



ADHD

ATTENTION DEFICIT HYPERACTIVITY DISORDER


Laboratorio per la Salute
Materno Infantile


MARIO NEGRI
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J Pediatr. 2008;152:101-05.

Folate Pathway Genetic Polymorphisms are Related to Attention Disorders in Childhood Leukemia Survivors.

Krull KR, Brouwers P, Jain N, et al.

Objective: To test the hypothesis that 5,10-methylenetetrahydroreductase (MTHFR) polymorphisms can partially explain the individual variation in developing attention-deficit/hyperactivity disorder (ADHD) after acute lymphoblastic leukemia (ALL) therapy. Study design: Parents of 48 survivors of childhood ALL completed a clinical diagnostic process to identify subtypes of ADHD. Genotyping was performed with peripheral blood DNA for MTHFR (C677T and A1298C) polymorphisms. Results: Eleven of the 48 patients (22.9%) had scores consistent with the inattentive symptoms of ADHD. Patients with genotypes related to lower folate levels (11 out of 39; 39.2%) were more likely to have ADHD. The A1298C genotype appeared to be the predominant linkage to the inattentive symptoms, leading to a 7.4-fold increase in diagnosis, compared with a 1.3-fold increase for the C677T genotype. Age at diagnosis and sex were not associated with inattentiveness. Conclusions: Preliminary data imply a strong relationship between MTHFR polymorphisms and the inattentive symptoms of ADHD in survivors of childhood ALL. (copyright) 2008 Mosby, Inc. All rights reserved.

Pediatr Blood Cancer. 2008;50:337-40.

Cognitive outcome in pediatric brain tumor survivors: Delayed attention deficit at long-term follow-up.

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Background. Treatment of childhood brain tumors has often been associated with long-term cognitive morbidity in children. Our previous research identified age at diagnosis, polytherapy and brain radiation dose as treatment factors affecting neuropsychological outcome most strongly in children with cancer [1]. Our current goal was to measure the change across different cognitive functions. Procedure. This study examined the cognitive outcome over repeat testing in a heterogeneous sample of 18 children with brain tumors. Tumor types included medulloblastoma and glioma. ANOVA's for repeated measures were used to evaluate the changes in cognitive domains across follow-up evaluations. Results. Consistent with previous findings, the most deleterious effects were seen on IQ indices of non verbal cognitive ability, visual perceptual skills and information processing speed. Analyses reveal that the attentional factor, Freedom from Distractibility, is the only IQ index that declines over subsequent testing. The statistical decline was attributable to a significant decline on the arithmetic subtest, as well as a non-significant trend for the auditory attention span subtest. Conclusions. This study reveals that while most indices remained stable over repeat testing, auditory attention and concentration skills decline. Long-term outcome is discussed in light of the high prevalence of attention and mathematic difficulties reported in these children and the need for preventive and remedial approaches. (copyright) 2007 Wiley-Liss, Inc

Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase e PsycINFO 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.

Genes Brain Behav. 2008;7:53-60.

Association study of the nicotinic acetylcholine receptor (alpha)4 subunit gene, CHRNA4, in attention-deficit hyperactivity disorder.

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Attention-deficit hyperactivity disorder (ADHD) is a common childhood-onset psychiatric condition with a strong genetic component. Evidence from pharmacological, clinical and animal studies has suggested that the nicotinic system could be involved in the disorder. Previous studies have implicated the nicotinic acetylcholine receptor (alpha)4 subunit gene, CHRNA4, in ADHD. Particularly, a polymorphism in the exon 2-intron 2 junction of CHRNA4 has been associated with severe inattention defined by latent class analysis. In the current study, we used the transmission disequilibrium test (TDT) to investigate four polymorphisms encompassing this region of CHRNA4 for association with ADHD in a sample of 264 nuclear families from Toronto. No significant evidence of biased transmission was observed for any of the marker alleles for ADHD defined as a categorical trait (all subtypes included), although one haplotype showed marginal evidence of under-transmission. No association was found with the ADHD predominantly inattentive subtype or with symptom dimension scores of inattention. On the contrary, nominally significant evidence of association of individual markers was obtained for the ADHD combined subtype and with teacher-rated hyperactivity-impulsivity scores, with the same haplotype being under-transmitted. Based on our results and others, CHRNA4 may be involved in ADHD; however, its role in ADHD symptomatology remains to be clarified. (copyright) 2007 Blackwell Publishing Ltd

J Int Neuropsychol Soc. 2008;14:119-29.

Differences in executive functioning in children with heavy prenatal alcohol exposure or attention-deficit/ hyperactivity disorder.

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Children with either fetal alcohol spectrum disorder (FASD) or attention-deficit/hyperactivity disorder (ADHD) display deficits in attention and executive function (EF) and differential diagnosis of these two clinical groups may be difficult, especially when information about prenatal alcohol exposure is unavailable. The current study compared EF performance of three groups: children with heavy prenatal alcohol exposure (ALC); nonexposed children with attention-deficit/ hyperactivity disorder (ADHD); and typically developing controls (CON). Both clinical groups met diagnostic criteria for ADHD. The EF tasks used were the Wisconsin Card Sorting Test (WCST), the Controlled Oral Word Association Test (COWAT), and the Trail Making Test (TMT). Results indicated different patterns of deficit; both clinical groups displayed deficits on the WCST and a relative weakness on letter versus category fluency. Only the ALC group displayed overall deficits on letter fluency and a relative weakness on TMT-B versus TMT-A. In addition, WCST performance was significantly lower than expected based on IQ in the ADHD group and significantly higher than expected in the ALC group. These results, which indicate that, although EF deficits occurred in both clinical groups, the degree and pattern of deficit differed between the ALC and ADHD groups, may improve differential diagnosis. (copyright) 2008 The International Neuropsychological Society

Child Care Health Dev. 2008;34:121-33.

Critical influences affecting response to various treatments in young children with ADHD: A case series.

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Background: While the use of stimulant medication as a treatment for children with attention deficit hyperactivity disorder (ADHD) has been the most studied therapy in child psychiatry, there is debate about its use with young children. This study describes a series of cases seen in a normal clinical context, treated with one of four different treatment programmes. Methods: Sixteen pre-school children diagnosed with ADHD and their parents were randomly assigned to receive one of four treatments: (1) 0.3mg/kg methylphenidate, parent training programme; (2) 0.3mg/kg methylphenidate, parent support programme; (3) placebo medication, parent training; and (4) placebo medication, parent support. Changes were assessed at the individual level, using clinical observations, parent and teacher rating scales and measures of parenting and family factors. Results: Children were more likely to improve when the treatment involved at least one active component (medication or parent training). However, there was notable variability in individual parental and child

participants' responses to all treatment conditions, indicating the importance of interactions between treatment variables and other factors. Conclusions: Findings are discussed within the framework of a transactional model, and inferences are drawn about the limitations of the idea that there is a 'best treatment' that is universally applicable. (copyright) 2007 The Authors; Journal compilation (copyright) 2007 Blackwell Publishing Ltd

Child Care Health Dev. 2008;34:111-20.

Children's and parents' perspectives on open-label use of placebos in the treatment of ADHD.

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Background: The purpose of this study was to examine the efficacy and acceptability of an open-label conditioned placebo dose reduction (CPDR) treatment in 70 children with attention deficit hyperactivity disorder (ADHD). This paper focuses on the qualitative data from the study. Methods: Following a double-blind, crossover dose finding procedure to determine each subject's optimal dose of stimulant medication, subjects were randomized to the CPDR treatment or one of two control groups. Outcome measures included parent and teacher ratings of ADHD behaviours and stimulant side effects. Qualitative assessments were based on open-ended interviews of children and parents. Positive responders to CPDR and controls were followed for 3 months to assess persistence of treatment benefits. Results: Children randomized to CPDR showed an excellent treatment response, well maintained over time. Parents and children were generally accepting of the treatment. Most parents reported treatment benefits and 80% of the children found the placebo to be useful. Full disclosure of the placebo to parents and children did not appear to negate the placebo's effectiveness. Participation effects and changes in caregiver behaviour may have contributed to positive treatment outcomes. Conclusions: Open-label use of placebos as part of CPDR treatment may represent an innovative, ethical way of harnessing the power of placebos in clinical therapeutics. (copyright) 2008 The Authors; Journal compilation (copyright) 2008 Blackwell Publishing Ltd

Child Care Health Dev. 2008;34:104-10.

Open-label use of placebos in the treatment of ADHD: A pilot study.

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Background: This study examined short-term efficacy, side effects and acceptability of a placebo treatment procedure designed to maintain children with attention deficit hyperactivity disorder (ADHD) on 50% of their usual stimulant dose. Methods: An open-label prospective crossover trial was conducted in 26 children with ADHD, ages 7-15 years, stable on stimulant therapy, followed at a community-based developmental paediatrics ADHD clinic. Subjects were randomly assigned to one of two orders of experimental conditions: (1) baseline (100%) dose (1week), then 50% dose (1week), then 50% dose + placebo (1week), or (2) baseline (100%), then 50% dose + placebo, then 50% dose. The inert nature of the placebo was fully disclosed to parent and child. Treatment was open-label for child, parents and physician, but single blind for teachers. Main outcome measures included weekly IOWA Conners parent and teacher rating scales, the Pittsburgh side effects rating scale (PSERS) and the Clinical Global Impressions (CGI) scale. Results: Parent IOWA showed ADHD behaviour tended to remain the same when the dose of stimulant medication was reduced with placebo but to deteriorate when the dose was reduced without placebo. There were no significant differences between conditions on the Teacher IOWA. PSERS scores were higher at baseline than on 50% dose. On the CGI, there was a significant difference ($P = 0.004$) between the 50% dose and the 50% + placebo conditions. Individual subject analysis showed that eight subjects met criteria for responder. Conclusions: Results indicate that the open-label placebo treatment was acceptable and efficacious in the short term for some children. (copyright) 2008 The Authors; Journal compilation (copyright) 2008 Blackwell Publishing Ltd

J Am Acad Child Adolesc Psychiatry. 2008;47:76-85.

Predictors of stability of attention-deficit/hyperactivity disorder subtypes from childhood to young adulthood.

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OBJECTIVE: To determine the 5-year prospective stability of population-based and DSM-IV subtypes of attention-deficit/hyperactivity disorder (ADHD) as well as to explore predictors of stability. **METHOD:** A total of 708 twins ages 7 to 19 years who were identified from birth records of the state of Missouri and had participated in a study of ADHD were reassessed 5 years later in a blinded fashion. Stabilities of DSM-IV and population-based ADHD subtypes were compared using percentage of agreement with significance tested by the (kappa) statistic. Predictors of stability of subtype diagnosis were determined using multivariate logistic regression. **RESULTS:** In general, 5-year ADHD subtype stability was poor to modest and ranged from 11.1% to 24.0% for DSM-IV for subtypes and from 14.3% to 35.3% for clinically significant population-derived subtypes. There were no predictors of diagnostic stability that applied across subtypes. There were subtype-specific predictors including a diagnosis of oppositional defiant disorder for DSM-IV primarily inattentive ADHD; lower verbal IQ for DSM-IV combined type ADHD; and younger age, oppositional defiant disorder, and medication use for population-defined severe combined ADHD. **CONCLUSIONS:** Population-defined ADHD subtype criteria demonstrated modestly improved diagnostic stability over 5 years compared to DSM-IV subtypes. Few correlates or predictors of stability were identified. Copyright 2008 (copyright) American Academy of Child and Adolescent Psychiatry

J Am Acad Child Adolesc Psychiatry. 2008;47:68-75.

Familial vulnerability to ADHD affects activity in the cerebellum in addition to the prefrontal systems.

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OBJECTIVE: Familial vulnerability to attention-deficit/hyperactivity disorder (ADHD) has been shown to be related to atypical prefrontal activity during cognitive control tasks. However, ADHD is associated with deficits in the cerebellum as well as deficits in frontostriatal circuitry and associated cognitive control. In this study, we investigated whether cerebellar systems are sensitive to familial risk for ADHD in addition to frontostriatal circuitry. **METHOD:** We used an event-related, rapid mixed-trial functional magnetic resonance imaging design. The paradigm was a variation on a go/no-go task, with expected (go) and unexpected (no-go) events at expected and unexpected times. A total of 36 male children and adolescents completed the study, including 12 sibling pairs discordant for ADHD and 12 matched controls. **RESULTS:** Children and adolescents with ADHD were less accurate on unexpected events than control subjects. Performance by unaffected siblings was intermediate, between that of children and adolescents with ADHD and controls. Functional neuroimaging results showed dissociation between activation in the cerebellum and anterior cingulate cortex: Activity in the anterior cingulate cortex was decreased for subjects with ADHD and their unaffected siblings compared with controls for manipulations of stimulus type (no-go trials), but not timing. In contrast, cerebellar activity was decreased for subjects with ADHD and their unaffected siblings for manipulations of timing, but not stimulus type. **CONCLUSIONS:** These findings suggest that activity in both the prefrontal cortex and cerebellum is sensitive to familial vulnerability to ADHD. Unaffected siblings of individuals with ADHD show deficits similar to affected probands in prefrontal areas for unexpected events and in cerebellum for events at unexpected times. Copyright 2008 (copyright) American Academy of Child and Adolescent Psychiatry

J Am Acad Child Adolesc Psychiatry. 2008;47:61-67.

Dopamine transporter genotype conveys familial risk of attention-deficit/ hyperactivity disorder through striatal activation.

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OBJECTIVE: The dopamine transporter (DAT1) gene has been implicated in attention-deficit/hyperactivity disorder (ADHD), although the mechanism by which it exerts its effects remains unknown. The polymorphism associated with ADHD has been shown to affect expression of the transporter in vitro and in vivo. Dopamine transporters are predominantly expressed in the striatum, but also in the cerebellar vermis. Stimulant

medication is often effective in ADHD and is believed to exert its effects by blocking dopamine transporters in the striatum. We set out to investigate the effect of the DAT1 genotype in ADHD in a small, preliminary study. We hypothesized that the DAT1 genotype would affect brain activation patterns in a manner similar to that of stimulant medication, with the lesser expressing allele mirroring its effects. **METHOD:** We investigated DAT1 gene effects on brain activation patterns in an all-male sample of sibling pairs discordant for ADHD ($n = 20$) and controls ($n = 9$). All of the subjects participated in a functional magnetic resonance imaging session using a go/no-go paradigm and provided a DNA sample for analysis. **RESULTS:** DAT1 genotype affected activation in the striatum and cerebellar vermis. The genotype interacted with familial risk of ADHD in the striatum but not the vermis. **CONCLUSIONS:** These preliminary results suggest that the DAT1 gene effects in the striatum are involved in translating the genetic risk of ADHD into a neurobiological substrate. As such, this study represents a first step in elucidating the neurobiological mechanisms underlying genetic influences in ADHD. Furthermore, these results may contribute to long-term possibilities for the development of new treatments: If the DAT1 genotype has differential effects on striatal activation, then it may be useful as a surrogate endpoint in individualized treatments targeting genotype/functional magnetic resonance imaging activation profiles. Copyright 2008 (copyright) American Academy of Child and Adolescent Psychiatry

Child Psychiatry Hum Dev. 2008;39:85-99.

Mothers' and fathers' attributions and beliefs in families of girls and boys with attention-deficit/hyperactivity disorder.

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This study examined parent and child gender effects on parents' attributions and beliefs in regards to child symptoms of attention-deficit/ hyperactivity disorder (ADHD). Participants included mothers and fathers of 19 girls and 17 boys with ADHD. Groups of boys and girls, aged 5-13 years, were equated on age and medication status, as well as ADHD symptom severity. These groups also were similar in the severity of comorbid oppositional behaviors and internalizing problems, as well as a variety of demographic characteristics. Parents' attributions for child behavior were assessed in response to written scenarios describing either hyperactive/impulsive or inattentive symptoms of ADHD. Parents also completed a questionnaire assessing beliefs and knowledge about ADHD. There were no child gender effects for parents' attributions or beliefs. All parents attributed inattentive symptoms to more internal, global and stable causes than impulsive symptoms. Mothers attributed both inattentive and impulsive child symptoms to more global and stable causes than did fathers. Fathers, but not mothers, reported more negative reactions to ADHD symptoms that were perceived as having an internal cause. Finally, mothers scored higher on beliefs in behavior management than did fathers, and fathers believed more in psychological causes and treatments for ADHD. Possible explanations for and implications of these results are explored. (copyright) 2007 Springer Science+Business Media, LLC

Child Psychiatry Hum Dev. 2008;39:27-38.

The stress response in adolescents with inattentive type ADHD symptoms.

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Objective: To investigate the hypothalamic pituitary adrenal (HPA) axis response to a stressor in adolescents with inattentive type attention-deficit hyperactivity disorder symptoms (ADHD-I). **Method:** Salivary cortisol was measured in threshold inattentive (TI, $n = 7$), moderately inattentive (MI, $n = 13$) and no symptom (comparison) ($n = 19$) groups of healthy, young adolescents, based on symptom counts, prior to and after an induced social/cognitive stressor. **Results:** The TI group displayed a significant decrease in cortisol post stressor whereas both the MI and comparison groups showed an increase in cortisol. **Conclusion:** The diagnostic threshold of inattentive type ADHD shows HPA axis dysregulation whereas the more mild form does not show dysfunction. (copyright) 2007 Springer Science+Business Media, LLC

Biol Psychol. 2008;77:53-62.

Stimulus context and motor preparation in attention-deficit/hyperactivity disorder.

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Aim: To investigate (1) whether and how local stimulus context variation may modify behavioural and preparatory motor processes in children, and (2) if these effects differ between healthy children and children with attention-deficit/hyperactivity disorder (ADHD) aged 9-12 years. Methods: Behavioural parameters and contingent negative variation (CNV) at cortical motor electrodes were recorded during a cued continuous performance task (AX-CPT) in three stimulus context conditions (Go, NoGo, neutral). Stimulus context was varied on the basis of stimulus types preceding the cue letter A. Results: In all children, responses were slowed in both the NoGo- and Go-conditions relative to the neutral condition. Stimulus context affected preparatory motor processes in both groups but differentially. ADHD children showed smaller CNV potentials and a functionally irrelevant over-activation of the ipsilateral motor area. Conclusions: Local stimulus context may modify behavioural and preparatory motor processes in children. In ADHD, local context variations may disrupt behaviour due to inefficient regulation of supervisory higher control systems. (copyright) 2007 Elsevier B.V. All rights reserved

Clin Linguist Phon. 2008;22:25-46.

Narrative organization skills in children with attention deficit hyperactivity disorder and language impairment: Application of the causal network model.

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Studies suggest that the oral narratives of children with attention deficit hyperactivity disorder (ADHD) are less organized than those of typically developing peers. Many studies, however, do not account for children's language abilities. Because language impairment (LI) is a frequent comorbid condition in children with ADHD, this exploratory study investigated language abilities and narrative organization skills in children with and without ADHD. Narratives were elicited using the picture-sequence task and the single-picture task from the Test of Narrative Language (Gillam & Pearson, 2004). The causal network model (Trabasso, Van den Broek, & Suh, 1989) was applied to analyse the narratives. Specifically, narratives were examined to identify complete and incomplete superordinate and subordinate Goal-Attempt-Outcome (GAO) units. The results revealed no differences among the groups in the picture-sequence task. Children with ADHD+LI produced significantly fewer complete superordinate GAO units than typical children in the single-picture task. Theoretical and clinical implications are discussed

Clin Neurophysiol. 2008;119:163-79.

Event-related wave activity in the EEG provides new marker of ADHD.

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Objective: This study examines the utility of new measures of event-related spatio-temporal waves in the EEG as a marker of ADHD, previously shown to be closely related to the P3 ERP in an adult sample. Methods: Wave activity in the EEG was assessed during both an auditory Oddball and a visual continuous performance task (CPT) for an ADHD group ranging in age from 6 to 18 years and comprising mostly Combined and Inattentive subtypes, and for an age and gender matched control group. Results: The ADHD subjects had less wave activity at low frequencies (~1 Hz) during both tasks. For auditory Oddball targets, this effect was shown to be related to smaller P3 ERP amplitudes. During CPT, the ~1 Hz wave activity in the ADHD subjects was inversely related to clinical and behavioral measures of hyperactivity and impulsivity. CPT wave activity at ~1 Hz was seen to "normalise" following treatment with stimulant medication. Conclusions: The results identify a deficit in low frequency wave activity as a new marker for ADHD associated with levels of hyperactivity and impulsivity. Significance: The marker is evident across a range of tasks and may be specific to ADHD. While lower ~1 Hz activity partly accounts for reduced P3 ERPs in ADHD, the effect also arises for tasks that do not elicit a P3. Deficits in behavioral inhibition are hypothesized to arise from underlying dysregulation of cortical inhibition. Crown Copyright (copyright) 2007

J Child Psychol Psychiatry Allied Discip. 2008;49:70-78.

Predictive validity of DSM-IV and ICD-10 criteria for ADHD and hyperkinetic disorder.

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Background: The goal of this study was to compare the predictive validity of the two main diagnostic schemata for childhood hyperactivity - attention-deficit hyperactivity disorder (ADHD; Diagnostic and Statistical Manual- IV) and hyperkinetic disorder (HKD; International Classification of Diseases- 10th Edition). Methods: Diagnostic criteria for ADHD and HKD were used to classify 419 children ages 6 to 16 years referred to a clinic for behavioral problems into one of four groups: HKD, ADHD combined subtype (ADHD-C), ADHD hyperactive-impulsive subtype (ADHD-HI), ADHD inattentive subtype (ADHD-IA). These groups were compared on clinical characteristics including total symptom severity, overall impairment, exposure to psychosocial and neuro-developmental risks, family history of ADHD in first-degree family members, rate and type of comorbidity, intelligence, academic achievement, and on laboratory tests of motor response inhibition and working memory with each other and with normal controls (47). Results: Of the 419 cases, there were 46 HKD (11.0%), 200 ADHD-C (47.7%), 60 ADHD-HI (14.3%) and 113 ADHD-IA (27.0%) cases. The HKD group had more symptoms and was more impaired on teachers' ratings than were the other groups. The ADHD-C and HKD groups had poorer inhibitory control than the ADHD-IA, ADHD-HI and control groups, and all four clinic groups showed inhibition deficit compared to controls. Groups did not differ in working memory. Compared to controls, the HKD, ADHD-C, ADHD-HI and ADHD-IA groups had higher familial risk of ADHD, greater psychosocial risk exposure, lower intellectual level and poorer academic attainment. However, we observed no differences among the clinic groups in these characteristics. Conclusions: Like earlier versions, ICD-10 and DSM-IV continue to delineate diagnostic entities with substantially different prevalence in clinic samples. However, HKD, ADHD-C, ADHD-IA and ADHD-HI groups overlap substantially in terms of important clinical characteristics, although HKD and ADHD-C may be somewhat more severe variants of the condition than ADHD-IA and ADHD-HI. (copyright) 2007 The Authors

Arch Clin Neuropsychol. 2008;23:21-32.

Cognitive switching processes in young people with attention-deficit/hyperactivity disorder.

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Patients with attention-deficit/hyperactivity disorder (ADHD) can be slow at switching between stimuli, or between sets of stimuli to control behaviour appropriate to changing situations. We examined clinical and experimental parameters that may influence the speed of such processes measured in the trail-making (TMT) and switch-tasks in cases with ADHD combined type, their non-affected siblings and unrelated healthy controls. The latency for completion of the trail-making task controlling for psychomotor processing (TMT-B-A) was longer for ADHD cases, and correlated with Conners' ratings of symptom severity across all subjects. The effect decreased with age. Switch-task responses to questions of "Which number?" and "How many?" between sets of 1/111 or 3/333 elicited differential increases in latency with condition that affected all groups. But there was evidence for increased symptom-related intra-individual variability among the ADHD cases, and across all subjects. Young siblings showed familiarity for some measures of TMT and switch-task performance but these were modest. The potential influences of moderator variables on the efficiency of processing stimulus change rather than the speed of processing are discussed. (copyright) 2007 National Academy of Neuropsychology

Arch Clin Neuropsychol. 2008;23:103-12.

Attentional problems in children born very preterm or with extremely low birth weight at 7-9 years.

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Behavioral rating scales and tests of attention were used to study attentional problems in children born very preterm (less-than or equal to)27 weeks gestation) or with extremely low birth weight (ELBW; (less-than or equal to)1000 g). Psychological tests of attention (viz., Digits and Spatial Span Forward, Visual Attention from the NEPSY, Trail Making Test B, and Stroop Color and Word Test) were administered to 45 children born very preterm/ELBW and 49 full-term controls, aged 7-9 years of age. Behavioral ratings on an ADHD scale were provided by parents and teachers on inattentive and hyperactive-impulsive symptoms. Children born

very preterm/ELBW were found to perform significantly more poorly on Spatial Span Forward, Visual Attention, and Trail Making B than controls. Group differences were also found on parents' ratings on inattentive and total symptoms. Finally, measures of psychological tests of attention were found to be significant predictors of parents' and teachers' ratings of symptoms. Crown Copyright (copyright) 2007

Eur Neuropsychopharmacol. 2008;18:79-86.

CYP2D6 metabolizer status and atomoxetine dosing in children and adolescents with ADHD.

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To determine whether physicians can adequately titrate atomoxetine without knowing genotype status for hepatic cytochrome P450 2D6, we pooled data from two open-label studies of atomoxetine in children and adolescents with attention-deficit/hyperactivity disorder. Patients were assessed weekly up to 10 weeks and doses titrated for efficacy and tolerability at the discretion of investigators (max. 1.8 mg/kg/d). Mean dose was 0.1 mg/kg/d lower in poor metabolizer (PM) patients (n = 87) than extensive metabolizers (EMs, n = 1239). PMs demonstrated marginally better efficacy on the ADHDRS-IV-Parent:Inv and had comparable safety profiles, except for a 4.0-bpm greater increase in mean pulse rate and a 1.0-kg greater weight loss. Changes from baseline in Fridericia QTc did not differ between groups or correlate with dose in PMs. Results suggest genotyping is unnecessary during routine clinical management, because investigators were able to dose atomoxetine to comparable efficacy and safety levels in EMs and PMs without knowledge of genotype metabolizer status. (copyright) 2007 Elsevier B.V. and ECNP

Clin Pediatr. 2008;47:15-20.

Correlation between hospitalization for pharmaceutical ingestion and attention deficit disorder in children aged 5 to 9 years old.

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To determine if attention deficit hyperactivity disorder is a risk factor for pharmaceutical ingestions leading to hospital admission in children between ages 5 and 9, a retrospective, case-controlled chart review was conducted at a children's hospital. Cases were children aged 5 to 9 admitted for oral ingestion of pharmaceuticals. Controls were children admitted during the same time period with abdominal pain, appendicitis, or gastroenteritis. Controls were matched to cases 3:1 by age and gender. An odds ratio was calculated to determine if attention deficit hyperactivity disorder is a statistically significant risk factor for hospitalization after pharmaceutical ingestion. A total of 36% of 31 identified cases had attention deficit hyperactivity disorder compared with 7% of controls. The odds ratio for attention deficit hyperactivity disorder in children hospitalized after pharmaceutical ingestion was 7.97 (95% confidence interval, 2.35-28.01; P <.01). Children hospitalized for pharmaceutical ingestion are nearly 8 times more likely to have attention deficit hyperactivity disorder than children hospitalized for an unrelated disorder. (copyright) 2008 Sage Publications

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:110-11.

No association between the DAT1 10-repeat allele and ADHD in the Iranian population.

Banoei MM, Majidzadeh T, Shirazi E, et al.

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Association studies between attention-deficit hyperactivity disorder (ADHD) and the 10-repeat allele of a polymorphism (a 40 bp variable number of tandem repeats) in the dopamine transporter gene (DAT1) have resulted in mixed findings in different populations. We performed a case/control study to clarify the contribution of this allele with ADHD in the Iranian population. No association was observed between the 10-allele and disease ($\chi^2 = 0.081$, $P < 0.9$). Furthermore, no significant difference was observed in the homozygosity of this allele between the case and control groups ($\chi^2 = 0.022$, $P < 0.9$). Implication of the dopamine transporter gene in the pathophysiology of ADHD warrants investigation of other functional polymorphisms within this gene in the Iranian ADHD patients. (copyright) 2007 Wiley-Liss, Inc

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:107-09.

Preliminary report of familial clustering of EEG measures in ADHD.

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The purpose of the present study is to examine the familiarity of electroencephalographic (EEG) measures among affected sibling pairs with Attention-Deficit Hyperactivity Disorder (ADHD). EEG was recorded during baseline (eyes open and eyes closed) and cognitive activation conditions on a sample of 58 children with ADHD (27 multiplex families), ages 6-18. EEG power in three frequency bands: theta (4-7 Hz), alpha (8-12 Hz) and beta (12-20 Hz) was tested for sibling correlation, familial co-segregation and association with behavioral task performance on a sustained attention task. Sibling correlation for EEG measures was moderate during baseline conditions and significantly higher for the cognitive activation condition. Familial clustering of frontal and parietal alpha power was evident, but only during the cognitive activation condition. Theta and alpha power correlated significantly with CPT response variability and omission errors, respectively. Cognitive task performance did not exhibit familial clustering in our sample. EEG measures (i.e., alpha power) recorded during cognitive activation is a strongly familial trait in ADHD and may be a putative endophenotype for ADHD. (copyright) 2007 Wiley-Liss, Inc

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:100-06.

Family-based association analysis of a statistically derived quantitative traits for ADHD reveal an association in DRD4 with inattentive symptoms in ADHD individuals.

Lasky-Su J, Lange C, Biederman J, et al.

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The objective of this study was to determine whether single nucleotide polymorphisms (SNPs) within candidate genes for ADHD are associated with quantitative phenotypes generated from inattentive and hyperactive-impulsive symptoms. One hundred forty-three SNPs were genotyped in and around five ADHD candidate genes. A highly heritable quantitative phenotype was generated at each SNP by weighting inattentive and hyperactive-impulsive symptoms. Once these phenotypes were generated, a screening procedure was used to select and test the five SNP/phenotype combinations with the greatest power to detect an association for each candidate gene. Adjacent SNPs in the promoter region of DRD4, hCV26775267 and hCV26775266, were associated with the quantitative phenotypes generated from the ADHD symptoms (corrected P-values = 0.012 for both SNPs). The correlations between the ADHD symptoms and quantitative phenotype revealed that inattentive symptoms had a strong influence on the generated phenotype. Subsequent family-based association test-principal components (FBAT-PC) analyses using inattentive symptoms only also had significant associations. SNPs in the promoter region of DRD4 are associated with the phenotypes generated from ADHD symptoms. The strong correlation of the inattentive symptoms with these quantitative phenotypes and the subsequent FBAT-PC analyses suggest this region is primarily associated with inattentive symptoms. This analysis adds to previous findings by suggesting that variants at these loci may be specifically associated with inattentive symptoms. (copyright) 2007 Wiley-Liss, Inc

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Differential dopamine receptor D4 allele association with ADHD dependent of proband season of birth.

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Season of birth (SOB) has been associated with attention deficit hyperactivity disorder (ADHD) in two existing studies. One further study reported an interaction between SOB and genotypes of the dopamine D4 receptor (DRD4) gene. It is important that these findings are further investigated to confirm or refute the findings. In this study, we investigated the SOB association with ADHD in four independent samples collected for molecular genetic studies of ADHD and found a small but significant increase in summer births compared to a large population control dataset. We also observed a significant association with the 7-repeat allele of the DRD4 gene variable number tandem repeat polymorphism in exon three with probands born in the winter season, with no significant differential transmission of this allele between summer and winter seasons. Preferential transmission of the 2-repeat allele to ADHD probands occurred in those who were born during the summer season, but did not surpass significance for association, even though the difference in transmission

between the two seasons was nominally significant. However, following adjustment for multiple testing of alleles none of the SOB effects remained significant. We conclude that the DRD4 7-repeat allele is associated with ADHD but there is no association or interaction with SOB for increased risk for ADHD. Our findings suggest that we can refute a possible effect of SOB for ADHD. (copyright) 2007 Wiley-Liss, Inc

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:49-53.

Testing for gene x environment interaction effects in attention deficit hyperactivity disorder and associated antisocial behavior.

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Gene x environment (G x E) interactions are increasingly thought to have substantial influence on the aetiology and clinical manifestations of complex disorders. In ADHD, although main effects of specific genetic variants and pre-or peri-natal variables have been reported and replicated using pooled analyses, few studies have looked at possible interactions. In a clinical sample of 266 children with ADHD, we tested for interaction between gene variants (in DRD4, DAT1, DRD5, and 5HTT) found to be associated with ADHD in pooled analyses and maternal smoking, alcohol use during pregnancy and birth weight. First, G x E effects on a diagnosis of ADHD were tested using conditional logistic regression analyses. Second, possible modifying effects of G x E on symptoms of associated conduct disorder and oppositional defiant disorder (ODD) were investigated using linear regression analysis. The sample size associated with each of the analyses differed as not each variant had been genotyped for each individual. No effects of G x E on ADHD diagnosis were observed. The results suggest that lower birth weight and maternal smoking during pregnancy may interact with DRD5 and DAT1 (birth weight only) in influencing associated antisocial behavior symptoms (ODD and conduct disorder). These preliminary findings showed no evidence of interaction between previously implicated variants in ADHD and specific environmental risk factors, on diagnosis of the disorder. There may be evidence of G x E on associated antisocial behavior in ADHD, but further investigation is needed. (copyright) 2007 Wiley-Liss, Inc

Biol Psychiatry. 2008;63:325-31.

Low Blood Lead Levels Associated with Clinically Diagnosed Attention-Deficit/Hyperactivity Disorder and Mediated by Weak Cognitive Control.

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Background: Attention-deficit/hyperactivity disorder (ADHD) and low-level lead exposure are high-prevalence conditions among children, and studies of large populations have suggested that these conditions are related. We examine this relationship in children from a community sample exposed to average background levels of lead who have a diagnosis of ADHD that is established by clinical criteria. Methods: One hundred fifty children ages 8-17 years participated (mean age = 14 years; 53 control subjects, 47 ADHD Predominantly Inattentive type, 50 ADHD-Combined type). Diagnosis was formally established with a semi-structured clinical interview and parent and teacher ratings. Children completed intelligence quotient (IQ) measures and the stop task (a neuropsychological measure). Lead was assayed from whole blood with inductively coupled plasma mass spectrometry. Results: Blood lead levels in this sample closely matched US population exposure averages, with a maximum level of 3.4 (μ)g/dL. Blood lead levels were statistically significantly higher in ADHD-combined type than in non-ADHD control ($p < .05$) children. Blood lead was associated with symptoms of hyperactivity-impulsivity but not inattention-disorganization, after control of covariates. Blood lead levels were linked with a lower IQ ($p < .05$), but IQ did not account for effects on hyperactivity. Instead, hyperactivity mediated effects of lead on IQ. Effects of blood lead on hyperactivity-impulsivity were mediated by poor performance on the stop task. This mediation effect was independent of effects of lead on IQ. Conclusions: Low-level lead exposure might be an important contributor to ADHD. Its effects seem to be mediated by less effective cognitive control, consistent with a route of influence via striatal-frontal neural circuits. (copyright) 2008 Society of Biological Psychiatry

Aten Prim. 2008;40:29-33.

Evaluation of the validity of AD/HD diagnoses in referrals from paediatrics to the child psychiatry clinic.

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Objectives. To evaluate the validity of clinical diagnoses of attention deficit/hyperactivity disorder (AD/HD). **Design.** Descriptive, cross-sectional study. **Setting.** Mental Health Care area 6, Murcia, Spain. **Participants.** The sample consists of those patients referred consecutively to the child psychiatry clinic between July and September 2005. **Main measurements.** The presumptive diagnosis of AD/HD in the paediatric department referral was compared with the definitive one in psychiatry (gold standard). Sensitivity, specificity and predictive values and probability quotients were calculated. **Results.** Seventy-five patients were included; 12% were lost. Sixty-six cases were studied, 15 with AD/HD and 51 with other diagnoses (23 with differential diagnoses from AD/HD). Sensitivity was 86.7% (95% CI, 69.5-100); specificity, 54.9% (95% CI, 41.3-68.6); positive predictive value, 36.1% (95% CI, 20.4-51.8); and negative predictive value, 93.3% (95% CI, 84.4-100). **Conclusions.** Validity of diagnosis was moderate with high sensitivity, low specificity and a low positive predictive value, the latter calculated for low AD/HD prevalence. The clinical picture of AD/HD tends to be oversized. The presumptive diagnosis in primary care behaved as a screening test. The clinical diagnosis in primary care should be complemented with other diagnostic tests that provide greater specificity

J Clin Rehab Tissue Eng Res. 2007;11:10500-02.

Adaptive behavior evaluation for 35 pupils with attention-deficit hyperactivity disorder.

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Aim: To analyze the behavioral characteristics and weak points of children with attention-deficit hyperactivity disorder (ADHD) by testing their adaptive behaviors, so as to provide evidence for the behavior modification of ADHD children by family and school. **Methods:** Forty pupils, diagnosed as ADHD in the Second Affiliated Hospital of Dalian Medical University and Dalian Children Hospital were selected between September 2004 and March 2005. Their suspected degree was examined by Conners Rating Scale for ADHD, and their behaviors were assessed by Adaptive Behavior Scale for Children complicated by Yao Shuqiao and Gong Yaonian, which was composed of 8 subscales such as sensory motor, self care, language development, private tendency, social responsibility, directional space-time, labor skill and economic behavior. The eight subscales were classified into independent factor, cognitive factor and social/self control factor. After factor integration, the values were increased, and convenient for total scores. The scale was scored by 8 grades and represented by social accommodate quotient: > 130 as very strong, 129-115 as strong, 114-85 as normal, 84-70 as edge, 69-55 as mild deficit, 54-40 as moderate deficit, 39-25 as severe deficit and < 25 as very severe deficit. The results were compared with normal norm for children and the percentage was counted. The data were analyzed by the Adaptive Behavior Scale for Children (urban version). **Results:** Forty questionnaires were sent out and 35 were retrieved with the efficacy of 87%. Thirty-five cases were finally involved in the result analysis including 29 males and 6 females (4.84:2). 1 In Conners Rating Scale for ADHD, there were 18, 9, 5, 2, and 1 person at the five stages scored 15-18, 19-21, 22-24, 25-27 and 28-30, respectively. The subjects with mild suspicious phrase were predominant with 15 points or more. 2 The scores in sensory motor and self care ability and the norm percentage were gradually decreased from grade 1 to 6 (6.6%-2.0%, 36.2%-3.0%); the scores of the language development subscale and the norm percentage at grade 3 were different from those at grade 1 and 2 (8.0%, 17.8%, 12.6%), and improved significantly at grade 6 (25.5%); there were no obvious rules in the scores in private tendency and the norm percentage from grade 1 to grade 6, but the scores were increased at grade 2 and 6; there were no significant differences in the scores of social responsibility subscale and norm percentage among pupils of each grade (1.1%-6.5%); the scores in directional space-time, labor skill and economic behavior and norm percentage were increased with age. 3 Among the adaptive standards, 10 persons were at normal level, 13 edge level (28.3%), 7 mild deficit (8.7%), and 2 serious deficit (6%). There were significant individual differences in adaptive behavior development; the scores in social responsibility were lower. In factor analysis, the scores in social/self control factor were the lowest; the adaptive level of pupils at grade 3 and 4 were the lowest. **Conclusion:** The educational diagnosis is accordance with medical diagnosis for ADHD children. There are problems in the social adaptability in most ADHD pupils, and the psychological fluctuation is evident in pupils at grade 3 and 4

Neuropsychiatr Dis Treat. 2007;3:949-54.

Effects of psycho-educational training and stimulant medication on visual perceptual skills in children with attention deficit hyperactivity disorder.

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Attention deficit hyperactivity disorder (ADHD) is treated with stimulants and psycho-educational remedial programs despite limited literature support for the latter. This study aimed to examine changes in a "Test of Visual Perceptual Skills" (TVPS) that has not been previously reported in children with ADHD enrolled in such a program. Methods: Sixteen children, 7-11 years old, with ADHD were involved in occupational therapy and special education geared towards attention training. Six months later methylphenidate 1 mg/kg/day was prescribed. It was not taken by eight children because of family choice. The TVPS was given twice, upon diagnosis, and 8 months post-intervention. The groups were compared by a repeated measures analysis of variance (ANOVA) with medication as a between groups factor and test-retest scores as within factor. Results: All children demonstrated increases in total scores in the second measurement. Medicated children scored higher but ANOVA showed a nonsignificant F for the two groups, medicated and unmedicated ($F=0.0031$, $p=0.9563$), indicating a nondifferential effect of the two levels of treatment. It revealed a significant F for the pre- and post-treatment total TVPS scores ($F=30.91$, $p<0.0001$) indicating a significant difference between pre- and post-treatment tests. The interaction between pre-post treatment and level of treatment (medicated-unmedicated) was nonsignificant ($F=2.20$, $p=0.1604$). Conclusion: TVPS scores improved in all children following intervention. Medicated children did better, but differences were nonsignificant. (copyright) 2007 Papavasiliou et al, Publisher and Licensee Dove Medical Press Ltd

J Pediatr Psychol. 2007;32:1203-13.

Attention deficit hyperactivity disorder symptoms predict nicotine dependence and progression to regular smoking from adolescence to young adulthood.

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Objective: To examine the association between retrospectively reported attention deficit hyperactivity disorder (ADHD) symptoms and progression to smoking and the association with nicotine dependence. Methods: Study sample consisted of a nationally representative cohort of U.S. adolescents ($n = 13,494$). Logistic regression was used to examine ADHD symptoms from both the inattentive (IN) and hyperactive-impulsive (HI) domains and smoking trajectories. Linear regression was used to examine nicotine dependence. Results: HI symptoms were associated with progression from nonsmoking to regular smoking (OR = 1.14, 95% CI = 1.07-1.21), and with progression from experimentation to regular smoking (OR = 1.16, 95% CI = 1.08-1.26). IN and HI symptoms were associated with nicotine dependence among current smokers (IN: (beta) = 0.17, SE = 0.03, $p < 0.0001$; HI: (beta) = 0.10, SE = 0.04., $p < .001$). Conclusions: These results have important implications for the development of prevention and treatment modalities. (copyright) The Author 2007. Published by Oxford University Press on behalf of the Society of Pediatric Psychology. All rights reserved

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Estimation of the prevalence of attention deficit/hyperactivity disorder among the standard population on the island of Majorca.

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Aim. To determine the rate of prevalence of attention-deficit/hyperactivity disorder (ADHD) in children of school age (6-11 years) in the Island of Mallorca. Subjects and methods. The epidemiological study was conducted using a community sample extracted by means of multi-stage stratified sampling according to areas (rural, city and touristy) and schooling (public, private and concerted) and consisted in 1,509 children of both sexes. The ADHD Rating Scales-IV (ADHD RS-IV) for home and school setting were used to collect data. The optimal approach to do a diagnostic evaluation, according with the literature, was using a cut-off point of 90 centil. Results. The estimated prevalence of ADHD was 4.57% (confidence interval at 99%: 3.0-5.8%) and we also obtained 1.26% for the hyperactive subtype, 1.06% for the disattentive subtype, and 2.25% for the combined subtype. Contrary to what was expected, prevalence was higher for females but no statistically significant. There were no statistically significant differences between levels, schools or areas.

Conclusions. The estimates for prevalence found in this study are consistent with those reported in the literature (between 3-5%). Using the ADHD RS-IV which has different cut-off point regarding age, sex and setting and the fact that it was a poblational based study could explain the higher prevalence in the females. We propose a normalization of the scales in our area in other to confirm our findings. (copyright) 2007, Revista de Neurologia

J Child Neurol. 2007;22:1342-47.

The prevalence of attention-deficit/hyperactivity disorder among persons with albinism.

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Attention-deficit/hyperactivity disorder (ADHD) is a common diagnosis in children and adults. Human albinism is an uncommon genetic condition associated with visual impairment that may affect behavior. To determine if there is a relationship between albinism and ADHD, the prevalence of ADHD was examined among 78 children (age range, 4-18 years) and among 44 adults (age range, 19-79 years) with ocular or oculocutaneous albinism. ADHD was diagnosed in the pediatric population using a combination of Diagnostic and Statistical Manual of Mental Disorders (Fourth Edition) criteria, Conners' Parent Rating Scale, and physician observation. Adults were diagnosed using the Utah criteria for ADHD as confirmed by physician history and interview. Seventeen children (22.7% [17 of 75]) (3 children with existing diagnoses of pervasive developmental disorder were identified but were not included in the data analysis) and 3 adults (6.8%) met the criteria for ADHD. The combined hyperactivity and impulsivity subtype of ADHD was most common, accounting for 50% of the diagnoses. Binocular best-corrected visual acuity and genetic type of albinism were not found to correlate with a diagnosis of ADHD. The prevalence of ADHD among children and adults with albinism is more frequent than that reported among the general population and is not related to binocular best-corrected visual acuity. (copyright) 2007 Sage Publications

Arq Neuro-Psiquiatr. 2007;65:1078-83.

Prevalence of attention deficit hyperactivity disorder and its comorbidities in a sample of school-aged children.

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Attention deficit hyperactivity disorder (ADHD) is a frequent condition in school-age children and commonly presents in comorbidity with other psychiatric diseases. In Brazil, there are few studies concerning non-clinical samples. Purpose: The present study aims to calculate the prevalence of this disorder and its comorbidities in a sample of school-age children. Method: Cross-sectional analytic study was conducted on a non-clinical sample of children and adolescents registered in 2003 in the elementary school of the Federal University of Rio de Janeiro. A screening questionnaire was used and parents of those possible affected children were invited for a clinical structured interview. Results: The prevalence of ADHD was 8.6%. Comorbidities were present in 58% of the cases and oppositional-defiant disorder was the most common, found in 38.5%. Conclusions: The prevalence of the ADHD and its comorbidities in this sample is similar to that observed in the literature

Eur Child Adolesc Psychiatry. 2007;16:505-09.

Predictors of diagnostic delay in a clinical sample of French children with attention-deficit/hyperactivity disorder.

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Background: Early recognition of attention-deficit/hyperactivity disorder (ADHD) may improve the educational and psychosocial outcome of most affected children. To date, factors associated with diagnostic delay of ADHD have not specifically been addressed. Aims of this study were to evaluate the mean diagnostic delay (time between first consultation and definite diagnosis) in a clinical sample of French children with ADHD referred to an outpatient university clinic, and to determine associated factors. Method: A total of 129 consecutively referred ADHD patients aged 6-16 years. A detailed history of the children was obtained from their parents. The Kiddie-SADS-PL, the ADHD-Rating Scale, and the Clinical Global Impression Scale were used for clinical assessment. Results: Mean diagnostic delay was 32.89 months. A previous suspicion of

ADHD by any health care professional, therapist or teacher was significantly associated with a reduced diagnostic delay. Co-morbidity with anxiety/depressive disorders and previous contact with a mental health professional were associated with a significant delay in diagnosis. Conclusion: Delay in diagnosis of ADHD in France is among the longest reported. Children with co-morbid anxiety or depressive disorders are particularly at risk of having a significant delay in the diagnosis. Health professionals, therapists and teachers may play a relevant role to accelerate the diagnostic procedure. (copyright) 2007 Steinkopff Verlag

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Impulsivity in overweight children.

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Objective: This study investigates whether or not obese children have a stronger tendency to act on impulse than normal weight children, taking into account the multidimensionality and complexity of the impulsivity construct. Method: A performance based test (Matching Familiar Figure Test, MFFT), a child interview and questionnaire, and parental reports were obtained from 56 overweight children and 53 normal weight children aged 10-18 years. Results: Overweight children responded in a more impulsive way on the MFFT ($P < .01$). On the child questionnaire, overweight boys reported more problems with focussing attention ($P < .05$) and both overweight boys and girls reported being worse at shifting their attention compared with normal weight children ($P < .05$). In particular, overweight boys showed more impulsivity ($P < .05$), hyperactivity ($P < .01$), and inattention symptoms ($P < .001$) as measured via the clinical interview. Parents of overweight children reported an equal amount of impulsivity and hyperactivity symptoms as parents of normal weight children, but scored their children lower on the Conscientiousness personality dimension ($P < .01$). Discussion: A subgroup of overweight children appears to have a stronger tendency to act on impulse than normal weight children, and demonstrated an impulsivity prone personality. Hence, overweight children should be screened for impulse control deficiencies. More research is needed to clear out the robustness of gender differences, the existence of a specific personality profile and possibly common underlying mechanisms of childhood obesity and Attention Deficit Hyperactivity Disorder. (copyright) 2007 Steinkopff Verlag

Dev Med Child Neurol. 2007;49:920-25.

Developmental coordination disorder in children with attention-deficit-hyperactivity disorder and physical therapy intervention.

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Although physical therapy (PT) is effective in improving motor function in children with developmental coordination disorder (DCD), insufficient data are available on the impact of this intervention in children with combined attention-deficit-hyperactivity disorder (ADHD) and DCD. This prospective study aimed to establish the prevalence of DCD among a cohort of patients with ADHD, characterize the motor impairment, identify additional comorbidities, and determine the role of PT intervention on these patients. DCD was detected in 55.2% of 96 consecutive children with ADHD (81 males, 15 females), mostly among patients with the inattentive type (64.3% compared with 11% of those with the hyperactive/impulsive type, $p < 0.05$). Mean age was 8 years 4 months (SD 2y). Individuals with both ADHD and DCD more often had specific learning disabilities ($p = 0.05$) and expressive language deficits ($p = 0.03$) than children with ADHD only. Twenty-eight patients with ADHD and DCD randomly received either intensive group PT (group A, mean age 9y 3mo, SD 2y 3mo) or no intervention (group B, mean age 9y 3mo, SD 2y 2mo). PT significantly improved motor performance (assessed by the Movement Assessment Battery for Children; $p = 0.001$). In conclusion, DCD is common in children with ADHD, particularly of the inattentive type. Patients with both ADHD and DCD are more likely to exhibit specific learning disabilities and phonological (pronunciation) deficits. Intensive PT intervention has a marked impact on the motor performance of these children. (copyright) 2007 Blackwell Publishing Ltd

Rev Neurol. 2007;44:S31-S35.

The psychopharmacology of the comorbid disorders associated with attention deficit hyperactivity disorder.

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Introduction. The pharmacological treatment most commonly used in attention deficit hyperactivity disorder (ADHD) has traditionally consisted in the administration of psychostimulants. The particular association with comorbid disorders makes it essential to utilise different therapeutic approaches and this accounts for the growing therapeutic arsenal currently available for use in this condition. Development. It is important to be familiar with the different comorbidities because they are especially frequent and also because of their effect on the prognosis. Thus, it is necessary to reach a good diagnosis as early as possible in order to implement a therapy that allows the problem to be curbed. To do so, we need to know about the different pharmaceuticals that have to some extent or other proved to be effective. Conclusions. This paper aims to offer a global view of the problem by analysing the characteristics of the comorbid disorders associated with ADHD and the pharmacological tools that enable us to modify their deleterious effects. (copyright) 2007, Revista de Neurologia

Rev Neurol. 2007;44:S27-S30.

Clinical variability and characteristics of attention deficit hyperactivity disorder in girls.

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Introduction. Attention deficit hyperactivity disorder (ADHD) is a neurobiological condition essentially characterised by inattention, hyperactivity and impulsiveness, and has a prevalence of around 5%. Because it is a biological disorder, both boys and girls with ADHD display these same symptoms, but more boys are diagnosed with ADHD (in a ratio of 3 to 1). Aim. To examine the differences between the two sexes, their prevalence and possible female subtypes in ADHD. Patients and methods. We conducted a retrospective study of 172 patients of both sexes who were attended as hospital neuropaediatric outpatients in the year 2004 according to Diagnostic and statistical manual of mental disorders (DSM-IV-TR) criteria. Their ages ranged between 4 and 14 years and they were divided into three groups: under 6, between 6 and 10, and from 11 to 14 years old. The girls were subdivided into four subtypes, in order of greater to lesser prevalence: shy, hypersociable, hyperactive and changeable. Results. Both sexes showed the same response to methylphenidate. Only the group of boys presented other comorbidities such as negativism and conduct disorders; approximately 25% of them required treatment with atypical neuroleptic drugs. Conclusions. a) Girls have certain specific clinical manifestations within the three common symptoms; b) methylphenidate is equally effective in both sexes; c) only boys display other disorders such as negativism and conduct disorders; and d) the brains of males and females are quite similar, but symptoms are expressed differently depending on environments and levels. (copyright) 2007, Revista de Neurologia

Rev Neurol. 2007;44:S23-S25.

Discipline styles in families with children with attention deficit hyperactivity disorder: Their influence on the course of the disorder.

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Introduction. Attention deficit hyperactivity disorder (ADHD) is caused by hereditary factors but it can only really be understood using a model that takes into account the interaction between genes and the environment. Discipline styles stand out among the factors offered by the familial environment that can influence the course of ADHD. Aims. To compare the discipline styles employed by mothers of children with and without ADHD and to analyse how the subtype of ADHD and the presence of oppositional defiant disorder influence the discipline styles utilised by mothers of children with ADHD. Subjects and methods. We divided 167 mothers into two groups, one consisting of those who had a child with ADHD (n = 114) and a control group (n = 53), and they were asked to answer a semi-structured interview and a questionnaire about discipline styles. Results. The statistical analyses showed that mothers of children with ADHD used more severe discipline strategies, especially if the ADHD was associated with oppositional defiant disorder.

Conclusions. Interventions must include family guidance focused on the dimensions of self-control and affective expression. (copyright) 2007, Revista de Neurologia

Emot Behav Difficulties. 2007;12:319-32.

The identification of children with behavioural manifestations of inattention, hyperactivity and impulsivity, in mainstream school: The development of the Scope Classroom Observation Checklist.

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The objective of this paper is to report the development and use of an observation checklist to identify typically developing children with behavioural manifestations associated with inattention, hyperactivity and impulsivity. This measure is termed the Scope Classroom Observation Checklist (SCOC). The SCOC was developed, assessed for reliability using an independent observer and teacher ratings, and administered to a sample of 157 mainstream schoolchildren. The SCOC revealed a normal distribution of scores on the checklist, and the top and bottom quartiles of this distribution were found, as would be expected, to differ significantly on SCOC score. The SCOC had good inter-observer reliability and a high rate of concordance with teacher ratings of attentional difficulties. The SCOC has emerged as a reliable measure that could prove to be a useful tool in a battery of screening measures to identify mainstream schoolchildren with difficulties characterised by inattention and hyperactivity-impulsivity

Pharmacoepidemiol Drug Saf. 2007;16:1268-72.

Methylphenidate use in children and risk of cancer at 18 sites: Results of surveillance analyses.

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Purpose: A recent report linked methylphenidate (MPH) use in children to cytologic abnormalities in plasma lymphocytes, a possible cancer biomarker. The purpose of this study was to investigate the association of MPH use and childhood cancer risk. Methods: Using automated pharmacy databases and the SEER-affiliated cancer registry of the Kaiser Permanente Medical Care Program (KPMCP), we compared cancer rates at 18 sites among 35 400 MPH users who received it before age 20 to rates among KPMCP membership (age, sex, and calendar year standardized). Medical records of MPH exposed cancer cases were reviewed to identify the presence of established risk factors. Results: There were 23 cancers among MPH users, versus 20.4 expected (standardized morbidity ratio, SMR = 1.13, 95% confidence interval (0.72, 1.70)). Given the small number of cancers, site-specific SMR estimates were imprecise. Only one SMR was statistically significant at the $p < 0.05$ level, which given the number of comparisons is consistent with the absence of a true association at any site. MPH use was associated with increased risk of lymphocytic leukemia (SMR = 2.64 (1.14, 5.20)), based on eight observed cases). The medical records of these exposed cases did not reveal any lymphocytic leukemia risk factors (prior cancer, radiotherapy or chemotherapy, or Down syndrome). Conclusions: Our results are consistent with no moderate or strong association between MPH use and cancer risk in children, although our ability to examine dose and duration of use or risk at specific sites was limited by small numbers. Further study of MPH use and lymphocytic leukemia risk is needed to determine whether results are due to chance alone. Copyright (copyright) 2007 John Wiley & Sons, Ltd

Rev Neurol. 2007;44:589-95.

Attention deficit hyperactivity disorder: Intellectual profile and the freedom from distraction factor.

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Introduction. Attention deficit hyperactivity disorder (ADHD) usually presents a neuropsychological profile in which the freedom from distraction factor (FDF) is affected to a greater extent than the verbal comprehension factor (VCF) and the perceptual organisation factor (POF). Aim. To determine the intellectual profile of clinical cases with ADHD through a specific analysis of the FDF, in which we evaluated the differences compared with the VCF and the POF, between types of ADHD and with WISC-R criteria, as well as the variables that affect the probability of $FDF < VCF$ and POF . Patients and methods. Our study involved a clinical sample of 167 cases of ADHD between 6 and 16 years of age. The cases were defined according to DSM-IV criteria and the evaluation was performed using WISC-R, the Child Symptom Inventory and the social and occupational activity assessment scale. Both descriptive and exploratory statistics were used. Means were

compared using ANOVA and/or t tests. Alpha was accepted if it was equal to or below 0.05 and a logistic regression method was used (alpha model parameters below or equal to 0.05). In each factor a 95% confidence interval and odds ratio were determined. Results. The criterion $FDF < VCF$ and FOP accounted for 71.3% of the cases with ADHD and $FDF < (VCF + POF) / 2$ represented 81.4% (sensitivity: 81.4%). The FDF is significantly lower than both the mean that corresponds to factorial criteria derived from the WISC-R and the VCF and POF in the cases that were analysed. The mean FDF scores were significantly higher in ADHD-H (a type in which hyperactive-impulsivity predominates) than in ADHD-C (combined type) and ADHD-I (inattentive type). Comorbidity, social or school activity and intellectual quotient do not have a significant influence on the probability that $FDF < VCF$ and POF . Conclusions. The FDF is a neuropsychological dimension that is useful in evaluating ADHD. (copyright) 2007, Revista de Neurologia

Rev Neurol. 2007;44:75-80.

Attention deficit and understanding of non-literal meanings: The interpretation of indirect speech acts and idioms.

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Aim. To report on the oral comprehension of the non-literal meanings of indirect speech acts and idioms in everyday speech by children with attention deficit hyperactivity disorder (ADHD). **Subjects and methods.** The subjects in this study consisted of a sample of 29 Chilean schoolchildren aged between 6 and 13 with ADHD and a control group of children without ADHD sharing similar socio-demographic characteristics. A quantitative method was utilised: comprehension was measured individually by means of an interactive instrument. The children listened to a dialogue taken from a cartoon series that included indirect speech acts and idioms and they had to choose one of the three options they were given: literal, non-literal or distracter. **Results.** The children without ADHD identified the non-literal meaning more often, especially in idioms. Likewise, it should be pointed out that whereas the children without ADHD increased their scores as their ages went up, those with ADHD remained at the same point. **Conclusions.** ADHD not only interferes in the inferential comprehension of non-literal meanings but also inhibits the development of this skill in subjects affected by it. (copyright) 2007, Revista de Neurologia

Aust New Zealand J Psychiatry. 2007;41:998-1004.

Health-related quality of life in methylphenidate-treated children with attention-deficit-hyperactivity disorder: Results from a Taiwanese sample.

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Objective: Attention-deficit-hyperactivity disorder (ADHD) is the most common neuropsychiatric disorder of childhood. The purpose of the present study was to assess the health-related quality of life (HRQL) in methylphenidate-treated school-age children with ADHD as compared with healthy children in a Taiwanese population. **Methods:** Subjects were 6-15 years of age with ADHD who were currently receiving methylphenidate treatment (total n = 119). Subjects were compared to 129 healthy children recruited from the community. Child Health Questionnaire Parent Form-50 (CHQ-PF-50), a functional health status measure of HRQL was arranged for parents to complete. Disease-related variables were analysed to determine their relationship and predictive power with HRQL of children. **Results:** The HRQL of methylphenidate-treated children with ADHD was rated worse than that of community children in all the psychosocial subscales and the Psychosocial Summary Score of CHQ-PF-50. In addition, the problems of ADHD children interfered with family activities and family cohesion significantly. Moreover, improvement of ADHD core symptoms after medication treatment predicted higher psychosocial functioning. This effect was independent of children's current age, age receiving diagnosis, age starting and duration of medication treatment but was not independent of ADHD comorbidity. **Conclusion:** This study may serve as one of the cross-cultural validations of ADHD as a common concern for children and families worldwide. After methylphenidate treatment, parents of Taiwanese children with ADHD still reported them to have poorer health outcomes than control children across almost all domains of HRQL. Improvement of HRQL should be integrated in the overall treatment plan for children with ADHD

Pediatr Emerg Care. 2007;23:909-11.

A 6-year-old girl with somnolence: Patching together the clues.

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J Psychiatry Neurosci. 2007;32:447.

Sitting on the edge: When to treat symptoms of inattention without the full DSM-IV criteria of ADHD.

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Tohoku J Exp Med. 2007;213:269-76.

Association between low serum ferritin and restless legs syndrome in patients with attention deficit hyperactivity disorder.

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Attention deficit hyperactivity disorder (ADHD) is a neurobehavioral disorder characterized by pervasive inattention and/or hyperactivity-impulsivity. It has been suggested that ADHD symptoms are associated with restless legs syndrome (RLS), which is a neurological condition that is defined by an irresistible urge to move the legs. Increasing evidence suggests iron deficiency may underlie common pathophysiological mechanisms in subjects with ADHD and with RLS. To further define the relationship between iron deficiency and RLS in children and adolescents with ADHD, we evaluated 87 ADHD subjects: 79 boys and 8 girls with age 9.3 (plus or minus) 2.5 years (6-16 years). Various psychopathologies and the severity of the ADHD symptoms and serum ferritin levels were assessed. Diagnosis of RLS was made according to the International RLS Group criteria. The patients were evaluated for the iron deficiency (ferritin < 12 ng/ml). RLS was found in 29 (33.3%) of the 87 ADHD subjects. Parent-and teacher-rated behavioral and emotional problems and the severity of ADHD symptoms were not significantly different between ADHD subjects with RLS and those without RLS (n = 58). The rate of iron deficiency was significantly higher in ADHD subjects with RLS (n = 6, 20.7%) when compared with ADHD subjects without RLS (n = 1, 1.7%, p = 0.005). Our results showed that depleted iron stores might increase the risk of having RLS in ADHD subjects. Iron deficiency, which is associated with both ADHD and RLS, seems to be an important modifying factor in the relationship between these two conditions. (copyright) 2007 Tohoku University Medical Press

Proc Natl Acad Sci U S A. 2007;104:19649-54.

Attention-deficit/hyperactivity disorder is characterized by a delay in cortical maturation.

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There is controversy over the nature of the disturbance in brain development that underpins attention-deficit/hyperactivity disorder (ADHD). In particular, it is unclear whether the disorder results from a delay in brain maturation or whether it represents a complete deviation from the template of typical development. Using computational neuroanatomic techniques, we estimated cortical thickness at >40,000 cerebral points from 824 magnetic resonance scans acquired prospectively on 223 children with ADHD and 223 typically developing controls. With this sample size, we could define the growth trajectory of each cortical point, delineating a phase of childhood increase followed by adolescent decrease in cortical thickness (a quadratic growth model). From these trajectories, the age of attaining peak cortical thickness was derived and used as an index of cortical maturation. We found maturation to progress in a similar manner regionally in both children with and without ADHD, with primary sensory areas attaining peak cortical thickness before polymodal, high-order association areas. However, there was a marked delay in ADHD in attaining peak thickness throughout most of the cerebrum: the median age by which 50% of the cortical points attained peak thickness for this group was 10.5 years (SE 0.01), which was significantly later than the median age of 7.5 years (SE 0.02) for typically developing controls (log rank test ($\chi^2(1) = 5,609$, $P < 1.0 \times 10^{-20}$). The delay was most prominent in prefrontal regions important for control of cognitive processes including attention and

motor planning. Neuroanatomic documentation of a delay in regional cortical maturation in ADHD has not been previously reported. (copyright) 2007 by The National Academy of Sciences of the USA

Rev Neurol. 2007;45:393-99.

ADHD Rating Scale-IV in a sample of Spanish schoolchildren: Normative data and internal consistency for teachers and parents.

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Introduction. The ADHD Rating Scale-IV (ADHD RS-IV) is one of the most use scales for attention deficit hyperactivity disorder (ADHD), because has cut-off point regarding age, gender and setting, but the normalization data is based on American school samples. Aim. Evaluation of cut-off point of ADHD-RS-IV for parents and teachers in a Spanish sample. Subjects and methods. The study used the score of ADHD-RS-IV from a prevalence study of ADHD in school children of 6-12 years. Using an intrasubject design between the three evaluators (parents and teachers) and the results of each subscale (IN, H/I, and TOT) according to gender and age factors. Then, we analyzed the reliability and internal consistency for each subscale and evaluator. Results. There are no significant differences between the father and the mother; but there are between teachers, and father and/or mother scores. In relation to gender factor, boys' score is higher on inattention and hyperactivity-impulsivity than girls'. Our results show a reversal tendency in comparison with the American samples, in our case parents' scores were significantly higher than teachers'. Conclusion. The use and normalization of the ADHD RS-IV will need to account not only for age, gender and setting but also for socio-cultural aspects. (copyright) 2007, Revista de Neurologia

Rev Neurol. 2007;44:146-49.

Motor assessment in school-aged children with indicators of the attention deficit/hyperactivity disorder.

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Introduction. Attention deficit/hyperactivity disorder (ADHD) is one of the most frequent disorders in childhood. In the literature there are claims that ADHD is associated with important comorbidities, which include disorders affecting motor coordination. Aim. To evaluate motor development of schoolchildren with ADHD indicators. Patients and methods. The sample used in our study consisted of 31 schoolchildren (aged between 7.3 and 10.8 years) studying in the first and second years of primary education in state-run schools in Florianopolis, SC, Brazil, who had ADHD indicators in accordance with DSM-IV (Diagnostic and statistical manual of mental disorders) and attention deficit with hyperactivity disorder evaluation scale (EDAH) criteria, which had been answered by teachers and parents. Motor evaluation was evaluated using the Motor Development Scale. The Epi Info 3.2.2 software application was used for descriptive statistics. Results. Findings showed that 48.4% of the schoolchildren had a motor development that was considered to be 'low average' according to the Motor Development Scale; 35.5% were 'inferior'; 9.7% were 'very inferior'; and 6.4% were found to be 'medium average'. The mean motor development of the group as a whole was classified as being 'low average'; the greatest difficulties were temporal organisation ('very inferior'), spatial organisation ('inferior') and balance ('inferior'). Fine motor control, general motor control and body schema were classified as 'low average'. With respect to laterality, 48.4% were right-handed, 48.4% had crossed laterality and 3.2% had undefined laterality. Conclusions. These results are in line with studies that suggest the existence of alterations in the motor coordination of children with symptoms of ADHD. (copyright) 2007, Revista de Neurologia

Drug Ther Bull. 2007;45:37-40.

Update on drugs for hyperactivity in childhood.

Anon.

In 2001, we concluded that methylphenidate or dexamfetamine can be useful adjunctive therapy for children with severe hyperactivity in whom non-drug approaches alone have been inadequate. Since then, (black down triangle)atomoxetine (pronounced a-toe-moks-e-teen; Strattera - Lilly) and three modified-release

formulations of methylphenidate have been launched for attention deficit hyperactivity disorder (ADHD). Here we reconsider drugs for ADHD in childhood, focusing on the newer products

J Altern Complement Med. 2007;13:1091-97.

A comprehensive approach to treating autism and attention-deficit hyperactivity disorder: A pre-pilot study.

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Objectives: The purpose of this study was to observe the effects of a multi dimensional treatment plan involving nutrition, environmental control, chelation, and behavioral/educational/physical/speech therapy to treat children with autistic spectrum disorder and attention-deficit hyperactivity (ADHD) disorder. This study is only a preliminary study, and its small size (10 patients) precludes statistical analysis of simultaneous multiple modal treatment regimes. **Design:** This was an open-label observational study. **Settings/location/subjects:** This study examined 10 children aged 4-10 years old who had been diagnosed with both autistic spectrum disorder and ADHD by outside physicians or psychologists. These 10 children presented consecutively in an environmental medicine clinic in Buffalo, New York. The children were given comprehensive nutritional/environmental/chelation treatment for 3 to 6 months in addition to their usual behavioral, educational, speech, and physical therapies. **Outcome measures:** Study outcomes were measured by objective/subjective improvement as judged by physicians/parents/teachers. Outcomes were also measured by changes in urinary heavy metal burdens over time. **Results:** All 10 children showed significant improvement in many areas of social interaction, concentration, writing, language, and behavior. Urinary lead burden dropped significantly in all 10 children. **Conclusions:** Autistic spectrum disorders and ADHD are complicated conditions that probably require multidimensional treatment strategies. Larger studies are needed to determine optimum treatment plans involving nutrition, environmental control, medication, and behavioral/education/speech/physical therapies. (copyright) Mary Ann Liebert, Inc. 2007

Pediatrics. 2008 Jan;121:e73-e84.

A randomized, double-blind, placebo-controlled study of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder.

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OBJECTIVE: With this study we assessed the efficacy and safety of an extended-release formulation of guanfacine compared with placebo for the treatment of children and adolescents with attention-deficit/hyperactivity disorder. **METHODS:** In this multicenter, double-blind, placebo-controlled, fixed-dosage escalation study, patients aged 6 to 17 years were randomly assigned to 1 of 3 treatment groups of guanfacine extended release (2, 3, or 4 mg/day) or placebo for 8 weeks. The primary outcome measurement was the Attention-Deficit/Hyperactivity Disorder Rating Scale IV total score. Secondary measurements included Clinical Global Impression of Improvement, Parent's Global Assessment, Conners' Parent Rating Scale-Revised: Short Form, and Conners' Teacher Rating Scale-Revised: Short Form. **RESULTS:** A total of 345 patients were randomly assigned to placebo (n = 86) or guanfacine extended release 2 mg (n = 87), 3 mg (n = 86), or 4 mg (n = 86) treatment groups. Least-squares mean changes from baseline to the end point in Attention-Deficit/Hyperactivity Disorder Rating Scale IV total scores were significant in all groups of children taking guanfacine extended release: -16.18 in the 2-mg group, -16.43 in the 3-mg group, and -18.87 in the 4-mg group, compared with -8.48 in the placebo group. All groups of children taking guanfacine extended release showed significant improvement on hyperactivity/impulsivity and inattentiveness subscales of the Attention-Deficit/Hyperactivity Disorder Rating Scale IV, Clinical Global Impression of Improvement, Parent's Global Assessment, Conners' Parent Rating Scale-Revised: Short Form, and Conners' Teacher Rating Scale-Revised: Short Form assessments compared with placebo. The most commonly reported treatment-emergent adverse events were headache, somnolence, fatigue, upper abdominal pain, and sedation. Small to modest changes in blood pressure, pulse rate, and electrocardiogram parameters were observed but were not clinically meaningful. **CONCLUSIONS:** Guanfacine extended release met the primary and secondary efficacy end points. It was well tolerated and effective compared with placebo

Pediatrics. 2008 Jan;121:e65-e72.

Managing attention-deficit/hyperactivity disorder in primary care: a systematic analysis of roles and challenges.

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OBJECTIVE: This study was designed to investigate the perceptions of primary care providers about their roles and the challenges of managing attention-deficit/hyperactivity disorder and to evaluate differences between providers who serve families primarily from urban versus suburban settings. **METHODS:** The ADHD Questionnaire was developed to assess primary care provider views about the extent to which clinical activities that are involved in the management of attention-deficit/hyperactivity disorder are appropriate and feasible in primary care. Participants were asked to rate each of 24 items of the questionnaire twice: first to indicate the appropriateness of the activity given sufficient time and resources and second to indicate feasibility in their actual practice. Informants used a 4-point scale to rate each item for appropriateness and feasibility. **RESULTS:** An exploratory factor analysis of primary care provider ratings of the appropriateness of clinical activities for managing attention-deficit/hyperactivity disorder identified 4 factors of clinical practice: factor 1, assessing attention-deficit/hyperactivity disorder; factor 2, providing mental health care; factor 3, recommending and monitoring approved medications; and factor 4, recommending nonapproved medications. On a 4-point scale (1 = not appropriate to 4 = very appropriate), mean ratings for items on factor 1, factor 2, and factor 3 were high, indicating that the corresponding domains of practice were viewed as highly appropriate. Feasibility challenges were identified on all factors, but particularly factors 1 and 2. A significant interaction effect, indicating differences between appropriateness and feasibility as a function of setting (urban versus suburban), was identified on factor 1. The challenges of assessing attention-deficit/hyperactivity disorder were greater for urban than for suburban primary care providers. **CONCLUSIONS:** Primary care providers believe that it is highly appropriate for them to have a role in the management of attention-deficit/hyperactivity disorder. Feasibility issues were particularly salient related to assessing attention-deficit/hyperactivity disorder and providing mental health care. The findings highlight the need not only for additional training of primary care providers but also for practice-based resources to assist with school communication and collaboration with mental health agencies, especially in urban practices

Ann Pharmacother. 2008 Jan;42:24-31.

Utilization of pharmacologic treatment in youths with attention deficit/hyperactivity disorder in Medicaid database.

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BACKGROUND: Little is known about longitudinal changes in drug utilization in attention-deficit/hyperactivity disorder (ADHD). **OBJECTIVE:** To describe longitudinal trends in ADHD drug utilization and explore demographic differences among youths eligible for a large Southern state Medicaid program. **METHODS:** A cross-sectional and longitudinal analysis of 10 years of claims data for all Medicaid beneficiaries younger than 20 years of age with 6 months or more of continuous insurance (N = 2,131,953) was conducted. Annual prevalence, incidence, and persistence in ADHD medication use (stimulants and atomoxetine) were estimated based on pharmacy claims and clinician-reported ADHD diagnosis. **RESULTS:** ADHD prevalence increased 1.70-fold (95% CI 1.67 to 1.73) from 3.10% (21,904 of 705,573 beneficiaries) in fiscal year 1995-1996 to 5.27% (41,681 of 790,338) in 2003-2004, paralleled by a 1.84-fold (95% CI 1.81 to 1.87) increase in drug use to 4.63%. In 2003-2004, 0.89% of youths were diagnosed and newly started on drugs, reflecting a 1.38-fold (95% CI 1.33 to 1.43) increase over 1995-1996. One in five white males between the ages of 10 and 14 years (19.24%; 95% CI 18.81 to 19.67) received ADHD medication in 2003-2004. Males continued to be more likely diagnosed and treated than females (prevalence ratio [PR] in 2003-2004 = 2.96; 95% CI 2.90 to 3.03 vs 3.82; 95% CI 3.69 to 3.96 in 1995-1996), as were whites when compared with Hispanics (PR in 2003-2004 = 2.65; 95% CI 2.57 to 2.73 vs 3.78; 95% CI 3.57 to 3.99 in 1995-1996) and blacks (PR in 2003-2004 = 1.81; 95% CI 1.76 to 1.85 vs 2.00; 95% CI 1.93 to 2.07 in 1995-1996). The most common starting age throughout the study period was 5-9 years, with 2.45% (95% CI 2.37 to 2.52) new ADHD drug users in 2003-2004, but largest increases in prevalence were observed in adolescents 15-19 years of age, with 2.47% (95% CI 2.38 to 2.55) in 2003-2004 compared with 0.45% (95% CI 0.41 to 0.49) in 1995-1996. Medication persistence varied, with only 49.9% (95% CI 49.4 to 50.5) of new users receiving drugs after 1 year, with yet another 17.2% (95% CI 16.4 to 18.0) continuing for 5 years or more. **CONCLUSIONS:** ADHD drug utilization continues to increase due to steady increases in diagnosis and chronic use of the drugs over several years.

While racial, ethnic, and sex differences persist, the age distribution of drug users has shifted toward older children. These findings emphasize the need for studies that analyze determinants of treatment as well as outcomes, both benefits and risks, associated with long-term medication use

Clin Pediatr (Phila). 2008 Jan;47:15-20.

Correlation between hospitalization for pharmaceutical ingestion and attention deficit disorder in children aged 5 to 9 years old.

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To determine if attention deficit hyperactivity disorder is a risk factor for pharmaceutical ingestions leading to hospital admission in children between ages 5 and 9, a retrospective, case-controlled chart review was conducted at a children's hospital. Cases were children aged 5 to 9 admitted for oral ingestion of pharmaceuticals. Controls were children admitted during the same time period with abdominal pain, appendicitis, or gastroenteritis. Controls were matched to cases 3:1 by age and gender. An odds ratio was calculated to determine if attention deficit hyperactivity disorder is a statistically significant risk factor for hospitalization after pharmaceutical ingestion. A total of 36% of 31 identified cases had attention deficit hyperactivity disorder compared with 7% of controls. The odds ratio for attention deficit hyperactivity disorder in children hospitalized after pharmaceutical ingestion was 7.97 (95% confidence interval, 2.35-28.01; $P < .01$). Children hospitalized for pharmaceutical ingestion are nearly 8 times more likely to have attention deficit hyperactivity disorder than children hospitalized for an unrelated disorder

Arch Clin Neuropsychol. 2008 Jan;23:21-32.

Cognitive switching processes in young people with attention-deficit/hyperactivity disorder.

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Patients with attention-deficit/hyperactivity disorder (ADHD) can be slow at switching between stimuli, or between sets of stimuli to control behaviour appropriate to changing situations. We examined clinical and experimental parameters that may influence the speed of such processes measured in the trail-making (TMT) and switch-tasks in cases with ADHD combined type, their non-affected siblings and unrelated healthy controls. The latency for completion of the trail-making task controlling for psychomotor processing (TMT-B-A) was longer for ADHD cases, and correlated with Conners' ratings of symptom severity across all subjects. The effect decreased with age. Switch-task responses to questions of "Which number?" and "How many?" between sets of 1/111 or 3/333 elicited differential increases in latency with condition that affected all groups. But there was evidence for increased symptom-related intra-individual variability among the ADHD cases, and across all subjects. Young siblings showed familiarity for some measures of TMT and switch-task performance but these were modest. The potential influences of moderator variables on the efficiency of processing stimulus change rather than the speed of processing are discussed. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

Arch Clin Neuropsychol. 2008 Jan;23:103-12.

Attentional problems in children born very preterm or with extremely low birth weight at 7-9 years.

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Behavioral rating scales and tests of attention were used to study attentional problems in children born very preterm (≈ 27 weeks gestation) or with extremely low birth weight (ELBW; ≈ 1000 g). Psychological tests of attention (viz., Digits and Spatial Span Forward, Visual Attention from the NEPSY, Trail Making Test B, and Stroop Color and Word Test) were administered to 45 children born very preterm/ELBW and 49 full-term controls, aged 7-9 years of age. Behavioral ratings on an ADHD scale were provided by parents and teachers on inattentive and hyperactive-impulsive symptoms. Children born very preterm/ELBW were found to perform significantly more poorly on Spatial Span Forward, Visual Attention, and Trail Making B than controls. Group differences were also found on parents' ratings on inattentive and total symptoms. Finally, measures of

psychological tests of attention were found to be significant predictors of parents' and teachers' ratings of symptoms. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

International Journal of Neuroscience. 2008 Jan;118:119-35.

Time reproduction disturbances in ADHD children: An ERP study.

González-Garrido AA, Gómez-Velázquez FR, Zarabozo D, et al.

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Sixteen ADHD children and a control group were asked to reproduce the varying time duration of successively presented visual stimuli. Time estimation was poorer in ADHD children, who showed more impulsive errors. ERPs exhibited similar grand-mean waveforms for both groups during the estimating period, but they were significantly different during the reproducing stage, when an early positive wave over frontal regions characterized the control group, interpreted as memory-guided motor output, followed by a slow negativity probably reflecting an inhibitory motor closure process, both probably involving central executive networks that seem to be improperly activated in ADHD children. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

Journal of Attention Disorders. 2008 Jan;11:427-36.

Interpersonal coping among boys with ADHD.

Hampel P, Manhal S, Roos T, et al.

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Objective: The authors investigate self-reported coping with interpersonal stressors among boys with and without ADHD in two studies and provide initial evidence for effects of different subgroups of ADHD on coping in Study 2. Method: In Study 1, 20 Austrian adolescents with ADHD were compared to 20 healthy controls. In Study 2, 44 German children and adolescents with ADHD (35 without and 9 with conduct disorders) were compared to 44 healthy controls matched by age and grade level, respectively. Results: Increased maladaptive coping was found in both studies. Study 2 revealed heightened maladaptive coping among both subgroups of ADHD, but the subgroup of ADHD with conduct disorders was more affected compared to healthy controls than the subgroup with ADHD alone. Conclusion: Results suggest an impaired interpersonal coping style in ADHD and point to the potential benefit of stress management and social skills trainings for boys with ADHD. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

Journal of Attention Disorders. 2008 Jan;11:437-44.

Duration of sleep and ADHD tendency among adolescents in China .

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Objective: This study investigates the association between duration of sleep and ADHD tendency among adolescents. Method: This population-based health survey uses a two-stage random cluster sampling design. Participants ages 13 to 17 are recruited from the total population of adolescents attending high school in one city of China. Duration of sleep is measured by self-reported time to bed and rise. ADHD tendency is assessed via a structured personal interview. Data are analyzed using linear regression modeling with adjustment for the effects of cluster sampling. Results: There is a highly significant and negative association between duration of sleep and ADHD tendency ($t = -4.99, p < .001$) with a regression coefficient of -0.73 after adjusting for the potential confounding factors. Conclusion: Duration of sleep is associated with ADHD tendency among adolescents. It would be prudent for clinicians to include the assessment of sleep problems, including lack of sleep, in evaluating potential ADHD patients for treatment programs. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

Journal of Attention Disorders. 2008 Jan;11:459-69.

Medications do not necessarily normalize cognition in ADHD patients.

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Objective: Although ADHD medications are effective for the behavioral components of the disorder, little information exists concerning their effects on cognition, especially in community samples. Method: A cross-sectional study of ADHD patients treated with three different ADHD drugs was conducted. Patients' performance on a computerized neurocognitive screening battery was compared to untreated ADHD patients and normal controls (NML). A total of 177 ADHD patients aged 10 to 18, achieved a favorable response to one of the following medications: Adderall XR (AMP), atomoxetine (ATMX), and Concerta (MPH-OROS) compared to 95 untreated ADHD patients and 101 NML. Results: Significant differences were detected between normals and untreated ADHD patients. Treated patients performed better than untreated patients but remained significantly impaired compared to normal subjects. Conclusion: Even with optimal treatment, based on parents' and teachers' opinions, subtle and not-so-subtle neurocognitive impairments persisted in the ADHD patients. Some ADHD patients may require additional educational assistance, even in the face of successful medication treatment. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

Journal of Attention Disorders. 2008 Jan;11:470-81.

Atomoxetine treatment of ADHD in children with comorbid tourette syndrome.

Spencer TJ, Sallee FR, Gilbert DL, et al.

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Objective: This study examines changes in severity of tics and ADHD during atomoxetine treatment in ADHD patients with Tourette syndrome (TS). Method: Subjects (7-17 years old) with ADHD (Diagnostic and Statistical Manual of Mental Disorders, DSM-IV) and TS were randomly assigned to double-blind treatment with placebo (n = 56) or atomoxetine (0.5-1.5 mg/kg/day, n = 61) for approximately 18 weeks. Results: Atomoxetine subjects showed significantly greater improvement on ADHD symptom measures. Treatment was also associated with significantly greater reduction of tic severity on two of three measures. Significant increases were seen in mean pulse rate and rates of treatment-emergent nausea, decreased appetite, and decreased body weight. No other clinically relevant treatment differences were observed in any other vital sign, adverse event, laboratory parameter, or electrocardiographic measure. Conclusion: Atomoxetine is efficacious for treatment of ADHD and its use appears well tolerated in ADHD patients with comorbid TS. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

Journal of Attention Disorders. 2008 Jan;11:482-92.

Sibling relationships among children with ADHD.

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Objective: This study investigated the quality of sibling relationships among children with ADHD relative to those without ADHD. Additional analyses examined whether externalizing and internalizing problems comorbid with ADHD affected sibling relationships. Method: Participants were 77 children with ADHD and 14 nonproblem control children. Sibling relationships were assessed via three informants: mother report, self-report, and sibling report. Results: In analyses utilizing hierarchical linear modeling to combine data from the three informants, children with ADHD showed increased conflict in sibling relationships, relative to nonproblem children. Comorbid externalizing problems were associated with less warmth/closeness and increased conflict in the sibling relationship and largely accounted for the finding that children with ADHD showed greater sibling relationship problems. Comorbid internalizing problems were associated with less warmth/closeness in the sibling relationship. Conclusion: It is recommended that sibling relationships be incorporated into theories of social impairment in ADHD. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

Journal of the American Academy of Child & Adolescent Psychiatry. 2008 Jan;47:61-67.

Dopamine transporter genotype conveys familial risk of attention-deficit/hyperactivity disorder through striatal activation.

Durston S, Fossella JA, Mulder MJ, et al.

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Objective: The dopamine transporter (DAT1) gene has been implicated in attention-deficit/hyperactivity disorder (ADHD), although the mechanism by which it exerts its effects remains unknown. The polymorphism associated with ADHD has been shown to affect expression of the transporter in vitro and in vivo. Dopamine transporters are predominantly expressed in the striatum, but also in the cerebellar vermis. Stimulant medication is often effective in ADHD and is believed to exert its effects by blocking dopamine transporters in the striatum. We set out to investigate the effect of the DAT1 genotype in ADHD in a small, preliminary study. We hypothesized that the DAT1 genotype would affect brain activation patterns in a manner similar to that of stimulant medication, with the lesser expressing allele mirroring its effects. Method: We investigated DAT1 gene effects on brain activation patterns in an all-male sample of sibling pairs discordant for ADHD (n = 20) and controls (n = 9). All of the subjects participated in a functional magnetic resonance imaging session using a go/no-go paradigm and provided a DNA sample for analysis. Results: DAT1 genotype affected activation in the striatum and cerebellar vermis. The genotype interacted with familial risk of ADHD in the striatum but not the vermis. Conclusions: These preliminary results suggest that the DAT1 gene effects in the striatum are involved in translating the genetic risk of ADHD into a neurobiological substrate. As such, this study represents a first step in elucidating the neurobiological mechanisms underlying genetic influences in ADHD. Furthermore, these results may contribute to long-term possibilities for the development of new treatments: If the DAT1 genotype has differential effects on striatal activation, then it may be useful as a surrogate endpoint in individualized treatments targeting genotype/functional magnetic resonance imaging activation profiles. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

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Familial vulnerability to ADHD affects activity in the cerebellum in addition to the prefrontal systems.

Mulder MJ, Baeyens D, Davidson MC, et al.

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Objective: Familial vulnerability to attention-deficit/hyperactivity disorder (ADHD) has been shown to be related to atypical prefrontal activity during cognitive control tasks. However, ADHD is associated with deficits in the cerebellum as well as deficits in frontostriatal circuitry and associated cognitive control. In this study, we investigated whether cerebellar systems are sensitive to familial risk for ADHD in addition to frontostriatal circuitry. Method: We used an event-related, rapid mixed-trial functional magnetic resonance imaging design. The paradigm was a variation on a go/no-go task, with expected (go) and unexpected (no-go) events at expected and unexpected times. A total of 36 male children and adolescents completed the study, including 12 sibling pairs discordant for ADHD and 12 matched controls. Results: Children and adolescents with ADHD were less accurate on unexpected events than control subjects. Performance by unaffected siblings was intermediate, between that of children and adolescents with ADHD and controls. Functional neuroimaging results showed dissociation between activation in the cerebellum and anterior cingulate cortex: Activity in the anterior cingulate cortex was decreased for subjects with ADHD and their unaffected siblings compared with controls for manipulations of stimulus type (no-go trials), but not timing. In contrast, cerebellar activity was decreased for subjects with ADHD and their unaffected siblings for manipulations of timing, but not stimulus type. Conclusions: These findings suggest that activity in both the prefrontal cortex and cerebellum is sensitive to familial vulnerability to ADHD. Unaffected siblings of individuals with ADHD show deficits similar to affected probands in prefrontal areas for unexpected events and in cerebellum for events at unexpected times. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

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Predictors of stability of attention-deficit/hyperactivity disorder subtypes from childhood to young adulthood.

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Objective: To determine the 5-year prospective stability of population-based and DSM-IV subtypes of attention-deficit/hyperactivity disorder (ADHD) as well as to explore predictors of stability. Method: A total of 708 twins ages 7 to 19 years who were identified from birth records of the state of Missouri and had participated in a study of ADHD were reassessed 5 years later in a blinded fashion. Stabilities of DSM-IV and population-based ADHD subtypes were compared using percentage of agreement with significance tested by the κ statistic. Predictors of stability of subtype diagnosis were determined using multivariate logistic regression. Results: In general, 5-year ADHD subtype stability was poor to modest and ranged from 11.1% to 24.0% for DSM-IV for subtypes and from 14.3% to 35.3% for clinically significant population-derived subtypes. There were no predictors of diagnostic stability that applied across subtypes. There were subtype-specific predictors including a diagnosis of oppositional defiant disorder for DSM-IV primarily inattentive ADHD; lower verbal IQ for DSM-IV combined type ADHD; and younger age, oppositional defiant disorder, and medication use for population-defined severe combined ADHD. Conclusions: Population-defined ADHD subtype criteria demonstrated modestly improved diagnostic stability over 5 years compared to DSM-IV subtypes. Few correlates or predictors of stability were identified. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

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Modafinil as a treatment for attention-deficit/hyperactivity disorder in children and adolescents: A double blind, randomized clinical trial.

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Attention-Deficit/Hyperactivity Disorder (ADHD) is the most prevalent psychiatric disorder currently afflicting children and is among the most common chronic conditions affecting school-age children. Modafinil is structurally different from the psychostimulants that are typically used to treat ADHD and has been reported to be effective in improving the symptoms of ADHD. The aim of the present study was to further evaluate, under double blind and controlled conditions, the efficacy of modafinil for ADHD in children and adolescents as compared to methylphenidate. Patients included 60 outpatients, children (47 boys and 13 girls) between the ages of 6-15 who clearly met the DSM-IV-TR diagnostic criteria for ADHD. Subjects were recruited from an outpatient child and adolescent clinic for a 6 week double blind, randomized clinical trial. All study subjects were randomly assigned to receive either treatment with modafinil film coated tablet (in doses of 200-300 mg/day) depending on weight (200 mg/day for <30 kg and 300 mg/day for >30 kg) (group 1) or methylphenidate (in doses of 20-30 mg/day) depending on weight (20 mg/day for <30 kg and 30 mg/day for >30 kg) (group 2). The principal measure of outcome was the Teacher and Parent ADHD Rating Scale-IV. Patients were assessed at baseline and at 21 and 42 days after the medication started. No significant differences were observed between the two groups on the Parent and Teacher Rating Scale scores. Side effects of decreased appetite and difficulty falling asleep were observed more in the methylphenidate group. The results of this study indicate that modafinil significantly improved symptoms of ADHD and was well tolerated and it is beneficial in the treatment of children with ADHD. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2008 Jan;32:243-48.

A case-control association study of the polymorphism at the promoter region of the DRD4 gene in Korean boys with attention deficit-hyperactivity disorder: Evidence of association with the -521 C/T SNP.

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Recent genetic studies at the 5' end of the dopamine D4 receptor (DRD4) gene have identified several polymorphisms having a possible relationship with attention deficit-hyperactivity disorder (ADHD). This study

examined the association between the -521 and -376 promoter single nucleotide polymorphisms (SNPs) of the DRD4 gene and ADHD through a case-control association study in Korean boys, who constitute a single ethnic population. Ninety-four ADHD and ninety-five control boys were enrolled in this study. All of the ADHD subjects completed a comprehensive and standardized diagnostic and psychological evaluation battery including the ADHD Rating Scale-IV (ARS). Genotyping for the 2 promoter SNPs was performed. There were significant differences in the genotype and allele frequencies of the -521 C/T SNP between the ADHD and control groups ($\chi^2 = 6.28$, $p = 0.043$ and $\chi^2 = 6.22$, $p = 0.013$, respectively). However, the distribution of the -376 C/T genotypes and alleles were similar in the ADHD and control groups. The subtypes of ADHD were not related to either of these two SNPs. In the ADHD subjects, the -521 TT genotype group had a higher score in the inattentive subscale and a lower score in the hyperactive subscale of the parents version of ARS, although these differences did not attain statistical significance ($p = 0.146$, $p = 0.082$). In conclusion, there was a significant association between the -521 C/T SNP and ADHD in Korean boys. These results suggest a role of the -521 C/T SNP in the susceptibility for ADHD. (PsycINFO Database Record (c) 2008 APA, all rights reserved) (from the journal abstract)

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Investigation of the G protein subunit G β -sub(olf) gene (GNAL) in attention deficit/hyperactivity disorder.

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The dopamine system plays an important role in the regulation of attention and motor behavior, subsequently, several dopamine-related genes have been associated with Attention Deficit/Hyperactivity Disorder (ADHD). Among them are the dopamine receptors D1 and D5 that mediate adenylyl cyclase activation through coupling with G-sub(s)-like proteins. We thus hypothesized that the G-sub(s)-like subunit G β -sub(olf), expressed in D1-rich areas of the brain, contributes to the genetic susceptibility of ADHD. To evaluate the involvement of the G β -sub(olf) gene, GNAL, in ADHD, we examined the inheritance pattern of 12 GNAL polymorphisms in 258 nuclear families ascertained through a proband with ADHD (311 affected children) using the transmission/disequilibrium test (TDT). Categorical analysis of individual marker alleles demonstrated biased transmission of one polymorphism in GNAL intron 3 (rs2161961; $P = 0.011$). We also observed significant relationships between rs2161961 and dimensional symptoms of inattention and hyperactivity/impulsivity ($P = 0.003$ and $P = 0.008$). In addition, because of recent evidence of imprinting at the GNAL locus, secondary analyses were split into maternal and paternal transmissions to assess a contribution of parental effects. We found evidence of strong maternal effect, with preferential transmission of maternal alleles for rs2161961A ($P = 0.005$) and rs8098539A ($P = 0.035$). These preliminary findings suggest a possible contribution of GNAL in the susceptibility to ADHD, with possible involvement of parent-of-origin effects. (PsycINFO Database Record (c) 2007 APA, all rights reserved) (from the journal abstract)

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"Sicurezza a lungo termine dei farmaci utilizzati nel trattamento di bambini in età scolare con sindrome da deficit di attenzione e iperattività ed epidemiologia della malattia nella popolazione italiana".

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