

# NEWSLETTER



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### 2. Documenti

Ferri R, et.al.

**TIME STRUCTURE OF LEG MOVEMENT ACTIVITY DURING SLEEP IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND EFFECTS OF LEVODOPA**

Sleep Medicine 2013;14:359-66

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**TERM THERAPY WITH METHYLPHENIDATE INDUCES MODEST EFFECTS ON GROWTH IN ADHD CHILDREN**

Eur Neuropsychopharmacol 2013;23:S80 [abstract]

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### 3. Segnalazioni

#### Convegno:

**“ADHD: per una condivisione dei percorsi diagnostico-terapeutici”**

Istituto di Ricerche Farmacologiche “Mario Negri;

A.O. Spedali Civili di Brescia

28-29 maggio 2013; Milano.

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#### IX Congresso Nazionale AIDAI-AIRIPA:

**“NUOVE PROSPETTIVE DI INTERVENTO NELL’ADHD”**

Servizio per il Trattamento dei Disturbi del Comportamento

30-31 maggio 2013; Perugia.

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## **BIBLIOGRAFIA ADHD GENNAIO 2013**

Adolesc Health Med Ther. 2012;3:51-66.

**LISDEXAMFETAMINE IN THE TREATMENT OF ADOLESCENTS AND CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

***Najib J.***

Attention-deficit/hyperactivity disorder is one of the most common neurobehavioral disorders defined by developmentally inappropriate levels of inattention, hyperactivity, and impulsivity. Symptoms begin in childhood and may persist into adolescence and adulthood. Currently available pharmacological treatment options for attention-deficit/hyperactivity disorder in children and adolescents include stimulants that are efficacious and well tolerated; however, many of these preparations require multiple daily dosing and have the potential for abuse. Lisdexamfetamine dimesylate, the first prodrug stimulant, was developed to provide a longer duration of effect. It demonstrates a predictable delivery of the active drug, d-amphetamine, with low interpatient variability, and has a reduced potential for abuse. A literature search of the MEDLINE database and clinical trials register from 1995-2011, as well as relevant abstracts presented at annual professional meetings, on lisdexamfetamine dimesylate in children and adolescents were included for review. This article presents the pharmacokinetic profile, efficacy, and safety of lisdexamfetamine dimesylate for the treatment of attention-deficit/hyperactivity disorder in children and, more recently, in adolescents.

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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 B Neuropsychiatr Genet. 2013;162:227-34.

**DISC1 IN ADULT ADHD PATIENTS: AN ASSOCIATION STUDY IN TWO EUROPEAN SAMPLES.**

**Jacobsen KK, Halmoy A, Sanchez-Mora C, et al.**

The DISC1 gene was named after its discovery in a Scottish pedigree with schizophrenia (SCZ) patients. However, subsequent studies have shown association of DISC1 variants with a range of different neurocognitive phenotypes and psychiatric disorders, including bipolar disorder (BPD), and major depression. Attention-deficit/hyperactivity disorder (ADHD) shares some symptoms with BPD and ADHD patients often suffer from comorbid affective disorders. We wanted to examine the role of DISC1 in ADHD, and with comorbid symptoms of mood disorders. Eleven single nucleotide polymorphisms (SNPs) previously implicated in SCZ and BPD, and a DISC1 duplication involving exon 1, were genotyped in 561 adult ADHD cases and 713 controls of Norwegian ancestry. The intronic SNP rs1538979 was associated with ADHD in the Norwegian sample [odds ratio (OR): 1.33, 95% confidence interval (CI) 1.03-1.73, P=0.03] and replicated in a Spanish adult ADHD sample of 694 cases and 735 controls, using the tagging SNP rs11122330 (meta-analysis: P=0.008, OR 1.25, 95% CI 1.06-1.47). In the Norwegian ADHD sample we also observed an association between the Phe607-variant of rs6675281 and a positive score on the Mood Disorder Questionnaire (MDQ; OR=1.44, 95% CI 1.08-1.93, P=0.01). To our knowledge, this is the first study to show an association between DISC1 variants and ADHD. Our study suggests that further studies are warranted to resolve if DISC1 variation is involved in several common neurodevelopmental disorders including ADHD.

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Am J Addict. 2013.

**DELINQUENCY, AGGRESSION, AND ATTENTION-RELATED PROBLEM BEHAVIORS DIFFERENTIALLY PREDICT ADOLESCENT SUBSTANCE USE IN INDIVIDUALS DIAGNOSED WITH ADHD.**

**Harty SC, Galanopoulos S, Newcorn JH, et al.**

**Objective:** To measure the degree to which childhood and adolescent ratings of aggression, attention, and delinquency are related to adolescent substance use outcomes in youth diagnosed with attention-deficit/hyperactivity disorder (ADHD).

**Background:** Childhood externalizing disorders have been shown to predict adolescent maladaptive substance use, but few studies have examined the differential predictive utility of two distinct dimensions of externalizing behavior: aggression and delinquency.

**Methods:** Ninety-seven clinically referred children with ADHD initially took part in this research protocol when they were on average 9.05 years of age, and were seen again on average 9.30 years later. Participants' parents were administered the Child Behavior Checklist (CBCL) at baseline and follow-up, and youth completed the Youth Self Report (YSR) in adolescence. At follow-up, substance use severity and diagnosis were assessed using semi-structured psychiatric interviews administered separately to parents and adolescents. Linear and binary logistic regressions were used to determine the association of CBCL- and YSR-rated attention problems, aggression, and delinquency to adolescent substance use.

**Results:** Childhood and adolescent delinquency, but not aggression, as rated by parents and youths, predicted adolescent substance use disorders and substance use severity (all p<.05). After accounting for the associations of delinquency and aggression with adolescent substance use, ratings of attention problems in childhood and adolescence were negatively associated with substance use outcome.

**Conclusions:** Children with ADHD who exhibit high rates of delinquency are at risk for later substance use and may require targeted prevention, intervention, and follow-up services.

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An Pediatr. 2013.

**ROLE OF IRON IN THE TREATMENT OF ATTENTION DEFICIT-HYPERACTIVITY DISORDER.**

**Soto-Insuga V, Calleja ML, Prados M, et al.**

**Introduction:** The aetiology of attention deficit hyperactivity disorder (ADHD) is attributed to different factors: genetic, environmental, and biological (neurotransmitters: dopaminergic system). Iron is essential for the correct functioning of the dopaminergic system. Iron deficiency is common in patients with ADHD, and its correction may be useful in the treatment.

**Objectives:** To analyse a possible relationship between iron deficiency and symptoms of inattention, hyperactivity and impulsivity in ADHD patients, and the potential benefit of iron therapy.

**Patients and methods:** A prospective study was conducted on non-anaemic and cognitively normal children, newly diagnosed with ADHD, according to DSM-IV criteria. Specific scales were used (SNAP-IV, ADHS) and serum ferritin was determined. Those with ferritin (less-than or equal to) 30 ng/ml were treated with ferrous sulphate (4 mg/kg/day) for 3 months, with its effect quantified being subsequently quantified.

**Results:** A total of 60 patients, with a mean age of 9.02 years (range: 6-14), were analysed. The inattentive subtype was the most frequent one (53.3%). Almost two-thirds (63.3%) had iron deficiency, which was more frequent among the inattentive group (38 vs 22,  $P < .02$ ). The iron treatment was completed by 17 patients. The treatment was not effective in 7 of the 8 non-inattentive subtypes, with a partial response in the remaining one. Of the 9 inattentive subtypes: the treatment was successful in the total control of symptoms in 5 of them, partially effective in other 3, and ineffective in one patient. The probability of complete response after treatment with iron was higher in inattentive patients with ADHD ( $P = .02$ ).

**Conclusions:** Treatment with iron supplements can be an effective alternative to treat patients with ADHD and iron deficiency, especially the inattentive subtype.

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Ann Epidemiol. 2013;23:179-84.

**CHRONIC HEALTH CONDITIONS AND SCHOOL PERFORMANCE AMONG CHILDREN AND YOUTH.**

**Crump C, Rivera D, London R, et al.**

**Purpose:** Chronic health conditions are common and increasing among U.S. children and youth. We examined whether chronic health conditions are associated with low school performance.

**Methods:** This retrospective cohort study of 22,730 children and youth (grades 2-11) in San Jose, California, was conducted from 2007 through 2010. Health conditions were defined as chronic if reported in each of the first 2 years, and school performance was measured using standardized English language arts (ELA) and math assessments.

**Results:** Chronic health conditions were independently associated with low ELA and math performance, irrespective of ethnicity, socioeconomic status, or grade level. Adjusted odds ratios for the association between any chronic health condition and low ("basic or below") performance were 1.25 (95% confidence interval [CI], 1.16-1.36;  $P < .001$ ) for ELA and 1.28 (95% CI, 1.18-1.38;  $P < .001$ ) for math, relative to students without reported health conditions. Further adjustment for absenteeism had little effect on these results. The strongest associations were found for ADHD, autism, and seizure disorders, whereas a weak association was found for asthma before but not after adjusting for absenteeism, and no associations were found for cardiovascular disorders or diabetes.

**Conclusions:** Chronic neurodevelopmental and seizure disorders, but not cardiovascular disorders or diabetes, were independently associated with low school performance among children and youth.

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Biol Psychiatry. 2013.

**WHITE MATTER ALTERATIONS AT 33-YEAR FOLLOW-UP IN ADULTS WITH CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Cortese S, Imperati D, Zhou J, et al.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is increasingly conceived as reflecting altered functional and structural brain connectivity. The latter can be addressed with diffusion tensor imaging (DTI).

We examined fractional anisotropy (FA), a DTI index related to white matter structural properties, in adult male subjects diagnosed with ADHD in childhood (probands) and matched control subjects without childhood ADHD. Additionally, we contrasted FA among probands with and without current ADHD in adulthood and control subjects.

**Methods:** Participants were from an original cohort of 207 boys and 178 male control subjects. At 33-year follow-up, analyzable DTI scans were obtained in 51 probands (41.3(plus or minus)2.8 yrs) and 66 control subjects (41.2(plus or minus)3.1 yrs). Voxel-based FA was computed with tract-based spatial statistics, controlling for multiple comparisons.

**Results:** Probands with childhood ADHD exhibited significantly lower FA than control subjects without childhood ADHD in the right superior and posterior corona radiata, right superior longitudinal fasciculus, and in a left cluster including the posterior thalamic radiation, the retrolenticular part of the internal capsule, and the sagittal stratum ( $p < .05$ , corrected). Fractional anisotropy was significantly decreased relative to control subjects in several tracts in both probands with current and remitted ADHD, who did not differ significantly from each other. Fractional anisotropy was not significantly increased in probands in any region.

**Conclusions:** Decreased FA in adults with childhood ADHD regardless of current ADHD might be an enduring trait of ADHD. White matter tracts with decreased FA connect regions involved in high-level as well as sensorimotor functions, suggesting that both types of processes are involved in the pathophysiology of ADHD.

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Brain Topogr. 2013;1-13.

#### **NEUROFEEDBACK IN ADHD: FURTHER PIECES OF THE PUZZLE.**

**Gevensleben H, Kleemeyer M, Rothenberger LG, et al.**

Among the different neuromodulation techniques, neurofeedback (NF) is gaining increasing interest in the treatment of children with attention-deficit/hyperactivity disorder (ADHD). In this article, a methodological framework is summarised considering the training as a neuro-behavioural treatment. Randomised controlled trials are selectively reviewed. Results from two smaller-scale studies are presented with the first study comprising a tomographic analysis over the course of a slow cortical potential (SCP) training and a correlational analysis of regulation skills and clinical outcome in children with ADHD. In the second study, ADHD-related behaviour was studied in children with tic disorder who either conducted a SCP training or a theta/low-beta (12-15 Hz) training (single-blind, randomised design). Both studies provide further evidence for the specificity of NF effects in ADHD. Based on these findings, a refined model of the mechanisms contributing to the efficacy of SCP training is developed. Despite a number of open questions concerning core mechanisms, moderators and mediators, NF (theta/beta and SCP) training seems to be on its way to become a valuable and ethically acceptable module in the treatment of children with ADHD.

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Can J Psychiatry. 2013;58:177-83.

#### **EXAMINING THE NATURE OF THE ASSOCIATION BETWEEN ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND NICOTINE DEPENDENCE: A FAMILIAL RISK ANALYSIS.**

**Biederman J, Petty CR, Hammerness P, et al.**

**Objective:** To use familial risk analysis to examine the association between attention-deficit hyperactivity disorder (ADHD) and nicotine dependence (ND).

**Method:** Subjects were children with ( $n=257$ ) and without ( $n=229$ ) ADHD of both sexes ascertained from pediatric and psychiatric referral sources and their first-degree relatives ( $N=1627$ ).

**Results:** ND in probands increased the risk for ND in relatives irrespective of ADHD status. There was no evidence of cosegregation or assortative mating between these disorders. Patterns of familial risk analysis suggest that the association between ADHD and ND is most consistent with the hypothesis of independent transmission of these disorders.

**Conclusions:** These findings may have important implications for the identification of a subgroup of children with ADHD at high risk for ND based on parental history of ND.

Child Psychiatry Hum Dev. 2013 Feb;44:166-85.

**EVALUATION OF PLANNING DYSFUNCTION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISTIC SPECTRUM DISORDERS USING THE ZOO MAP TASK.**

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

Attention-Deficit-Hyperactivity-Disorders (ADHD) and Autistic-Spectrum- Disorders (ASD) share overlapping clinical and cognitive features that may confuse the diagnosis. Evaluation of executive problems and planning dysfunction may aid the clinical diagnostic process and help disentangle the neurobiological process underlying these conditions. This study evaluates the planning function problems in 80 male children and adolescents diagnosed with ADHD and 23 male children and adolescents with ASD using the Zoo Map Task; both groups were comparable in terms of age and IQ. The relationship between planning function and other executive functions is also assessed. In comparison to the ADHD groups, ASD children presented more errors in the open-ended tasks; these planning function problems seem to be mediated by processing speed and motor coordination, however it does not seem to be mediated by other executive function problems, including attention, working memory or response inhibition. In the time for planning, an interaction between the specific subgroups and working memory components was observed. ADHD and ASD present with different patterns of planning function, even when other components of executive function are taken into account; clinical and educational implications are discussed.

Clin Neurophysiol. 2013 Apr;124:644-57.

**TEN YEARS ON: A FOLLOW-UP REVIEW OF ERP RESEARCH IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Johnstone SJ, Barry RJ, Clarke AR .**

This article reviews the event-related potential (ERP) literature in relation to attention-deficit/hyperactivity disorder (AD/HD) over the years 2002-2012. ERP studies exploring various aspects of brain functioning in children and adolescents with AD/HD are reviewed, with a focus on group effects and interpretations in the domains of attention, inhibitory control, performance monitoring, non-pharmacological treatments, and ERP/energetics interactions. There has been a distinct shift in research intensity over the past 10 years, with a large increase in ERP studies conducted in the areas of inhibitory control and performance monitoring. Overall, the research has identified a substantial number of ERP correlates of AD/HD. Robust differences from healthy controls have been reported in early orienting, inhibitory control, and error-processing components. These data offer potential to improve our understanding of the specific brain dysfunction(s) which contribute to the disorder. The literature would benefit from a more rigorous approach to clinical group composition and consideration of age effects, as well as increased emphasis on replication and extension studies using exacting participant, task, and analysis parameters.

Clin Neuropharmacol. 2013;36:37-41.

**REBOXETINE TREATMENT FOR AUTISTIC SPECTRUM DISORDER OF PEDIATRIC PATIENTS WITH DEPRESSIVE AND INATTENTIVE/HYPERACTIVE SYMPTOMS: AN OPEN-LABEL TRIAL.**

**Golubchik P, Sever J, Weizman A.**

**Background:** Reboxetine is a norepinephrine reuptake inhibitor that may be useful in treating pediatric depression as well as attention-deficit/ hyperactivity disorder (ADHD). Both are often comorbid with autistic spectrum disorder (ASD). We evaluated the effectiveness of reboxetine treatment in pediatric patients with ASD with symptoms of depression and ADHD.

**Method:** Eleven adolescent patients with ASD (9 boys and 2 girls, aged 12.2 (plus or minus) 3.6 years) with depressive and ADHD symptoms were treated with reboxetine (maximal dose, 4 mg/d) in an open-label trial during a 12-week period. The severity of depressive and ADHD symptoms was assessed by the Child Depression Rating Scale (CDRS) and Attention-Deficit/Hyperactivity Disorder Rating Scale (ADHD-RS), respectively.

**Results:** Significant, but modest, decreases in the severity of depressive symptoms (CDRS before vs after scores: 65.5 (plus or minus) 10.8 vs 58.3 (plus or minus) 8.2; paired t test, 3.1; df, 10; P=0.01) and ADHD symptoms (Attention Deficit/Hyperactivity Disorder Rating Scale before vs after: 36.4 (plus or minus) 5 vs 32.8 (plus or minus) 5; paired-t test, 2.94; df, 10; P=0.015) were obtained after reboxetine treatment. The patients (n=5) with high baseline scores of CDRS (T score >75) showed a trend toward larger response to reboxetine than those (n=6) with low (T score <75) basal CDRS scores ((Delta), 12.8 (plus or minus) 5.4 vs 2.3 (plus or minus) 5.2; P=0.07). A significant positive correlation was found between the changes in the total scores of the depression and the ADHD severity (Spearman correlation  $r=0.65$  [95% confidence interval, 0.09-0.9]; n=11; P=0.029). Most of the patients (approximately 90%) reported tolerable adverse effects.

**Conclusions:** Reboxetine treatment may reduce, modestly but significantly, depressive and ADHD symptoms in adolescents with ASD. High rate of adverse effects requires close monitoring.

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Clin Ther. 2013.

**DESCRIPTIVE COMPARISON OF DRUG TREATMENT-PERSISTENT, -NONPERSISTENT, AND NONDRUG TREATMENT PATIENTS WITH NEWLY DIAGNOSED ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN GERMANY.**

**Braun S, Russo L, Zeidler J, et al.**

**Background:** Attention deficit/hyperactivity disorder (ADHD) is a heterogeneous behavioral disorder commonly found in children, with serious lifetime health and social consequences for both children and their parents. Public awareness of ADHD in Germany has increased in the past decade, but little is known about the costs of treating newly diagnosed patients in clinical practice.

**Objective:** This study aimed to describe the resource utilization and treatment costs of patients aged 6 to 17 years with newly diagnosed ADHD, using patient data from a German sickness fund, and to quantify resource utilization by drug treatment and treatment persistence.

**Methods:** To identify patients with newly diagnosed ADHD, the second largest German sickness fund was utilized. Complete claims data of all de-identified patients meeting eligibility criteria for 2007 and 2008 were extracted. Patients were divided into 1 of 3 treatment groups: drug treatment-persistent, drug treatment-nonpersistent, and nondrug treatment. The differences in costs and resource utilization are reported in a descriptive manner, with paired and unpaired 2-sample Wilcoxon tests used.

**Results:** Of 3407 newly diagnosed patients with ADHD, 1105 (32%) received an ADHD-specific drug following diagnosis; the remaining 2302 comprised the nondrug treatment group. Of the total number of drug-treated patients, 1-year observational data were available for only 786 methylphenidate users (71%). Of these, 503 patients (64%) comprised the drug treatment-persistent group (those having at least 1 prescription every 3 months during the 12 months following their first ADHD prescription) and 283 (36%) comprised the drug treatment-nonpersistent group. After excluding those patients with <12 months of follow-up, 1779 patients (52%) were included in the nondrug-treatment group. Outpatient visits and the number of drug prescriptions and associated costs were highest in the drug treatment-persistent group (P=0.05); however, the number of hospital admissions and days spent in-hospital were lowest in this group. Significant average savings of (euro) 187/y in overall costs (P=0.05) were noted for the drug treatment-persistent group compared with the drug treatment-nonpersistent group. These mean savings were (euro) 739/y and (euro) 552/y (drug treatment-persistent group and drug treatment-nonpersistent group, respectively) compared with nondrug-treated patients.

**Conclusions:** There are potential cost-savings benefits when patients are treatment persistent. Therefore, future disease-management programs might consider treatment persistence as potentially reducing overall payer costs. Additionally, the clinical and psychosocial situations of patients and their families should be taken into account.

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Crim Behav Ment Health. 2013;23:86-98.

**LONG-TERM CRIMINAL OUTCOME OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Dalsgaard S, Mortensen PB, Frydenberg M, et al.**

**Background** Long-term outcome studies of child psychiatric populations are often limited by attrition. Our study uses the Danish National Crime Register to report on the largest and most complete prospective study of adult criminality as an outcome for children with socioeconomic status attention deficit hyperactivity disorder (ADHD) and is the first to report on the adult criminal outcome of girls with ADHD.

**Aims** To estimate the relative risk (RR) of adult criminal convictions of children with ADHD compared with the rate in the general population.

**Methods** A clinical sample of 206 children who had attended a regional child and adolescent psychiatric clinic in Denmark between 1968 and 1989 and received a diagnosis of ADHD was identified. Official criminal conviction data were collected for all of them up to the year 2000 when their mean age was 31 years. Their rate of sustaining at least one criminal conviction was compared with that in an age-matched general population sample.

**Results** Ninety-seven (47%) of the children with ADHD had criminal convictions in adulthood. Children with ADHD were about five times more likely to sustain convictions than their peers in the general population (rate ratio (RR) 5.6, 95% confidence interval 5.2-6.1) and twelve times more likely to have violent convictions (RR 12.0, 95% confidence interval 9.9-14.5). Fifty-four (26%) of the children with ADHD without any conduct problems in childhood were convicted in adulthood. Girls with ADHD were also at increased risk of criminal convictions.

**Conclusions** Children with ADHD have a higher risk of criminal convictions in adulthood than previously documented, and both girls and boys are at increased risk. Co-morbid conduct problems in childhood are highly predictive of criminal convictions in adulthood. Even in the absence of conduct problems, however, childhood ADHD is associated with increased risk of criminality.

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Curr Psychiatry Rep. 2013;15:1-11.

**ANTIPSYCHOTIC AND PSYCHOSTIMULANT DRUG COMBINATION THERAPY IN ATTENTION DEFICIT/HYPERACTIVITY AND DISRUPTIVE BEHAVIOR DISORDERS: A SYSTEMATIC REVIEW OF EFFICACY AND TOLERABILITY.**

**Linton D, Barr AM, Honer WG, et al.**

This systematic review examines treatment guidelines, efficacy/effectiveness, and tolerability regarding the use of antipsychotics concurrently with psychostimulants in treating aggression and hyperactivity in children and adolescents. Articles examining the concurrent use of antipsychotics and psychostimulants to treat comorbid attention deficit/hyperactivity disorder (ADHD) and disruptive behavior disorders (DBDs) were identified and their results were summarized and critically analyzed. Antipsychotic and stimulant combination therapy is recommended by some guidelines, but only as a third-line treatment following stimulant monotherapy and stimulants combined with behavioral interventions to treat aggression in patients with ADHD. Some studies suggest efficacy/effectiveness for an antipsychotic and stimulant combination in the treatment of aggression and hyperactivity in children and adolescents. However, the data do not clearly demonstrate superiority compared to antipsychotic or psychostimulant monotherapy. Most studies were performed over short time periods, several lacked blinding, few studies used any placebo control, and no comparisons were made with behavioral interventions. There are concerns about the tolerability of combination therapy, but data do not suggest significantly worse adverse effects for combination compared to either antipsychotic or stimulant monotherapy. Conversely, and contrary to speculation, use of a stimulant does not significantly reduce metabolic effects of antipsychotics.

Combination treatment with antipsychotics and psychostimulants is used frequently, and increasingly more often. Few studies have directly examined this combination for the treatment of ADHD and DBDs. Further studies are necessary to confirm the efficacy and tolerability of the concurrent use of antipsychotics and psychostimulants in children and adolescents.

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Dev Med Child Neurol. 2013 Apr;55:296.

**MORE ATTENTION TO ADHD.**

**Sakakihara Y.**

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Epilepsy Behav. 2013;27:337-41.

**ATTENTION IMPAIRMENT IN CHILDHOOD ABSENCE EPILEPSY: AN IMPULSIVITY PROBLEM?**

**Cerminara C, D'Agati E, Casarelli L, et al.**

Although attention problems have often been described in children with childhood absence epilepsy (CAE), the use of different methodological approaches, neuropsychological tests, and heterogeneous experimental groups has prevented identification of the selective areas of attention deficit in this population. In this study, we investigated several components of attention in children with CAE using a unique computerized test battery for attention performance. Participants included 24 patients with CAE and 24 controls matched for age and sex. They were tested with a computerized test battery, which included the following tasks: selective attention, impulsivity, focused attention, divided attention, alertness, and vigilance. Compared with healthy controls, patients with CAE made more commission errors in the Go/No-Go task and more omission errors in the divided attention task. Childhood absence epilepsy patients also showed decreased reaction times in measures of selective attention and a great variability of reaction times in alertness and Go/No-Go tasks. Our findings suggest that patients with CAE were impaired in tonic and phasic alertness, divided attention, selective attention, and impulsivity.

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Eur Child Adolesc Psychiatry. 2013;1-2.

**METHYLPHENIDATE AND ATOMOXETINE FOR TREATMENT OF NOCTURNAL ENURESIS IN A CHILD WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.**

**Bahali K, Ipek H, Uneri OS.**

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Eur Child Adolesc Psychiatry. 2013;1-18.

**BARRIERS TO, AND FACILITATORS OF, PARENTING PROGRAMMES FOR CHILDHOOD BEHAVIOUR PROBLEMS: A QUALITATIVE SYNTHESIS OF STUDIES OF PARENTS' AND PROFESSIONALS' PERCEPTIONS.**

**Koerting J, Smith E, Knowles MM, et al .**

Disruptive behaviour problems (DBPs) during childhood exert a high burden on individuals, families and the community as a whole. Reducing this impact is a major public health priority. Early parenting interventions are recommended as valuable ways to target DBPs; however, low take-up of, and high drop-out rates from, these programmes seriously reduce their effectiveness. We present a review of published qualitative evidence relating to factors that block or facilitate access and engagement of parents with such programmes using a thematic synthesis approach. 12 papers presenting views of both parents and professionals met our inclusion and quality criteria. A large number of barriers were identified highlighting the array of challenges parents can face when considering accessing and engaging with treatment for their child with behavioural problems. Facilitating factors in this area were also identified. A series of recommendations were made with regard to raising awareness of programmes and recruiting parents,

providing flexible and individually tailored support, delivering programmes through highly skilled, trained and knowledgeable therapists, and highlighting factors to consider when delivering group-based programmes. Clinical guidelines should address barriers and facilitators of engagement as well as basic efficacy of treatment approaches.

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Eur Child Adolesc Psychiatry. 2013;1-12.

**AUTISTIC TRAITS IN CHILDREN WITH ADHD INDEX CLINICAL AND COGNITIVE PROBLEMS .**

**Cooper M, Martin J, Langley K, et al.**

Traits of autistic spectrum disorders (ASD) occur frequently in attention deficit hyperactivity disorder (ADHD), but the significance of their presence in terms of phenotype and underlying neurobiology is not properly understood. This analysis aimed to determine whether higher levels of autistic traits, as measured by the Social Communication Questionnaire (SCQ), index a more severe presentation in a large, rigorously phenotyped sample of children with ADHD (N = 711). Regression analyses were used to examine association of SCQ scores with core ADHD features, clinical comorbidities and cognitive and developmental features, with adjustment for putative confounders. For outcomes showing association with total SCQ score, secondary analyses determined levels of differential association of the three ASD sub-domains. Results suggest that increasing ASD symptomatology within ADHD is associated with a more severe phenotype in terms of oppositional, conduct and anxiety symptoms, lower full-scale IQ, working memory deficits and general motor problems. These associations persisted after accounting for ADHD severity, suggesting that autistic symptomatology independently indexes the severity of comorbid impairments in the context of ADHD. Sub-domain scores did not show unique contributions to most outcomes, except that social deficits were independently associated with oppositional symptoms and repetitive behaviours independently predicted hyperactive-impulsive symptoms and motor problems. It would be worthwhile for clinicians to consider levels of socio-communicative and repetitive traits in those with ADHD who do not meet diagnostic criteria for ASD, as they index higher levels of phenotypic complexity, which may have implications for efficacy of interventions.

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Eur Neuropsychopharmacol. 2013;23:S80.

**LONG TERM THERAPY WITH METHYLPHENIDATE INDUCES MODEST EFFECTS ON GROWTH IN ADHD CHILDREN.**

**Balia C, Anedda A, Granitzio F, et al.**

**Background:** Although stimulants are the most effective medication for Attention Deficit Hyperactivity Disorder (ADHD), poor growth is a common concern, especially with children already on the lower growth percentiles. Studies providing longitudinal data indicate a reduction in both height and weight gain: these effects are usually minimal, but there is substantial variability with some children completely unaffected, whereas others shows significant growth suppression [1].

**Objectives:** To evaluate whether long term immediate release methylphenidate (IR-MPH) therapy (one or two years) interferes with the growth of ADHD children and to assess whether the effects on growth are related to the length of the treatment or to the daily dose.

**Methods:** Growth parameters were collected from 90 ADHD aged 6 to 14, enrolled at one of the site of the Italian National Register for ADHD. All patient were on IR-MPH and with a minimum follow-up of 12 months. 65 were Drug Naive (DN), 25 were already on MPH since 1-3 years prior to enrollment in the Registry (PR). Weight, height, BMI, height Z-score and BMI Z-score were recorded at each follow-up visit (baseline and after 6, 12, 18, 24 months). Growth velocity SDS and height deficit were calculated after 12 and 24 months. Data Analysis: Categorical data were analysed using contingency tables (c2), continuous variables were compared by one-way ANOVA. Repeated measures ANOVA was performed for height and BMI z scores at baseline, 6, 12, 18, 24 month follow up and for height velocity SDS at 12 and 24 months.

**Results:** At baseline Height Z-scores of the entire sample was -0.33(plus or minus)0.98, BMI Z-score was equal to 0.19(plus or minus)1.14. During the 24 months in the study, subjects gained in absolute values of height and weight. Height Z-score showed a significant decrease only from T12 to T24 (p = 0.05). BMI Z-

score decreased significantly at T12 ( $p < 0.001$ ) remaining essentially unchanged at T24. Height deficit was about 0.5 cm at 12 months and 1.3 cm after 24 months. MPH dose/kg/day changed from 0.49 (plus or minus) 0.21 mg when starting medication, to 0.68 (plus or minus) 0.24 at T12 and to 0.75 (plus or minus) 0.25 at T24. No significant differences were found on growth parameters at baseline when stratifying between DN and PR. As in the total sample, in both groups a significant decrease in BMI Z-score from baseline to T12 ( $p < 0.001$ ) and in height Z-score between T12 and T2 ( $p = 0.05$ ) was found. No changes in growth velocity from baseline to the different times considered, were observed, neither in DN nor in PR.

**Discussion:** The findings of the present study suggest that the effects of MPH on growth are relatively small and unlikely to be of clinical concern for this population. Expected and actual deficit in growth should be considered in the context of the benefits the patient receives from the medication. In the present sample the height deficit appears to be more related to the maximum pro/die dose rather than to the length of therapy. More research is needed to better elucidate the mechanism of growth suppression and to implement specific treatment strategies for ADHD children.

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Front Psychiatry. 2011;2.

**THE ROLE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN THE ASSOCIATION BETWEEN VERBAL ABILITY AND CONDUCT DISORDER.**

**Smith AK, Stasi SM, Rhee SH, et al.**

Although there is clear evidence that low verbal ability is a risk factor for conduct disorder (CD), some researchers have questioned whether this association is due to the common comorbidity between attention-deficit/hyperactivity disorder (ADHD) and CD. The present study examined the association among verbal ability, ADHD, and CD in a genetically informative sample in order to examine the role of genes and/or environmental influences shared in common with ADHD on the covariation between verbal ability and CD. Participants were 2744 adolescents from the Center for Antisocial Drug Dependence (CADD), and included 360 monozygotic (MZ) female twin pairs, 221 dizygotic (DZ) female twin pairs, 297 MZ male twin pairs, 220 DZ male twin pairs, and 274 opposite-sex DZ twin pairs. The Diagnostic Interview Schedule for Children (DISC-IV) was used to assess lifetime symptoms of ADHD and CD. Verbal ability was assessed via the Vocabulary subtest of the Wechsler Adult Intelligence Scale III (WAIS-III) for individuals over the age of 16 and the Vocabulary subtest of the Wechsler Intelligence Scale for Children III (WISCIII) for individuals under the age of 16. There was a small but significant negative covariance between verbal ability and CD and between verbal ability and ADHD. Results also suggest that the covariation between verbal ability and CD is due to influences shared in common with ADHD.

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Front Psychiatry. 2012;2.

**A SYSTEMATIC REVIEW OF GLOBAL PUBLICATION TRENDS REGARDING LONG-TERM OUTCOMES OF ADHD.**

**Hodgkins P, Arnold LE, Shaw M, et al.**

There is increased global recognition of attention deficit hyperactivity disorder (ADHD) as a serious medical condition with long-term consequences. Although originally conceived of as a childhood disorder, ADHD is being increasingly recognized in adults. Individual geographic regions may have specific interests and objectives for the study of ADHD. A systematic review of long-term outcomes (LTOs) in ADHD was conducted to evaluate research on ADHD LTOs on a global scale. Studies that were at least 2 years in duration were examined. A total of 351 studies were identified in the final analysis. We identified nine outcomes of interest and classified studies by specific geographical regions, age groups studied and study design by region and over time. Published studies of LTOs in ADHD have increased in all geographical regions over the past three decades, with a peak number of 42 publications in 2008. This rise in publications on ADHD LTOs may reflect a rise in global interest and recognition of consequences and impairment associated with ADHD. Although many world regions have published on ADHD LTOs, the majority of studies have emerged from the US and Canada, followed by Europe. While investigators in the US and Canada were predominantly interested in drug addiction as a LTO, European researchers were

more interested in antisocial behavior, and Eastern Asian investigators focused on both of these LTOs as well as self-esteem. Geographical differences in the focus of ADHD LTO studies may reflect regional variations in cultural values. Proportionally fewer prospective longitudinal studies and proportionally more retrospective and cross-sectional studies have been published in more recent decades. Finally, more studies focusing on ADHD in adolescents and adults have been conducted in recent years, and particularly adolescents in Eastern Asia. These changes in basic study design may reflect an increase in the recognition that ADHD is a lifetime chronic disorder. This systematic review analysis of publication trends in ADHD LTOs reflects geographically based interests that change over time.

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Front Psychiatry. 2012;3.

**ALTERED CORTICO-STRIATAL-THALAMIC CONNECTIVITY IN RELATION TO SPATIAL WORKING MEMORY CAPACITY IN CHILDREN WITH ADHD.**

**Mills KL, Bathula D, Dias TGC, et al.**

**Introduction:** Attention deficit hyperactivity disorder (ADHD) captures a heterogeneous group of children, who are characterized by a range of cognitive and behavioral symptoms. Previous resting-state functional connectivity MRI (rs-fcMRI) studies have sought to understand the neural correlates of ADHD by comparing connectivity measurement between those with and without the disorder, focusing primarily on cortical-striatal circuits mediated by the thalamus. To integrate the multiple phenotypic features associated with ADHD and help resolve its heterogeneity, it is helpful to determine how specific circuits relate to unique cognitive domains of the ADHD syndrome. Spatial working memory has been proposed as a key mechanism in the pathophysiology of ADHD.

**Methods:** We correlated the rs-fcMRI of five thalamic regions of interest (ROIs) with spatial span working memory scores in a sample of 67 children aged 7-11 years [ADHD and typically developing children (TDC)]. In an independent dataset, we then examined group differences in thalamo-striatal functional connectivity between 70 ADHD and 89 TDC (7-11 years) from the ADHD-200 dataset. Thalamic ROIs were created based on previous methods that utilize known thalamo-cortical loops and rs-fcMRI to identify functional boundaries in the thalamus.

**Results/Conclusion:** Using these thalamic regions, we found atypical rs-fcMRI between specific thalamic groupings with the basal ganglia. To identify the thalamic connections that relate to spatial working memory in ADHD, only connections identified in both the correlational and comparative analyses were considered. Multiple connections between the thalamus and basal ganglia, particularly between medial and anterior dorsal thalamus and the putamen, were related to spatial working memory and also altered in ADHD. These thalamo-striatal disruptions may be one of multiple atypical neural and cognitive mechanisms that relate to the ADHD clinical phenotype.

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Front Psychiatry. 2012;2.

**RESTING STATE FUNCTIONAL CONNECTIVITY CORRELATES OF INHIBITORY CONTROL IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**Mennes M, Potler NV, Kelly C, et al.**

Motor inhibition is among the most commonly studied executive functions in attention-deficit/hyperactivity disorder (ADHD). Imaging studies using probes of motor inhibition such as the stop signal task (SST) consistently demonstrate ADHD-related dysfunction within a right-hemisphere fronto-striatal network that includes inferior frontal gyrus and pre-supplementary motor area. Beyond findings of focal hypo- or hyperfunction, emerging models of ADHD psychopathology highlight disease-related changes in functional interactions between network components. Resting state fMRI (R-fMRI) approaches have emerged as powerful tools for mapping such interactions (i.e., resting state functional connectivity, RSFC), and for relating behavioral and diagnostic variables to network properties. We used R-fMRI data collected from 17 typically developing controls (TDC) and 17 age-matched children with ADHD (aged 8-13 years) to identify neural correlates of SST performance measured outside the scanner. We examined two related inhibition

indices: stop signal reaction time (SSRT), indexing inhibitory speed, and stop signal delay (SSD), indexing inhibitory success. Using 11 fronto-striatal seed regions-of-interest, we queried the brain for relationships between RSFC and each performance index, as well as for interactions with diagnostic status. Both SSRT and SSD exhibited connectivity-behavior relationships independent of diagnosis. At the same time, we found differential connectivity-behavior relationships in children with ADHD relative to TDC. Our results demonstrate the utility of RSFC approaches for assessing brain/behavior relationships, and for identifying pathology-related differences in the contributions of neural circuits to cognition and behavior.

Genes Brain Behav. 2013;12:305-10.

**A STUDY OF THE POSSIBLE ASSOCIATION BETWEEN ADENOSINE A2A RECEPTOR GENE POLYMORPHISMS AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER TRAITS.**

**Molero Y, Gumpert C, Serlachius E, et al.**

The adenosine A2A receptor (ADORA2A) is linked to the dopamine neurotransmitter system and is also implicated in the regulation of alertness, suggesting a potential association with attention-deficit hyperactivity disorder (ADHD) traits. Furthermore, animal studies suggest that the ADORA2A may influence ADHD-like behavior. For that reason, the ADORA2A gene emerges as a promising candidate for studying the etiology of ADHD traits. The aim of this study was to examine the relationship between ADORA2A gene polymorphisms and ADHD traits in a large population-based sample. This study was based on the Child and Adolescent Twin Study in Sweden (CATSS), and included 1747 twins. Attention-deficit hyperactivity disorder traits were assessed through parental reports, and samples of DNA were collected. Associations between six single nucleotide polymorphisms (SNPs) and ADHD traits were examined, and results suggested a nominal association between ADHD traits and three of these SNPs: rs3761422, rs5751876 and rs35320474. For one of the SNPs, rs35320474, results remained significant after correction for multiple comparisons. These results indicate the possibility that the ADORA2A gene may be involved in ADHD traits. However, more studies replicating the present results are warranted before this association can be confirmed. When examining the relationship between adenosine A2A receptor (ADORA2A) gene polymorphisms and ADHD traits in a population-based sample of 1747 twins, results showed nominal associations between ADHD traits and three SNPs in the ADORA2A gene: rs3761422, rs5751876 and rs35320474. For one of the SNPs, rs35320474, results remained significant after correction for multiple comparisons. These results indicate the possible involvement of the ADORA2A in ADHD traits, a plausible notion as adenosine plays a role in ADHD-related neurobiological mechanisms such as dopamine neurotransmission and regulation of alertness. However, these results should be viewed as preliminary and more studies replicating the present results are warranted before this association can be confirmed.

Gent Test and Mol Biomarkers. 2013;17:301-06.

**ASSOCIATION BETWEEN TPH2 GENE POLYMORPHISMS AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN KOREAN CHILDREN.**

**Park TW, Park YH, Kwon HJ, et al.**

Attention deficit hyperactivity disorder (ADHD) is a common disorder of the school-age population. ADHD is a familial disorder and genetic studies estimate heritability at 80%-90%. The aim of the present study was to investigate the association between the genetic type and alleles for the TPH2 gene in Korean children with ADHD. The sample consisted of 142 ADHD children and 139 control children. We diagnosed ADHD according to the Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition). ADHD symptoms were evaluated with Conners' Parent Rating Scales and Dupaul Parent ADHD Rating Scales. Blood samples were taken from the 281 subjects, DNA was extracted from blood lymphocytes, and polymerase chain reaction was performed for TPH2 polymorphism. Alleles and genotype frequencies were compared using the chi-square test. We compared the allele and genotype frequencies of TPH2 gene polymorphism in the ADHD and control groups. This study showed that there was a significant correlation among the

frequencies of the rs11179027 (odd ratio [OR]=2.12, 95% confidence interval [CI]=1.13-3.97, p=0.020) and rs1843809 (OR=0.48, 95% CI=0.24-0.97, p=0.040) of alleles of TPH2, but the final conclusions are not definite. Follow-up studies with larger patient or pure subgroups are expected. These results suggested that TPH2 might be related to ADHD symptoms.

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J Autism Dev Disord. 2013 Apr;43:917-23.

**INHIBITION OF RETURN IN RESPONSE TO EYE GAZE AND PERIPHERAL CUES IN YOUNG PEOPLE WITH ASPERGER'S SYNDROME.**

**Marotta A, Pasini A, Ruggiero S, et al.**

Inhibition of return (IOR) reflects slower reaction times to stimuli presented in previously attended locations. In this study, we examined this inhibitory after-effect using two different cue types, eye-gaze and standard peripheral cues, in individuals with Asperger's syndrome and typically developing individuals. Typically developing participants showed evidence of IOR for both eye-gaze and peripheral cues. In contrast, the Asperger group showed evidence of IOR to previously peripherally cued locations but failed to show IOR for eye-gaze cues. This absence of IOR for eye-gaze cues observed in the participants with Asperger may reflect an attentional impairment in responding to socially relevant information.

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J Child Adolesc Psychopharmacol. 2013;23:130-35.

**WORSENING BEHAVIORAL DYSREGULATION IN A TRIPLET PAIR: UNDERTREATED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER OR UNTREATED PSYCHIATRIC COMORBID DISORDERS?**

**Mitrani P, Coffey DB.**

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Journal of Clinical Child and Adolescent Psychology. 2013 Mar;42:251-61.

**ONE-YEAR FOLLOW-UP OF COMBINED PARENT AND CHILD INTERVENTION FOR YOUNG CHILDREN WITH ADHD.**

**Webster-Stratton C, Reid MJ, Beauchaine TP.**

Efficacies of the Incredible Years (IY) interventions are well-established in children with oppositional defiant disorder (ODD) but not among those with a primary diagnosis of attention-deficit/hyperactivity disorder (ADHD). We sought to evaluate 1-year follow-up outcomes among young children with ADHD who were treated with the IY interventions. Four- to 6-year-olds with ADHD (n = 49, 73% male) participated in 6 months of treatment using the IY parent and child interventions. Immediate posttreatment results indicated improvements in parenting, children's externalizing and attention problems, and social contact at school. At 1-year follow up, 22 of 27 variables that showed significant posttreatment effects demonstrated maintenance to 1-year follow up. Children with higher ODD symptoms at baseline showed more improvement in oppositionality and total behavior problems, and their mothers showed more improvement on harsh discipline scores. Approximately 70 to 75% of children were reported by their parents and teachers to fall below clinical cutoffs on measures of externalizing symptoms at the 1-year follow up (compared to 50% at baseline), and more than 50% fell below clinical cutoffs on measures of hyperactivity and inattentiveness (all were in the clinical range at baseline). Children with ADHD who were treated with the IY parent and child treatment programs showed maintenance of treatment effects 1 year after treatment.

Journal of Clinical Child and Adolescent Psychology. 2013 Mar;42:197-207.

**MEASURING ADHD AND ODD SYMPTOMS AND IMPAIRMENT USING HIGH SCHOOL TEACHERS' RATINGS.**

**Evans SW, Brady CE, Harrison JR, et al.**

We analyzed the results of high school teachers' ratings of symptoms of attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder, as well as school-related impairment of 875 adolescents. One hundred forty-three teachers at 19 high schools across 4 states each rated 6 students from their first-period classes according to selection criteria that led to ratings for 3 male and 3 female students. Factor analyses were conducted on the symptom measure to test hypotheses pertaining to the divergence of impulsivity and hyperactivity dimensions. Normative values for the Disruptive Behavior Disorder–Teacher Rating Scale and Impairment Rating Scale are reported, as well as important differences related to age, race, and gender. Gender and age contrasts revealed that boys were rated as more symptomatic and impaired than girls and younger adolescents were rated as having more problems than older adolescents in most areas. African American adolescents were rated higher on measures of symptoms and impairment than their Caucasian peers. Large differences in normative levels of hyperactivity/impulsivity and inattention are reported that are consistent with a reduced likelihood of a diagnosis of ADHD-C as children get older. Implications for the interpretation of ratings from high school teachers are discussed.

Journal of Clinical Child and Adolescent Psychology. 2013 Mar;42:243-50.

**THE EFFECTS OF SINGLE VERSUS MIXED GENDER TREATMENT FOR ADOLESCENT GIRLS WITH ADHD.**

**Babinski DE, Sibley MH, Ross JM, et al.**

This study evaluated the social behavior of adolescents with attention deficit hyperactivity disorder (ADHD) in single and mixed gender treatment settings. We collected ratings of social behavior (i.e., prosocial peer interactions, assertiveness, self-management, compliance, physical aggression, relational aggression) during single and mixed gender games within the Summer Treatment Program–Adolescent for 10 girls (M age = 13.17, 80% Hispanic) and 11 boys (M age=12.89, 54.55% Hispanic). Counselors completed ratings immediately following 10 recreational periods for each adolescent they supervised (5 single gender games, 5 mixed gender games). Gender (female vs. male) × Setting (single vs. mixed gender) ANOVAs were conducted. If a significant interaction emerged, post hoc tests were also conducted. Several Gender × Setting interactions emerged, suggesting that girls benefit more from single gender formats than mixed gender formats. Girls showed more assertiveness, self-management, and compliance in single compared to mixed gender settings. A somewhat different pattern of results emerged for boys, which showed more appropriate social behavior (i.e., self-management, compliance) and less inappropriate social behavior (i.e., physical and relational aggression) in mixed gender settings compared to single gender settings. In contrast to previous ADHD treatment studies, these findings suggest that gender may impact treatment response for adolescents. Therefore, it is important that future studies evaluate whether current treatments for ADHD are appropriate for girls with ADHD and whether gender-specific treatments are necessary to address the unique difficulties of adolescent girls with ADHD.

Journal of Clinical Child and Adolescent Psychology. 2013 Mar;42:187-96.

**ARE COGNITIVE CONTROL AND STIMULUS-DRIVEN PROCESSES DIFFERENTIALLY LINKED TO INATTENTION AND HYPERACTIVITY IN PRESCHOOLERS?**

**Miller CJ, Miller SR, Healey DM, et al.**

Temperament and attention-deficit/hyperactivity disorder (ADHD) are both typically viewed as biologically based behavioral constructs. There is substantial overlap between ADHD symptoms and specific temperamental traits, such as effortful control, especially in young children. Recent work by Martel and colleagues (2009, 2011) suggests that cognitive control temperamental processes are more closely related to inattention symptoms, whereas stimulus-driven temperamental processes are linked to hyperactivity-impulsivity. The present study tested a model of temperament and ADHD symptoms in typically developing

preschoolers and those at risk for ADHD using structural equation modeling. Data were from larger study on ADHD in a short-term longitudinal sample with parent/teacher reports and neurocognitive testing. Participants included 214 preschool children (72.9% male) from diverse ethnic/racial backgrounds and a wide range of socioeconomic status from a large metropolitan center. Cognitive control processes, such as effortful control, but not stimulus-driven processes, are related to inattention and hyperactivity. In contrast, stimulus-driven processes, such as emotional reactivity, were related only to hyperactivity symptoms longitudinally. These results suggest that early temperament behaviors and cognitive processes may be indicators of later childhood behavioral difficulties with lasting consequences.

Journal of Clinical Child and Adolescent Psychology. 2013 Mar;42:232-42.

**ADOLESCENT GIRLS' ADHD SYMPTOMS AND YOUNG ADULT DRIVING: THE ROLE OF PERCEIVED DEVIANT PEER AFFILIATION.**

**Cardoos SL, Loya F, Hinshaw SP.**

Our goal was to examine the role of adolescent perceived deviant peer affiliation in mediating or moderating the association between adolescent attention-deficit/hyperactivity disorder (ADHD) symptoms and young adult driving risk in females with and without ADHD. The overall sample included 228 ethnically and socioeconomically diverse girls with or without a diagnosis of ADHD in childhood (Wave 1; 6–12 years) followed through adolescence (Wave 2; 11–18 years) and into young adulthood (Wave 3; 17–24 years). A subsample of 103 girls with a driving license by Wave 3 and with full data for all study variables was utilized in this investigation. In adolescence, mothers and teachers reported on ADHD symptoms (inattention and hyperactivity/impulsivity), and participants reported on perceived deviant peer affiliation. In young adulthood, participants reported on driving behavior and outcomes, including number of accidents, number of moving vehicle citations, and ever having driven illegally. Covariates included age and adolescent oppositional defiant disorder/conduct disorder. Inattention directly predicted citations. Perceived deviant peer affiliation mediated the association between inattention and (a) accidents and (b) citations. In addition, perceived deviant peer affiliation moderated the association between hyperactivity/impulsivity and accidents, with hyperactivity/impulsivity predicting accidents only for those with low perceived deviant peer affiliation. Perceived deviant peer affiliation appears to play an important role in the association between ADHD symptoms and driving outcomes. Our findings provide preliminary evidence that both ADHD symptoms and peer processes should be targeted in interventions that aim to prevent negative driving outcomes in young women with and without ADHD.

Journal of Clinical Child and Adolescent Psychology. 2013 Mar;42:174-86.

**INTERACTION OF DOPAMINE TRANSPORTER GENE AND OBSERVED PARENTING BEHAVIORS ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A STRUCTURAL EQUATION MODELING APPROACH.**

**Li JJ, Lee SS.**

Emerging evidence suggests that some individuals may be simultaneously more responsive to the effects from environmental adversity and enrichment (i.e., differential susceptibility). Given that parenting behavior and a variable number tandem repeat polymorphism in the 3'untranslated region of the dopamine transporter (DAT1) gene are each independently associated with attention-deficit/hyperactivity disorder (ADHD), our goal was to evaluate the potential interactive effects of child DAT1 genotype with positive and negative parenting behaviors on childhood ADHD. We recruited an ethnically diverse sample of 150 six- to nine-year-old boys and girls with and without ADHD. Children were genotyped for a common polymorphism of the DAT1 gene, and objective counts of observed parenting behavior (i.e., negativity and praise) were obtained from a valid parent-child interaction task. Structural equation modeling was used to examine the interactive effects of DAT1 and observed parenting with a latent ADHD factor. We detected a significant interaction between observed praise and child DAT1 (coded additively), which suggested that praise was associated with increased ADHD, but only among youth with the 9/10 genotype. In addition, a marginally significant interaction between DAT1 (coded additively and recessively) and observed negativity emerged

for ADHD, such that negativity was positively associated with ADHD but only for youth with the 9/9 genotype. Although differential susceptibility theory was not fully supported, these preliminary results suggest that interactive exchanges between parenting behavior and child genotype potentially contribute to the development of ADHD. Clinical implications for interactions between parenting behavior and child genotype are discussed.

Journal of Clinical Child and Adolescent Psychology. 2013 Mar;42:161-73.

**DISTINGUISHING SLUGGISH COGNITIVE TEMPO FROM ADHD IN CHILDREN AND ADOLESCENTS: EXECUTIVE FUNCTIONING, IMPAIRMENT, AND COMORBIDITY.**

***Barkley RA.***

Controversy continues as to whether sluggish cognitive tempo (SCT) is a subtype of attention-deficit/hyperactivity disorder (ADHD) or a distinct disorder. This study examined differences between these disorders in demographics, executive functioning (EF), impairment, and prior professional diagnoses to address the issue. There were 1,800 children 6 to 17 years of age of both sexes from various U.S. ethnic backgrounds who were divided into four groups: (a) high SCT but not ADHD (N=41), (b) high ADHD but not SCT (N=95), (c) high in both SCT and ADHD (N=61), and (d) the control group (N=1,603). Besides providing demographics, parents completed scales assessing ADHD and SCT symptoms, EF deficits, and psychosocial impairment and reported their child's history of professional diagnoses. SCT symptoms formed two distinct but interrelated factors separate from those for ADHD. SCT differed from ADHD in demographics (age, sex ratio, parental education, income). ADHD was associated with more severe and pervasive EF deficits than SCT, whereas SCT was chiefly associated with mild deficits in Self-Organization. ADHD contributed far more variance to EF deficits than did SCT. Both disorders were impairing, but ADHD was more severely and pervasively so than SCT, especially in Home-School domains; SCT was most impairing in Community-Leisure domains. Different patterns of comorbidity were evident between SCT and ADHD. SCT showed less comorbidity and was particularly associated with depression. SCT may comprise a distinct disorder from ADHD but both may coexist in 39% to 59% of cases each.

Journal of Clinical Child and Adolescent Psychology. 2013 Mar;42:220-31.

**MOTORSPORTS INVOLVEMENT AMONG ADOLESCENTS AND YOUNG ADULTS WITH CHILDHOOD ADHD.**

***Wymbs BT, Molina BSG, Belendiuk KA, et al.***

Although children with attention-deficit/hyperactivity disorder (ADHD) are at risk for impulsive, health-endangering behavior, few studies have examined nonsubstance, use-related risk-taking behaviors. This study examined whether adolescents and young adults with ADHD histories were more likely than those without ADHD histories to report frequent engagement in motorsports, a collection of risky driving-related activities associated with elevated rates of physical injury. Path analyses tested whether persistent impulsivity, comorbid conduct disorder or antisocial personality disorder (CD/ASP), and heavy alcohol use mediated this association. Analyses also explored whether frequent motorsporting was associated with unsafe and alcohol-influenced driving. Two hundred twenty-one adolescent and young adult males (16–25 years old) diagnosed with ADHD in childhood and 139 demographically similar males without ADHD histories reported their motorsports involvement. Persistent impulsivity, CD/ASP, heavy drinking, and hazardous driving were also measured in adolescence/young adulthood. Adolescents and young adults with ADHD histories were more likely to report frequent motorsports involvement than those without childhood ADHD. Impulsivity, CD/ASP, and heavy drinking partially mediated this association, such that individuals with ADHD histories, who had persistent impulsivity or CD/ASP diagnoses, were more likely to engage in heavy drinking, which was positively associated with frequent motorsporting. Motorsports involvement was associated with more unsafe and alcohol-influenced driving, and this association was

more often found among those with, than without, ADHD histories. Adolescents and young adults with ADHD histories, especially those with persisting impulsivity, comorbid CD/ASP and heavy drinking tendencies, are more likely to engage in motorsports, which may heighten risk of injury.

Journal of Clinical Psychology in Medical Settings. 2013;1-10.

**TREATMENT EFFECTIVENESS OF A BRIEF BEHAVIORAL INTERVENTION FOR PRESCHOOL DISRUPTIVE BEHAVIOR.**

**Axelrad ME, Butler AM, Dempsey J, et al.**

Parent management training is an evidence-based treatment for disruptive behavior. However, the number of treatment sessions can be high, contributing to high attrition rates. The purpose of this study was to examine post-treatment, 6-month, and 1-year treatment outcomes of the Brief Behavioral Intervention. One hundred twenty children aged 2-6.5 years demonstrating clinically significant disruptive behavior were referred to an outpatient clinic for treatment and participated in the study. Attrition was below reported rates in the literature. Significant decreases in child disruptive behavior and parent stress were found from pre-to-post intervention, and improvements were maintained at follow-ups. Significant pre-to-post intervention teacher reported decreases in behavior were reported.

J Clin Psychopharmacol. 2013.

**NOREPINEPHRINE GENES PREDICT RESPONSE TIME VARIABILITY AND METHYLPHENIDATE-INDUCED CHANGES IN NEUROPSYCHOLOGICAL FUNCTION IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Kim BN, Kim JW, Cummins TDR, et al.**

Noradrenergic dysfunction may be associated with cognitive impairments in attention-deficit/hyperactivity disorder (ADHD), including increased response time variability, which has been proposed as a leading endophenotype for ADHD. The aim of this study was to examine the relationship between polymorphisms in the (alpha)-2A-adrenergic receptor (ADRA2A) and norepinephrine transporter (SLC6A2) genes and attentional performance in ADHD children before and after pharmacological treatment. One hundred one medication-naive ADHD children were included. All subjects were administered methylphenidate (MPH)-OROS for 12 weeks. The subjects underwent a computerized comprehensive attention test to measure the response time variability at baseline before MPH treatment and after 12 weeks. Additive regression analyses controlling for ADHD symptom severity, age, sex, IQ, and final dose of MPH examined the association between response time variability on the comprehensive attention test measures and allelic variations in single-nucleotide polymorphisms of the ADRA2A and SLC6A2 before and after MPH treatment. Increasing possession of an A allele at the G1287A polymorphism of SLC6A2 was significantly related to heightened response time variability at baseline in the sustained (P=2.0 null 10) and auditory selective attention (P=1.0 null 10) tasks. Response time variability at baseline increased additively with possession of the T allele at the Dral polymorphism of the ADRA2A gene in the auditory selective attention task (P=2.0 null 10). After medication, increasing possession of a G allele at the MspI polymorphism of the ADRA2A gene was associated with increased MPH-related change in response time variability in the flanker task (P=1.0 null 10). Our study suggested an association between norepinephrine gene variants and response time variability measured at baseline and after MPH treatment in children with ADHD. Our results add to a growing body of evidence, suggesting that response time variability is a viable endophenotype for ADHD and suggesting its utility as a surrogate end point for measuring stimulant response in pharmacogenetic studies.

Journal of Neuropsychology. 2013 Mar;7:1-11.

**RESPONSE INHIBITION IN CHILDREN WITH AND WITHOUT ADHD AFTER TRAUMATIC BRAIN INJURY.**

**Ornstein TJ, Max JE, Schachar R, et al.**

Children with attention-deficit hyperactivity disorder (ADHD) and traumatic brain injury (TBI) show deficient response inhibition. ADHD itself is a common consequence of TBI, known as secondary ADHD (S-ADHD). Similarity in inhibitory control in children with TBI, S-ADHD, and ADHD would implicate impaired frontal-striatal systems; however, it is first necessary to delineate similarities and differences in inhibitory control in these conditions. We compared performance of children with ADHD and those with TBI without pre-injury ADHD on a stop signal, response inhibition task. Participants were 274 children aged 6–14 years. There were 92 children with ADHD, 103 children with TBI, and 79 typically developing children who served as controls. Among the TBI participants, injury severity ranged from mild to severe. Children with ADHD and TBI showed deficient inhibition. The deficit in children with ADHD was as great as or greater than that in children with TBI, regardless of degree of TBI severity or the presence of S-ADHD. The finding indicates that TBI results in deficient inhibition regardless of the development of S-ADHD.

J Pediatr. 2013.

**INTELLECTUAL DISABILITY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Ahuja A, Martin J, Langley K, et al.**

**Objective:** To determine whether children with attention deficit hyperactivity disorder (ADHD) and mild intellectual disability (ID) are a clinically distinct ADHD subgroup.

**Study design:** This was a cross-sectional study comparing clinical characteristics (ADHD subtypes, total number of symptoms, and rates of common comorbidities) between children with ADHD and mild ID and those with ADHD and IQ test scores >70, and also between children with ADHD and ID and a general population sample of children with ID alone. The sample comprised a clinical sample of children with ADHD with ID (n=97) and without ID (n=874) and a general population sample of children with ID and without ADHD (n=58).

**Results:** After correcting for multiple statistical tests, no differences were found between the 2 ADHD groups on any measure except the presence of conduct disorder (CD) symptoms and diagnoses. Children with ADHD and ID had higher rates of both (OR, 2.38; 95% CI, 1.71-3.32 and OR, 2.69; 95% CI, 1.69-4.28, respectively). Furthermore, children with ADHD and ID had significantly higher rates of oppositional defiant disorder (OR, 5.54; 95% CI, 2.86-10.75) and CD (OR, 13.66; 95% CI, 3.25-57.42) symptoms and a higher incidence of oppositional defiant disorder diagnoses (OR, 30.99; 95% CI, 6.38-150.39) compared with children with ID without ADHD.

**Conclusion:** Children with ADHD and mild ID appear to be clinically typical of children with ADHD except for more conduct problems. This finding has implications for clinicians treating these children in terms of acknowledging the presence and impact of ADHD symptoms above and beyond ID and dealing with a comorbid CD.

J Psychopathol Behav Assess. 2013;1-14.

**A PILOT TRIAL OF SUPPORTING TEENS' ACADEMIC NEEDS DAILY (STAND): A PARENT-ADOLESCENT COLLABORATIVE INTERVENTION FOR ADHD.**

**Sibley MH, Pelham J, Derfinko KJ, et al.**

Behavior therapy is one of two evidence-based treatments for ADHD—the other being stimulant medication. However, there are only a handful of studies of behavioral treatment for ADHD in adolescents (Smith et al. Clinical Child and Family Psychology Review 3:243-267, 2000). Supporting Teens' Academic Needs Daily (STAND) is a parent-adolescent collaborative behavioral intervention for adolescents with ADHD that can be delivered in clinic, school, and community settings. This pilot study evaluates the feasibility, acceptability, and preliminary efficacy of STAND. Thirty-six male and female middle school students with ADHD and diverse ethnic backgrounds were randomly assigned to STAND or a Treatment as Usual (TAU)

control group. Participants were evaluated at baseline, mid-treatment, and post-treatment assessments. Results suggest that STAND can be implemented by even beginner therapists with high treatment fidelity and is accessible to and popular with families. Relative to the TAU group, participants who received STAND showed greater improvements in parent-rated and observed academic and symptom indices. Treatment effects were not present for teacher ratings. Although the STAND group made significant gains in GPA (compared to TAU), these gains were small in size ( $d = .25$ ). The future of STAND as an academic intervention for adolescents with ADHD is discussed, as well as general implications for behavioral treatment delivery to ADHD adolescents.

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J Am Coll Nutr. 2012;31:239-42.

**ATTENTION-DEFICIT DISORDER ASSOCIATED WITH BREAST-FEEDING: A BRIEF REPORT.**

**Shamberger R.**

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurodevelopmental disorders that develop in children. In the United States and Canada, the prevalence is about 6%. The causes of ADHD are not known. ADHD, like autism, occurs mainly in boys aged 3-6, and there are some thoughts that both diseases may have a common mechanism.

**Methods:** This study uses nutritional epidemiology linked to exclusive 6-month breast-feeding. The Centers for Disease Control and Prevention (CDC) has reported in 2003 and 2007 extensive studies on ADHD involving several million children in 50 states. The prevalence of ADHD in each state in 2003 or 2007 was compared to the average of exclusive 6-month breast-feeding from 2001 to 2004 or 3-month exclusive breast-feeding in 2007 in each of the 50 states. Several parameters, such as premature births, low birth weight, and very low birth weight, that had previously associated with ADHD were compared to ADHD incidence. Other parameters such as obesity, infant death rate, neonatal death rate, poverty, per capita income, and the percentage of individuals enrolled in the U.S. WIC (Women, Infants, and Children) program were also compared to ADHD incidence.

**Results:** A highly significant inverse relationship of ADHD to exclusive 6-month and 3-month breast-feeding in 2007 was observed. Direct relationships were observed between premature births, low birth weight and very low birth weight, obesity, infant deaths, neonatal deaths, and ADHD.

**Interpretation:** Breast milk contains components that appear to prevent ADHD.

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Journal of Vocational Behavior. 2013 Apr;82:79-84.

**DYSFUNCTIONAL CAREER THOUGHTS AND ATTITUDES AS PREDICTORS OF VOCATIONAL IDENTITY AMONG YOUNG ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Dipeolu A, Sniatecki JL, Storlie CA, et al.**

This study examined dysfunctional career thoughts and attitudes as predictors of vocational identity among high school students with Attention Deficit Hyperactivity Disorder (ADHD). Regression analysis results indicated that dysfunctional career thoughts and attitudes were significant predictors of vocational identity, accounting for 42% of the explained variance. Dysfunctional career thinking, measured by the Career Thoughts Inventory (Sampson, Peterson, Lenz, Reardon, & Saunders, 1996) and the Career Maturity Inventory-Revised (Crites & Savickas, 1996), displayed important predictive relationships with vocational identity as measured by the Vocational Identity Scale (Holland, Daiger, & Power, 1980). Implications for interventions and further research in vocational psychology and career counseling with ADHD students are discussed.

Nat Med J China. 2013;93:172-76.

**PRACTICAL EXECUTIVE FUNCTION PERFORMANCE IN HIGH INTELLIGENCE QUOTIENT CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.**

**He XX, Qian Y, Wang YF.**

**Objective:** To explore the practical executive function profiles in high IQ (intelligence quotient) children and adolescents with attention deficit hyperactivity disorder (ADHD) in a Chinese sample population.

**Methods:** For this cross-sectional study, we identified 124 outpatients aged 6.8-13.1 years with a high IQ fulfilling the diagnostic criteria for ADHD according to the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV), 68 children and adolescents without ADHD aged 6.5-13.1 years with a high IQ matched by high IQ children and adolescents with ADHD, 124 outpatients aged 6.8-13.2 years with an average IQ with ADHD and 68 normal children and adolescents aged 6.4 - 13.1 years with an average IQ matched by IQ. We operationalized high IQ as having a full scale intelligence quotient (IQ or FSIQ) (greater-than or equal to) 120 on Chinese version Wechsler intelligence scale for children (C-WISC) and an average IQ as 90(less-than or equal to) IQ<110. All the above groups were matched by age. All subjects completed practical executive function tests, including Stroop color-word, trail-making, digit span, Tower of Hanoi task and verbal fluency to assess their ability in the aspects of inhibition, shifting, working memory, planning and verbal fluency.

**Results:** ADHD group with a high IQ performed worse on the Stroop color-word (3.18 (plus or minus)0.05) and trail-making tests (4.38 (plus or minus)0.55) than normal control group with a high IQ (2.92 (plus or minus)0.07 and 4.05 (plus or minus)0.07) ( $P < 0.01$ ). The test performances of trail-making, digit span (4.86 (plus or minus) 0.13) and fluency (23.0 (plus or minus) 0.5) were significantly better in high IQ ADHD group than average IQ ADHD group (4.10 (plus or minus) 0.07 and 19.9 (plus or minus)0.5) ( $P<0.01$ ).

**Conclusion:** Though a bit better than average IQ ADHD group in shifting, working memory and verbal fluency, the high IQ children and adolescents with ADHD perform worse than high-IQ controls on inhibition and shifting. IQ may protect practical executive function.

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NeuroImage Clin. 2013;2:366-76.

**OSMOTIC RELEASE ORAL SYSTEM-METHYLPHENIDATE IMPROVES NEURAL ACTIVITY DURING LOW REWARD PROCESSING IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.**

**Mizuno K, Yoneda T, Komi M, et al.**

Attention-deficit/hyperactivity disorder (ADHD) is neurobehavioral disorder characterized by inattention, hyperactivity/impulsivity and impaired reward system function, such as delay aversion and low reward sensitivity. The pharmacological treatment for ADHD includes methylphenidate (MPH), or osmotic release oral system-MPH (OROS-MPH), which increases extrasynaptic dopamine and noradrenaline levels by blocking their reuptake. Although previous functional magnetic resonance imaging (fMRI) studies revealed that acute treatment with MPH alters activation of the nucleus accumbens during delay aversion in children and adolescents with ADHD, the effects a relatively long period of OROS-MPH treatment on delay aversion as well as reward sensitivity remain unclear. Thus, we evaluated brain activation with fMRI during a reward sensitivity paradigm that consists of high monetary reward and low monetary reward conditions before and after a 3-month treatment with OROS-MPH in 17 children and adolescents with ADHD (mean age, 13.3 (plus or minus) 2.2) and 17 age- and sex-matched healthy controls (mean age, 13.0 (plus or minus) 1.9). We found that before treatment there was decreased activation of the nucleus accumbens and thalamus in patients with ADHD during only the low monetary reward condition, which was improved to same level as those of the healthy controls after the treatment. The observed change in brain activity was associated with improved ADHD symptom scores, which were derived from Japanese versions of the ADHD rating scale-IV. These results suggest that treatment with OROS-MPH for a relatively long period is effective in controlling reward sensitivity in children and adolescents with ADHD.

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NeuroMol Med. 2013 Mar;15:122-32.

**GENETIC EVIDENCE FOR THE ASSOCIATION OF THE HYPOTHALAMIC–PITUITARY–ADRENAL (HPA) AXIS WITH ADHD AND METHYLPHENIDATE TREATMENT RESPONSE.**

**Fortier MÈ, Sengupta SM, Grizenko N, et al.**

Exposure to stressors results in a spectrum of autonomic, endocrine, and behavioral responses. A key pathway in this response to stress is the hypothalamic–pituitary–adrenal (HPA) axis, which results in a transient increase in circulating cortisol, which exerts its effects through the two related ligand-activated transcription factors: the glucocorticoid receptor (GR) and mineralocorticoid receptor (MR). Genetic polymorphisms in these receptors have been shown to influence HPA axis reactivity, and chronic dysregulation of the HPA axis has been associated with the development of several psychiatric disorders. The objective of the study was to test the association between four functional polymorphisms in NR3C1 (encoding GR: ER22/23EK-rs6189, N363S-rs6195, BclI-rs41423247, A3669G-rs6198) and two in NR3C2 (encoding MR: 215G/C-rs2070951, I180 V-rs5522) with childhood ADHD. Family-based association tests (FBAT) were conducted with the categorical diagnosis of ADHD, behavioral and cognitive phenotypes related to ADHD, as well as with treatment response assessed in a 2-week, double-blind, placebo-controlled trial with methylphenidate. A specific haplotype (G:A:G:G; ER22/23EK-N363S-BclI-A3669G) of NR3C1 showed a significant association with behaviors related to ADHD (particularly thought and attention problems, aggressive behavior), comorbidity with oppositional defiant disorder, and executive function domains. An association was also observed with treatment response (assessed by the Conners'-Teachers and Restricted Academic Situation Scale). In contrast, MR gene polymorphisms were not associated with any of the variables tested. To the best of our knowledge, this is the first report showing an association between functional polymorphisms in NR3C1 and ADHD, providing genetic evidence for involvement of the HPA axis in the disorder and treatment response.

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Neuropsychologia. 2013;51:1085-93.

**INFLUENCE OF ATTENTIONAL LOAD ON SPATIAL ATTENTION IN ACQUIRED AND DEVELOPMENTAL DISORDERS OF ATTENTION.**

**Bellgrove MA, Eramudugolla R, Newman DP, et al.**

Converging evidence suggests that right-hemisphere dominant spatial attention systems can be modulated by non-spatial processes such as attentional capacity. The severity of neglect in right-hemisphere stroke patients for example, is correlated with impairments in non-lateralized attention. Evidence also suggests the coexistence of lateralized inattention and reduced capacity in developmental disorders of attention, such as attention deficit hyperactivity disorder (ADHD), which is marked by cognitive impairments suggestive of right hemisphere dysfunction. These lines of evidence argue against a coincident damage hypothesis and suggest instead a direct modulation of spatial attention by non-spatial processes. Here we sought experimental evidence for this relationship in both acquired and developmental disorders of attention. Six adult stroke patients with focal right brain injury and 19 children with ADHD were studied in comparison to control groups of both healthy older adults and typically developing children. The participants were required to detect transient, unilateral visual targets while simultaneously monitoring a stream of alphanumeric characters at fixation. Load at fixation was manipulated by asking participants either to ignore the central stream and focus on the peripheral detection task (no report condition), or to monitor the central stream for a probe item that was defined by either a unique feature (low load condition) or a conjunction of features (high load condition). As expected, in all participants greater load at fixation slowed responses to peripheral targets. Crucially, in right brain injured patients but not older healthy adults left target detection was slowed significantly more than central and right target detection. A qualitatively similar pattern was seen in children with ADHD, but not in typically developing children. The imposition of load at fixation slowed responses to left compared with right targets, and this response time asymmetry was correlated with the severity of ADHD symptoms. These results suggest that a direct manipulation of

non-spatial attention can reveal lateralised attention deficits in both acquired and developmental forms of inattention. Our findings support the view that spatial attention networks are tightly integrated with non-lateralized aspects of attention.

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Neuropsychology. 2012;26:407-13.

**FIT AND VIGILANT: THE RELATIONSHIP BETWEEN POORER AEROBIC FITNESS AND FAILURES IN SUSTAINED ATTENTION DURING PREADOLESCENCE.**

**Pontifex MB, Scudder MR, Drollette ES, et al.**

With the growing trend toward engagement in sedentary behaviors during childhood, a greater understanding of the relationship between cardiorespiratory fitness and cognition during development is of increasing importance. Objective: The aim of this investigation was to assess the extent to which failures in sustained attention may underlie deficits in cognition associated with poorer aerobic fitness. Method: A sample of 62 preadolescent children between the ages of 9 and 10 years were separated into higher and lower-fit groups according to their cardiorespiratory fitness. Results: Findings indicated that lower-fit children exhibited poorer overall response accuracy during a task requiring aspects of cognitive control relative to their higher-fit counterparts, with a disproportionately greater number of errors of omission, and longer, more frequent sequential errors of omission. Conclusions: These findings suggest that poorer vigilance may contribute to deficits in cognitive control associated with poorer aerobic fitness.

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Noropsikiyatr Ars. 2013;50:59-64.

**PSYCHIATRIC EVALUATION OF CHILDREN BORN WITH ASSISTED REPRODUCTIVE TECHNOLOGIES AND THEIR MOTHERS: A CLINICAL STUDY.**

**Ozbaran B, Kose S, Ardic UA, et al.**

**Background:** The number of parents who have children through assisted reproductive technologies (ART) is increasing. In this cross-sectional study, we aimed to evaluate the psychiatric diagnostic profiles and behavioral characteristics of children born after ART as well as to evaluate the anxiety and depressive symptoms in their mothers.

**Methods:** Thirty-five children (13 girls and 22 boys) born after ART (ART group) were compared with 35 naturally conceived children, matched for gender and age (control group). The Kiddie Schedule for Affective Disorders and Schizophrenia, the Diagnostic and Statistical Manual of Mental Disorders, 4th. Edition (DSM-IV) criteria and the Child Behavior Checklist (CBCL) were used for evaluation of the children. The Beck Depression Inventory (BDI) and the State-Trait Anxiety Inventory (STAI) were used for evaluating their mothers.

**Results:** The most common psychiatric diagnoses were attention deficit hyperactivity disorder, pervasive developmental disorders and anxiety disorders in both groups. Feeding disorders were significantly more frequent in children born following ART than in controls. Mothers of ART group had higher scores in BDI and STAI. Between both groups, there was a statistically significant difference in some CBCL subscales (e.g. withdrawn, social problems, internalizing and externalizing problems).

**Conclusion:** It is important to know that children born after ART may have some behavioral and psychiatric problems and working with their mothers' psychological status is also important.

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Paediatr Croat. 2013;57:57-60.

**EVALUATION OF AWAKE ELECTROENCEPHALOGRAPHY FINDINGS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER BEFORE PSYCHOSTIMULANT TREATMENT.**

**Bayram E, Topcu Y, Karaarslan D, et al.**

Attention deficit hyperactivity disorder is one of the most common neuropsychiatric disorders in childhood. Electroencephalographic abnormalities may be observed but it is controversial to perform electroencephalography before starting the treatment. Awake electroencephalography findings, demographic and psychometric variables of patients with attention deficit hyperactivity disorder treated between January 2005 and December 2010 were retrospectively evaluated. The study included 386 patients aged 4-18 (mean 9.61(plus or minus)3.04) years, who were diagnosed with attention deficit hyperactivity disorder according to the DSM-IV-TR (2000) diagnostic criteria. Epileptiform electroencephalography pattern was observed in 22/386 (5.7%) patients. Seven of 386 (1.8%) patients had a history of epilepsy diagnosis and antiepileptic medication. When patients with seizure history (with or without epilepsy diagnosis) and those with epileptic abnormalities on electroencephalography were excluded, the incidence of epileptiform abnormalities in attention deficit hyperactivity disorder patients was 12/386 (3.1%). After psychostimulant medication, epileptic seizures occurred in only three patients with epilepsy. The prevalence rate of epileptiform discharges on awake electroencephalography, observed in attention deficit hyperactivity disorder patients before psychostimulant treatment is similar to that in healthy schoolchildren. Since the seizures increased only in epileptic patients, we do not recommend routine awake electroencephalography evaluation in children with attention deficit hyperactivity disorder before psychostimulant medication.

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Pediatr Res. 2013;73:492-96.

**ASSOCIATION OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH DIABETES: A POPULATION-BASED STUDY.**

**Chen HJ, Lee YJ, Yeh GC, et al.**

**Background:** Cognitive impairment has been documented in adult diabetes but is unclear in pediatric diabetes. No study had been conducted to explore the relationship between attention-deficit/hyperactivity disorder (ADHD) and diabetes. Using a population-based data set, we aimed to examine the association between ADHD and a prior diagnosis of diabetes mellitus (DM) in Taiwan.

**Methods:** A total of 4,302 patients with ADHD were selected as cases and 21,510 randomly selected subjects as controls. We used conditional logistic regression to calculate the odds ratio (OR) for having previously received a diagnosis of DM between subjects with and without ADHD.

**Results:** In this study, 116 of the 25,812 sampled subjects (0.5%) had received a diagnosis of DM prior to their index date. Subjects with ADHD had a higher proportion of prior DM diagnoses than controls (0.9% vs. 0.4%,  $P < 0.001$ ). After adjusting for age, sex, index year, geographic location, and obesity, ADHD was significantly associated with a prior diagnosis of type 2 DM (OR=2.75, 95% confidence interval (CI)=1.82-4.16). However, no significant association was observed between ADHD and type 1 DM.

**Conclusion:** The findings suggest that ADHD was associated with a previous diagnosis of type 2 DM.

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Pediatrics. 2013;131:637-44.

**MORTALITY, ADHD, AND PSYCHOSOCIAL ADVERSITY IN ADULTS WITH CHILDHOOD ADHD: A PROSPECTIVE STUDY.**

**Barbaresi WJ, Colligan RC, Weaver AL, et al.**

**OBJECTIVE:** We examined long-term outcomes of attention-deficit/ hyperactivity disorder (ADHD) in a population-based sample of childhood ADHD cases and controls, prospectively assessed as adults.

**METHODS:** Adults with childhood ADHD and non-ADHD controls from the same birth cohort (N = 5718) were invited to participate in a prospective outcome study. Vital status was determined for birth cohort members. Standardized mortality ratios (SMRs) were constructed to compare overall and cause-specific mortality between childhood ADHD cases and controls. Incarceration status was determined for childhood ADHD cases. A standardized neuropsychiatric interview was administered.

**RESULTS:** Vital status for 367 childhood ADHD cases was determined: 7 (1.9%) were deceased, and 10 (2.7%) were currently incarcerated. The SMR for overall survival of childhood ADHD cases versus controls was 1.88 (95% confidence interval [CI], 0.83-4.26;  $P = .13$ ) and for accidents only was 1.70 (95% CI, 0.49-5.97;  $P = .41$ ). However, the cause-specific mortality for suicide only was significantly higher among ADHD cases (SMR, 4.83; 95% CI, 1.14-20.46;  $P = .032$ ). Among the childhood ADHD cases participating in the prospective assessment ( $N = 232$ ; mean age, 27.0 years), ADHD persisted into adulthood for 29.3% (95% CI, 23.5-35.2). Participating childhood ADHD cases were more likely than controls ( $N = 335$ ; mean age, 28.6 years) to have (greater-than or equal to) 1 other psychiatric disorder (56.9% vs 34.9%; odds ratio, 2.6; 95% CI, 1.8-3.8;  $P < .01$ ).

**CONCLUSIONS:** Childhood ADHD is a chronic health problem, with significant risk for mortality, persistence of ADHD, and long-term morbidity in adulthood.

Pharm Weekbl. 2013;148:9.

**PSYCHOTROPIC AGENTS IN YOUNG PEOPLE ARE PARTICULARLY FOR ADHD.**

Anon.

Pharmacoepidemiol Drug Saf. 2013;22:386-93.

**A COHORT STUDY OF THE RISK OF SEIZURES IN A PEDIATRIC POPULATION TREATED WITH ATOMOXETINE OR STIMULANT MEDICATIONS.**

**Mcafee AT, Landon J, Jones M, et al.**

**Purpose:** Stimulant medications used for treating attention deficit hyperactivity disorder (ADHD) can be associated with an increased risk of seizures. Atomoxetine is a non-stimulant medication approved for treating ADHD. This retrospective cohort analysis evaluated risk of seizures among pediatric patients naive to ADHD medication therapy, with exposure to atomoxetine relative to stimulant medications.

**Methods:** Among members of a large US health plan from 1/1/2003 to 12/31/2006, aged 6-17 years, we identified initiators of atomoxetine or stimulants with no evidence of prior study drug use. We created study cohorts using propensity score matching within 6-month calendar blocks. The outcome was a seizure event in the 6-month follow-up period verified through medical record review. Relative risks (RR) based on current use of each study drug adjusted for baseline covariates were calculated using Poisson regression. We estimated hazard ratios from Cox proportional hazards models for the comparison of atomoxetine to stimulants based on initial cohort assignment.

**Results:** We matched 13398 initiators of atomoxetine to 13322 initiators of stimulants. We identified 97 seizure events. After adjustment, current atomoxetine therapy was associated with a non-statistically significant 28% lower risk of seizure compared to current stimulant therapy (RR 0.72; 95%CI 0.37, 1.38). The adjusted RR of seizure with atomoxetine compared to stimulants based on initial cohort assignment was 0.90 (95%CI 0.54, 1.49).

**Conclusions:** These results do not support an increase in the risk of seizure with atomoxetine therapy. The risk of seizure was not significantly different between pediatric patients taking atomoxetine compared with those taking stimulants.

PLoS ONE. 2013;8.

**MOBILE PHONE USE, BLOOD LEAD LEVELS, AND ATTENTION DEFICIT HYPERACTIVITY SYMPTOMS IN CHILDREN: A LONGITUDINAL STUDY.**

**Byun YH, Ha M, Kwon HJ, et al.**

**Background:** Concerns have developed for the possible negative health effects of radiofrequency electromagnetic field (RF-EMF) exposure to children's brains. The purpose of this longitudinal study was to

investigate the association between mobile phone use and symptoms of Attention Deficit Hyperactivity Disorder (ADHD) considering the modifying effect of lead exposure.

**Methods:** A total of 2,422 children at 27 elementary schools in 10 Korean cities were examined and followed up 2 years later. Parents or guardians were administered a questionnaire including the Korean version of the ADHD rating scale and questions about mobile phone use, as well as socio-demographic factors. The ADHD symptom risk for mobile phone use was estimated at two time points using logistic regression and combined over 2 years using the generalized estimating equation model with repeatedly measured variables of mobile phone use, blood lead, and ADHD symptoms, adjusted for covariates.

**Results:** The ADHD symptom risk associated with mobile phone use for voice calls but the association was limited to children exposed to relatively high lead.

**Conclusions:** The results suggest that simultaneous exposure to lead and RF from mobile phone use was associated with increased ADHD symptom risk, although possible reverse causality could not be ruled out.

PLoS ONE. 2013;8.

**PROCESSING OF CONTINUOUSLY PROVIDED PUNISHMENT AND REWARD IN CHILDREN WITH ADHD AND THE MODULATING EFFECTS OF STIMULANT MEDICATION: AN ERP STUDY.**

**Groen Y, Tucha O, Wijers AA, et al.**

**Objectives:** Current models of ADHD suggest abnormal reward and punishment sensitivity, but the exact mechanisms are unclear. This study aims to investigate effects of continuous reward and punishment on the processing of performance feedback in children with ADHD and the modulating effects of stimulant medication.

**Methods:** 15 Methylphenidate (Mph)-treated and 15 Mph-free children of the ADHD-combined type and 17 control children performed a selective attention task with three feedback conditions: no-feedback, gain and loss. Event Related Potentials (ERPs) time-locked to feedback and errors were computed.

**Results:** All groups performed more accurately with gain and loss than without feedback. Feedback-related ERPs demonstrated no group differences in the feedback P2, but an enhanced late positive potential (LPP) to feedback stimuli (both gains and losses) for Mph-free children with ADHD compared to controls. Feedback-related ERPs in Mph-treated children with ADHD were similar to controls. Correlational analyses in the ADHD groups revealed that the severity of inattention problems correlated negatively with the feedback P2 amplitude and positively with the LPP to losses and omitted gains.

**Conclusions:** The early selective attention for rewarding and punishing feedback was relatively intact in children with ADHD, but the late feedback processing was deviant (increased feedback LPP). This may explain the often observed positive effects of continuous reinforcement on performance and behaviour in children with ADHD. However, these group findings cannot be generalised to all individuals with the ADHD, because the feedback-related ERPs were associated with the severity of the inattention problems. Children with ADHD-combined type with more inattention problems showed both deviant early attentional selection of feedback stimuli, and deviant late processing of non-reward and punishment.

Prostaglandins Leukotrienes Essent Fatty Acids. 2013.

**FATTY ACID CORRELATES OF TEMPERAMENT IN ADOLESCENT BOYS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Sumich AL, Matsudaira T, Heasman B, et al.**

Atypical fatty acid metabolism has been reported in attention deficit hyperactivity disorder (ADHD), however, its relationship with temperament in this population is unclear. The current study investigated the association between blood levels of fatty acids implicated in brain structure and function (omega-3, omega-6, omega-9) and personality traits of stability (neuroticism, conscientiousness and agreeableness) and plasticity (extraversion and openness). Twenty right-handed adolescent boys with ADHD completed a self-report NEO-FFI personality questionnaire, and had fatty acid content assessed from red blood using gas chromatography. Pearson's correlations showed no significant associations between omega-3 levels and

personality. After correction for multiple comparisons, Adrenic Acid (C22:4n6) was inversely associated with stability. Oleic acid (C18:1n9) was positively associated with plasticity. Results are in line with a role of fatty acids in brain function. They suggest that those fatty acids that are involved in myelination (Adrenic, Oleic) have the strongest associations with temperament in adolescents with ADHD.

Res Dev Disabil. 2013;34:1922-27.

**INFLUENCE OF METHYLPHENIDATE ON MOTOR PERFORMANCE AND ATTENTION IN CHILDREN WITH DEVELOPMENTAL COORDINATION DISORDER AND ATTENTION DEFICIT HYPERACTIVE DISORDER.**

**Bart O, Daniel L, Dan O, et al.**

Individuals with attention deficit hyperactive disorder (ADHD) often have coexisting developmental coordination disorder (DCD). The positive therapeutic effect of methylphenidate on ADHD symptoms is well documented, but its effects on motor coordination are less studied. We assessed the influence of methylphenidate on motor performance in children with comorbid DCD and ADHD. Participants were 30 children (24 boys) aged 5.10-12.7 years diagnosed with both DCD and ADHD. Conners' Parent Rating Scale was used to reaffirm ADHD diagnosis and the Developmental Coordination Disorder Questionnaire was used to diagnose DCD. The Movement Assessment Battery for Children-2 and the online continuous performance test were administered to all participants twice, with and without methylphenidate. The tests were administered on two separate days in a blind design. Motor performance and attention scores were significantly better with methylphenidate than without it ( $p < 0.001$  for improvement in the Movement Assessment Battery for Children-2 and  $p < 0.006$  for the online continuous performance test scores). The findings suggest that methylphenidate improves both attention and motor coordination in children with coexisting DCD and ADHD. More research is needed to disentangle the causality of the improvement effect and whether improvement in motor coordination is directly affected by methylphenidate or mediated by improvement in attention.

Rev Neurol. 2013;56:S107-S118.

**EXECUTIVE FUNCTIONING AND EVOKED POTENTIALS P300 PRE- AND POST- TREATMENT IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.**

**Roca P, Mulas F, Gandia R, et al.**

**Introduction.** Evoked potentials P300 and the analysis of executive functions have shown their utility in the monitoring of patients with symptoms of attention deficit hyperactivity disorder (ADHD).

**Patients and methods.** Neuropsychological profiles and evoked potentials P300 have been analysed for two groups of children with an ADHD treatment with atomoxetine and methylphenidate respectively. Correlations between P300 and the selected neuropsychological parameters are studied, and the differences between basal values and 1 year follow-up are analysed. Two groups were performed: a group of 22 children ADHD in the atomoxetine condition, and a group of 24 children ADHD in the methylphenidate condition.

**Results.** The results show a global improvement of all the parameters, in terms of executive function and P300 values in both, the atomoxetine and the methylphenidate group.

**Conclusion.** Executive functions and evoked potentials P300 reflect an underlying processing and they are very useful in the clinical practice. This exploratory study shows the importance of designing personalized objective variables-based treatments.

Sleep Med. 2013;14:359-66.

**TIME STRUCTURE OF LEG MOVEMENT ACTIVITY DURING SLEEP IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND EFFECTS OF LEVODOPA.**

**Ferri R, Bruni O, Novelli L, et al.**

**Objectives:** To evaluate the leg movement (LM) time structure (periodicity and night distribution) during sleep in children with attention-deficit/hyperactivity disorder (ADHD) and their eventual changes after treatment with levodopa (L-DOPA).

**Subjects and methods:** One group of ADHD patients (n= 18) and another group of normal controls (n= 17) were recruited; those with ADHD were randomized to L-DOPA or placebo therapy. At baseline (both groups) and after therapy (only patients) subjects underwent full-night polysomnography (PSG) and the leg motor pattern was evaluated with advanced tools of analysis particularly able to detect and describe LM time structure (periodicity and distribution).

**Results:** With respect to controls ADHD children showed prolonged sleep latency, increased number of stage shifts, awakenings, and percentage of sleep stage 1. Arousal index was higher in ADHD and also their PLMS index was slightly but considerably higher than controls; however, their periodicity was low and not different from controls. Only sleep latency was significantly reduced by L-DOPA treatment with all the other parameters (sleep scoring and LM activity) remaining substantially unmodified.

**Conclusions:** LMs during sleep in children with ADHD do not show a highly periodic character and are not considerably modified by L-DOPA treatment; this finding has potential implications for drug treatment that might target the most prominent changes observed in our study including arousals and sleep structure disruption.

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## Original Article

## Time structure of leg movement activity during sleep in attention-deficit/hyperactivity disorder and effects of levodopa

Raffaele Ferri<sup>a,\*</sup>, Oliviero Bruni<sup>b</sup>, Luana Novelli<sup>b</sup>, Matthew A. Picchiatti<sup>c</sup>, Daniel L. Picchiatti<sup>d</sup><sup>a</sup>Sleep Research Centre, Department of Neurology I.C., Oasi Institute (IRCCS), Troina, Italy<sup>b</sup>Centre for Pediatric Sleep Disorders, Department of Developmental Neurology and Psychiatry, University of Rome "La Sapienza", Rome, Italy<sup>c</sup>Department of Psychology, Southern Illinois University, Carbondale, IL, USA<sup>d</sup>University of Illinois School of Medicine and Carle Foundation Hospital, Urbana, IL, USA

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## ABSTRACT

**Objectives:** To evaluate the leg movement (LM) time structure (periodicity and night distribution) during sleep in children with attention-deficit/hyperactivity disorder (ADHD) and their eventual changes after treatment with levodopa (L-DOPA).

**Subjects and methods:** One group of ADHD patients ( $n = 18$ ) and another group of normal controls ( $n = 17$ ) were recruited; those with ADHD were randomized to L-DOPA or placebo therapy. At baseline (both groups) and after therapy (only patients) subjects underwent full-night polysomnography (PSG) and the leg motor pattern was evaluated with advanced tools of analysis particularly able to detect and describe LM time structure (periodicity and distribution).

**Results:** With respect to controls ADHD children showed prolonged sleep latency, increased number of stage shifts, awakenings, and percentage of sleep stage 1. Arousal index was higher in ADHD and also their PLMS index was slightly but considerably higher than controls; however, their periodicity was low and not different from controls. Only sleep latency was significantly reduced by L-DOPA treatment with all the other parameters (sleep scoring and LM activity) remaining substantially unmodified.

**Conclusions:** LMs during sleep in children with ADHD do not show a highly periodic character and are not considerably modified by L-DOPA treatment; this finding has potential implications for drug treatment that might target the most prominent changes observed in our study including arousals and sleep structure disruption.

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## 1. Introduction

Clinical studies have suggested the existence of an association between restless legs syndrome (RLS)/Willis-Ekbom disease, periodic limb movements in sleep (PLMS), and attention-deficit/hyperactivity disorder (ADHD); approximately one-quarter of school-age children with ADHD meet the criteria for RLS and conversely that 12% to 35% of those with RLS meet the criteria for ADHD [1–3]. A meta-analysis study on sleep in children with ADHD showed that PLMS were the only polysomnography (PSG) measure to show a small but significant overall size effect and that children with ADHD displayed more PLMS than control children [4]. Additionally, it is known that approximately 63% to 74% of pediatric RLS cases have PLMS [5–7].

Different hypotheses have been formulated to account for these associations [4,8–14]: (1) sleep disruption associated with RLS and

periodic leg movement during sleep may lead to inattentiveness and hyperactivity; (2) daytime manifestations of RLS may mimic ADHD symptoms [15–18]; and (3) RLS, PLMS, and a subset of ADHD might share a common central nervous system pathophysiology, such as dopamine underactivity [19,20] or brain iron deficiency [17,21,22].

The potential disruption of sleep mediated by RLS and PLMS and the postulated common dopaminergic deficit could be involved in the pathogenesis of ADHD. However, the multifactor etiology of ADHD and the fact that most children with ADHD do not have significant PLMS suggest that PLMS could not be considered as a major causal factor in this disorder [4]; therefore, the specific role of leg motor activity in ADHD children is still to be determined.

Ferri et al [23] have suggested a new approach for the detection and analysis of leg movements (LMs) recorded from the anterior tibialis muscles during sleep in patients with RLS, with particular attention to their quantity, duration, amplitude and periodicity. They also have suggested that a synthesis of the features of LMs during sleep can be achieved by considering three main parameters including, the total number of LMs per hour of sleep, the periodicity of the LMs and the distribution of the LMs throughout the

\* Corresponding author. Address: Sleep Research Centre, Department of Neurology I.C., Oasi Institute for Research on Mental Retardation and Brain Aging (IRCCS), Via C. Ruggiero 73, 94018 Troina, Italy. Tel.: +39 0935 936111; fax: +39 0935 936694.

E-mail addresses: [rferri@oasi.en.it](mailto:rferri@oasi.en.it), [raffaele.ferri@tiscali.it](mailto:raffaele.ferri@tiscali.it) (R. Ferri).

night. Different studies have shown that periodicity develops with age and is unusual in normal children or children with RLS [24,25] because LMs tend to show clear-cut periodicity in subjects with RLS only after the second decade and in normal controls after the fourth decade of life. From the analysis of LM periodicity, important implications arise with respect to pharmacologic treatment; in fact, Manconi et al [26] showed that only a subset of LMs during sleep with intermovement intervals six to 46 seconds and duration of two to four seconds and corresponding to the periodic component of the whole leg motor activity during sleep, responded to pramipexole treatment and isolated LMs do not. Finally, the fine analysis of LMs during sleep, which takes into consideration their real periodicity and time distribution throughout the night, has proven to be able to differentiate leg motor patterns in distinctly different clinical conditions, whereas simple consideration of PLMS index has not [27–29].

For this reason, it can be hypothesized that the same type of detailed analysis of the leg motor activity in children with ADHD might help to clarify the relationships between RLS, PLMS, and ADHD, as in these children the association has only been analyzed using the simple PLMS index. Thus, the aim of our study was to evaluate the leg motor pattern during sleep in children with ADHD with advanced tools of analysis particularly able to detect and describe LMs periodicity and distribution and their eventual changes after treatment with levodopa (*L-DOPA*).

## 2. Methods

### 2.1. Subjects

As part of a multisite study investigating the effects *L-DOPA* in children with ADHD, baseline end point PSG was performed; the results of the study have been reported earlier [30,31]. In our paper, we have reanalyzed data from a subsample of children aged seven to 12 years recruited at the Carle Foundation Hospital/University of Illinois. There was institutional review board approval. Written parental consent and verbal assent from the child were obtained for each subject.

ADHD was diagnosed using the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria [32]. Exclusion criteria were any central nervous system active pharmacologic therapies in the last three months, a history of any notable psychiatric disorder other than ADHD (assessed by the National Institute of Mental Health Diagnostic Interview Schedule for Children version 4.0) [33], mental retardation, severe Tourette syndrome, blindness, deafness, severe learning disability, chronic snoring, severe obesity, micrognathia, and an obstructive respiratory disturbance index of greater than two per hour of sleep on PSG [34,35]. A diagnosis of RLS was based on consensus pediatric definitions [36,37]. Recruitment was stratified to include approximately half of subjects having ADHD with RLS and half of subjects having ADHD without RLS.

A normal control group was enrolled with age range similar to that of the patients. None of the control subjects had any physical, neurological or psychiatric disorder or history of sleep concerns, and none were taking medication at the time of recording. Exclusion criteria included, a sleep disorder diagnosis (including sleep apnea), a major mental illness, a notable history of cognitive difficulties, and current or prior (within one year) use of central nervous system drugs.

### 2.2. Study design

ADHD children were randomly assigned to receive either carbidopa/*L-DOPA* 25/100 CR (marketed by Bristol-Myers Squibb,

Princeton, NJ) or placebo. The drug and placebo were packaged identically (Drug Product Services Laboratory, University of California, San Francisco, CA). The physician in charge of treatment was blinded to the study group to which a child was assigned. Nausea is common with *L-DOPA*, and for this reason domperidone 10 mg was provided for use as needed for nausea. Domperidone was chosen because unlike other anti-nausea medications, it does not cross the blood–brain barrier and therefore does not counteract the effects of *L-DOPA* centrally.

The drug (carbidopa 25 mg/*L-DOPA* 100 mg CR per tablet) or placebo was increased gradually by half a tablet every four days to a maximum dosage of one and a half tablets four times a day (breakfast, lunch, afternoon, and evening) depending on patient response. Dosage was increased if reports of symptoms of ADHD sleep disruption, or symptoms of RLS/PLMS had not resolved as assessed by the physician during clinic visits and phone consultations. Final dosages ranged from two and a half to six tablets per day (250–600 mg of *L-DOPA*).

More detailed information on excluded patients and those who dropped out can be found in the above mentioned report [30].

### 2.3. Polysomnographic recordings

Each subject attended an overnight PSG; two baseline and two end point night recordings were available for each child with ADHD. However, for our study only the second baseline (baseline night and the first end point (treatment) night were analyzed. For normal controls, only a single-night recording was available for analysis.

The following parameters were measured, electroencephalogram, eye movements, chin electromyogram, nasal and oral airflow, chest and abdominal movement, LMs, electrocardiogram, and oxygen saturation. Airflow was assessed by both pressure transducer and thermal sensors. Infrared video monitoring and a sensitive intercom also were used. LMs were measured using anterior tibialis leg leads bilaterally. An obstructive apnea was defined as a decrease of at least 75% in airflow from the baseline value for at least two breaths with continuing respiratory effort. A hypopnea was defined as a discernable decrease in airflow on the pressure transducer waveform from the preceding baseline accompanied by either a decrease in oxygen saturation of at least 3% percent or followed by an arousal [34,35].

### 2.4. Sleep scoring and detection and analysis of LMs

Sleep stages were scored following Rechtschaffen and Kales [38] standard criteria using 30-second epochs; arousals also were scored for calculation of the arousal index [39].

LMs during sleep were first detected by the software Hypnolab 1.2 (SWS Soft, Italy), which allows their computer-assisted detection. With this software, the detection is performed using a human-supervised automatic approach controlled by the scorer that uses WASM–IRLSSG [40] and American Association of Sleep Medicine criteria [39]. The performance of this system has been evaluated and validated [41], but in this study one scorer visually edited the detections proposed by the automatic analysis before computing a final result. In particular, 0.5 to 10 seconds LMs were detected and the total LM Index was calculated to represent the total number of LMs per hour of sleep, and the PLMS index was calculated (for total, REM, and NREM sleep) as the number of LMs included in a series of four or more separated by at least five and no more than 90 seconds per hour of sleep [39,40]. Finally, we calculated the Periodicity Index (PI) [23], which is defined by the formula,

$$PI = \frac{\text{No. of sequences of 3 inter-LM intervals } 10 < i \leq 90 \text{ seconds}}{\text{total number of inter-LM intervals}}$$

This index can vary between 0 (absence of periodicity) and 1 (all intervals with length  $10 < i \leq 90$  s). PI is independent on the absolute number of LMs recorded and was calculated for all the subjects with tibialis anterior electromyogram recording included in our study. PLMS associated with arousals also were counted and the PLMS/arousal index calculated following standard criteria [40].

### 2.5. Statistical data analysis

All comparisons between groups were carried out using the nonparametric Mann–Whitney test for independent data sets; within group comparisons were performed by the nonparametric Wilcoxon signed rank test for paired data sets. Differences were considered significant when they reached a  $p < 0.05$  level. The data analysis software system STATISTICA (StatSoft, Inc. 2004, version 6. www.statsoft.com) was used for statistical analysis.

## 3. Results

Eighteen patients with ADHD were enrolled in our study (11 boys and seven girls; mean age, 8.9 years; 1.35 standard deviation [SD]); eight of them were assigned to the placebo subgroup (five

boys and three girls; mean age, 9.5 years; 1.77 SD) and the remaining 10 were assigned to the L-DOPA subgroup (six boys and four girls; mean age, 8.5 years; 0.71 SD). A diagnosis of definite RLS was made in eight of the 18 children at the time of enrollment. However, over a two-year period of clinical follow-up, three more met definite RLS status and two had remission of the RLS sensory symptoms. In only one of these five cases the change in RLS status could be explained by iron status (a remission).

The normal control group was formed by 17 children (nine boys and eight girls; mean age, 9.4 years; 2.00 SD). Age and gender composition were not significantly different from those of the ADHD group.

### 3.1. ADHD children vs normal controls

Comparison of sleep scoring and leg motor activity parameters between the two groups of subjects is reported in Table 1. ADHD children showed prolonged sleep latency and increased number of stage shifts, awakenings, and percentage of sleep stage 1 with respect to the controls. The arousal index was significantly higher in ADHD children (in both REM and NREM sleep). In addition, their PLMS index (total and during NREM sleep) was slightly but significantly higher than controls as well as the number of PLMS

**Table 1**  
Comparison between the sleep scoring and leg motor activity during sleep parameters found in the two groups of subjects.

	ADHD (n = 18)		Controls (n = 17)		Mann–Whitney test
	Mean	SD	Mean	SD	p <
TIB, min	572.8	29.24	546.1	62.33	NS
SPT, min	509.9	37.83	507.6	58.23	NS
TST, min	492.2	37.58	481.1	58.79	NS
SOL, min	62.4	43.98	21.2	15.68	0.0014
FRL, min	129.7	57.84	104.0	60.51	NS
SS/h	7.0	1.96	5.0	1.12	0.0019
AWN/hr	1.0	0.55	0.5	0.63	0.0065
Sleep efficiency, %	86.1	7.14	88.3	7.26	NS
WASO, %	3.5	2.66	5.0	7.07	NS
S1, %	2.3	1.57	4.8	3.87	0.039
S2, %	50.9	5.83	47.6	8.27	NS
SWS, %	24.2	4.95	21.3	4.56	NS
REM, %	19.1	3.72	21.2	5.31	NS
Arousal index, total sleep	4.9	2.03	2.1	1.76	0.0003
Arousal index, NREM	5.5	2.63	2.3	1.69	0.0002
Arousal index, REM	2.7	1.46	1.0	1.42	0.0026
<i>Total sleep</i>					
Total index	15.3	7.84	11.4	4.91	NS
PLMS index	7.7	7.35	4.1	3.97	0.027
Isolated LM index	7.6	1.65	7.3	1.79	NS
<i>NREM</i>					
Total index	15.6	9.51	11.3	5.24	NS
PLMS index	8.8	8.60	4.5	4.62	0.029
Isolated LM index	6.8	1.90	6.8	1.73	NS
<i>REM</i>					
Total index	14.3	5.64	11.9	5.69	NS
PLMS index	3.3	4.86	2.4	3.57	NS
Isolated LM index	10.9	3.25	9.4	3.96	NS
PLMS sequence number	7.8	3.54	5.1	4.62	0.036
PLMS sequence duration, s	16.1	26.77	2.7	6.00	NS
PLMS duration in REM, s	3.5	0.94	2.9	1.78	NS
PLMS duration in NREM, s	3.0	0.76	3.0	1.65	NS
Isolated LM duration in REM, s	2.8	0.95	3.0	1.31	NS
Isolated LM duration in NREM, s	2.9	0.76	3.2	1.31	NS
Periodicity index, total	0.210	0.177	0.204	0.149	NS
Periodicity index, NREM	0.254	0.199	0.200	0.147	NS
Periodicity index, REM	0.093	0.134	0.106	0.169	NS
PLMS/arousal index, total sleep	1.0	0.47	0.4	0.63	0.0008
PLMS/arousal index, NREM	1.2	0.61	0.5	0.73	0.0016
PLMS/arousal index, REM	0.2	0.52	0.1	0.38	NS

TIB, Time in bed; SPT, sleep period time; TST, total sleep time; SOL, sleep onset latency; SS/h, stage shifts per hour; AWN/h, awakenings per hour; SE, sleep efficiency; WASO, wakefulness after sleep onset; S1, S2, NREM sleep stages 1 and 2; SWS, slow-wave sleep; NREM, nonrapid eye movement sleep; REM, rapid eye movement sleep; NS, nonsignificant.

sequences and the PLM/arousal index in NREM sleep. None of the other parameters was significantly different from controls including the periodicity indexes. These findings also are confirmed by the analysis of the distribution histograms of inter-LM intervals shown in the top panel of Fig. 1, in which a prominent peak is evident only at approximately four seconds followed by a progressive decrease of the number of LMs with increasing interval, both in ADHD children and normal controls. However, the rate of decrease is smaller in ADHD children with consequent higher graph values than controls approximate range, 8–42 s), reaching statistical significance in several points (grey-shaded areas).

Periodicity indices were not different between ADHD children and controls (Table 1). In both groups the mean periodicity indices were low, indicating that the majority of motor activity was of low periodicity. However, all activity that occurs in the five to 90 second-interval range is classified as PLMS, as long as there is a sequence of four or more and amplitude as well as duration criteria are met. Fig. 2 contains a visual example of highly periodic LM activity recorded in one of the ADHD children (top panel), with all consecutive intervals in the approximate range of 20 to 40 seconds. This finding was not the rule and was observed only in the minority of patients but contributes to the middle part of the graph reported in the top panel of Fig. 1. The bottom panel of Fig. 2 shows an example of the much more common low periodicity LM activity, usually appearing during arousals in another child

with ADHD depicting shorter and more variable interval LMs. These findings contribute to the first peak on the left of the graph in the top panel of Fig. 1. Also, any LM with intermovement interval (IMI) of five to 90 seconds contributes to the PLMS index.

The time distribution throughout the night of PLMS has a vaguely bell-shaped aspect with maximum during the third recording hour, in both groups (Fig. 1, bottom panel). Isolated LMs show no particular distribution. None of the comparisons between ADHD and controls in our analysis were statistically significant.

### 3.2. Comparison between ADHD children with or without RLS

Table 2 reports the comparison of sleep scoring and leg motor activity parameters between ADHD children subgrouped on the basis of the presence or absence of RLS symptoms at the time of the recording. Only marginal differences were found in this comparison. Additionally, the time distribution of LMs during the night was similar to the same observed in the whole group and in both subgroups (data not shown).

Finally, the effects of L-DOPA treatment in ADHD children and the subject-by-subject analysis of LM periodicity are reported in the online-only Appendix.

## 4. Discussion

To our knowledge this is the first study to analyze the time structure of LMs during sleep in children with ADHD. Using a computer-assisted advanced scoring algorithm, we assessed the three main features of LMs during sleep, PLMS index, periodicity index and IMI interval histogram, and time of night distribution.

The primary findings were an increased PLMS index in ADHD children compared to controls but a low periodicity index and little time of night decrement in both groups. The intermovement interval histogram showed that children with ADHD had slightly more periodic leg activity than controls falling in the 10 to 50-second IMI range. However, although this was within the PLMS range, the peak was not prominent and most of the activity was quite irregular (Fig. 2, bottom panel) with lack of the fixed stereotypic pattern characteristic of adult RLS. In fact, the mean periodicity indices of 0.21 for ADHD children and 0.15 for control children were much lower than those typical for adult RLS (>0.6), narcolepsy (0.4), rapid eye movement sleep behavior disorder (0.55), and controls >40 years of age (>0.4) but more similar to controls <40 years of age (0.24–0.26) [23,25,27,28,42]. Our findings are consistent with two other studies in children, one of which did not find a prominent 10 to 50-second PLMS IMI peak in children with sickle cell disease [43] and another that found a low periodicity index (0.251) and only a small increase in 10 to 50-second IMI range in children with iron deficiency anemia [44]. Thus, low periodicity, and irregular PLMS appear to be typical for children with these conditions.

Interestingly, the difference between PLMS activity in ADHD and control children was not accountable by RLS status at the time of PSG in spite of the study design, which resulted in eight of 18 ADHD children having comorbid RLS. None of the three main features of LMs during sleep were significantly different, suggesting that the findings are characteristic of ADHD rather than an effect of the RLS subgroup. In addition, these data for children with RLS are congruent with our previous work in RLS, in which we found the following age-related changes in PLMS: (1) PLMS index increased up to age ages 15 to 25 years then plateaued until age 65 years when there was another increase, (2) periodicity index progressively increased up to the age of 35 years and then remained stable up to age 85, and (3) time of night decrement was evident at 15 to 75 years of age but not <15 or >75 years [25].

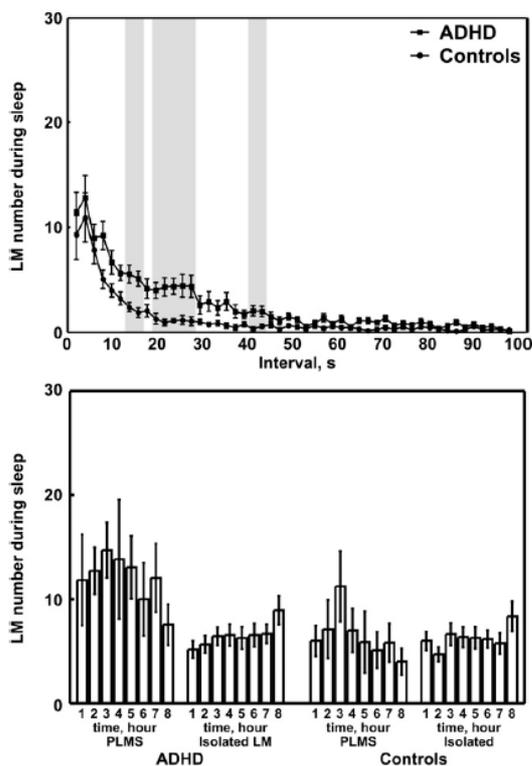
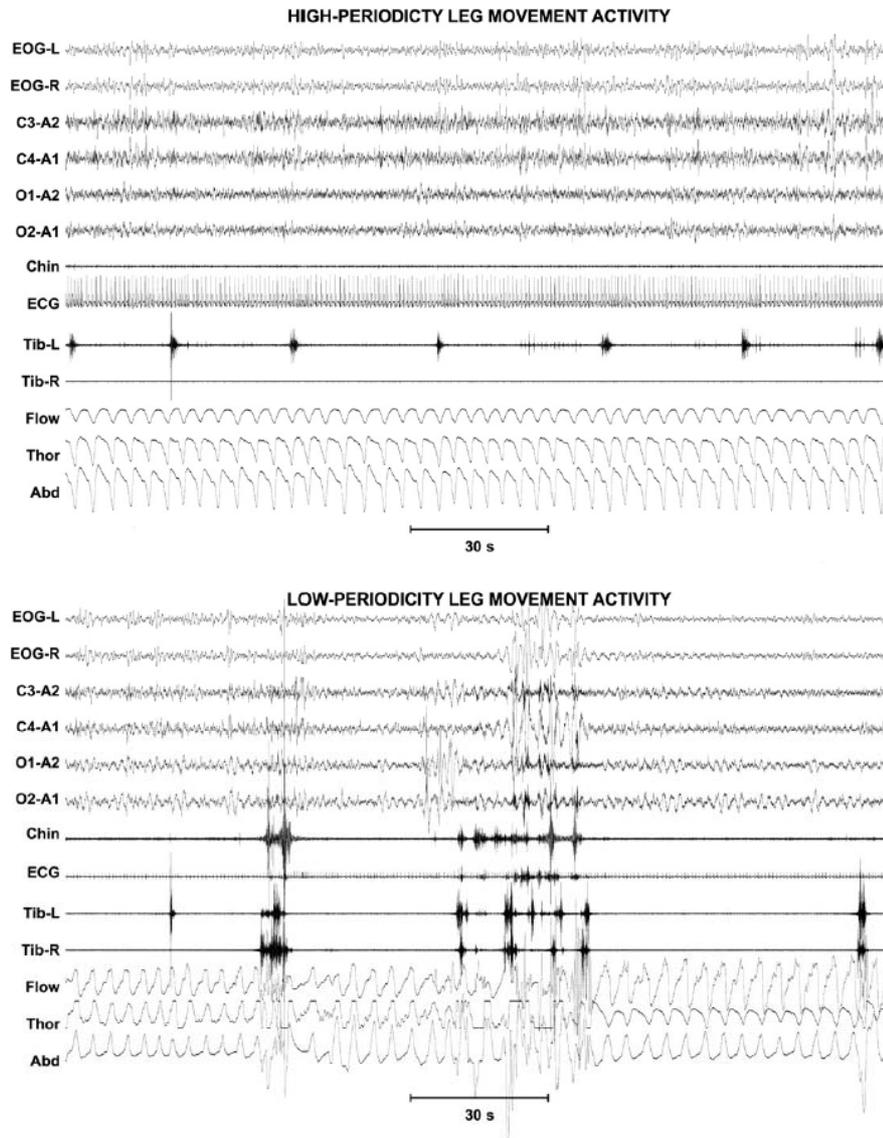


Fig. 1. Top panel: distribution histograms of intervals between consecutive LMs during sleep in the two groups of subjects. Grey-shaded areas indicate points where the two patient graphs significantly differ from controls (Mann-Whitney test,  $p < 0.05$ ). Bottom panel: distribution of the number of LMs per hour of sleep in the two groups of subjects.



**Fig. 2.** Top panel: example of high periodicity leg movement activity recorded in one of the ADHD children, with all consecutive intervals in the approximate range of 20 to 40 seconds. Bottom panel: example of low periodicity leg movement activity in another child with ADHD with several short-interval LMs.

We believe these results may help explain why some studies have found significantly more PLMS in children with ADHD [9,10,45] and others have not [46,47]. As pointed out in an early publication [9] and defined quantitatively in our current study, PLMS in these children tended to occur in small clusters with a varied IMI, whereas long runs of stereotypic LMs were uncommon. Given the atypical appearance of these movements as illustrated in Fig. 2 (bottom panel), many laboratories may not score them, though they fall within a technically scorable range based on previous and current scoring criteria.

It has been postulated that rather than a direct relationship between ADHD and PLMS, the link may be mediated by sleep fragmentation associated with PLMS-associated arousals [48]. However, the association between PLMS and arousals is not always consistent and isolated LMs have been shown to be associated with greater encephalography changes than PLMS [49]. It is intriguing to speculate that individual differences in response to medication for ADHD may be at least partially accounted for by the presence or absence of comorbid sleep disturbance [50].

The lack of response to *L-DOPA* (see Appendix) of all but one of the measures of sleep disturbance suggests that a dopaminergic

**Table 2**  
Comparison between the sleep scoring and leg motor activity during sleep parameters found in ADHD children with or without RLS.

	ADHD wo. RLS (n = 10)		ADHD with RLS (n = 8)		Mann-Whitney test
	Mean	SD	Mean	SD	p<
TIB, min	571.0	32.11	575.2	27.18	NS
SPT, min	519.4	38.77	498.0	35.38	NS
TST, min	503.9	40.93	477.6	28.93	NS
SOL, min	50.5	32.57	77.4	53.62	NS
FRL, min	105.5	44.86	160.0	60.42	NS
SS/h	7.3	1.81	6.6	2.18	NS
AWN/h	0.9	0.59	1.1	0.52	NS
Sleep efficiency, %	88.3	5.90	83.3	7.95	NS
WASO, %	3.0	2.64	4.0	2.76	NS
S1, %	3.2	1.53	1.2	0.78	0.007
S2, %	48.4	5.74	54.0	4.48	NS
SWS, %	24.4	5.22	24.1	4.93	NS
REM, %	21.1	3.53	16.6	2.21	0.013
Arousal index, total sleep	5.8	2.06	3.9	1.57	NS
Arousal index, NREM	6.6	2.72	4.2	1.93	0.054
Arousal index, REM	2.7	1.32	2.6	1.71	NS
<i>Total sleep</i>					
Total index	14.3	3.53	16.6	11.40	NS
PLMS index	6.6	4.31	9.2	10.14	NS
Isolated LM index	7.8	1.84	7.4	1.48	NS
<i>NREM</i>					
Total index	15.0	5.24	16.5	13.52	NS
PLMS index	8.0	5.65	9.9	11.67	NS
Isolated LM index	7.0	1.93	6.6	1.97	NS
<i>REM</i>					
Total index	11.5	4.50	17.8	5.10	0.013
PLMS index	1.1	1.31	6.2	6.25	0.062
Isolated LM index	10.4	3.58	11.6	2.85	NS
PLMS sequence number	7.3	3.02	8.4	4.24	NS
PLMS sequence duration, s	14.5	29.32	18.1	25.05	NS
PLMS duration in REM, s	3.5	0.99	3.4	0.95	NS
PLMS duration in NREM, s	2.8	0.87	3.2	0.56	NS
Isolated LM duration in REM, s	3.2	0.61	2.3	1.06	0.033
Isolated LM duration in NREM, s	2.9	0.69	2.9	0.89	NS
Periodicity index, total	0.232	0.236	0.182	0.051	NS
Periodicity index, NREM	0.300	0.257	0.197	0.066	NS
Periodicity index, REM	0.044	0.079	0.147	0.166	NS
PLMS/arousal index, total sleep	1.0	0.45	1.0	0.52	NS
PLMS/arousal index, NREM	1.2	0.61	1.1	0.63	NS
PLMS/arousal index, REM	0.1	0.23	0.4	0.72	NS

TIB, Time in bed; SPT, sleep period time; TST, total sleep time; SOL, sleep onset latency; SS/h, stage shifts per hour; AWN/h, awakenings per hour; SE, sleep efficiency; WASO, wakefulness after sleep onset; S1, S2, NREM sleep stages 1 and 2; SWS, slow-wave sleep; NREM, nonrapid eye movement; REM, rapid eye movement sleep; NS, nonsignificant.

gic mechanism may not be primarily responsible. This postulation is consistent with recent findings in adult RLS, in which a single oral dose of the dopamine agonist pramipexole was not found to improve NREM sleep instability [51], and gabapentin was found to improve sleep but the dopamine agonist ropinirole was not [52]. Similarly, clonazepam improved sleep instability without suppressing PLMS, whereas pramipexole had the opposite effect [53]. Furthermore, pramipexole has been found to target the highly periodic portion of motor activity between 10 and 50 seconds [26], a range that is not particularly prominent in children. These findings raise an interesting question of what types of medication would be most effective to treat ADHD-related sleep disturbance? We are aware of three randomized clinical trials for ADHD-related sleep disturbance. A larger L-DOPA study, of which these data are a subset, did show a slight decrease in PLMS, but not improvement in other sleep study parameters or ADHD symptoms [30]. A randomized clinical trial of melatonin showed improved sleep onset and total sleep time measured by actigraphy but no significant effect on behavior, cognition, or quality of life [54]. Zolpidem did not show improvement of polysomnographic latency to persistent sleep, efficiency, or ADHD measures but improvement in clinical global impression scores [55]. Therefore, based on data available in the literature, the specific effect of each treatment on LM activity, sleep structure, and daytime

symptoms should be considered. Possibly, a combination of drugs effectively targeting NREM sleep instability and LM activity at the same time might represent a valid treatment for sleep disturbance in children with ADHD. In any case, the results of our study should discourage the use of L-DOPA (and possibly of dopamine agonists) in children with ADHD, especially if this use is based on the detection of increased, but low-periodicity LM activity during sleep.

Limitations of our study include: (1) the lack of a comparison group of children with RLS but not ADHD; (2) no data on iron status, a factor that can influence PLMS, RLS, and ADHD [1]; (3) the results are more relevant for children with ADHD accompanied by sleep disturbance than for ADHD in general; and (4) due to the method used for the analysis of sleep breathing, we might have included subjects with flow limitations. However, we believe this limitation is unlikely, as we used pressure transducer airflow recording, a respiratory effort-related arousal definition, a very low respiratory disturbance index cutoff of one per hour, and excluded cases with chronic snoring (this was an exclusionary criterion for entry into the original study).

In conclusion, our study shows subtle but considerable differences in PLMS and arousal measures in children with ADHD compared to normal control children, regardless of RLS status. L-DOPA had little effect on the polysomnographic measures. These findings

have potential implications for the treatment of ADHD-related sleep disturbance.

## 5. Financial disclosures

Raffaele Ferri has consulted for Merck & Co., Sapio Life, and EB Neuro; Oliviero Bruni has consulted for Sapio Life; for the remaining authors there are no financial interests that represent potential conflict of interest.

## Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflict of Interest associated with this article can be viewed by clicking on the following link: <http://dx.doi.org/10.1016/j.sleep.2012.12.012>.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.sleep.2012.12.012>.

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**P4.015 Long term therapy with methylphenidate induces modest effects on growth in ADHD children**

C. Balia<sup>1\*</sup>, A. Anedda<sup>1</sup>, F. Granitzio<sup>1</sup>, S. Carucci<sup>1</sup>, A. Zuddas<sup>1</sup>. <sup>1</sup>Cagliari University Hospital, Dept Biomedical Science, Cagliari, Italy

**Background:** Although stimulants are the most effective medication for Attention Deficit Hyperactivity Disorder (ADHD), poor growth is a common concern, especially with children already on the lower growth percentiles. Studies providing longitudinal data indicate a reduction in both height and weight gain: these effects are usually minimal, but there is substantial variability with some children completely unaffected, whereas others shows significant growth suppression [1].

**Objectives:** To evaluate whether long term immediate release methylphenidate (IR-MPH) therapy (one or two years) interferes with the growth of ADHD children and to assess whether the effects on growth are related to the length of the treatment or to the daily dose.

**Methods:** Growth parameters were collected from 90 ADHD aged 6 to 14, enrolled at one of the site of the Italian National Register for ADHD. All patient were on IR-MPH and with a minimum follow-up of 12 months. 65 were Drug Naïve (DN), 25 were already on MPH since 1–3 years prior to enrollment in the Registry (PR). Weight, height, BMI, height Z-score and BMI Z-score were recorded at each follow-up visit (baseline and after 6, 12, 18, 24 months). Growth velocity SDS and height deficit were calculated after 12 and 24 months.

**Data Analysis:** Categorical data were analysed using contingency tables ( $\chi^2$ ), continuous variables were compared by one-way ANOVA. Repeated measures ANOVA was performed for height and BMI z scores at baseline, 6, 12, 18, 24 month follow up and for height velocity SDS at 12 and 24 months.

**Results:** At baseline Height Z-scores of the entire sample was  $-0.33 \pm 0.98$ , BMI Z-score was equal to  $0.19 \pm 1.14$ . During the 24 months in the study, subjects gained in absolute values of height and weight. Height Z-score showed a significant decrease only from T12 to T24 ( $p=0.05$ ). BMI Z-score decreased significantly at T12 ( $p < 0.001$ ) remaining essentially unchanged at T24. Height deficit was about 0.5 cm at 12 months and 1.3 cm after 24 months. MPH dose/kg/day changed from  $0.49 \pm 0.21$  mg when starting medication, to  $0.68 \pm 0.24$  at T12 and to  $0.75 \pm 0.25$  at T24. No significant differences were found on growth parameters at baseline when stratifying between DN and PR. As in the total sample, in both groups a significant decrease in BMI Z-score from baseline to T12 ( $p < 0.001$ ) and in height Z-score between

T12 and T2 ( $p=0.05$ ) was found. No changes in growth velocity from baseline to the different times considered, were observed, neither in DN nor in PR.

**Discussion:** The findings of the present study suggest that the effects of MPH on growth are relatively small and unlikely to be of clinical concern for this population. Expected and actual deficit in growth should be considered in the context of the benefits the patient receives from the medication. In the present sample the height deficit appears to be more related to the maximum pro/die dose rather than to the length of therapy. More research is needed to better elucidate the mechanism of growth suppression and to implement specific treatment strategies for ADHD children.

**Reference(s)**

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## RELATORI

Daniele Arisi  
UONPIA, A.O. Ist. Ospedalieri di Cremona

Umberto Balottn  
Neuropsichiatria Infantile, IRCCS Mondino, Univ. degli Studi di Pavia

Claudio Bissoli  
UONPIA, IRCCS "Ca'Granda" Ospedale Maggiore Policlinico di Milano

Maurizio Bonati  
IRCCS Ist. "Mario Negri" di Milano

Erika Buzzi  
Scuola di Specialità, Univ. degli Studi di Milano

Mauro Camuffo  
UONPIA, A.USL 9 di Grosseto

Daniela Candeloro  
Scuola di Specialità Univ. Degli Studi di Pavia

Tristana Castrignanò  
Scuola di Specialità, Univ. degli Studi di Varese

Giuseppe Chiarenza  
UONPIA, A.O. "G. Salvini" di Garbagnate Milanese

Antonio Clavenna  
IRCCS Ist. "Mario Negri" di Milano

Stefano Conte  
Neuropsichiatria Infantile, A.O. Ospedali Riuniti di Bergamo

Antonella Costantino  
UONPIA, IRCCS "Ca' Granda" Osp. Maggiore Policlinico di Milano

Gianluca Daffi  
UONPIA, A.O. Spedali Civili Presidio Ospedaliero dei Bambini di Brescia

Anna Didoni  
UONPIA, IRCCS "Ca'Granda" Ospedale Maggiore Policlinico di Milano

Patrizia Di Noia  
Genitore di Muggiò

Paola Effedri  
UONPIA, A.O. Spedali Civili Presidio Ospedaliero dei Bambini di Brescia

Elena Filippini  
UONPIA, A.O. Spedali Civili Presidio Ospedaliero dei Bambini di Brescia

Maria Teresa Foà  
Scuola Primaria "Vinci", 1° Circolo, di Vimercate

Emiddio Fornaro  
UONPIA, A.O. Ospedale Niguarda "Ca'Granda" di Milano

Andrea Gardini  
Direttore Sanitario, A.O. Università di Ferrara

Stefano Guerini  
Scuola di Specialità, Univ. degli Studi di Brescia

Gian Marco Marzocchi  
Psicologia dello Sviluppo, Univ. degli Studi di Milano-Bicocca

Silvia Merati  
UONPIA, A.O. Fatebenefratelli e Oftalmico di Milano

Corrado Meraviglia  
UONPIA, A.O. Valtellina Valchiavenna di Sondrio

Paolo Moderato  
Ist. Comunicazione Comportamento e Consumi, IULM di Milano

Massimo Molteni  
IRCCS, Ist. Scientifico Eugenia Medea di Boasio Parini

Paola Morosini  
UONPIA, A.O. della Provincia di Lodi

Gaia Oldani  
UONPIA, A.O. Fatebenefratelli e Oftalmico di Milano

Laura Reale  
Scuola di Specialità, Univ. degli Studi di Milano; Ist. "Mario Negri" di Milano

Francesco Rinaldi  
UONPIA, ASL Vallecambonica-Sebino

Ippolita Roncoroni  
Pediatra di Famiglia, ASL di Pavia

Monica Sacconi  
UONPIA, A.O. San Paolo, Univ. degli Studi di Milano

Roberto Segala  
UONPIA, A.O. "Carlo Poma" di Mantova

Cristiano Termine  
UONPIA, Ospedale di Circolo, Fondazione "Macchi" di Varese

Alessandra Tiberi  
UONPIA A.O. Spedali Civili Presidio Ospedaliero dei Bambini di Brescia

Davide Villani  
Neuropsichiatria Infantile, A.O. Provincia di Lecco

Antonio Viza  
DSM, AO Spedali Civili di Brescia, Università di Brescia

Gian Vincenzo Zuccotti  
Clin. Pediatrica, A.O. Ospedale Luigi Sacco, Univ. degli Studi di Milano



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

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Se fermate a Bovisio ricordatevi di scendere le scale che si trovano sul lato destro della stazione.

**Segreteria organizzativa:**

Laboratorio per la Salute Materno Infantile  
Dipartimento di Salute Pubblica  
IRCCS - Istituto di Ricerche Farmacologiche Mario Negri  
Via Giuseppe La Masa, 19, Milano  
Tel. 02 39014511 – fax 02 3550924  
ADHD@marionegri.it

Neuropsichiatria Infantile - Polo Ospedaliero UONPIA  
A. O. Spedali Civili di Brescia  
P.le Spedali Civili, 1, Brescia  
Tel. 030.3995722 - 030.3995723

La partecipazione è gratuita e prevede l'assegnazione dei crediti ECM.

L'iscrizione al Convegno è obbligatoria e deve essere effettuata entro il 15 maggio 2013 accedendo al link:

[ADHD.marionegri.it](http://ADHD.marionegri.it)



Milano, 28-29 maggio 2013  
Ore 9.00-18.00 - AULA A

**IRCCS**  
**Istituto di Ricerche Farmacologiche Mario Negri**  
Via G. La Masa 19 - 20156 Milano



Il Progetto: "Condivisione di percorsi diagnostico-terapeutici per l'ADHD in Lombardia" è stato in parte finanziato dalla Regione Lombardia e coinvolge 18 Centri di Riferimento per l'ADHD e il Laboratorio per la Salute Materno Infantile dell'IRCCS - Istituto di Ricerche Farmacologiche Mario Negri.  
Coordinatore del Progetto è la UONPIA degli Spedali Civili di Brescia

## ADHD: PER UNA CONDIVISIONE DEI PERCORSI DIAGNOSTICO-TERAPEUTICI

Il disturbo da deficit di attenzione e iperattività (ADHD) è una delle più frequenti sindromi neuropsichiatriche infantili, sebbene la stima della prevalenza vari tra le nazioni.

La complessità della diagnosi necessita dell'uso di strumenti appropriati che consentano di valutare la presenza dei sintomi nei diversi contesti di vita del bambino. Così anche ogni terapia va adattata alle caratteristiche specifiche del bambino e del suo contesto di vita. L'effettiva scelta terapeutica è basata sulla valutazione di diversi fattori, tra cui la comorbidità, la situazione familiare e la collaborazione con la scuola. Il trattamento farmacologico rappresenta una delle scelte possibili che, comunque, va ad integrarsi agli altri interventi terapeutici che devono essere attivati. Tuttavia gli approcci diagnostici e terapeutici e assistenziali variano ampiamente tra i Centri di Riferimento.

Per meglio comprendere quali sono i determinanti significativi che caratterizzano i percorsi assistenziali per i pazienti con ADHD e per le loro famiglie, e contemporaneamente agire per migliorarne l'appropriatezza, a partire dal gennaio 2010 con il contributo della Regione Lombardia è stato attivato uno specifico progetto di NPIA per la creazione di una rete di Centri di Riferimento per l'ADHD con la finalità principale di definire e condividere pratiche basate sull'evidenza.

Le attività previste dal progetto sono organizzate in 3 sottoprogetti paralleli e sinergici:

- **Analisi dei percorsi esistenti in Lombardia per l'ADHD**  
La costruzione e l'aggiornamento continuo di un Registro regionale per l'ADHD consente di raccogliere informazioni approfondite relative a: dati anagrafici e anamnestici, percorsi di valutazione, diagnosi, interventi terapeutici sia non farmacologici che farmacologici.
- **Formazione e informazione**  
La formazione degli operatori sanitari e la sensibilizzazione della popolazione mira a diagnosi e interventi più tempestivi e appropriati.
- **Definizione di percorsi diagnostico-terapeutici condivisi**  
La condivisione di percorsi di riferimento comuni vuole garantire approcci e gestioni più omogenei da parte di tutti i Centri di Riferimento della Regione Lombardia.

## PRIMA GIORNATA – 28 MAGGIO 2013

09.00 - 10.30

### I BISOGNI PER IL PAZIENTE CON ADHD E PER LA SUA FAMIGLIA

Maurizio Bonati

La percezione del/la

Genitore  
Insegnante  
Pediatra  
Psicologo  
Neuropsichiatra

Patrizia Di Noia

Maria Teresa Foà

Ippolita Roncoroni

Gian Marco Marzocchi

Paola Morosini

10.30 - 11.00

Dal Registro regionale

Anna Didoni

### LE CRITICITÀ NELL'APPROCCIO ALL'ADHD

Diagnosi categoriali o dimensionali?

Massimo Molteni

11.00 - 13.30

### L'IMPIEGO CRITICO DEGLI STRUMENTI DIAGNOSTICI

Paolo Moderato

L'appropriatezza degli strumenti

nei processi diagnostici

Paolo Moderato

L'osservazione clinica e la valutazione  
neuropsicologica

Davide Villani

Questionari e scale di valutazione

Daniele Arisi

qEEG e mapping cerebrale

Giuseppe Chiarenza

14.30 - 15.30

Dal Registro regionale

Paola Effedri, Elena Filippini

Cosa mi porto a casa?

Daniela Candeloro

DISCUSSIONE

15.30 - 18.00

### COMORBIDITÀ

Gian Vincenzo Zuccotti

Comorbidità vs coesistenza e interazioni

dei disturbi

Gian Vincenzo Zuccotti

Disturbi dell'apprendimento

Emidio Fornaro

Disturbo oppositivo-provocatorio

Monica Saccani

I disturbi organici

Roberto Segala

Dal Registro regionale

Cristiano Termine

Cosa mi porto a casa?

Stefano Guerini

DISCUSSIONE

## SECONDA GIORNATA – 29 MAGGIO 2013

09.00 - 13.00

### TERAPIA

Andrea Gardini

Per una cura appropriata, sostenibile, equa,  
attenta alla persona e all'ambiente

Andrea Gardini

Interventi sul contesto

Child training

Silvia Merati, Gaia Oldani

Parent training

Claudio Bissoli

Teacher training

Gianluca Daffi

Approccio integrato psicodinamico

Umberto Balottin

L'uso razionale degli psicofarmaci

Antonio Clavenna

Dal Registro regionale

Stefano Conte

Cosa mi porto a casa?

Erika Buzzi

DISCUSSIONE

14.30 - 18.00

### RISPOSTE ORGANIZZATIVE PER I BISOGNI

Antonella Costantino

Modelli organizzativi e Servizi di NPIA

centrati sulla famiglia

Antonella Costantino

Le criticità per i servizi

Francesco Rinaldi

I percorsi di passaggio alla maggiore età

Le evidenze

Laura Reale

La pratica

Neuropsichiatria

Mauro Camuffo

Psichiatria

Antonio Vita

Dal Registro regionale

Corrado Meraviglia

Cosa mi porto a casa?

Tristana Castrignanò

DISCUSSIONE GENERALE

CONCLUSIONI E PROSPETTIVE

Alessandra Tiberti, Maurizio Bonati

Con il patrocinio della:



**SINPIA**

Società Italiana di Neuropsichiatria  
dell'Infanzia e dell'Adolescenza



IX CONGRESSO NAZIONALE AIDAI-AIRIPA  
 “NUOVE PROSPETTIVE DI INTERVENTO  
 NELL’ADHD”



PERUGIA 30-31 MAGGIO 2013

UNIVERSITA' DEGLI STUDI

FACOLTA' DI SCIENZE DELLA FORMAZIONE

PIAZZA ERMINI

*Con il patrocinio:*

*Regione Umbria*

*Provincia di Perugia*

*Comune di Perugia*

*Università degli Studi di Perugia, Facoltà di Scienze della Formazione*

*Ufficio Scolastico Regionale per l'Umbria*

*Ordine degli Psicologi Regione Umbria*

*Azienda USL Umbria 1*

*CESVOL (Centro Servizi per il Volontariato)*

*AUPI (Associazione Unitaria Psicologi Italiani)*

*SIPNEI (Società Italiana di PsicoNeuroEndocrinoImmunologia)*

*AIFA (Associazione Italiana Famiglie ADHD)*

PROGRAMMA

GIOVEDÌ 30 MAGGIO

8:00-9:00 Apertura e registrazione partecipanti

AULA MAGNA	AULA 3
9:00-9:30 Saluto delle autorità	
9:30-11:00 Lettura magistrale: D. Daley, University of Nottingham <b>Beyond symptom control for ADHD: What can parents do to improve outcomes?</b>	
11:00-12:30 Lettura Magistrale: C. Cornoldi, Università di Padova <b>Disturbi della scrittura e ADHD: nuovi orientamenti di interpretazione ed intervento.</b>	
12:30-13:00 <b>In ricordo di Mariangela Quatrini</b> , a cura di AIDAI Marche	
13:00-14:00 Pausa pranzo	
14:00-16:00 Simposio: <b>Valutazione delle funzioni esecutive, dell'attenzione, nuovi marker per l'ADHD</b> Coordinatore: F. Benso, Università di Genova e Polo M.T. Bozzo. - M. Filippini, UOC di NPI, Ospedale Bellaria di Bologna, "Correlati neurobiologici ed elettrofisiologici e delle funzioni esecutive-attentive nei bambini con epilessia: dati preliminari di uno studio in età scolare". - S. Gazzellini <sup>1</sup> , A. Napolitano <sup>2</sup> <sup>1</sup> Dip. di Neuroscienze e Neuroriabilitazione, Ospedale Pediatrico B. Gesù, Roma. <sup>2</sup> Enterprise Risk Management, Ospedale Pediatrico B. Gesù, Roma. "Analisi time-frequency di segnali EEG e Rts: studio su pazienti pediatrici con deficit di attenzione sostenuta da lesione cerebrale acquisita". - M.C. Usai, Università di Genova e Polo MT Bozzo, "I sistemi di autoregolazione nella prima infanzia". - M. Margheriti <sup>1</sup> , M. Baciarelli <sup>1</sup> , M.T. Barberini <sup>1</sup> , M.S. Ghilardi <sup>1</sup> , G. Tinarelli <sup>1</sup> , L. Michelazzo <sup>2</sup> <sup>1</sup> Centro di Neuropsicologia Clinica dell'Età Evolutiva "G. Sabbadini", Perugia. <sup>2</sup> Università di Roma Tor Vergata. "Funzioni esecutive e disprassia". - F. Benso, Università di Genova e Polo M.T. Bozzo.	14:00-16:00 Simposio: <b>Il comportamento dirompente: dalla prevenzione all'urgenza</b> Coordinatore: S. Pezzica, Università di Firenze - E. Menesini, Università di Firenze, "La prevenzione dei comportamenti aggressivi". - D. Fedeli, Università di Udine, "Ragazzi con Disturbo della condotta in classe". - P. Muratori, IRCCS Fondazione Stella Maris, Università di Pisa, "Cosa cambia nel gruppo e grazie al gruppo: fra clinica e ricerca". - C. Buonanno, Scuola di Psicoterapia Cognitivo-comportamentale, Grosseto, "La psicoterapia cognitivo-comportamentale". - D. Calderoni, UOC TSMREE, ASL Roma B, "Il ricovero Ospedaliero nei disturbi del comportamento". Segue discussione.

<p>“Valutazione dei diversi marker utili per la diagnosi di ADHD”. Segue discussione.</p>	
<p>16:00-18:00 Simposio: <b>Nuove prospettive e Parent Training</b> Coordinatore: A.M. Re, Università di Padova - A.M. Re, A. Paiano, E. Boatto, E. Ferruzza, C. Cornoldi “Un nuovo modello di Parent Training” - S. Spagnoletti, Unità Operativa NPI, San Donà di Piave, “L'intervento di Parent Training nei prescolari” - S. Pezzica, Università di Firenze, “L'utilizzo dell'autocaratterizzazione nell'intervento con i genitori” - L. Benedetto, e M. Ingrassia, Università di Messina, “La valutazione del cambiamento nel parenting. L'Alabama Parenting Questionnaire (APQ) per la fascia prescolare”. Segue discussione.</p>	<p>16:00-18:00 Workshop: <b>Il Coping Power Program</b> L. Polidori, IRCCS Fondazione Stella Maris, Pisa</p>
<p>18:30 Assemblea dei soci AIDAI</p>	

## VENERDI' 31 MAGGIO

<p>9:00-10:30 Lettura magistrale J. Van der Meere, University of Groningen <b>Regulation and emotions in ADHD</b></p>	
<p>10:30-13:00 Simposio: <b>Attaccamento, relazioni e regolazione emotiva: video, video feedback e interventi sulla genitorialità nell'ADHD e severe mood dysregulation</b> Coordinatore: R. Bertaccini, Scuola Bolognese Psicoterapia Cognitiva, Centro Terapia Cognitiva, Forlì - R. Bertaccini, “Itinerari di sviluppo, stili di regolazione emotiva e ADHD”. - F. Manaresi, ASTREA, Roma, “Circle of Security, parent training e regolazione”. - C. Paloscia, ASTREA, Roma, “Manchester Child Attachment Story Task, video feedback e regolazione”. Segue discussione.</p>	<p>10:30-13:00 Simposio: <b>Le Istituzioni e l'ADHD</b> Coordinatore: P. Panei, Istituto Superiore di Sanità - R. Arcieri, Istituto Superiore di Sanità, “Il registro nazionale: sintesi di 5 anni di attività”. - G. Mazzotta, Università di Perugia e F. Guccione, ASL NO, “I centri di riferimento: obiettivi raggiunti e potenzialità inesprese”. - F. Ragazzo, Centro di Riferimento ADHD Savigliano, ASL CN1, “La presa in carico globale da parte dei servizi e delle istituzioni: luci e ombre” - S. Bianchi, Associazione Culturale Pediatri, Perugia, “Il punto di vista del pediatra”. Segue discussione.</p>
<p>13:00-14:00 Pausa pranzo</p>	
<p>14:00-16:00 Simposio: <b>Dalla diagnosi alla progettazione in una scuola inclusiva</b> Coordinatore: L. Arcangeli, Università di Perugia - L. Arcangeli, Università di Perugia, “I Bisogni Educativi Speciali nella prospettiva coevolutiva” - F. Falcinelli, Università di Perugia, “Nuove tecnologie e didattica inclusiva” - R. Ciambrone, MIUR, Roma, “La presa in carico dei Bisogni Educativi Speciali: dall'approccio clinico a quello pedagogico”. - C. Scheriani, Dirigente scolastico I.C. Divisione Julia, Trieste “La valutazione scolastica per i ragazzi con ADHD” - P. Stacconi, Presidente AIFA, “Le esigenze delle famiglie”</p>	
<p>16:00-18:00 Tavola rotonda: <b>L'intreccio delle responsabilità</b> Coordinatore: M. Margheriti, Presidente AIDAI Partecipano: L. Arcangeli, Università di Perugia. S. Bianchi, Associazione Culturale Pediatri, Perugia. S. Boarelli, Ufficio Scolastico Regionale dell'Umbria. P. Catanelli, Regione Umbria. R. Ciambrone, MIUR, Roma F. Falcinelli, Università di Perugia. G. Mazzotta, Università di Perugia. P. Panei, Istituto Superiore di Sanità, Roma. P. Stacconi, Presidente AIFA.</p>	
<p>18:00-19:00 Compilazione questionari ECM</p>	

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Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza  
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia  
(in attuazione della D.G. sanità n. 3250 del 11/04/2011)  
Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia"  
"Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia".

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**IRCCS ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI**  
**DIPARTIMENTO DI SALUTE PUBBLICA**  
**Laboratorio per la Salute Materno Infantile**  
Via Giuseppe La Masa, 19 - 20156 Milano MI - Italia - [www.marionegri.it](http://www.marionegri.it)  
tel +39 02 39014.511 - fax +39 02 3550924 - [mother\\_child@marionegri.it](mailto:mother_child@marionegri.it)