



# ADHD

ATTENTION DEFICIT HYPERACTIVITY DISORDER

  
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**NEWSLETTER**

**Numero 11 - Novembre 2008**

Clin Case Stud. 2008;7:521-37.¶

## **A comparison of cognitive and psychosocial function for males within the ADHD continuum.**

**Padolsky I.**

Two case studies are presented illustrating neurophysiological dysfunction suggesting input or output deficits in ADHD assessed across multiple domains. Data included child and family history, behavior ratings, information processing, speed, cognitive, neurophysiological, and academic function. Pretreatment data indicated impaired processing speed, excessive slow to fast wave ratios indicative of attentional dysregulation, and poor psychosocial function evident in both children. Posttreatment assessment indicated improvement in slow to fast wave ratios and psychosocial functioning for both children. Additional improvement was also noted in cognitive and academic function in MH, the child with learning disabilities, and in processing speed for CX, the child with elevated cognitive function. Neurophysiological dysregulation in ADHD may result in input or output impairment differentially affecting cognitive, academic, and psychosocial functioning. Heterogeneity within the ADHD continuum underscores the need for multifaceted assessment to guide diagnosis and treatment. In ADHD children nonresponsive to stimulants, neurofeedback can be a viable treatment to enhance attentional focus and on-task behavior.

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Eur Psychiatry. 2008;23:512-20.¶

## **A study of neuropsychological deficit in children with obsessive-compulsive disorder.¶**

**Shin MS, Choi H, Kim H, et al. ¶**

This study was conducted to examine the neuropsychological deficits in children with obsessive compulsive disorder (OCD). Furthermore, the focus of present study was to explore whether OCD children show the same executive dysfunction as adult OCD patients. The participants consisted of 106 children between the ages of 6 and 16 years who visited the department of child-adolescent psychiatry, Seoul National University Children's Hospital (17 OCD, 25 ADHD, 21 tic disorder, 20 depressive disorder, and 23 healthy children). The OCD children showed higher verbal ability compared to other psychiatric groups, but performed the worst on WISC-R subtests assessing perceptual organization ability under time pressure. The OCD children did not show any significant deficits in verbal intellectual function, memory, attention and concentration abilities. However, similar to the ADHD children, the OCD children had significantly more errors and completed fewer categories on the WCST compared to the healthy group. Through neuropsychological tests, the OCD children showed cognitive strength and weakness similar to those of OCD adults that were reported in previous research. Specifically, they had executive function deficits in mental set shifting, supporting the frontal-striatal dysfunction hypothesis of OCD in children as well as in adults.

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

Psychol Med. 2008;38:1607-16.

**ADHD and Stroop interference from age 9 to age 41 years: A meta-analysis of developmental effects.**  
**Schwartz K, Verhaeghen P.**

**Background:** In this meta-analysis, we investigated whether response inhibition is sensitive to attention deficit hyperactivity disorder (ADHD) status and, if so, what influence maturation has on this attentional symptom of ADHD.

**Method:** We examined 25 studies that reported data on the Stroop color word test in children and adults with ADHD and in age-matched controls; average ages ranged from 9 to 41 years. We utilized a hierarchical approach to analyze the strength of the Stroop effect and whether the effect varies as a function of age. Additionally, we assessed potential differences in maturation rates based on reaction time (RT) of color and color-word conditions.

**Results:** First, we found that the relationship between color-word and color RT was multiplicative, and the slope of this function (the ratio of color-word RT over color RT) was identical across age groups and ADHD status. Second, we found that although ADHD individuals were on average 1.14 times slower than age-matched controls in both the color and the color-word condition, the maturation rate was identical for both groups.

**Conclusions:** The results from this analysis indicate that the Stroop interference effect is not larger in ADHD individuals than in age-matched controls. Further, we did not find evidence for differential maturation rates for persons with ADHD and the control groups. The Stroop interference effect appears to be immune to age, regardless of ADHD status.

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Neurology. 2008 Nov;71:1514-20.

**Age-related changes in motor subtle signs among girls and boys with ADHD.**

**Cole WR, Mostofsky SH, Larson JC, et al.**

**OBJECTIVE:** To examine differences in age-related improvement in motor speed and neurologic subtle signs (overflow and dysrhythmia) among boys and girls with and without attention-deficit hyperactivity disorder (ADHD).

**METHOD:** Diagnosis of ADHD was determined by structured parent interview and administration of ADHD-specific and broad behavior rating scales. Motor function was assessed using the revised Physical and Neurological Assessment of Subtle Signs. Three primary outcome variables were obtained: 1) total time, 2) total overflow, and 3) total dysrhythmia. Effects of age, group, and sex were assessed.

**RESULTS:** Both control and ADHD groups showed improvement on timed tasks with age; however, controls were consistently faster across the age span. Controls and girls with ADHD showed steady age-related reduction of overflow and dysrhythmia, whereas boys with ADHD had little improvement in these signs through age 14 years.

**CONCLUSION:** Results indicated that girls with attention-deficit hyperactivity disorder (ADHD) performed similarly to age-matched controls on a quantified motor examination. These results parallel patterns of findings from neuroimaging studies, in which neurologic anomalies in areas related to motor control are present in boys with ADHD, but more equivocal in girls with ADHD. Sex-related differences observed in children with ADHD likely extend beyond symptom presentation to development of motor control, and are likely related to earlier brain maturation in girls

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Child Adolesc Ment Health. 2008;13:188-92.

**Association between colonic symptoms and inattention/hyperactivity in British children.**

**Ryan CW.**

**Background:** Functional faecal retention and attention deficit hyperactivity disorder (ADHD) are common in childhood. There is some evidence, mostly from clinical samples, of an association between them.

**Methods:** The association between parental reports of inattention/ hyperactivity and colonic symptoms in children between four and ten years of age was examined using the Health Survey for England 2000.

**Results:** Boys were about twice as likely to be rated by their parents as inattentive/hyperactive if they had colon symptoms.

**Conclusions:** This study adds to existing evidence associating bowel function and behavioural symptoms, especially in boys. Given the high prevalence of gastrointestinal symptoms in general, and the increasing personal and societal impact of childhood behavioural problems, further exploration of the relationship is warranted, with particular attention to causal pathways.

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Neurosci Lett. 2008;446:108-11.

**Association between the alpha-2C-adrenergic receptor gene and attention deficit hyperactivity disorder in a Korean sample.**

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

Findings from preclinical and clinical research support the involvement of central noradrenergic dysregulation in the etiology of attention deficit hyperactivity disorder (ADHD). Previous studies have suggested that the alpha-2C-adrenergic receptor gene (ADRA2C) is associated with ADHD. The aims of this study were to examine the association between the ADRA2C (GT)<sub>n</sub> repeat polymorphism (STR marker adra2c1) and ADHD in a Korean sample. In this case-control and family-based association study, we assessed 184 ADHD probands, 150 normal controls, and 98 trios. There were no significant differences in the allele frequencies of the ADRA2C polymorphism between the ADHD and control groups ( $p > 0.05$ ). The overall allele-wise transmission disequilibrium test (TDT) analysis showed statistical significance ( $(\chi)^2 = 19.07$ ,  $p = 0.025$ ). We found a trend for preferential transmission of the 183-bp allele ( $(\chi)^2 = 3.72$ ,  $p = 0.054$ ), and a significantly lower-than-expected rate of transmission of the 187-bp allele ( $(\chi)^2 = 6.26$ ,  $p = 0.012$ ). With regard to the temperament profiles of the Junior Temperament and Character Inventory (JTCI), the ADHD subjects with the 183/183 genotype at the ADRA2C polymorphism showed a trend toward a lower score in the Novelty Seeking ( $p = 0.020$ ) profile than did those with the other genotypes. Our findings provide important evidence that the ADRA2C polymorphism is involved in the etiology of ADHD in Korean subjects. In addition, our results provide evidence that the temperament of Novelty Seeking and ADHD might share molecular genetic characteristics related to the noradrenergic system.

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J Abnorm Child Psychol. 2008 Nov;36:1237-50.

**Associations between maternal attention-deficit/hyperactivity disorder symptoms and parenting.**

**Chronis-Tuscano A, Raggi VL, Clarke TL, et al.**

Mothers of children with attention-deficit/hyperactivity disorder (ADHD) are at increased risk for an ADHD diagnosis themselves, which is likely associated with impairments in parenting. The present study utilized a multi-method assessment of maternal ADHD and parenting to examine the extent to which maternal ADHD symptoms are associated with maladaptive parenting. Participants included 70 6-10 year old children with DSM-IV ADHD and their biological mothers. Results suggested that mothers with higher levels of ADHD symptoms reported lower levels of involvement and positive parenting and higher levels of inconsistent discipline. During observed parent-child interactions, maternal ADHD symptoms were negatively associated with positive parenting, and positively associated with negative parenting and repeated commands before giving the child an opportunity to comply. Given prior research suggesting that maladaptive parenting behaviors are risk factors for the later development of conduct problems among children with ADHD, these findings have important clinical implications for family-based assessment and treatment of ADHD.

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J Child Adolesc Psychopharmacol. 2008;18:539-41.

**Atomoxetine-induced mydriasis.**

**Alhatem FJ, Decker DH.**

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J Burn Care Res. 2008;29:724-29.

**Attention deficit-hyperactivity disorder in children with burn injuries.**

**Badger K, Anderson L, Kagan RJ.**

This study explored the characteristics of children with burns who were also diagnosed with attention deficit disorder (ADD) or attention deficit hyperactivity disorder (ADHD). The study was intended to identify and better understand the risk factors for such injuries and to help direct future burn prevention and education efforts for children with these underlying disorders. We performed a retrospective, comparison group study of 103 pediatric burn patients ranging in age from 5 to 18 years. Forty-four children who were diagnosed with ADD or ADHD at the time of their burn injury were compared with a random sample of 59 burn-injured children without the diagnosis of ADD or ADHD. Variables analyzed included patient demographics, cause of burn, length of hospitalization, engagement in high risk behavior at the time of injury, presence of other developmental, mental health diagnoses, and/or school behavior problems. The ADD or ADHD group had a significantly greater incidence of mental health and school behavior problems than other children with burn injuries. They also had a significantly greater history of high risk behavior at the time of injury than the comparison group. Children with ADD or ADHD who also had an additional mental health diagnosis had a higher incidence of school behavior problems. Our findings suggest the need for additional studies of children with ADD or ADHD who sustain burn injuries. Children with ADD or ADHD who have school behavior problems and/or a tendency to engage in high-risk behavior may be at greatest risk for burn injuries and most likely to benefit from educational counseling or other modalities of burn prevention.

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J Autism Dev Disord. 2008;38:1797-802.

**Brief report: Attention effect on a measure of social perception.**

**Fine JG, Semrud-Clikeman M, Butcher B, et al.**

A measure of social perception (CASP) was used to assess differences in social perception among typically developing children, children with autistic spectrum disorders (ASD), and children with Attention Deficit/Hyperactivity Disorder (ADHD). Significant between-group differences were found in recognition of emotions in video, with children diagnosed with ADHD or ASD performing more poorly than controls on measures of knowledge of nonverbal cues and emotional expression. The number of inattention symptoms was found to be a significant contributor to poorer video interpretation across diagnostic groups. An effect of attention on poor social perception was found that may be unique to the ASD group. Clinicians may overestimate the social deficits of children with ASD if they also have symptoms of inattention, while researchers may need to control for the effects of inattention in their studies.

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J Child Adolesc Psychopharmacol. 2008;18:537-38.

**Bruxism arising during monotherapy with methylphenidate.**

**Mendhekar DN, Andrade C.**

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J Am Acad Child Adolesc Psychiatry. 2008;47:1151-57.

**CBCL pediatric bipolar disorder profile and ADHD: Comorbidity and quantitative trait loci analysis.**

**McGough JJ, Loo SK, McCracken JT, et al.**

**Objective:** The pediatric bipolar disorder profile of the Child Behavior Checklist (CBCL-PBD), a parent-completed measure that avoids clinician ideological bias, has proven useful in differentiating patients with attention-deficit/hyperactivity disorder (ADHD). We used CBCL-PBD profiles to distinguish patterns of comorbidity and to search for quantitative trait loci in a genomewide scan in a sample of multiple affected ADHD sibling pairs.

**Method:** A total of 540 ADHD subjects ages 5 to 18 years were assessed with the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present and Lifetime version and CBCL. Parents were assessed with the Schedule for Affective Disorders and Schizophrenia-Lifetime version supplemented by the Schedule for Affective Disorders and Schizophrenia for School-Age Children for disruptive behavioral disorders. Patterns of psychiatric comorbidity were contrasted based on the CBCL-PBD profile. A quantitative trait loci variance component analysis was used to identify potential genomic regions that may harbor susceptibility genes for the CBCL-PBD quantitative phenotype.

**Results:** Bipolar spectrum disorders represented less than 2% of the overall sample. The CBCL-PBD classification was associated with increased generalized anxiety disorder ( $p = .001$ ), oppositional defiant disorder ( $p = .008$ ), conduct disorder ( $p = .003$ ), and parental substance abuse ( $p = .005$ ). A moderately significant linkage signal (multipoint maximum lod score = 2.5) was found on chromosome 2q.

**Conclusions:** The CBCL-PBD profile distinguishes a subset of ADHD patients with significant comorbidity. Linkage analysis of the CBCL-PBD phenotype suggests certain genomic regions that merit further investigation for genes predisposing to severe psychopathology.

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J Clin Psychiatry. 2008;69:1477-84.

**Childhood attention-deficit/hyperactivity disorder and the emergence of personality disorders in adolescence: A prospective follow-up study.**

**Miller CJ, Flory JD, Miller SR, et al.**

**Objectives:** Adults with attention-deficit/hyperactivity disorder (ADHD) experience considerable functional impairment. However, the extent to which comorbid Axis II personality disorders contribute to their difficulties and whether such comorbidities are associated with the childhood condition or the persistence of ADHD into adulthood remain unclear.

**Method:** This study examined the presence of personality disorders in a longitudinal sample of 96 adolescents diagnosed with ADHD when they were 7 through 11 years old, as compared to a matched, never ADHD-diagnosed, control group ( $N = 85$ ). Participants were between 16 and 26 years old at follow-up. On the basis of a psychiatric interview, the ADHD group was subdivided into those with and without persistent ADHD. Axis II symptoms were assessed by using the Structured Clinical Interview for DSM-IV Axis II Personality Disorders. Data were analyzed using logistic regression, and odds ratios (ORs) were generated. The study was conducted from 1994 through 1997.

**Results:** Individuals diagnosed with childhood ADHD are at increased risk for personality disorders in late adolescence, specifically borderline (OR = 13.16), antisocial (OR = 3.03), avoidant (OR = 9.77), and narcissistic (OR = 8.69) personality disorders. Those with persistent ADHD were at higher risk for antisocial (OR = 5.26) and paranoid (OR = 8.47) personality disorders but not the other personality disorders when compared to those in whom ADHD remitted.

**Conclusion:** Results suggest that ADHD portends risk for adult personality disorders, but the risk is not uniform across disorders, nor is it uniformly related to child or adult diagnostic status.

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Clin Child Psychol Psychiatry. 2008;13:515-30.

**Differences in dropout between diagnoses in child and adolescent mental health services.**

**Johnson E, Mellor D, Brann P.**

Dropout from treatment is a significant problem in child and adolescent mental health services, and findings regarding the role of possible contributing factors are inconsistent. It is argued that this inconsistency may be

the result of the confounding effects of different definitions of dropout, and different dropout rates for different diagnoses. A file review of 520 new cases over a 12-month period in a large Child and Adolescent Mental Health Service in Melbourne, Australia was performed. Information was collected about the intake, parents, family, child, diagnoses and treatment. A significant relationship was found between diagnosis and dropout rate, with clients experiencing family problems or conduct disorder and ADHD being more likely to dropout, and those experiencing negative life events, anxiety disorders or those not having a diagnosis being less likely to dropout. These findings offer potential directions for services to consider specific strategies for retaining their clients. Possible reasons for these findings, methodological issues and future research directions are discussed.

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Schizophr Res. 2008;105:216-23.

**Different psychological effects of cannabis use in adolescents at genetic high risk for schizophrenia and with attention deficit/hyperactivity disorder (ADHD).**

**Hollis C, Groom MJ, Das D, et al.**

**Background:** Controversy exists regarding whether young people at risk for schizophrenia are at increased risk of adverse mental effects of cannabis use.

**Methods:** We examined cannabis use and mental health functioning in three groups of young people aged 14-21; 36 non-psychotic siblings of adolescents with schizophrenia (genetic high risk group), 25 adolescents with attention deficit hyperactivity disorder (ADHD) and 72 healthy controls. The groups were sub-divided into 'users' and 'non-users' of cannabis based on how often they had used cannabis previously. Mental health functioning was quantified by creating a composite index derived from scores on the Schizotypal Personality Questionnaire (SPQ), Strengths and Difficulties Questionnaire (SDQ) and Global Assessment of Function (GAF).

**Results:** A significant positive association between cannabis use and mental health disturbance was confined to young people at genetic high risk for schizophrenia. To determine whether the relationship was specific to particular dimensions of mental health function, a second composite index was created based on scores from the SPQ Disorganisation and SDQ hyperactivity-inattention sub-scales. Again, there was a significant positive association between cannabis use and factor scores which was specific to the genetic high risk group. There was a trend for this association to be negative in the ADHD group ( $p = 0.07$ ).

**Conclusions:** The findings support the view that young people at genetic high risk for schizophrenia are particularly vulnerable to mental health problems associated with cannabis use. Further research is needed to investigate the basis of relationships between cannabis and mental health in genetically vulnerable individuals.

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J Abnorm Psychol. 2008 Nov;117:881-95.

**Divided attention in youth-onset psychosis and attention deficit/hyperactivity disorder.**

**Karatekin C, White T, Bingham C.**

The authors used pupillary dilations to test whether divided attention deficits in youth-onset psychosis and attention deficit/hyperactivity disorder (ADHD) were because of limitations in recruitment of cognitive resources or abnormalities in attention allocation. Eight- to 19-year-olds with youth-onset psychosis or ADHD were administered a divided attention test consisting of an auditory digit span (DS) task and a simple visual response time (RT) task. In 4 conditions, participants performed neither (no task), 1 (DS or RT only), or both tasks (dual). Dependent variables were DS accuracy, RT, and pupillary dilation to digits as an estimate of recruitment of cognitive resources. The authors found no evidence for an abnormal attention strategy in either disorder. Instead, results were consistent with the hypothesis that both clinical groups have limitations in resource recruitment. These limitations were more severe in psychosis than in ADHD. Findings indicate that both clinical groups had difficulties in regulating physiological arousal on a moment-to-moment basis in accordance with task demands. Findings also demonstrate the importance of taking into account difficulties that constrain performance on simple tasks before interpreting impairments on complex tasks.

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Arch Pediatr Adolesc Med. 2008;162:916-21.

**Effect of prior stimulant treatment for attention-deficit/hyperactivity disorder on subsequent risk for cigarette smoking and alcohol and drug use disorders in adolescents.**

**Wilens TE, Adamson J, Monuteaux MC, et al.**

**Objective:** To examine the effects of early stimulant treatment on subsequent risk for cigarette smoking and substance use disorders (SUDs) in adolescents with attention-deficit/hyperactivity disorder (ADHD).

**Design:** Case-controlled, prospective, 5-year follow-up study. Setting: Massachusetts General Hospital, Boston.

**Participants:** Adolescents with and without ADHD from psychiatric and pediatric sources. Blinded interviewers determined all diagnoses using structured interviews. Intervention: Naturalistic treatment exposure with psychostimulants for ADHD.

**Main Outcome Measures:** We modeled time to onset of SUDs and smoking as a function of stimulant treatment. Results: We ascertained 114 subjects with ADHD (mean age at follow-up, 16.2 years) having complete medication and SUD data; 94 of the subjects were treated with stimulants. There were no differences in SUD risk factors between naturalistically treated and untreated groups other than family history of ADHD. We found no increased risks for cigarette smoking or SUDs associated with stimulant therapy. We found significant protective effects of stimulant treatment on the development of any SUD (hazard ratio [HR], 0.27; 95% confidence interval [CI], 0.13-0.60;  $\chi^2_{1132} = 10.57$ ,  $P = .001$ ) and cigarette smoking (HR, 0.28; 95% CI, 0.14-0.60;  $\chi^2_{1112} = 10.05$ ,  $P = .001$ ) that were maintained when controlling for conduct disorder. We found no effects of time to onset or duration of stimulant therapy on subsequent SUDs or cigarette smoking in subjects with ADHD.

**Conclusion:** Stimulant therapy does not increase but rather reduces the risk for cigarette smoking and SUDs in adolescents with ADHD.

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Clin Neurophysiol. 2008;119:2476-93.

**Error and feedback processing in children with ADHD and children with Autistic Spectrum Disorder: An EEG event-related potential study.**

**Groen Y, Wijers AA, Mulder LJM, et al.**

**Objective:** Performance monitoring was investigated in typically developing (TD) children, children with Autistic Spectrum Disorder (ASD), and Methylphenidate (Mph)-treated and medication-free children with Attention Deficit Hyperactivity Disorder (ADHD).

**Methods:** Subjects performed a feedback-based learning task. Event-related Potentials (ERPs) time locked to responses and feedback were derived from the EEG.

**Results:** Compared to the TD and ASD groups, the medication-free ADHD group showed a decreased response-locked Error Related Negativity (ERN) and error Positivity (Pe), particularly as learning progressed throughout the task. Compared to the medication-free ADHD group, the Methylphenidate-treated group showed a normalised Pe. All clinical groups showed or tended to show a decreased feedback-locked late positive potential to negative feedback.

**Conclusions:** The ERPs suggest that medication-free children with ADHD, but not with ASD, have a diminished capacity to monitor their error responses when they are learning by performance feedback. This capacity partially 'normalises' in Mph-treated children with ADHD. Both children with ADHD and children with ASD are suggested being compromised in affective feedback processing.

**Significance:** This study shows that measuring ERPs of error and feedback processing is a useful method for (1) dissociating ADHD from ASD and (2) elucidating medication effects in ADHD on component processes of performance monitoring.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1182-85.

**Family based association study of pediatric bipolar disorder and the dopamine transporter gene (SLC6A3).**

**Mick E, Jang WK, Biederman J, et al.**

The dopamine transporter gene (SLC6A3) is a compelling candidate for pediatric bipolar disorder because (a) it has been associated with ADHD, (b) bipolar comorbidity with ADHD has been hypothesized to be an etiologically distinct familial subtype (c) blockade of the dopamine transporter with psychostimulants can

induce mania in susceptible individuals and (d) previous studies have implicated the gene in bipolar disorder in adults. We conducted a family-based association study of SLC6A3 in 170 affected offspring trios defined by a child (12.9(plus or minus)5.3 years of age) with DSM-IV Bipolar-I disorder. Twenty-eight tag SNPs were chosen from the CEU (European) population of the International HapMap project ([www.hapmap.org](http://www.hapmap.org)). Results indicated nominally positive association for 4 SNPs (rs40184, rs11133767, rs3776512, and rs464049), but only rs40184 survived correction for multiple statistical comparisons ( $P=0.038$ ). This is the first examination of the association with SLC6A3 and bipolar disorder in children and, like previous findings in adults with bipolar disorder, we found evidence of association with SNPs in the 30 region of the gene. These data provide suggestive evidence supporting a role for SLC6A3 in the etiology of pediatric bipolar disorder. (copyright) 2008 Wiley-Liss, Inc

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J Am Acad Child Adolesc Psychiatry. 2008;47:1141-50.

**fMRI of intrasubject variability in ADHD: Anomalous premotor activity with prefrontal compensation.**

**Suskauer SJ, Simmonds DJ, Caffo BS, et al.**

**Objective:** Children with attention-deficit/hyperactivity disorder (ADHD) consistently display increased intrasubject variability (ISV) in response time across varying tasks, signifying inefficiency of response preparation compared to typically developing (TD) children. Children with ADHD also demonstrate impaired response inhibition; inhibitory deficits correlate with ISV, suggesting that similar brain circuits may underlie both processes. To better understand the neural mechanisms underlying increased ISV and inhibitory deficits in children with ADHD, functional magnetic resonance imaging was used to examine the neural correlates of ISV during Go/No-go task performance.

**Method:** Event-related functional magnetic resonance imaging was used to study 25 children with ADHD and 25 TD children ages 8 to 13 years performing a simplified Go/No-go task. Brain-behavior correlations were examined between functional magnetic resonance imaging activation and ISV within and between groups.

**Results:** For TD children, increased rostral supplementary motor area (pre-supplementary motor area) activation during No-go events was associated with less ISV, whereas the reverse was true for children with ADHD for whom increased pre-supplementary motor area activation was associated with more ISV. In contrast, children with ADHD with less ISV showed greater prefrontal activation, whereas TD children with more prefrontal activation demonstrated more ISV.

**Conclusions:** These findings add to evidence that dysfunction of premotor systems may contribute to increased variability and impaired response inhibition in children with ADHD and that compensatory strategies eliciting increased cognitive control may improve function. However, recruitment of prefrontal resources as a compensatory mechanism for motor task performance may preclude the use of those prefrontal resources for higher order, more novel executive functions with which children with ADHD often struggle.

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Can J Clin Pharmacol. 2008;15:e411-e419.

**Gender and attention deficits in children diagnosed with a fetal alcohol spectrum disorder.**

**Herman LE, Acosta MC, Chang PN.**

**Background:** A portion of children are born with Fetal Alcohol Spectrum Disorders (FASD). Most present with significant difficulties in attention, with attention-deficit/hyperactivity disorder (ADHD) being the most common psychiatric co-morbidity.

**Objectives:** The current study will describe behavioral and executive functioning (EF) deficits in attention in a group of children with FASD. Effects of gender and ADHD diagnosis will be explored.

**Methods:** Existing data from the University of Minnesota's Pediatric Psychology clinic was utilized. Of 191 children with FASD in the database, 36 children (ages 6-16) had complete scores on measures of behavioral and EF attention deficits. Multivariate Analyses of Variance (MANOVA) were used to examine the impact of gender and ADHD diagnosis on behavioral checklist scores and on a variety of EF measures.

**Results:** FASD males were significantly more likely to be diagnosed with ADHD (68%) than FASD females (29%). No impact of gender or diagnosis was found for behavioral measures of attention, but an interaction of gender and diagnosis emerged for EF. Females with ADHD evidenced deficits in EF compared to females without ADHD. However, males with ADHD performed better on measures of EF than their non-ADHD counterparts.

**Conclusion:** An ADHD diagnosis in FASD children needs to be reconsidered, especially for males.  
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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1306-09.

**No association between two polymorphisms of the serotonin transporter gene and combined type attention deficit hyperactivity disorder.**

**Xu X, Aysimi E, Anney R, et al.**

Several independent studies have reported association between serotonin transporter gene (SLC6A4) polymorphisms and attention deficit hyperactivity disorder (ADHD). Five studies found evidence for association between the long-allele of a 44-bp insertion/deletion polymorphism (5-HTTLPR) and ADHD. Another two studies corroborated this finding while a further six studies did not find such an association. For a second polymorphism within the gene, a variable number tandem repeat (VNTR) within intron 2, one study demonstrated that the 12/12 genotype was significantly less frequent in ADHD cases compared to controls, while a second study found that the 12-allele was preferentially transmitted to offspring affected with ADHD. To provide further clarification of the reported associations, we investigated the association of these two markers with ADHD in a sample of 1,020 families with 1,166 combined type ADHD cases for the International Multi-Centre ADHD Genetics project, using the Transmission Disequilibrium Test. Given the large body of work supporting the association of the promoter polymorphism and mood disorders, we further analyzed the group of subjects with ADHD plus mood disorder separately. No association was found between either of the two markers and ADHD in our large multisite study or with depression within the sample of ADHD cases.

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J Abnorm Child Psychol. 2008 Nov;36:1199-210.

**Novel measures of response performance and inhibition in children with ADHD.**

**Morein-Zamir S, Hommersen P, Johnston C, et al.**

Fifteen children with ADHD aged 8 to 12 years and age and gender matched controls performed two different stopping tasks to examine response performance and inhibition and their respective moment-to-moment variability. One task was the well-established stop-signal task, while the other was a novel tracking task where the children tracked a spaceship on the screen until an alarm indicated they should stop. Although performance was discrete in the stop signal task and continuous in the tracking task, in both tasks latencies to the stop signal were significantly slowed in children with ADHD. Go performance and variability did not significantly differ between ADHD and control children in either task. Importantly, stopping latency in the novel spaceship tracking task also was more variable in children with ADHD. As stopping variability cannot be measured using the standard stop signal task, the new task offers compelling support for the heretofore untested prediction that stopping is both slowed and more variable in children with ADHD. The results support a response inhibition impairment in ADHD, whilst limiting the extent of an intra-trial variability deficit.

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J Clin Psychiatry. 2008;69:1462-68.

**Olfactory impairments in child attention-deficit/hyperactivity disorder.**

**Karsz FR, Vance A, Anderson VA, et al.**

**Objective:** This study compared unilateral olfactory identification abilities in children with and without attention-deficit/hyperactivity disorder (ADHD) and evaluated the utility of the University of Pennsylvania Smell Identification Test (UPSIT) as a potential screening tool for the diagnosis of ADHD.

**Method:** Subjects comprised 44 children with DSM-IV ADHD (aged 7-16 years) from 2 Melbourne, Australia, hospital outpatient clinics and 44 healthy children matched for age and sex. The children were assessed from March 2004 to October 2004 for olfactory identification ability using the UPSIT, and behavioral data were gathered using the Rowe Behavioral Rating Inventory. Background and demographic data were also obtained through hospital records and parental interview.

**Results:** Children with ADHD demonstrated significantly poorer olfactory identification ability compared to healthy controls ( $p < .01$ ). A significant right nostril advantage for smell identification was evident in the control group ( $p < .01$ ), whereas significant right nostril impairment was evident among the children with ADHD ( $p < .01$ ).

**Conclusion:** The results provide the first evidence of olfactory identification deficits in children with ADHD. As such deficits implicate orbitofrontal regions, this finding is consistent with previous reports of prefrontal compromise in children with ADHD.

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J Abnorm Psychol. 2008 Nov;117:869-80.

**Relations between multi-informant assessments of ADHD symptoms, DAT1, and DRD4.**

**Gizer IR, Waldman ID, Abramowitz A, et al.**

Researchers conducting candidate gene studies of attention-deficit/hyperactivity disorder (ADHD) typically obtain symptom ratings from multiple informants (i.e., mothers, fathers, and teachers) and use a psychologist's best estimate or a simple algorithm, such as taking the highest symptom ratings across informants, to construct diagnostic phenotypes for estimating association. Nonetheless, these methods have never been empirically validated in the context of a molecular genetic study. In the current study, the authors systematically evaluated several methods of operationalizing phenotypes and the resulting evidence for association between ADHD and the candidate genes: dopamine transporter gene (DAT1) and dopamine D4 receptor gene (DRD4). Use of symptom scores as continuous scales in regression analysis suggested that the combination of mother and teacher ratings yielded the strongest evidence for association between hyperactive-impulsive ADHD symptoms and DAT1 and between inattentive ADHD symptoms and DRD4. Teacher ratings alone were sufficient for evaluating the association between inattentive symptoms and DAT1. Further, this regression-based method consistently yielded stronger evidence for association among ADHD symptoms, DAT1, and DRD4 than did three simple algorithms (i.e., the and, or, and averaging rules). The implications of these results for future molecular genetic studies of ADHD are discussed.

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Pharm Weekbl Wet Platform. 2008;2:183-87.

**Retrospective, observational study of switching or discontinuing ADHD medication.**

**Pauw RT, Dieleman HG, De Vogel EM, et al.**

**Objective:** In patients starting ADHD medication, we investigated the percentage that continued, switched or stopped the medication. Secondly, we wanted to define determinants that could predict switching or discontinuing ADHD medication.

**Design and methods:** Included were ADHD patients (according to DSM IV criteria), aged 6-21 years and treated in outpatient clinics for child and adolescent psychiatry in Dordrecht and Gorinchem, The Netherlands. They all started their ADHD medication between January 2005 and December 2006. We collected age, gender, severity of ADHD (AVL < or (greater-than or equal to)20, which is the Dutch version of the ADHD rating scale-IV), initial medication, switch or no switch, reason for switch, co-medication, co-

morbidity (psychological and somatic) and treating psychiatrist from the electronic patient file. A multiple regression analysis was performed.

**Results:** 169 patients were included. 87% started with short-acting methylphenidate. 42.0% continued the initial medication, 50.3% switched at least once and 7.7% discontinued medication. 80% switched from short-acting to long-acting methylphenidate. Switches or stops were observed more in patients with AVL (greater-than or equal to)20 and/or with co-medication ( $p < 0.05$ ). We also observed a trend to switch and stop medication in patients older than 12 years and/or with somatic co-morbidity ( $p = 0.1$ ). Reasons to switch or stop were inefficacy, non-adherence and rebound. Side-effects did not affect the frequency of switching or stopping.

**Conclusion:** This study shows that 42.0% of the ADHD-patients appear to be satisfied with the started ADHD medication, 50.3% switches to other ADHD-medication and that 7.7% quits their medication. In patients over 12 years old, with 'severe ADHD', co-medication and/or somatic co-morbidity, doctors might consider starting long-acting ADHD-medication initially

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Eur J Paediatr Neurol. 2008;12:461-69.

**Somatosensory functioning and experienced pain in ADHD-families: A pilot study.**

**Scherder EJA, Rommelse NNJ, Broring T, et al .**

**Background:** An issue somewhat overlooked in children with Attention Deficit/Hyperactivity Disorder (ADHD) is somatosensory functioning. Some studies show a deficit in the processing of tactile and kinesthetic stimuli, but more research is needed to confirm these findings. A related topic, namely the subjective experience of pain, has not been investigated. Also unknown is the somatosensory functioning and experienced pain of non-affected siblings of children with ADHD, which may shed light on the familiarity of possible alterations in somatosensory functioning and experienced pain. Therefore, the present study aimed to investigate these aspects in children with ADHD and their non-affected siblings, and to investigate how these aspects were related to each other.

**Method:** Somatosensory functioning (tactile perception and kinesthesia) and subjective intensity and emotionality of pain experiences were examined in 50 children with ADHD, their 38 non-affected siblings and 35 normal controls.

**Results:** Both children with ADHD and their non-affected siblings showed deficits in tactile perception, though kinesthesia appeared unimpaired. Non-affected siblings reported a significant lower intensity and emotionality of past experienced pain than controls. The 'objective' tests of somatosensory functioning did not relate to the subjective sensation of pain.

**Conclusions:** Alterations in tactile perception may relate to a familial susceptibility for ADHD. Clinicians should be aware of possible under reportage of experienced pain in siblings of children with ADHD. The intensity and emotionality of pain appears difficult to objectify with somatosensory test.

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J Child Adolesc Psychopharmacol. 2008;18:449-59.

**Stimulant treatment in children with attention-deficit/hyperactivity disorder moderates adolescent academic outcome.**

**Powers RL, Marks DJ, Miller CJ, et al.**

Treatment with psychostimulant medication has been shown to improve scholastic functioning in children with attention-deficit/hyperactivity disorder (ADHD). However, the extent to which long-term academic gains are apparent in those having received such treatment remains elusive. This study examined prospectively the relationship of childhood stimulant treatment to academic functioning during adolescence. Children ( $n = 169$ ) were initially recruited and diagnosed with ADHD when they were 7-11 years old. A subsample of those with childhood ADHD ( $n = 90$ ) was reevaluated on average 9.13 (SD = 1.5) years later. Probands who did and did not receive treatment with stimulant medication were compared to each other and to a never-ADHD comparison group ( $n = 80$ ) on three subtests from the Wechsler Individual Achievement Test-II (WIAT-II), as well as high school grade point average (GPA) and number of retentions in school as derived from school records. Analyses of covariance controlling for severity of childhood ADHD symptoms indicated that

probands treated with psychostimulant medication achieved better academic outcomes, as measured by WIAT-II subtests and high school GPA, than those not treated with psychostimulants ( $p < .05$ ). However, treated probands did not fare as well as the never-ADHD comparison group. Psychostimulant treatment for children with ADHD may benefit long-term adolescent academic performance, although the extent of improvement is likely to vary as a function of multiple factors. (copyright) 2008 Mary Ann Liebert, Inc

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Psychol Med. 2008;38:1595-606.

**Support for an independent familial segregation of executive and intelligence endophenotypes in ADHD families.**

**Rommelse NNJ, Altink ME, Oosterlaan J, et al.**

**Background:** Impairments in executive functioning (EF) and intelligence quotient (IQ) are frequently observed in children with attention deficit hyperactivity disorder (ADHD). The aim of this paper was twofold: first, to examine whether both domains are viable endophenotypic candidates for ADHD and second to investigate whether deficits in both domains tend to co-segregate within families.

**Method:** A large family-based design was used, including 238 ADHD families (545 children) and 147 control families (271 children). Inhibition, visuospatial and verbal working memory, and performance and verbal IQ were analysed.

**Results:** Children with ADHD, and their affected and non-affected siblings were all impaired on the EF measures and verbal IQ (though unimpaired on performance IQ) and all measures correlated between siblings. Correlations and sibling cross-correlations were not significant between EF and IQ, though they were significant between the measures of one domain. Group differences on EF were not explained by group differences on IQ and vice versa. The discrepancy score between EF and IQ correlated between siblings, indicating that siblings resembled each other in their EF-IQ discrepancy instead of having generalized impairments across both domains. Siblings of probands who had an EF but not IQ impairment, showed a comparable disproportionate lower EF score in relation to IQ score. The opposite pattern was not significant.

**Conclusions:** The results supported the viability of EF and IQ as endophenotypic candidates for ADHD. Most findings support an independent familial segregation of both domains. Within EF, similar familial factors influenced inhibition and working memory. Within IQ, similar familial factors influenced verbal and performance IQ.

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J Consult Clin Psychol. 2008;76:905-08.

**Teacher Key Opinion Leaders and Mental Health Consultation in Low-Income Urban Schools.**

**Atkins MS, Frazier SL, Leathers SJ, et al.**

Diffusion theory posits that information is disseminated throughout a social network by the persuasion of key opinion leaders (KOLs). This study examined the relative and combined influence of peer-identified KOL teachers ( $n = 12$ ) and mental health providers ( $n = 21$ ) on classroom teachers' ( $n = 61$ ) self-reported use of commonly recommended classroom practices for children with attention-deficit/hyperactivity disorder in 6 low-income urban African American communities, relative to teachers ( $n = 54$ ) at 4 matched schools who received mental health provider consultation only. Mixed-effects regression models showed that KOLs in collaboration with mental health providers promoted higher rates of teachers' self-reported use of recommended strategies than mental health providers alone, and that these effects were mediated by KOL support but not by mental health provider support. The results suggest an expanded role for KOL teachers as indigenous and natural supports for the dissemination and implementation of school-based mental health programs.

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J Child Adolesc Psychopharmacol. 2008;18:461-73.

**The attention-deficit/hyperactivity disorder medication-related attitudes of patients and their parents.**  
*Harpur RA, Thompson M, Daley D, et al.*

Patient perspectives represent an increasingly important focus in clinical trials of medical treatments for pediatric mental health conditions. This paper describes the development and initial testing of a short, easy to complete, condition specific, measure of patients' and their parents' attitudes regarding drugs used for the treatment of their attention-deficit/hyperactivity disorder (ADHD) - the Southampton ADHD Medication Behaviour and Attitudes scale. On the basis of an initial qualitative study and pilot data, subscales were constructed for both the child and parent versions covering perceived costs and benefits of treatment, patient stigma, and resistance to treatment. The parent version had additional subscales for parental stigma, treatment inconsistency, and flexibility. Factor and reliability analysis of data from 356 parents and 123 of their children supported the distinction between these subscale domains. Children were aged between 5 and 18 years (mean age 10.95 years). Parent and child scores were correlated, although as in previous research parents rated ADHD medications as having more benefits and children rated them as having more costs. The Southampton ADHD Medication Behaviour and Attitudes scale represents a useful addition to the growing portfolio of patient-reported outcomes for ADHD treatments. Future research should focus on the scales value in predicting treatment adherence as it impacts on medication effectiveness.

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J Child Psychol Psychiatry Allied Discip. 2008;49:1053-60.

**The dopamine receptor D4 7-repeat allele and prenatal smoking in ADHD-affected children and their unaffected siblings: No gene-environment interaction.**

*Altink ME, rias-Vasquez A, Franke B, et al.*

**Background:** The dopamine receptor D4 (DRD4) 7-repeat allele and maternal smoking during pregnancy are both considered as risk factors in the aetiology of attention deficit hyperactivity disorder (ADHD), but few studies have been conducted on their interactive effects in causing ADHD. The purpose of this study is to examine the gene by environment (GxE) interaction of the DRD4 7-repeat allele and smoking during pregnancy on ADHD and oppositional behavior in families from the International Multicenter ADHD Genetics project; and further, to test the hypothesis that the direction of effect of the DRD4 7-repeat allele differs between ADHD affected and unaffected children.

**Methods:** Linear mixed models were used to assess main and interactive effects of the DRD4 7-repeat allele and smoking during pregnancy in 539 ADHD-affected children and their 407 unaffected siblings, aged 6-17 years.

**Results:** There was some evidence pointing to differential effects of the DRD4 7-repeat allele on ADHD and oppositional symptoms in the affected (fewer symptoms) and unaffected children (increasing ADHD symptoms of teacher ratings). Affected children were more often exposed to prenatal smoking than unaffected children. There were limited main effects of prenatal smoking on severity of symptoms. Given the number of tests performed, no indication was found for GxE interactions.

**Conclusion:** Despite the large sample size, no GxE interactions were found. The impact of the DRD4 7-repeat allele might differ, depending on affected status and rater. This finding is discussed in terms of differences in the activity of the dopaminergic system and of different genes involved in rater-specific behaviors.

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Biol Psychol. 2008;79:329-36.

**The effects of childhood disruptive disorder comorbidity on P3 event-related brain potentials in preadolescents with ADHD.**

*Yoon HH, Iacono WG, Malone SM, et al.*

The present study examined the degree to which the P300 component of the visual brain event-related potential and associated task performance deficits often observed in children with attention-deficit hyperactivity disorder (ADHD) are attributable to comorbid childhood disruptive disorders using a community

sample of 11-year olds from the Minnesota Twin Family Study. Subjects were divided into "ADHD-pure" (ADHD without oppositional defiant disorder, ODD, or conduct disorder, CD), "ADHD-comorbid" (ADHD with ODD or CD), and comparison (no childhood disruptive disorder) groups using DSM-III-R diagnoses. Results showed that ADHD-comorbid but not ADHD-pure subjects displayed significant P3 amplitude reduction and poorer task performance compared to controls. No group effects for P3 latency or reaction time were seen. Although ADHD-comorbid children had marginally more ADHD symptoms compared to ADHD-pure children, this did not account for their reduced P3, suggesting that the observed neurobehavioral deficits reflected the effects of co-occurring childhood disruptive disorders.  
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Nicotine Tob Res. 2008;10:1549-58.

**The familial association between cigarette smoking and ADHD: A study of clinically referred girls with and without ADHD, and their families.**

**Monuteaux MC, Faraone SV, Hammerness P, et al.**

Attention-deficit/hyperactivity disorder (ADHD) is a strong risk factor for smoking. Since both ADHD and smoking are familial disorders, one way to further our understanding of this association is to examine the familial relationship between them. Our aim was to evaluate the familial association between ADHD and smoking in families ascertained from girls with and without ADHD. Subjects were derived from a longitudinal case-control family study of girls with (n = 140) and without (n = 122) ADHD ascertained from pediatric and psychiatric clinics, and their biological first-degree relatives. Diagnoses of ADHD and smoking (i.e., full or subthreshold nicotine dependence) were made with structured psychiatric interviews. We stratified the relatives into four groups based on probands' ADHD and smoking status: (1) relatives of controls without smoking (probands n = 100, relatives n = 317), (2) relatives of controls with smoking (probands n = 22, relatives n = 71), (3) relatives of ADHD girls without smoking (probands n = 100, relatives n = 320), and (4) relatives of ADHD girls with smoking (probands n = 39, relatives n = 133). We compared the rates of ADHD and smoking across the four relative groups using survival analysis. ADHD in the proband increased the risk for ADHD in the relatives irrespective of probands' smoking and smoking in the proband increased the risk for smoking in the relatives irrespective of probands' ADHD status. Furthermore, we found statistically significant evidence for cosegregation of smoking and ADHD, suggesting that the two disorders are transmitted together through families more often than expected by chance. These findings support the hypothesis that the combination of ADHD and smoking comprises an etiologically distinct familial subtype of ADHD in girls

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