009,  $p=0.02$ ).

**Conclusions:** Although the increase in the annual prevalence of maternal depression during pregnancy, ADHD and ASD could be partly explained by increased detection, the increase in children with ADHD and ASD is higher than expected and could be explained by an epigenetic phenomenon.

Pharmacoepidemiol Drug Saf. 2013;22:379.

**DOES DRUG TREATMENT FOR ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD) PREVENT INJURIES AMONG CHILDREN WITH ADHD?**

**Schmedt N, Mikolajczyk RT, Horn J, et al.**

**Background:** Children with attention deficit / hyperactivity disorder (ADHD) have a higher risk of accidents and injuries compared to children without ADHD. Methylphenidate (MPH) and atomoxetine (ATX) are widely used to reduce the symptoms of ADHD, but it remains unclear if they can decrease the risk of injuries.

**Objectives:** To investigate whether the use of MPH or ATX reduces the risk of injuries among children with ADHD using the case-crossover (CCOD) and self-controlled case series design (SCCSD).

**Methods:** We used the German Pharmacoepidemiological Research Database (GePaRD) to identify incident cases of ADHD among children aged 3-17 years in 2005-2007. Among all ADHD children, we identified those with an inpatient injury diagnosis (classified by the Injury Mortality Diagnosis Matrix) subsequent to their first ADHD diagnosis up to the end of follow up (December 2008). For the CCOD, exposure to MPH and ATX was assessed at the time of hospitalization with an injury diagnosis and at the control time point 90 days prior to the hospitalization. For the SCCSD, the time dependent exposure was assessed between the initial ADHD diagnosis and the end of follow up. Conditional logistic regression was used to calculate odds ratios (ORs) in the CCOD. Methods described by Whitaker et al. were used for the SCCSD analysis. In additional analyses, we restricted the sample to children with brain injuries only.

**Results:** Among 37,650 ADHD children, 2,186 had received an injury diagnosis. The ORs of experiencing an injury under MPH or ATX use were 0.86 (95% CI: 0.73-1.02) in the SCCSD and 0.98 (95% CI: 0.76-1.28) in the CCOD. When we restricted the outcomes to brain injuries only, the risk for injury was reduced under MPH or ATX in the SCCSD (OR: 0.66; 95% CI: 0.49-0.91), but not in the CCOD (OR: 0.98; 95% CI: 0.75-1.29).

**Conclusions:** No preventive effect of ADHD drugs on injuries in ADHD children was observed overall, but there was a preventive effect regarding the risk of brain injuries in the SCCSD. Different estimates from SCCSD and CCOD might be explained by the inability to control for exposure trends in the CCOD.

Pharmacoepidemiol Drug Saf. 2013;22:345.

**RELATIVE AGE IN CLASS AND STIMULANT DRUG UTILIZATION FOR ADHD.**

**Potteganullrd A, Hallas J, Hernandez-Diaz S, et al.**

**Background:** Recent studies have demonstrated that the youngest children in a class are up to twice as likely as their older classmates to be prescribed stimulants for ADHD.

**Objectives:** To investigate whether younger age in class is associated with an increased risk of being prescribed stimulants for ADHD among school-aged children in Denmark.

**Methods:** For all children in Denmark we obtained data from The Danish National Prescription Registry and the Danish Student Registry between July 1, 2000 and June 31, 2012. We estimated the prevalence proportion ratio (PPR) of receiving stimulant prescriptions between the youngest children in class (born in October-December) and the oldest in class (born in January-March). PPRs were stratified by study year, children's grade level, and gender. The main analysis was restricted to children in 1st through 6th grade (7-12 years), who started school on their age assigned grade level.

**Results:** We identified 932,032 eligible children for the main analysis, of which 246,596 (26.5%) were relatively young in class and 161,116 (17.3%) relatively old. Overall, 40% of those relatively young were delayed in school, i.e. did not attend school at their age assigned grade level, and were thus excluded from the main analyses. Over the study period, annual prevalence proportion of stimulant use from age 7 to 12 increased from 0.13 to 1.03 per 1,000 children among those relatively young and from 0.15 to 1.47 per 1,000 children among those relatively old in class. The average PPR over the entire study period, comparing the relatively youngest with the relatively oldest, was 1.08 (95% CI, 1.04-1.12). When including children not on their age assigned grade level, i.e. classifying children based on their age assigned school grade, the PPR was 1.09 (1.06-1.12).

**Conclusions:** Contrary to previous studies, we observed almost no relative age-effect on ADHD use among children in Denmark. This may be explained by a high proportion of relatively young children with delayed school entry, which may effectively serve as an alternative to investigating immature children for an ADHD diagnosis.

Pharmacoepidemiol Drug Saf. 2013;22:379.

#### **INSTRUMENTAL VARIABLE ANALYSIS OF ADHD TREATMENT AND SERIOUS ADVERSE EVENTS .**

**Dormuth CR, Brookhart MA, Miller TA, et al.**

**Background:** A dearth of evidence exists on the association between treatment for Attention-Deficit-Hyperactivity- Disorder (ADHD) and serious adverse events (SAE). A strong correlation between birth month and treatment provides an opportunity to study SAEs using instrumental variable (IV) analysis.

**Objectives:** To estimate SAE risk associated with ADHD treatment and to assess the value of IV analysis to adjust for confounding in ADHD populations.

**Methods:** We performed a fixed cohort study in the U.S. MarketScan database. Exposed patients were children 6-18 years of age between 2007 and 2011, diagnosed with ADHD and treated with a stimulant. The control group consisted of the siblings of the treated patients. Follow-up for treated patients began the day after they started their stimulant. Controls were assigned the same follow-up start dates as their siblings. We estimated the one-year risk difference for SAEs (defined as an emergency admission to hospital for any reason). IV analysis was used to adjust for confounding factors using two-stage ordinary least squares regression. First and second stage models also included additional covariates for age, sex and geographic region. The analysis was repeated using two IVs: quarter of birth (modeled as a categorical variable), and month of birth (modeled as 11 binary variables).

**Results:** Our study included 141,266 ADHD-treated patients and 191,286 sibling controls, among whom there were 1,382 events and 902 events, respectively. The crude one-year risk difference was 5.07 events per 1,000 patients (95% CI 4.50-5.64). Adjustment for age, sex and geographic region did not appreciably alter the risk difference. The IV adjusted risk differences were 3.75 per 1,000 when birth quarter served as the instrument (95% CI -14.73 to 22.22), and -2.66 per 1,000 when birth month was used (95% CI -21.2 to 15.90).

**Conclusions:** ADHD patients in our study population were at significantly greater risk of SAEs than their siblings. IV analysis lacked sufficient power to estimate a precise adjusted risk difference, but adjusted point estimates were closer to the null, suggesting that some or all of the elevated crude risk was attributable to unmeasured confounding.

Pharmacoepidemiol Drug Saf. 2013;22:448-49.

#### **CORRELATES OF NONMEDICAL USE OF ADHD-TYPE STIMULANTS VS. NONMEDICAL USE OF OTHER STIMULANTS IN A U.S. NATIONAL SAMPLE.**

**Chen LY, Kaufmann CN, Alexander C, et al.**

**Background:** ADHD stimulants have the highest abuse potential among the legally approved drugs, but few studies focus on nonmedical use of ADHD stimulants.

**Objectives:** To compare sociodemographic characteristics, mental health status, deviant behaviors, and other substance use in nonmedical ADHD stimulant users and other stimulant users.

**Methods:** Using data from the 2009-2011 National Survey on Drug Use and Health (NSDUH), 11,370 individuals reporting nonmedical use of ADHD stimulants and 4,732 reporting nonmedical use of other stimulants were compared. Data were analyzed via binary logistic regressions adjusting for sociodemographics.

**Results:** Compared to other stimulant users, nonmedical ADHD stimulant users were more likely to be male, young, white, never married, from lower income families, unemployed, and to have some college education. Among adults, nonmedical ADHD stimulant users were more likely to use marijuana, cocaine, heroin, hallucinogens, ecstasy, prescription opioids, tranquilizers, and sedatives, while adolescents were only more likely to use marijuana, hallucinogens, ecstasy, tranquilizers, and alcohol, compared to other stimulant users. Adult nonmedical ADHD stimulant users (vs. other stimulant users) were more likely to have past-year major depression (aOR = 1.4[1.1,1.7]) and to receive mental health treatment (aOR = 1.3[1.1, 1.5]), while adolescent users showed lower likelihood of major depression (aOR = 0.5[0.3, 0.8]) as compared to other stimulant users. Adolescent ADHD stimulant users were more likely to engage in deviant behaviors than other stimulant users, including being arrested and booked (aOR=2.8[1.7, 4.8]), selling illegal drugs (aOR=3.2 [2.0, 5.1]), stealing (aOR=2.3[1.5, 3.6]), and attacking others (aOR=1.67[1.1, 2.5]), while adult ADHD stimulant users were only more likely than their other stimulant user counterparts to sell illegal drugs.

**Conclusions:** This study provides evidence that nonmedical ADHD stimulant users have different substance use, mental health and deviant behavior profiles as compared to other stimulant users. The findings have implications for policy aimed at curbing nonmedical use of prescription stimulants.

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**INTERACTION OF AGE AND PSYCHIATRIC DIAGNOSIS ON ANTIPSYCHOTIC USE AMONG PUBLICLY-INSURED YOUTH WITH ADHD OR DISRUPTIVE BEHAVIOR DISORDERS.**

**Burcu M, Zito JM, Safer DJ.**

**Background:** Since the introduction of atypical antipsychotic medications, antipsychotic (ATP) use has expanded at a greater rate in youth than in adults and often for unlabeled indications, particularly for attention deficit hyperactivity disorder (ADHD) or disruptive disorders. No previous study has detailed the differential effect of age and comorbid psychiatric diagnosis on ATP use and its duration of use among publicly-insured youth with such behavioral disorders.

**Objectives:** The study aims to characterize annual ATP use and median duration of use among publiclyinsured youth with ADHD or disruptive disorder, mainly by comorbid psychiatric diagnosis across age groups.

**Methods:** A cohort of youth with ADHD or disruptive disorder was identified using claims data from a mid-Atlantic state Medicaid program for youth aged 2- 17 years with continuous enrollment in 2006. Bivariate analyses, age-stratified multivariable quantile and logistic regression models were employed. Study variables included age groups (2-5; 6-12; 13-17 years), psychiatric diagnosis, Medicaid-eligibility groups, gender, race/ethnicity, and region.

**Results:** The majority of the study population (N = 22,055) was African American, aged 6-12 years, and Medicaid-eligible by low family income. The annual prevalence of ATP use in this behavioral disorder cohort increased from 17.6% for 2-5 year-olds to 30.0% for 13-17 year-olds. Overall, median duration of ATP use was 189 days. Youth with comorbid bipolar disorder had significantly greater adjusted odds (AOR) of ATP use and greater adjusted median days of ATP exposure compared to youth without bipolar disorder, whereas these findings were most prominent for 2-5 year-olds (AOR:28.9; +76.5 median days). Depressive and anxiety disorders were also associated with greater ATP use, in particular for youth aged (less-than or equal to) 12 years.

**Conclusions:** Antipsychotic use for ADHD or disruptive disorders was substantial regardless of age group. Comorbid psychiatric conditions, especially clinician-reported bipolar disorder for young children, increase the likelihood of ATP treatment. Clinical monitoring and Medicaid program oversight are warranted.

Psychol Assess. 2013.

**DIFFERENTIATING BIPOLAR DISORDER FROM UNIPOLAR DEPRESSION AND ADHD: THE UTILITY OF THE GENERAL BEHAVIOR INVENTORY.**

***Pendergast LL, Youngstrom EA, Merkitch KG, et al.***

Adolescence and early adulthood are the peak ages for the onset of unipolar and bipolar mood disorders. Moreover, for most individuals with attention-deficit/hyperactivity disorder (ADHD), symptoms and impairment begin in childhood but persist well into adolescence and adulthood (e.g., Barkley, 2010). Thus, adolescence and early adulthood represent a developmental window wherein individuals can be affected by mood disorders, ADHD, or both. Because treatment protocols for unipolar depression (UPD), bipolar disorder (BD), and ADHD are quite different, it is crucial that assessment instruments used among adolescents and young adults differentiate between these disorders. The primary objectives of this study were to evaluate the predictive and diagnostic validity of General Behavior Inventory (GBI; Depue et al., 1981) scores in discriminating BD from UPD and ADHD. Participants were drawn from adolescent (n=361) and young adult (n=614) samples. Based on findings from logistic regression and receiver-operating characteristics analyses, the diagnostic efficiency of the GBI scales range from fair (discriminating UPD from BD) to good (discriminating BD participants from nonclinical controls). Multilevel diagnostic likelihood ratios are also provided to facilitate individual decision making.

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**ATOMOXETINE FOR THE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) IN ADULTS.**

***Bartel C, Kraemer S, Schneider E, et al.***

The attention deficit hyperactivity disorder (ADHD) is a well-established diagnosis among children and adolescents. Symptoms of ADHD can persist well into adulthood. Abundant research and medical evidence support the diagnosis of ADHD in adults, but due to insufficient diagnostic criteria in the ICD-10 and DSM-IV-TR manuals, uncertainties exist regarding the validity and reliability of the diagnosis among this age group. DSM-5, published in May 2013 constitutes an advancement in this respect. Stimulants are the most common types of pharmacological treatment used in ADHD, but because they are controlled substances, their availability is restricted. Since several years, however, atomoxetine is available for the treatment of ADHD in children and adolescents. As a selective norepinephrine reuptake inhibitor, atomoxetine has a different mechanism of action from stimulant drugs, and is the only non-stimulant drug approved in Germany for the treatment of ADHD in pediatric patients. Based on data generated during the past years that establish the efficacy and safety of atomoxetine in adults, an extended indication has been granted in Germany in June 2013.

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## RESEARCH ARTICLE

## Open Access

# Neuropsychopathological comorbidities in learning disorders

Lucia Margari\*, Maura Buttiglione, Francesco Craig, Arcangelo Cristella, Concetta de Giambattista, Emilia Matera, Francesca Operto and Marta Simone

**Abstract**

**Background:** Learning Disorders (LD) are complex diseases that affect about 2-10% of the school-age population. We performed neuropsychological and psychopathological evaluation, in order to investigate comorbidity in children with LD.

**Methods:** Our sample consisted of 448 patients from 7 to 16 years of age with a diagnosis of LD, divided in two subgroups: Specific Learning Disorders (SLD), including reading, writing, mathematics disorders, and Learning Disorders Not Otherwise Specified (LD NOS).

**Results:** Comorbidity with neuropsychopathologies was found in 62.2% of the total sample. In the LSD subgroup, ADHD was present in 33%, Anxiety Disorder in 28.8%, Developmental Coordination Disorder in 17.8%, Language Disorder in 11% and Mood Disorder in 9.4% of patients. In LD NOS subgroup, Language Disorder was present in 28.6%, Developmental Coordination Disorder in 27.5%, ADHD in 25.4%, Anxiety Disorder in 16.4%, Mood Disorder in 2.1% of patients. A statistically significant presence was respectively found for Language and Developmental Coordination Disorder comorbidity in LD NOS and for ADHD, mood and anxiety disorder comorbidity in SLD subgroup.

**Conclusions:** The different findings emerging in this study suggested to promote further investigations to better define the difference between SLD and LD NOS, in order to improve specific interventions to reduce the long range consequences.

**Keywords:** Learning disorders, Comorbidity, Language disorder, Motor coordination disorder, ADHD, Mood and anxiety disorders

**Background**

Learning Disorders (LD) affect about 2-10% of the school-age population. They are characterized by an academic functioning that is below the level that would be expected given their age, Intelligent Quotient (IQ) and grade level in school, and interfere significantly with academic performances or daily life activities that require reading, writing or calculation skills. LD are distinguished in Specific Learning Disorders (SLD) and Learning Disorders Non-Otherwise Specified (LD NOS), two categories separated for the clinic and care. SLD include Reading, Written Expression and Calculation

Disorder. LD NOS refer to a disability in acquiring new knowledge and skills, that are not limited to one or more specific school areas (reading, writing, mathematics) but also extended to other areas.

LD are neurobiological disorders that are not diagnosed before school age, accompanying the subject during the course of their life. Genetic and acquired factors may occur alone or in combination in determining LD. Dyslexia is present in 35-45% of ascending and colaterals; the concordance is 84% in monozygotic and 50% in dizygotic twins; moreover it has been demonstrated a genetic association with different chromosomes, including 6, 15, 18 [1-3], and about 15 genes have been found associated with dyslexia [4,5]. Recently, Giraud and Ramus [6] reviewed the current literature and described a putative mechanistic model that linked

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neuronal micro-architecture of the auditory cortex to specific alterations of phonological processing. The authors suggested that dyslexia could be related to a disconnection syndrome, signaling candidate genes (DCDC2, KIAA0319, DYX1C1) associated with neuroanatomical alterations, involving both the white and the gray matter of a fronto-temporo-parietal network, suggestive of dysfunction in cortical connectivity. Several acquired factors have been also involved such as: childbirth dystocias, neonatal asphyxia, neonatal icterus, cardiorespiratory arrest, status epilepticus, low birth weight and preterm birth [7-9], smoker mother during pregnancy [10], exposure to more than 2 general anesthesia within the fourth year of life [11,12], parental history of alcoholism or substance abuse [13] and prenatal exposure to cocaine [14]. School, family and social context are also interweave with neurobiological and contribute to determine the multifactorial nature of LD.

LD show variable clinical features and often associate to other disorders [15], that complicate the LD clinical presentation. The knowledge of these aspects is important from a preventive and therapeutic point of view. For these reasons, in this study we analyzed comorbidities in LD, considering separately the SLD and LD NOS subgroups, in order to deepen clinical and etiopathogenic knowledge of these disorders and improve their treatment.

## Methods

### Subjects

The sample consisted of 448 patients with a diagnosis of Learning Disorder, formulated by a child and adolescent neuropsychiatrist. The patients were divided in 2 subgroups: SLD (including Reading, Writing and Calculation Disorders) and LD NOS. All participants had Italian as their first language and they referred to the Child Neuropsychiatric Unit of the University of Bari "Aldo Moro", Italy, during the period between October 2010 and December 2012. The study was approved by the local ethical committee "Azienda Ospedaliero-Universitaria Consorziale Policlinico di Bari". All children were recruited in this study after obtaining written informed consent by their parents. In addition, patients aged from 8 to 16 years of age, gave their written informed consent.

All patients underwent anamnesis (familiar, physiological, pathological and academic), physical and neurological examination, routine laboratory tests and electroencephalogram.

### Assessment

In this study we performed a clinical assessment of LD and specific comorbidities. Diagnosis was formulated, according to the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition-Text Revision (DSM IV TR) [16], and it was supported by

diagnostic standardized tests for neuropsychological and psychopathological evaluation.

Neuropsychological evaluation assessed cognitive level, reading, writing and arithmetic skills, visual motor abilities and language.

The cognitive level was assessed with Italian version of Wechsler Intelligence Scale for Children, Third Edition (WISC-III) [17], we could not use WISC IV [18] because it was validated for Italian language only on February 2012; Leiter International Performances Scale Revised-Visualization and Reasoning battery (Leiter-R) [19] was administered, as an alternative to WISC-III, to subjects with verbal disorders. The cognitive level was classified according to DSM IV TR criteria as follows: normal intellectual functioning, IQ > 84; borderline intellectual functioning, IQ 71-84; mild intellectual impairment, IQ 50/55-70; moderate intellectual impairment, IQ 35/40-50/55; severe intellectual impairment, IQ 20/25-35/40.

Academic achievement was assessed with the following batteries of tests, validated for the Italian language: MT Group Reading Tests for Primary School [20]; MT Group Reading Tests for Middle School [21]; MT Group Advanced Reading and Mathematics Tests [22] for the first biennium of Secondary School; Battery for the Evaluation of Developmental Dyslexia and Dysorthography [23] for Primary and Middle school; Evaluation Tests of Calculation Ability for Primary School [24] and Evaluation Tests of Calculation Ability and Problem Solving for Middle School [25].

Visual motor abilities were evaluated by using the Visual Motor Integration Developmental test [26].

Language was evaluated with the following tests, validated for the Italian language: Test for the Evaluation of Language [27] and Evaluation Test for the Language Comprehension [28].

Psychopathological evaluation included the following tests, assessing behavioral, anxiety, mood and interpersonal problems: Child Behaviour Checklist (CBCL, Achenbach, 2001) [29]; Kiddies Schedule for Affective Disorders and Schizophrenia for School-Age Children - Present and Lifetime Version (Kaufman et al. 2004) [30]; Screen for Childhood Anxiety Related Disorders [31]; Children Depression Inventory [32]; Conner's Parent Rating Scale - Revised-Long Version [33]; Swanson Nolan and Pelham-IV [34].

The tests assessing cognitive level, skills of reading, writing and arithmetic and the CBCL were administered to all patients. The other listed tests were administered case by case to support diagnosis of neurodevelopmental and psychopathological disorders.

### Statistical analysis

All demographic and clinical variables were subjected to statistical analysis. Descriptive analysis was carried out

for the sociodemographic characteristics of the two samples. To compare age and gender between SLD and LD NOS group, we used respectively Student's t tests and Chi-square independence ( $\chi^2$ ) test. In order to examine the difference of neuropsychopathological comorbidities in a sample of SLD children compared with LD NOS children, the Chi-square independence was used. Statistical significance was considered for p-values  $\leq 0.05$ . We used the Software Statistical Package for Social Science version 20.

### Results

The sample included 448 Caucasian patients (319 males and 129 females) aged from 7 to 16 years (mean age 10.45,  $DS \pm 2.57$ ). The SLD subgroup included 240 patients (53.5%), mean age of 10.39 years,  $SD \pm 2.45$ . The subgroup of LD NOS included 208 subjects (46.4%), mean age of 10.2 years,  $SD \pm 2.67$ .

Normal intellectual functioning was present in 218 patients (48.6%), borderline intellectual functioning in 68 (16.2%), mild intellectual impairment in 132 (31.4%) and moderate intellectual impairment in 30 (7.2%).

In total sample, comorbidity with one or more neuropsychopathologies was found in 279 patients (62.2%). In SLD subgroup, one or more neuropsychopathological comorbidity were present in 140 patients (58.3%): Attention Deficit Hyperactivity Disorder (ADHD) combined or isolated in 63 (33%), 55 males and 8 females, Anxiety Disorder in 55 (28.8%), 39 males and 16 females, Language Disorder in 21 (11%), 18 males and 3 females, Developmental Coordination Disorder in 34 (17.8%), 30 males and 4 females, Mood Disorder in 18 (9.4%), 14 males and 4 females.

In LD NOS subgroup, one or more neuropsychopathological comorbidity were present in 139 patients (66.8%): Language Disorder in 54 (28.6%), 36 males and 18 females, Developmental Coordination Disorder in 52 (27.5%), 34 males and 18 females, Attention Deficit Hyperactivity Disorder (ADHD) combined or isolated in 48 (25.4%), 41 males and 7 females, Anxiety Disorder in 31 (16.4%), 16 males and 15 females, Mood Disorder in 4 (2.1%), 2 males and 2 females.

Statistically significant differences between the group of SLD and LD NOS for the presence of comorbidities ( $p = 0.64$ ) did not emerge.

Considering each comorbidity, in the LD NOS subgroup, language and coordination disorders were more frequent with a statistical significant difference ( $p = 0.00$ ); in the SLD subgroup, ADHD, anxiety and mood disorders comorbidity were more frequent with a statistical significant difference ( $p = 0.00$ ).

Neuropsychopathological comorbidities in both subgroups are summarized in Table 1.

**Table 1 Neuropsychopathological comorbidity in SLD<sup>1</sup> and LD NOS<sup>2</sup> subgroups**

|                                       | SLD             | LD Nos          | p     |
|---------------------------------------|-----------------|-----------------|-------|
| <b>Number</b>                         | 240             | 208             | -     |
| <b>Gender</b>                         |                 |                 |       |
| Male                                  | 184             | 135             | -     |
| Female                                | 56              | 73              | -     |
| <b>Age (mean <math>\pm</math> sd)</b> | 10.3 $\pm$ 2.45 | 10.2 $\pm$ 2.67 | -     |
| <b>Total Comorbidity %</b>            | 58.3%           | 66.8%           | 0.64  |
| ADHD                                  | 33%             | 25.4%           | 0.00* |
| Anxiety disorder                      | 28.8%           | 16.4%           | 0.00* |
| Mood disorder                         | 9.4%            | 2.1%            | 0.00* |
| Language disorder                     | 11%             | 28.6%           | 0.00* |
| Motor coordination disorder           | 17.8%           | 27.5%           | 0.00* |

<sup>1</sup>Specific Learning Disorders; <sup>2</sup>Learning Disorders Not Otherwise Specified; \* $p < 0.005$ .

### Discussion and conclusions

The epidemiology of LD is highly variable according to the type of LD, the spoken language and the tools used for the diagnosis. International epidemiological studies report a prevalence of 4-17% for dyslexia, 2-8% for dysorthography and 1-5% for dyscalculia [35-39]. SLD are more frequent in males than females [37,40].

Different languages have different writing systems and variations in prevalence depend on factors like the spelling opacity of each language. The Italian language has a shallow orthographical system, for this reason, we would expect a lower prevalence of SLD in Italy, where, however, the prevalence range is very large, between 0.88% and 10% [41-46]. In Italy, SLD represent about 30% of the users of local Neuropsychiatry Services and about 50% of patients which undergo rehabilitation [47].

Comorbidity are very common in Neuropsychiatric diseases, including LD, during developmental age. Understanding comorbidity is important because the presence of an additional disorder may affect the expression and severity of the clinical picture, requiring specific treatments and interventions. Patients with comorbidity compared to those without comorbidity usually exhibit more severe neurocognitive impairment, negative academic experience and social outcomes and lower treatment response.

Dyslexia is the most extensively investigated learning disorder in the national and international studies regarding its features and also its comorbidity.

Language disorders may precede or be associated with dyslexia. International studies have estimated that 30-40% of children with Specific Language Disorder receive a diagnosis of reading disorder later on [48-50] and a percentage between 55% [51] and 77% [52] of dyslexics meets the diagnostic criteria for Specific Language Disorder. In Italy, comorbidity with Specific Language Disorder has

been found from 15% to 20% of dyslexic children [53,54]. These data support the hypothesis that Language Disorder and Dyslexia may have common genetic or etiologic factors and may be different manifestations of the same cognitive impairment [55-58].

In addition, children with LD often present motor, sensory, perceptual abnormalities [59-63]. Huc Chabrolle et al. [15] in a review found that the impairment of motor development is a feature of nearly 50% of patients with dyslexia and that dyslexia is common among dyspraxic patients. Motor coordination disorder was reported in a percentage from 10.3% to 26% of dyslexics [53,54]. These data support the “cerebellar theory” of dyslexia [64] according to which, the cerebellum, that is responsible for motor control and automate overlearned tasks (i.e. reading), in LD may exert an insufficient motor control influencing articulation, phonological representation and ability to form appropriate connections between graphemes and phonemes.

Comorbidity with other disorders also is known in LD. It is reported that approximately 60% of patients with dyslexia also meet the criteria for at least one neuropsychiatric disorder [65,66]. Comorbidity with ADHD is present from 10% to 50% of LD children, while comorbidity with dyslexia is present from 25 to 40% of ADHD patients [65,67-69]. Comorbidity with anxiety and mood disorders has been reported in some studies but in others no difference was detected in the symptoms of anxiety and depressed mood among children with and without LD [53,67,70-75].

We did not find comparative data between SLD and LD NOS in literature.

In our sample we detected a comorbidity with neuropsychopathological disorders in both analyzed subgroups with some differences. A more significant presence of language and motor coordination disorders was found in the LD NOS compared to SLD subgroup. This could be linked to a higher degree of functional impairment in LD NOS patients, which presented, in the majority of cases, intellectual disability that might interfere with the normal evolution of neurolinguistic and motor development.

A meaningful presence of ADHD, anxiety and depressed mood was detected in the SLD subgroup. Some old and less replicated studies have suggested that reading disorder might be the primary deficit which causes secondary symptoms of ADHD [76-79]. Recent data have shown that there are common cognitive deficits between the two disorders [80] according to a possible similar genetic etiology, as demonstrated by families studies in twins [81,82]. Our results might support these latter theories, as demonstrated by the higher frequency of ADHD in SLD patients. With regards to anxiety and depressed mood, a bi-directional relationship between anxiety, depression and academic achievement has recently been hypothesized [83].

Anxiety and depressed mood could negatively impact learning process, alternatively children with LD may develop anxiety and mood problems, because they often reported adverse academic experiences. In our study we can assume that the symptoms of anxiety and depression are more frequent in the SLD subgroup, due to the greater introspective capacities of these children which are more aware of their difficulties compared to LD NOS patients, most of which have cognitive impairments.

In May 2013, it was published the DSM-5 [84] that provides the diagnostic category of LSD as a single, overall diagnosis. New criteria give detailed specifiers for the areas of reading, mathematics and written expression and specifiers for grade of severity (mild, moderate, severe). The classification system DSM-5 does not provide diagnostic category LD unspecified/NOS but admit that SLD can co-occurs with neurodevelopmental (e.g. ADHD, communication disorders, developmental coordination disorder, autistic spectrum disorder) or other mental disorders (e.g. anxiety disorders, depressive and bipolar disorders). Further investigations, in according to new classification criteria, are need to better define comorbidities and LSD prognostic profiles to implement appropriate intervention strategies.

#### Competing interests

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

None of the authors has any competing interest to disclose.

All co-authors have seen and approved the final version of the paper and accept responsibility for the data presented.

There is no financial or others conflict of interest that may be related to the authors.

#### Authors' contributions

LM conceived of the study and participated in final approval of the version to be published, MB conceived of the study and participated in its design and coordination and helped to draft the manuscript, FC participated in the design of the study and performed the statistical analysis, AC carried out substantial contributions to conception, design and acquisition of data, CdG carried out substantial contributions to conception, design and acquisition of data, EM participated in the sequence alignment and drafted the manuscript FO carried out contributions to interpretation of data, MS carried out contributions to conception and design and acquisition of data. All authors have seen and approved the final version of the paper and accept responsibility for the data presented.

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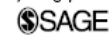
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Article

## Change Blindness in Children With ADHD: A Selective Impairment in Visual Search?

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### Abstract

**Objective:** This study evaluated change blindness and visual search efficiency in children with ADHD in searching for central and marginal changes. **Method:** A total of 36 drug-naïve children (18 ADHD/18 controls) performed a flicker task that included changes in objects of central or marginal interest. The task required observers to search for a change until they detected it. **Results:** Children with ADHD performed more slowly and less accurately than did typically developing children, specifically in detecting marginal-interest changes. **Conclusion:** In contrast to more standard visual search tasks, flicker tasks seem to be more sensitive to highlight focused attention deficits in children diagnosed with ADHD. Concretely, ADHD attentional deficits were more apparent when the task involved serial top-down strategies. (*J. of Att. Dis.* 2013; 17(7) 620-627)

### Keywords

ADHD, change detection, change blindness, focused attention, flicker task, visual search

ADHD is one of the most common childhood psychiatric disorders (Goldman, Genel, Bezman, & Slanetz, 1998; Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007) that might be characterized by symptoms of inattention, hyperactivity, and impulsiveness (American Psychiatric Association [APA], 2000). Inattention is the most commonly studied symptom of ADHD, and, although the diagnosis of ADHD involves attentional deficits according to the diagnostic criteria of the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; APA, 1994), attention is not formally defined in cognitive terms. Despite several studies having assessed experimentally different components of attention (alertness, selective attention, divided attention, spatial attention, visual search, executive attentional control) in children with ADHD, the actual mechanisms underlying attention deficits in ADHD remain poorly understood (for reviews, see Huang-Pollock & Nigg, 2003; Lansberger, Kenemans, & Van Engeland, 2007; Luman, Oosterlaan, & Sergeant, 2005; Mullane & Klein, 2008). Thus, further research that investigates the specific attentional abilities that are affected in ADHD is still necessary.

Important issues in the field of visual attention are concerned with whether processing occurs automatically or it requires top-down attentional control and whether certain pathological states affect, differentially, these ways of processing. Regarding ADHD, some studies have assessed whether children diagnosed with ADHD show any deficit when attention is devoted to searching for a target stimulus presented among distracter stimuli. A bulk of evidence comes from visual search tasks that take the feature-integration theory of attention by Treisman and Gelade (1980) as the theoretical framework. In a typical visual search task, participants are required to keep in memory a template of what (the target) they are told to search for, scan the scene, and detect the

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target stimulus among distracter items when it is presented. When the target differs from the distracters on the basis of one simple dimension (e.g., shape), the “single-feature search” is relatively easy, automatic, and not affected by the number of distracters in the display (set size). It is as if the target pops out from the visual display. When target and distracters share some perceptive features (e.g., shape and color), the “conjunction search” is harder, carried out in a serial and intentional way, and it is usually affected by the set size. By allowing ADHD participants to perform these kinds of visual search tasks, researchers might be able to assess how automatic and controlled processes operate in these children.

By reviewing the results of seven studies that used standard visual search tasks in a combined sample of 180 children with ADHD and 193 typically developing children, Mullane and Klein (2008) concluded that automatic search is rather preserved in ADHD participants, but serial search produced inconsistent results. Concerning the single-feature search tasks, children with ADHD showed significantly longer reaction times (RTs) than did typically developing children, but group and display size factors did not interact ever. In the conjunction search tasks, all examined studies reported longer RTs as the set size increased, and that pattern of results was observed in both ADHD and typically developing children. Six out of seven studies showed longer RTs in children with ADHD than in typically developing children, and only three studies found a significant group by display size interaction. Mullane and Klein suggested that these inconsistent results could be partially due to low statistical power (sample sizes ranged from 12 to 22 per group) and methodological differences among the studies.

However, we would like to suggest that a potential factor that might have contributed to the aforementioned inconsistent results with the serial visual search tasks is *demotivation*. Standard visual search tasks, as they are usually used in experimentally based settings might be declared as both boring and unappealing, about all by children with ADHD whose main attention impairment seems to be concerned with alertness (Bellgrove, Hawi, Kirley, Gill, & Robertson, 2005; Johnson et al., 2007). ADHD children’s abilities to keep a sustained state of alertness are also usually assessed through tedious and monotonous tasks (Casagrande, Violani, Curcio, & Bertini, 1997; for a review, see Parasuraman, 1998). Thus, the attentional deficits frequently reported associated with ADHD might be confounded by low motivation or disinterest to perform the tasks.

In line with the above contention, when visual search is assessed with more engaging videogame tasks, the differences between ADHD and typically developing children in both RTs and accuracy measures, as well as any interaction involving the groups, disappear (Mason, Humphreys, &

Kent, 2004). Thus, using extremely boring and demotivating tasks, such as the standard visual search tasks, or extremely motivating and arousing ones, such as video games, might obscure potential deficits associated with intentional controlled processing or focused attention in ADHD. In other words, the former tasks might spuriously maximize the differences between children diagnosed with ADHD and typically developing children, and the latter tasks might spuriously minimize potential group differences.

The current study was aimed to assess performance of children diagnosed with ADHD on a specific type of visual search task, the flicker task (Rensink, 2000; Rensink, O’Regan, & Clark, 1997, 2000). This task is supposed to tap focused attention abilities, and to our knowledge it has never been used with children diagnosed with ADHD (with the exception of a study reported in the unpublished Cohen’s dissertation). An advantage of the flicker task to assess potential attention deficits in ADHD is that it seems to be more motivating than the standard visual search tasks, but less intriguing than video games.

In the flicker task, pictures of daily life scenes are used to assess visual search efficiency (Rensink, 2000). Two versions of a picture are presented. The pictures are identical except in a specific detail. The pictures alternate repeatedly and are separated by a brief gray screen. The observers have to search the scene for what has changed between the two pictures until they detect it. As the task uses pictures of natural scenes, participants tend to give priority to some areas of the scene than to others. Consequently, they detect changes in objects of central interest (CI) faster than changes in marginal-interest (MI) objects (Rensink et al., 1997). Both perceptual and semantic characteristics of the visual scene might be taken to create a sort of priority list that determines which items are going to be attended first. Changes in objects of CI pop out from the pictures, and they are usually efficiently detected. Changes in objects of MI are more difficult to detect and require serial visual search, and therefore performance is less efficient.

As change detection usually occurs under focused attention conditions (Rensink, 2002; Rensink et al., 1997, 2000), attention abilities can be evaluated in children diagnosed with ADHD by means of more ecologic stimuli within a rather enjoyable context. According to previous findings (e.g., Mullane & Klein, 2008), we expect ADHD and typically developing children to differ in detecting changes in objects of MI, but not in detecting objects of CI.

## Method

### Participants

A total of 36 children participated in the study: 18 were diagnosed with ADHD (mean age:  $10.7 \pm 1.5$  years;



17 males/1 female) and 18 were typically developing children (mean age:  $10.6 \pm 1.5$  years; 17 males/1 female). The ADHD group included 10 children who met the criteria for the ADHD/C subtype (exhibit both inattentiveness and hyperactivity/impulsiveness symptoms) and 8 who met the criteria for ADHD/I (show prevalently inattentive symptoms; *Diagnostic and Statistical Manual of Mental Disorders* [4th ed., text rev.; *DSM-IV-TR*; APA, 2000]). All children with ADHD were drug-naïve patients first admitted to the Day Hospital of the Child Psychiatry Unit of the University of Rome “Tor Vergata.” Children included in this study did not have a prior history of stimulant treatment. A psychopathological evaluation was performed by a team of child psychiatrists by means of the Kiddie Schedule of Affective Disorders (K-SADS; Kaufman, Birmaher, Brent, Rao, & Ryan, 1996), the Conners’ Parent Rating Scale (CPRS), the Conners’ Teacher Rating Scale (CTRS; Conners, 1989), the Children Depression Inventory (Kovacs, 1985), and the Multidimensional Anxiety Scale for Children (March, 1997). The inclusion criteria to participate in the study were the diagnosis of ADHD (based on the *DSM-IV* criteria and confirmed by K-SADS), no history of mental retardation, brain trauma, neurological diseases or physical impairment, a lack of comorbid mental disorders with the exception of oppositional defiant disorder (ODD), and learning disabilities.

The participants for the control group were matched in gender and age with the ADHD group and were selected from a wider group of 86 children recruited from two public schools in Rome. The control group participants had no history of cerebral injury or other neurological or psychiatric disorders.

All children aged 11 years and older had a full-scale IQ that fell above the 75th percentile on the Progressive Colored Matrices (PCM; Raven, Court, & Raven, 1990; Raven, Raven, & Court, 1993), and all children aged 10.5 years or younger had an IQ greater than 80 on the Progressive Standard Matrices (PSM; Raven, et al., 1990; 1993). The presence of ADHD in children from the control group was assessed via an independent evaluation carried out by the teacher and by one parent who completed a *DSM-IV-TR* report card (APA, 2000). Any child with a possible indication of ADHD was not considered. The mean age and IQ scores of children from the two groups did not differ significantly. Demographic data are reported in Table 1. The Child Psychiatry and Neurology Institute Ethical Committee approved the study. All parents or legal guardians of children gave written informed consent before testing.

### Apparatus

The stimuli were presented using E-Prime software on a Pentium 4 PC and were displayed on a 21-inch color VGA

monitor from a viewing distance of approximately 56 cm (with a headrest). Responses were collected via the computer keyboard.

### Stimuli

Three judges jointly selected 16 pictures from a larger sample identified through Google Images (see Figure 1 for some examples). The pictures depicted familiar scenes for children such as a group of children playing. Each picture measured  $640 \times 480$  pixels. By removing a single object using Photoshop we created an alternate version of each picture. To make CI and MI changes, we followed the method indicated by Rensink et al. (1997).

A group of 31 children (mean age  $10.2 \pm 1.6$ ), who were not participants in this experiment, viewed each picture for 3 s and generated a written list of scene elements of highest interest. Items chosen by no more than 2 children were defined as MI objects and those chosen by all children were defined as CI objects.

Half of the changes referred to MI objects and the other half referred to CI objects. Changes consisted in removing one object from the scene, and the size of the changes averaged  $49 \times 49$  pixels, approximately.

### Procedure

Children were tested individually in a silent and dimly illuminated room. On each trial, an original and modified version of a picture alternated repeatedly (240-ms display time), separated by a gray screen (80 ms), until the participants pressed the space bar to indicate they had detected the change (see Figure 2). Children were instructed to press the space bar as soon as they detected that one object appeared and disappeared, and then they were told to verbally describe the change. An experimenter noted whether they accurately named the changing object.

Two pictures were used for practice. One depicted the Italian actor Roberto Benigni jumping on his chair during the Oscar Award ceremony, and the other depicted three race car drivers holding a trophy. After practice, children completed 16 experimental trials randomly presented for each participant. ADHD children performed the task in the Sant’Alessandro Clinic in Rome, and children from the control group performed the task at school.

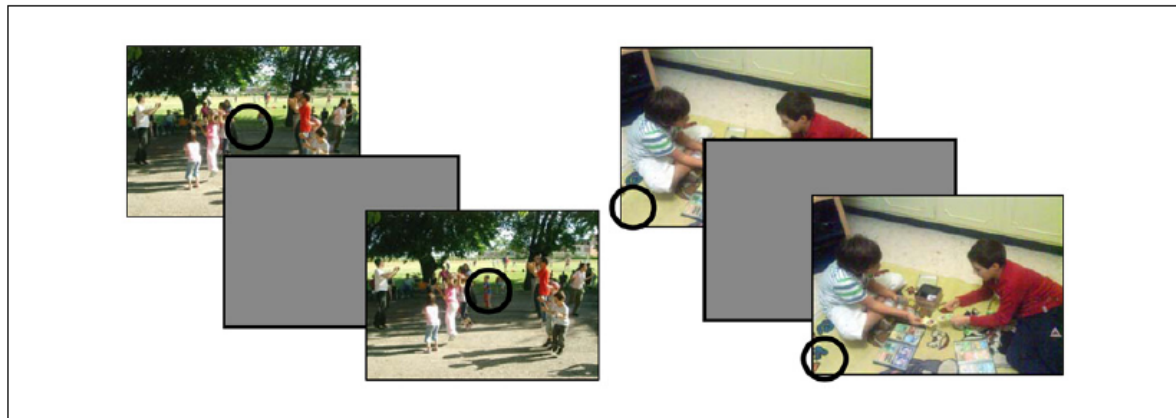
### Data Analysis

A Group (ADHD, Control)  $\times$  Change Type (CI, MI) mixed ANOVA was carried out on both change detection RTs and errors. RTs in trials in which participants did not detect the change were replaced by the mean RTs + 2 *SD* for that condition. Post hoc comparisons were conducted using the

**Table 1.** Participant Demographic and Descriptive Characteristics.

|  | Children with ADHD | Typically developing children | <i>F</i> | <i>p</i> |
|--|--------------------|-------------------------------|----------|----------|
| Gender                                   | 17 males/1 female  | 17 males/1 female             |          |          |
| Age                                      | 10.1 (± 1.7)       | 10 (± 1.2)                    | 0.37     | .71      |
| PCM and PSM corrected responses          | 35.9 (± 7.9)       | 35.7 (± 4.4)                  | 0.11     | .82      |
| Number of children with ADHD/I           | 10                 |                               |          |          |
| Number of children with ADHD/C           | 8                  |                               |          |          |
| Parents Inattention Conners' scores      | 64.7 (± 8.9)       |                               |          |          |
| Parents Hyperactivity Conners' scores    | 63.5 (± 10.3)      |                               |          |          |
| Parents ADHD index                       | 64.5 (± 9.1)       |                               |          |          |
| Teachers Inattention Conners' scores     | 69.2 (± 11.9)      |                               |          |          |
| Teachers Hyperactivity Conners' scores   | 70.9 (± 10.2)      |                               |          |          |
| Teachers ADHD index                      | 74.5 (± 12.9)      |                               |          |          |
| ADHD/I: number of inattention symptoms   | 6.1 (± 1.8)        |                               |          |          |
| ADHD/I: number of hyperactivity symptoms | 3.6 (± 0.6)        |                               |          |          |
| ADHD/I: number of impulsivity symptoms   | 1.3 (± 0.8)        |                               |          |          |
| ADHD/C: number of inattention symptoms   | 4.1 (± 2.7)        |                               |          |          |
| ADHD/C: number of hyperactivity symptoms | 4.5 (± 1.1)        |                               |          |          |
| ADHD/C: number of impulsivity symptoms   | 2.7 (± 0)          |                               |          |          |
| Oppositional defiant disorder            | 3                  | 0                             |          |          |
| Conduct disorder                         | 0                  | 0                             |          |          |
| Learning disabilities                    | 3                  | 0                             |          |          |
| Depression/anxiety disorders             | 0                  | 0                             |          |          |

Note: PCM = Progressive Colored Matrices; PSM = Progressive Standard Matrices; ADHD/I = children showing prevalently inattentive symptoms; ADHD/C = children showing inattentiveness and hyperactivity/impulsiveness symptoms.

**Figure 1.** Examples of the stimuli.

Note: CI = central interest; MI = marginal interest. All the changes were deletion type, half the trials were of CI (on the left) and half of MI (on the right). The black circle indicates which item appears and disappears during the flicker sequence. The choice of the changed item was made based on an independent attentional evaluation of the stimuli.

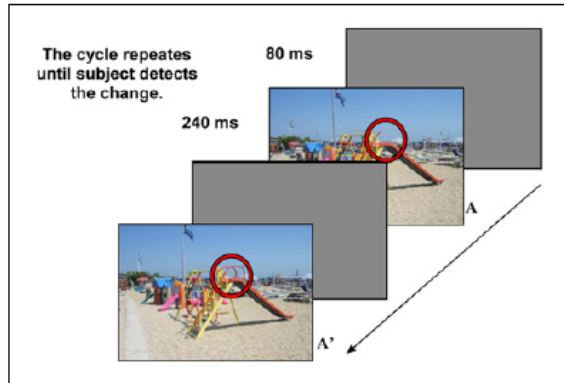
Duncan test. A  $\alpha$  value of .05 was used to establish statistical significance for all analyses.

## Results

Mean RTs ( $\pm SD$ ) and mean errors ( $\pm SD$ ) are reported in Table 2.

## RTs Analysis

Children with ADHD took longer to detect the changes than did their typically developing peers (38,082.29 ms vs. 24,545.13 ms),  $F(1, 34) = 7.77$ ;  $p < .01$ ; partial  $\eta^2 = .19$ . All participants detected CI changes faster than MI changes (16,882.23 ms vs. 45,745.09 ms),  $F(1, 34) = 74.37$ ;  $p <$



**Figure 2.** General design of the flicker paradigm.

Note: Original image A (a playground with a slide on the foreground) and modified image A' (a playground with the slide without the handrails) are displayed in the order A, A', A, A'... with a gray blank screen between the two images.

.000001; partial  $\eta^2 = .69$ . The Group  $\times$  Change Type interaction was also significant,  $F(1, 34) = 4.88$ ;  $p = .03$ ; partial  $\eta^2 = .13$ . The Duncan test revealed that children with ADHD showed significant slower RTs compared with typically developing children, but only when changes were of MI ( $p < .001$ ; see Figure 3).

Group differences in MI changes detection were further examined with proportional change scores to reduce the effects of ADHD-related generalized slowing. For each participant, MI/CI proportion scores were calculated by dividing mean RTs for MI changes by mean RTs for CI changes. Differences between the two groups were not significant ( $t = 0.46$ ;  $p = .65$ ).

### Accuracy Analysis

Children with ADHD made more errors than their typically developing peers (1.41 vs. 0.22),  $F(1, 34) = 16.03$ ;  $p < .0001$ ; partial  $\eta^2 = .32$ . All participants were more accurate when detecting CI changes than MI changes (0.31 vs. 1.33),  $F(1, 34) = 19.01$ ;  $p < .0001$ ; partial  $\eta^2 = .38$ . The Group  $\times$  Change Type interaction was also significant,  $F(1, 34) = 6.64$ ;  $p < .01$ ; partial  $\eta^2 = .16$ . Children with ADHD made significantly more errors than did typically developing peers only when they detected marginal changes.

### Discussion

To our knowledge, this is the first time the flicker task has been used to assess attention deficits in children diagnosed with ADHD. The only exception is the unpublished dissertation by Cohen (2009). In Cohen's study, children with ADHD were faster than were children from the control group in detecting marginal changes. This inconsistency with our results could be due to differences in the

way error trials were treated in both studies. In the current study, RTs in error trials were replaced by the mean RTs + 2 SD of the specific experimental condition. In the aforementioned Cohen's experiment, only RTs from correct trials entered into the analyses. This way of dealing with error trials might have favored rejection of slow RTs data from difficult trials, that is, when participants have to detect marginal changes. This data rejection procedure might have affected more dramatically ADHD children who might have found marginal trials difficult to detect.

The present study confirms that ADHD children are slower and perform poorer than typically developing children in a task that is thought to tap focused attention abilities. These results agree with previous findings that associate ADHD with important attentional deficits (Andreou et al., 2007; Johnson et al., 2007). However, the present findings do not replicate those observed by Cohen and Shapiro (2007) who concluded that the flicker task was not sensitive to uncouple people with and without ADHD. Some methodological differences between the two studies might be the cause of such inconsistent results. Our ADHD participants were drug-naïve children, whereas Cohen and Shapiro's study examined ADHD adults under current and/or previous pharmacological treatment. The flicker task might have been more sensitive to capture group differences under nontreatment conditions.

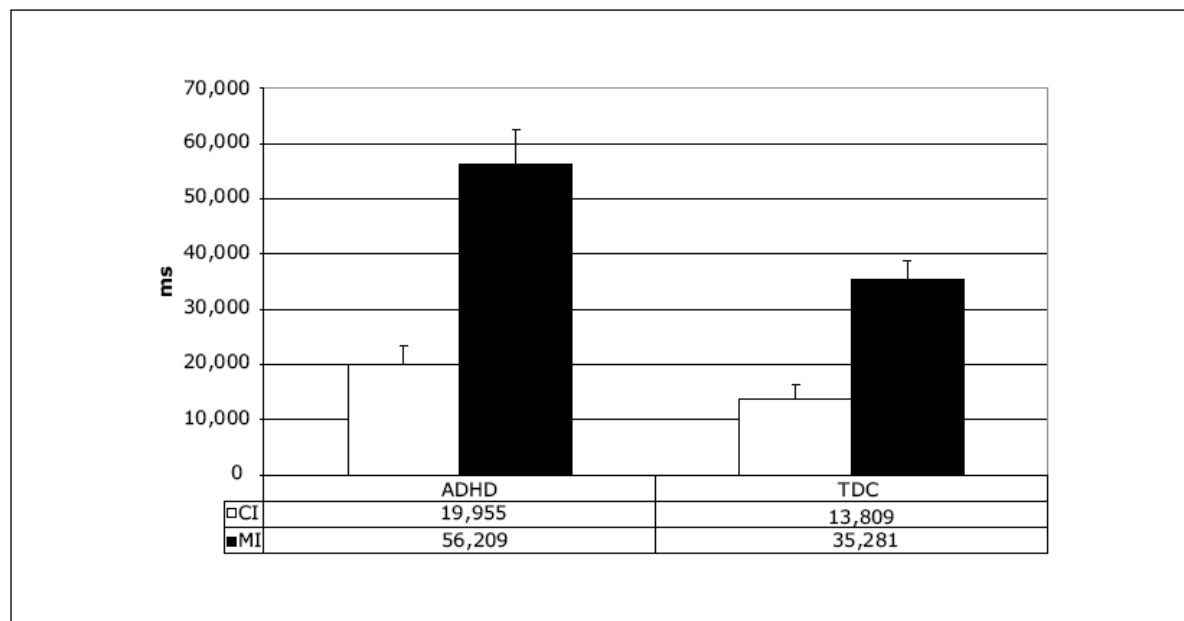
Results of the present study replicate the findings consistently observed with the flicker task (Fletcher-Watson, Collis, Findlay, & Leekam, 2009), demonstrating the robust nature of change blindness. All the children showed a strong change blindness effect and a clear difference between CI and MI trials. Detection of CI changes required less than half the time needed to detect MI changes. Faster CI changes detection agrees with the assumption that these changes pop out from the picture, inducing an automatic capture of attention. However, the greater amount of time needed to detect MI changes confirms the use of serial top-down visual search strategies in these trials (Rensink, 2000). In the absence of a CI change that rapidly attracts the observers' attention, observers must implement a serial top-down strategy to detect a MI change. Through a serial search strategy, the observers actively explore new locations of the picture until a change is detected (Caplovitz, Fendrich, & Hughes, 2008). This strategy is implemented in a top-down manner for at least two reasons: (a) It is goal directed; that is, it is aimed to search for changes outside the CI elements of the scene; and (b) it is driven by implicit information about the portion of the scene previously explored (Wolfe, Butcher, Lee, & Hyle, 2003). Once the general scene-schema has been extracted, knowledge-based information can be used to help guide attention (Henderson, 2003).

Importantly, the flicker task has proved to be useful to dissociate attentional performance in children with ADHD from performance of typically developing children. Whereas children from the two groups did not differ in their efficiency to detect CI changes, both RTs (only raw scores)

**Table 2.** Mean RTs, Standard Deviations, and Mean Number of Errors, as a Function of CI and MI Changes in Children With ADHD and TDC.

|    | ADHD     |         | Errors | TDC      |          | Errors |
|----|----------|---------|--------|----------|----------|--------|
|    | RTs (ms) | SD      |        | RTs (ms) | SD       |        |
| CI | 19,955.4 | 3,411.5 | 0.61   | 13,809.3 | 10,954.6 | 0      |
| MI | 56,209.2 | 6,212.2 | 2.22   | 35,280.9 | 15,101.4 | 0.44   |

Note: CI = central interest; MI = marginal interest; TDC = typically developing children; RTs = reaction time.



**Figure 3.** Response times (in ms) for detecting the CI (white column) and the MI (black column) in children with ADHD and TDC. Note: CI = central interest; MI = marginal interest; TDC = typically developing children.

and error data showed that ADHD children were impaired in detecting MI changes.

The results with error data are of special clinical and neuropsychological relevance. According to the attentional resources hypothesis (e.g., Helton & Warm, 2008; Kahneman, 1973), as task demands increase, so will errors. The poor accuracy of children with ADHD on the highest demanding condition (e.g., detection of MI changes) is consistent with a deficit in attentional resources, or with a specific impairment in using serial top-down strategies due to their limited attentional resources.

It is important to remark that only a small number of studies (three out of seven) found serial search deficits in ADHD compared with control participants by using standard visual search tasks (Mullane & Klein, 2008). The more appealing nature of the current flicker task did not preclude any attentional impairment in children with ADHD to be

uncovered, despite the fact that it might have raised their motivational levels (see Mason et al., 2004). The task uses attractive ecological stimuli that children are familiar with, and it allows the possibility of further exploring the effect of semantic context on attention. Thus, the present flicker task seems to be a useful tool for assessing focused attention abilities in clinical and nonclinical populations.

## Conclusion

For the first time, the flicker task has been used to assess focused attention, serial visual search strategies, and change blindness in children with ADHD. Of particular relevance is the fact that our patients were drug-naïve children, in whereas most of the previous studies have ADHD participants were medication free either on the day of testing or just 24 to 72 hr prior to testing. It allowed us to determine

the effects of the ADHD disease on focused attention without the influence of medication. In other words, our results reflect the actual framework of attention in ADHD. However, the strict criteria followed for selecting our participants are also the source of a primary weakness of the present study, the small number of participants. Future studies should address that limitation by both increasing the sample of participants and evaluating attentional performance in the ADHD subtypes.

Finally, some characteristics of the current flicker task deserve further comments. First, regarding motivation, our task falls in between extremely boring tasks, such as the standard visual serial tasks, and extremely arousing ones, such as those that use video games. Second, from our point of view, the present task might be better situated to overcome the current gap between the clinical definition and the cognitive performance characterizing attentional disorder in ADHD.

In summary, the results of the present study allow us to conclude that children diagnosed with ADHD show a specific impairment in developing serial top-down strategies that have been proved to be useful to solve a rather difficult task, what might be attributed to their limited attentional resources.

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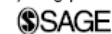
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## Introduction to the Special Section on Sleep and ADHD

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Human sleep is considered to be a global phenomenon, orchestrated by central nervous system neuronal networks, and a local phenomenon. Sleep and wakefulness may be restricted to small groups of neurons, to individual cortical columns, or to larger brain regions. Cognitive impairment and performance deficits induced by sleep deprivation (reduced attention and vigilance, decision-making ability, and memory functions) may reflect the occurrence of cortical and subcortical local “islands of sleep” in participants who are behaviorally fully awake.

The similarity between the spectrum of cognitive consequences of sleep loss and the profile of ADHD makes the relationship between sleep and ADHD an intriguing issue for basic researchers and clinicians on account of its implications in the diagnosis and choice of therapies. Data on the occurrence of “islands of sleep” during wakefulness in ADHD are based on electroencephalography (EEG) studies of oscillatory power during the resting state, which point to abnormally high slow oscillatory activity (i.e., theta) and reduced fast oscillatory activity (i.e., alpha and beta), as well as on neuroimaging studies, which have detected hypoactivation in systems involved in executive function (frontoparietal network) and attention (ventral attentional network).

In their review, Owens and coauthors explain the functions of the three main sleep regulatory processes: the circadian process, named “Process C,” which couples the timing for sleep and wakefulness with the light–dark cycle; the homeostatic process, named “Process S,” which modulates sleep intensity and is strongly dependent on the duration of and activity during wakefulness; and, finally, the ultradian process, which regulates the intrasleep non-rapid eye movement (NREM)–REM alternation. The authors describe the main neurotransmitters involved in the regulation of sleep, arousal, vigilance, and attention. The review by Owens et al. is the outcome of a meeting held in November 2010, by a multidisciplinary group of experts in pediatric sleep medicine and ADHD. The aim of the meeting was to review the current literature, identify gaps in knowledge, and formulate recommendations regarding future research directions and priorities. The participants at

the meeting summarized the similarities between the cognitive, emotional, and behavioral consequences of sleep loss and ADHD. This is a fundamental field of research when differentiating ADHD participants with major sleep disorders (such as restless legs syndrome [RLS], periodic leg movements, and obstructive sleep apnea, which all result in sleep loss) from those without sleep problems. Moreover, they raised the question of whether participants with ADHD have a chronobiological vulnerability, expressed by a delayed endogenous circadian pacemaker. I personally believe that Question Number 4 (“Are there specific phenotypes of ADHD that may be delineated in which sleep problems such as delayed sleep onset and/or night wakings are more or less prominent, and does their identification have a significant impact on the efficacy and tolerability of specific pharmacologic therapeutic choices for the treatment of ADHD?”) is the question that most urgently needs to be addressed. Delineating different sleep phenotypes of ADHD may reduce the heterogeneity and complexity of the sleep–ADHD relationship.

With regard to sleep phenotypes, the authors who wrote the second article (Modestino & Winchester) wanted to study the relationship between ADHD and hypersomnia, hypothesizing that in some cases ADHD may be part of a primary disorder of vigilance, and the core symptoms of ADHD may be an attempt to stay alert, to counteract daytime sleepiness. This overlap between ADHD and symptoms of hypersomnia is often ignored by clinicians, notwithstanding some cases of adults with narcolepsy receiving a diagnosis of ADHD during childhood has been described. According to this hypothesis, the authors investigated the presence of symptoms of childhood ADHD in a large population of 161 adults with a diagnosis of narcolepsy (age range from 18 to 86 years, 109 female), by means of the retrospective self-report questionnaire Wender Utah Rating Scale (WURS). The authors found that more than 37% of patients have had symptoms of ADHD during childhood, and that the score of WURS correlated positively with the mean sleep latency measured by the Multiple Sleep Latency Test (MSLT). Daytime sleepiness has been investigated in children with ADHD,

by objective measures such as MSLT and by questionnaires, with contradictory results, which can be explained by the fact that a disorder of vigilance may be present only in a subgroup of children with ADHD and that hypersomnolence usually is more evident in adulthood. The same differences may be reported in participants with obstructive sleep apnea syndrome: Adults often showed clear daytime sleepiness and sleep attacks, whereas children manifest symptoms of ADHD. The results of this study confirm the hypothesis that a subgroup of children with ADHD display a primary disorder of vigilance, narcolepsy being the extreme sleep phenotype.

The growing interest in the distinction of sleep phenotypes associated with ADHD also emerges from the study design adopted in the third article by Fargason et al. The authors investigate sleep quality by means of a standardized scale administered to a “pure” ADHD subtype of adults without referred insomnia or other circadian rhythm disorders, and with no psychiatric comorbidities. The participants’ age ranged from 19 to 65 years, two thirds were below 40 years of age, 53% were men, and the participants were composed of four groups: ADHD + stimulants ( $n = 39$ ), ADHD + nonstimulants ( $n = 15$ ), ADHD-no medication ( $n = 26$ ), and controls ( $n = 25$ ). The authors found that the ADHD participants did not display any circadian delay but did suffer unrecognized subclinical sleep problems and prolonged sleep latency, which appeared to be independent of medications. Moreover, positive correlations between the later timing of stimulant medications and higher stimulant dosages, which in turn led to delayed sleep onset, were observed. By contrast, only ADHD participants on stimulants did not display any daytime dysfunction due to sleepiness, thus resembling controls. This finding suggests that daytime sleepiness may be a core deficit of ADHD. The authors should have excluded not only participants who complain of insomnia but also those with other major sleep disorders (such as RLS, periodic limb movements, obstructive sleep apnea, nocturnal seizures), to obtain a “pure” group of ADHD participants. Indeed, any correlation between stimulants and sleepiness that might have emerged from a “pure” ADHD group would have been more interesting as it might be related to a “primary” condition of hypoarousability, as it is observed in narcolepsy.

It is somewhat surprising that the authors of these three articles discuss sleep phenotypes but do not mention alterations in sleep quality due to either epilepsy or interictal epileptiform discharges. Sleep activates focal and

generalized spikes in about one third of all individuals with epilepsy. Some types of epilepsy are closely related to sleep, with the clinical onset occurring exclusively or mainly during sleep (i.e., rolandic epilepsy and nocturnal frontal lobe epilepsy). A large body of data in the literature point to a high prevalence of interictal or ictal discharges during sleep in ADHD children (approximately 50% of those who underwent a full-night video-polysomnography for suspected sleep disorders, with seizures occurring in fewer than 10%). One in four nonepileptic children examined for ADHD had epileptiform discharges (focal in more than half), which were detected by means of sleep EEG recording and sleep-deprivation EEG recording. The majority of the EEG abnormalities occurred in the sleep and sleep-deprived recordings, whereas the highest prevalence of epileptiform discharges was usually observed in prolonged sleep recordings.

On the basis of all these findings that point to the need to distinguish between different sleep phenotypes, the fourth article attempts to describe each ADHD sleep phenotype and its clinical and therapeutic implications by presenting case reports of children with ADHD and learning disabilities who had been referred to a sleep center for suspected sleep disorders according to the following classification: (a) the hypoarousal state of the “primary” form of ADHD, (b) the sleep phase advanced disorder, (c) sleep disordered breathing (SDB), (d) RLS and/or periodic limb movements disorder (PLMD), and (e) epilepsy. The first case report is an example of ADHD and SDB, with resolution of sleep apnea and daytime hypersomnolence after continuous positive airway pressure therapy. The second case highlights the efficacy of melatonin on delayed sleep phase advanced disorder and cognitive performance. The third case report describes the association between ADHD and PLMD, with a significant improvement following iron supplementation. The other two cases are examples of ADHD associated with epilepsy (nocturnal frontal lobe epilepsy and benign occipital epilepsy), which improved after the start of antiepileptic treatment.

In conclusion, the sleep model of the hypoarousal state resembling narcolepsy of the primary ADHD phenotype may be related to alterations in the ultradian process, which regulates the intrasleep NREM-REM alternation; the model of sleep loss with varying levels of arousal (such as the obstructive sleep apnea syndrome phenotype, the RLS and periodic limb movements phenotype, the sleep occurrence of ictal and interictal epileptiform discharges during



**Table 1.** The Relationship Between Sleep Process and ADHD.

|                                      | Process C   | Process S  | Ultradian process  |
|--------------------------------------|---|--|--|
| Neurophysiological function          | Couples timing for sleep and wakefulness with the light–dark cycle                                | Modulates sleep intensity and is strongly dependent on wakefulness duration and activity | Regulates intrasleep NREM–REM alternation                            |
| Central nervous system area involved | Hypothalamic suprachiasmatic nucleus, retinohypothalamic projections, pineal gland, raphe nucleus | Thalamus, corticothalamic projections, prefrontal cortex                                 | REM on neurons: pontine reticular formation, mesencephalic tegmentum |
| Sleep ADHD phenotype                 | Sleep loss secondary to sleep delay onset insomnia  | Sleep loss secondary to major sleep problems or to epilepsy                              | Hypoarousability, mimicking narcolepsy                               |
| Therapeutic suggestions              | Melatonin, light therapy  | Therapy of major sleep problems or antiepileptic drugs                                   | Stimulants, serotonergic agents                                      |

Note. NREM = non-rapid eye movement.

sleep) may instead be related to an alteration in the homeostatic “Process S”; and, finally, the sleep-onset delay insomnia in ADHD is a sleep model related to an alteration in the circadian “Process C.” Not only does this hypothesis have numerous research implications, which are not limited to clinical aims, but also it provides a better definition

of our genetic, biochemical, and basic knowledge of ADHD (see Table 1).

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