



ADHD

ATTENTION DEFICIT HYPERACTIVITY DISORDER


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Journal of Attention Disorders. 2009 Jan;12:341-52.

Selective and sustained attention as predictors of social problems in children with typical and disordered attention abilities.

Andrade BF, Brodeur DA, Waschbusch DA, et al.

Objective: Investigated the relationship between selective and sustained attention and social behavior in children with different degrees of attentional disturbance.

Method: Participants were 101 6- to 12-year-old children, including 18 who were diagnosed with Attention Deficit Hyperactivity Disorder (AD/HD), 61 who were clinically referred for attentional difficulties but did not meet criteria for ADHD, and 22 typically developing children. Two groups of children completed either a sustained attention task or a selective attention task. Task performance was compared with teacher reported social behavior.

Results: In support of the investigator's hypothesis poor performance on the sustained attention task correlated with social behavior problems. However, contrary to expectation, poor performance on the selective attention task was not correlated with teacher reported social problems. Results are discussed with specific emphasis on the need to identify underlying cognitive contributions to social dysfunction.

Conclusion: The findings support a growing body of research highlighting the negative relationship between inattention and social functioning.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1369-78.

Conduct disorder and ADHD: Evaluation of conduct problems as a categorical and quantitative trait in the international multicentre ADHD genetics study.

Anney RJL, Lasky-Su J, O'Dushlaine C, et al.

Attention-deficit/hyperactivity disorder (ADHD) is typically characterized by inattention, excessive motor activity, impulsivity, and distractibility. Individuals with ADHD have significant impairment in family and peer relations, academic functioning, and show high co-morbidity with a wide range of psychiatric disorders including oppositional defiant disorder (ODD), conduct disorder (CD), anxiety disorder, depression, substance abuse, and pervasive developmental disorder (PDD). Family studies suggest that ADHD + CD represents a specific subtype of the ADHD disorder with familial risk factors only partly overlapping with those of ADHD alone. We performed a hypothesis-free analysis of the GAIN-ADHD sample to identify markers and genes important in the development of conduct problems in a European cohort of individuals with ADHD. Using the Family-Based Association Test (FBAT) package we examined three measures of conduct problems in 1,043,963 autosomal markers. This study is part of a series of exploratory analyses to identify candidate genes that may be important in ADHD and ADHD-related traits, such as conduct problems. We did not find genome-wide statistical significance ($P < 5 \times 10^{-7}$) for any of the tested markers and the three conduct problem traits. Fifty-four markers reached strong GWA signals ($P < 10^{-2}$). We discuss these findings in the context of putative candidate genes and the implications of these findings in the understanding of the etiology of ADHD + CD. We aimed to achieve insight into the genetic etiology of a trait

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.

using a hypothesis-free study design and were able to identify a number of biologically interesting markers and genes for follow-up studies.
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Psychiatr Hung. 2008;23:324-35.

[Neuropsychological impairments in adult attention deficit hyperactivity disorder: a literature review].

Balint S, Czobor P, Meszaros A, et al.

INTRODUCTION: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most frequently diagnosed childhood psychiatric disorders. Based on various empirical estimates, symptoms of ADHD persist into adulthood in about 30-50% of the childhood cases.

METHOD: The objective of the present investigation was to conduct a systematic review of neuropsychological studies to characterize executive and attentional performance in subjects with adult ADHD and to examine whether these neuropsychological tools are useful to diagnose the disorder. 29 relevant publications were identified from 1993 to 2007 via a comprehensive research in Medline and Pubmed databases.

RESULTS: The neuropsychological characteristics of adults with ADHD are comparable to those described in the pediatric population. Results indicate that in ADHD the frontal lobe neurocognitive functions, such as attention, planning, behaviour inhibition and problem solving, are the ones primarily impaired in the disorder.

DISCUSSION: A better understanding of the nature and extent of the impairment of the cognitive functions involved in the disorder would offer opportunities for the development of disease-specific cognitive therapies and psychopharmacological therapies for patients with ADHD. Furthermore, a finer specification of the neurocognitive profile in adult ADHD might be of great importance as a sensitive marker for the efficacy of pharmaceutical agents

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1511-18.

Sexually dimorphic effects of four genes (COMT, SLC6A2, MAOA, SLC6A4) in genetic associations of ADHD: A preliminary study.

Biederman J, Kim JW, Doyle AE, et al.

A growing body of literature finds gender differences in ADHD. However, little is known about the causes of these differences. One possibility is that ADHD risk genes have sexually dimorphic effects. We have investigated four ADHD candidate genes (COMT, SLC6A2, MAOA, SLC6A4) for which there is evidence of sexually dimorphic effects. Past neurobiological and genetic studies suggest that COMT, and SLC6A4 variants may have a greater influence on males and that SLC6A2, and MAOA variants may have a greater influence on females. Our results indicate that genetic associations are stronger when stratified by sex and in the same direction as the previous neurobiological studies indicate: associations were stronger in males for COMT, SLC6A4 and stronger in females for SLC6A2, MAOA. Moreover, we found a statistically significant gender effect in the case of COMT ($P = 0.007$) when we pooled our work with a prior study. In conclusion, we have found some evidence suggesting that the genetic association for these genes with ADHD may be influenced by the sex of the affected individual. Although our results are not fully validated yet, they should motivate further investigation of gender effects in ADHD genetic association studies.

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Tijdschr Geneesk. 2008;64:1237-40.

Stimulants in the treatment of ADHD in children.

Boie A, Verhelst H.

ADHD is a common psychiatric disorder during childhood and adolescence. The increasing use of psychoactive drugs to treat children with ADHD has raised major concerns about their adverse effects. The most common adverse effects of the most frequently used product, methylphenidate, include: anorexia, weight loss, sleeping disorders and fluctuations in blood pressure. The casuistic reports of sudden death upon administering methylphenidate occur mainly in children with a cardiac risk. The use of psychoactive drugs is not linked to the risk for substance abuse disorder in later life. Thus and although methylphenidate has been proven safe, it remains important to select those children who really need medication and to evaluate carefully the advantages and the possible risks of this treatment.

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1519-23.

Association of ADHD with genetic variants in the 5'-region of the dopamine transporter gene: Evidence for allelic heterogeneity.

Brookes KJ, Xu X, Anney R, et al.

Multiple studies have reported an association between attention deficit hyperactivity disorder (ADHD) and the 10-repeat allele of a variable number tandem repeat (VNTR) polymorphism in the 30-untranslated region (3'UTR) of the dopamine transporter gene (DAT1). Yet, recent meta-analyses of available data find little or no evidence for this association; although there is strong evidence for heterogeneity between datasets. This pattern of findings could arise for several reasons including the presence of relatively rare risk alleles on common haplotype backgrounds or the functional interaction of two or more loci within the gene. We previously described the importance of a specific haplotype at the 30 end of DAT1, as well as the identification of associated single nucleotide polymorphisms (SNPs) within or close to 50 regulatory sequences. In this study we replicate the association of SNPs at the 50 end of the gene and identify a specific risk haplotype spanning the 50 and 30 markers. These findings indicate the presence of at least two loci associated with ADHD within the DAT1 gene and suggest that either additive or interaction effects of these two loci on the risk for ADHD. Overall these data provide further evidence that genetic variants of the dopamine transporter gene confer an increased risk for ADHD. (copyright) 2008 Wiley-Liss, Inc

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1531-35.

Association of the steroid sulfatase (STS) gene with attention deficit hyperactivity disorder.

Brookes KJ, Hawi Z, Kirley A, et al.

Attention deficit hyperactivity disorder (ADHD) is the most common behavioral disorder affecting children worldwide. The male bias in the prevalence of the disorder, suggests that some susceptibility genes may lie on the X chromosome. In this study we present evidence for a role of the X-linked steroid sulfatase (STS) gene and neurosteroids in the development of ADHD. Previously it has been observed that probands with ADHD have lower serum concentrations of the neurosteroids DHEA, which is synthesized from DHEA-S-bySTS. In further support, boys that suffer from XLI, a skin disorder caused by the deletion of the STS gene, have higher rates of ADHD, in particular the inattentive subtype. In a moderately sized sample of ADHD families (N = 384), we genotyped seven single nucleotide polymorphisms, tagging the entire gene. TDT analysis of the data yielded two polymorphisms that were significantly associated with ADHD (rs2770112 - Transmitted: 71 Not Transmitted: 48; rs12861247 - Transmitted: 43 Not Transmitted: 21), located towards the 5' end of the gene (P < 0.05). We conclude that the STS gene may play a role in susceptibility for ADHD, and that the neurosteroids pathways should be investigated further to assess their potential contribution in susceptibility to the disorder. (copyright) 2008 Wiley-Liss, Inc

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1450-60.

DSM-IV combined type ADHD shows familial association with sibling trait scores: A sampling strategy for QTL linkage.

Chen W, Zhou K, Sham P, et al.

Attention deficit hyperactivity disorder (ADHD) is a discrete clinical syndrome characterized by the triad of inattention, hyperactivity, and impulsivity in the context of marked impairments. Molecular genetic studies have been successful in identifying genetic variants associated with ADHD, particularly with DSM-IV inattentive and combined subtypes. Quantitative trait locus (QTL) approaches to linkage and association mapping have yet to be widely used in ADHD research, although twin studies investigating individual differences suggest that genetic liability for ADHD is continuously distributed throughout the population, underscoring the applicability of quantitative dimensional approaches. To investigate the appropriateness of QTL approaches, we tested the familial association between 894 probands with a research diagnosis of DSM-IV ADHD combined type and continuous trait measures among 1,135 of their siblings unselected for phenotype. The sibling recurrence rate for ADHD combined subtype was 12.7%, yielding a sibling recurrence risk ratio ((lambda)sib) of 9.0. Estimated sibling correlations around 0.2-0.3 are similar to those estimated from the analysis of fraternal twins in population twin samples. We further show that there are no threshold effects on the sibling risk for ADHD among the ADHD probands; and that both affected and unaffected siblings contributed to the association with ADHD trait scores. In conclusion, these data confirm the main requirement for QTL mapping of ADHD by demonstrating that narrowly defined DSM-IV combined type probands show familial association with dimensional ADHD symptom scores amongst their siblings. (copyright) 2008 Wiley-Liss, Inc

Cyberpsychol Behav. 2008;11:735-37.

Biogenetic temperament and character profiles and attention deficit hyperactivity disorder symptoms in Korean adolescents with problematic internet use.

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

The objective of this study was to evaluate the biogenetic temperament and character profiles in Korean adolescents with problematic Internet use. Six hundred eighty-six high school students completed the Internet Addiction Test (IAT), Junior Temperament and Character Inventory (JTCI), and Conners/Wells Adolescent Self-Report Scale: Short Form (CASS: Short). The problematic Internet use group showed higher scores in the Self-Directedness and Cooperativeness profiles and lower scores in the Novelty Seeking and Self-Transcendence profiles of the JTCI, compared with the nonproblematic Internet use group, after controlling for the ADHD symptoms. The results of this study suggest that temperament/character patterns should be considered in accounts of the etiology of problematic Internet use.

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Zh Nevrol Psikhiatr Im S S Korsakova. 2008;108:75-80.

[Attention deficit hyperactivity disorder: clinical heterogeneity and possibilities of therapy].

Chutko LS, Surushkina SI.

Journal of Attention Disorders. 2009 Jan;12:330-40.

ADHD and health services utilization in the National Health Interview Survey.

Cuffe SP, Moore CG, McKeown R.

Objective: Describe the general health, comorbidities and health service use among U.S. children with ADHD.

Method: The 2001 National Health Interview Survey (NHIS) contained the Strengths and Difficulties Questionnaire (SDQ; used to determine probable ADHD), data on medical problems, overall health, and health care utilization.

Results: Asthma was two and headaches were three times more prevalent, and overall health was significantly lower, among children with SDQ ADHD. Of children with SDQ ADHD, 45% saw a mental health professional in the past year and over half were not taking medication regularly. Urban residence, age (9-13), higher family education, having health insurance, and having comorbid emotional problems were associated with mental health care utilization in children with SDQ AD/HD, while race, gender and family income were not associated.

Conclusions: Children with SDQ AD/HD had more medical problems and were more likely to visit the emergency room. Treatment data suggest a problem with under-treatment of ADHD in the United States. Interventions should be targeted in rural areas, and among families with low education and without health insurance. (PsychINFO Database Record (c) 2009 APA, all rights reserved) (from the journal abstract)

J Child Adolesc Psychopharmacol. 2008;18:565-71.

A review of co-morbid depression in pediatric ADHD: Etiology, phenomenology, and treatment.

Daviss WB.

This paper reviews the literature and highlights the need for further research regarding the phenomenology, etiology, assessment, and treatment of co-morbid depression in patients with attention-deficit/hyperactivity disorders (ADHD). Depression occurs in youths with ADHD at a significantly higher rate than in youths without ADHD. Youths with ADHD and depression together have a more severe course of psychopathology and a higher risk of long-term impairment and suicide than youths with either disorder alone. Assessment of such co-morbid depression is complicated by overlapping symptoms with ADHD and with other disorders that commonly occur with ADHD. Depressive disorders typically emerge several years after the onset of ADHD and may arise from environmental difficulties associated with chronic ADHD that interact with genetic risks as the child gets older. Despite a scarcity of well-designed treatment studies for youths with ADHD and co-morbid depression, there is increasing preliminary evidence for the role of stimulants, selective serotonergic reuptake inhibitors, bupropion, and atomoxetine to target either or both disorders. There is also some indirect evidence for the benefit of combining pharmacological treatments with psychosocial interventions that specifically target relevant environmental factors and functional impairments.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1399-411.

Multivariate genomewide linkage scan of neurocognitive traits and ADHD symptoms: Suggestive linkage to 3q13.

Doyle AE, Ferreira MAR, Sklar PB, et al.

Family and twin studies suggest that a range of neurocognitive traits index the inherited liability to ADHD; however, the utility of such measures as endophenotypes in molecular genetic studies remains largely untested. The current article examined whether the inclusion of neurocognitive measures in a genomewide linkage analysis of ADHD could aid in identifying QTL linked to the behavioral symptoms of the condition. Data were from an affected sibling pair linkage study of DSM-IV ADHD conducted at Massachusetts General Hospital. The sample included 1,212 individuals from 271 families. ADHD symptoms were assessed with the K-SADS-E. The neurocognitive battery included Wechsler Intelligence Scales subtests, the Stroop, the Wisconsin Card Sorting Test (WCST), the Rey-Osterreith Complex Figure, a working memory CPT, the CVLT and WRAT-III subscales. Evidence for linkage was assessed using a simulation-based method that combines information from univariate analyses into the equivalent of a multivariate test. After correction for multiple trait testing, a region on chromosome 3q13 showed suggestive linkage to all neurocognitive traits examined and inattention symptoms of ADHD. The second highest peak occurred on 22q12 but showed linkage to a single subscale of the WCST. In univariate analysis, this region retained criteria for suggestive linkage to this measure after correction for multiple trait testing. Our primary findings raise the possibility that one or more genes on 3q13 influence neurocognitive functions and behavioral symptoms of inattention. Overall, these data support the utility of neurocognitive traits as ADHD endophenotypes, but also highlight their limited genetic overlap with the disorder.

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Z Kinder- Jugendpsychiatr Psychother. 2008;36:419-26.

Attention deficit disorders after stroke in childhood.

Eikermann A, Petermann F, Daseking M.

Objective: The present study investigates whether attention deficits increase after stroke in childhood and identifies influencing factors.

Methods: The attentional functions of 78 children who suffered strokes were evaluated by means of neuropsychological assessments for attention abilities, the CBCL/4-18, and a standardized observation of behavior. The results were compared for age at the time of the stroke, affected hemisphere, and localisation.

Results: Children and adolescents develop attention deficits due to stroke. There seems to be no influence of sex, age at stroke or localisation of stroke. Children with right-hemispheric brain damage tend to develop more attention deficits than children with left-hemispheric stroke.

Conclusions: There is a need for an early diagnosis and the initiation of an effective treatment to avoid collateral disorders and school problems.

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European Child & Adolescent Psychiatry. 2008 Dec;17:106-15.

Psychometric properties of two ADHD questionnaires: comparing the Conners' scale and the FBB-HKS in the general population of German children and adolescents--Results of the BELLA study.

Erhart M, Döpfner M, Ravens-Sieberer U.

Background and objective To examine and compare the psychometric properties of two short screening instruments for children and adolescents suffering from attention deficit-/ hyperactivity disorder (ADHD). The Conners' Hyperactivity Index consists of ten items that assess symptoms of hyperactivity through self-report and parents' proxy. The German ADHD Rating scale (FBBHKS/ ADHS) consists of 20 items that assess the severity and perceived burden of inattention, hyperactivity, and impulsiveness as defined by the ICD-10 and DSM-IV. **Methods** Within the BELLA module of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS), the parents of 2,863 children and adolescents rated the Conners' Hyperactivity Index and the FBB-HKS. **Results** The internal consistency of item responses was assessed via Cronbach's α and showed that both instrument scores were able to obtain a reliable measurement. The factorial validity of the FBBHKS measurement model as well as the unidimensionality of the Conners' scale was tested by means of exploratory and confirmatory factor analysis (EFA and CFA), indicating satisfactory goodness of fit for the FBB-HKS (RMSEA = 0.06) and some deviation from the unidimensionality assumption of the Conners' scale. Stability of results across age could be confirmed with few exceptions. Mean scores differences were found between both sexes, age groups, and different socioeconomic status groups (Winkler-Index) with males, younger respondents, and children with low socioeconomic status displaying

more ADHD-related behaviour. Correlation coefficients between the two instruments' scores and other scales assessing emotional and behavioural problems hinted at convergent validity. Conclusion Both instruments' scores showed reliability as well as factorial and convergent/discriminant validity. The pros and cons of the two instruments as well as for which purpose and under which circumstances one of the measures can be favoured must be considered prior to applying such a measure.
(PsycINFO Database Record (c) 2009 APA, all rights reserved) (from the journal abstract)

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1387-91.

Linkage analysis of attention deficit hyperactivity disorder.

Faraone SV, Doyle AE, Lasky-Su J, et al.

Results of behavioral genetic and molecular genetic studies have converged to suggest that both genes contribute to the development of ADHD. Although prior linkage studies have produced intriguing results, their results have been inconsistent, with no clear pattern of results emerging across studies. We genotyped 5,980 SNPs across the genome in 1,187 individuals from families with children diagnosed with ADHD. We then performed two nonparametric linkage analyses on ADHD families: (1) an affected sibling pair linkage analysis on 217 families with 601 siblings diagnosed with ADHD and (2) a variance components linkage analysis using the number of ADHD symptoms as the phenotype on 260 families with 1,100 phenotyped siblings. The affection status linkage analysis had a maximum LOD score of 1.85 on chromosome 8 at 54.2 cM. The maximum LOD score in the variance components linkage analysis was 0.8 on chromosome 8 at 93.4 cM. The absence of regions of significant or suggestive linkage in these data suggest that there are no genes of large effect contributing to the ADHD phenotype.
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Journal of Attention Disorders. 2009 Jan;12:308-15.

Effects of once-daily oral and transdermal methylphenidate on sleep behavior of children with ADHD.

Faraone SV, Glatt SJ, Bukstein OG, et al.

Objective: Methylphenidate is a leading first-line treatment for ADHD (AD/HD). This stimulant has long been suspected to adversely affect sleeping patterns of treated individuals, especially children. There are few studies on the effects of recently developed longer-acting methylphenidate treatments, such as once-daily oral or transdermal formulations, on sleep.

Method: The authors examined eight indices of sleep behavior among children treated with either of these two methylphenidate preparations or placebo in a randomized, double-blind, multicenter, parallel-group study.

Results: The main predictor of sleep problems was baseline numbers or severity of preexisting sleep problems, whereas the different treatments and placebo varied little in their propensity to elicit such problems. There was no significant relationship between dosage and severity or frequency of sleep problems.

Conclusion: The authors found little evidence that methylphenidate treatment (at least in sustained-release forms) was a significant cause of sleep problems in treated children who were carefully titrated to an optimal dose.

(PsycINFO Database Record (c) 2009 APA, all rights reserved) (from the journal abstract)

Journal of the American Academy of Child & Adolescent Psychiatry. 2009 Jan;48:25-34.

ADHD and poor motor performance from a family genetic perspective.

Fliers E, Vermeulen S, Rijdsdijk Fh, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is frequently accompanied by motor problems (MPs). We investigated a possible shared etiology between the two traits in the Dutch sample of the International Multicenter ADHD Genetics study comprising 275 children with ADHD and their affected or unaffected sibling and 146 unrelated control children.

Method: Exploratory data analysis and bivariate structural equation modeling were used to estimate the familiarity of MP rated by parents (Developmental Coordination Disorder Questionnaire [DCD-Q]) or teachers (Groningen Motor Observation Scale [GMO]) and to determine the familial and environmental correlation between MP and ADHD. Furthermore, the nature of the familiarity was explored by studying the siblings of ADHD-affected children.

Results: The ADHD-affected children had significantly more MP than their unaffected siblings, who in turn had significantly more MP than the control subjects. The familial component of MP measured by DCD-Q and GMO was 47% and 22%, respectively. The familial correlation between motor performance measures and ADHD was -0.38 for DCD-Q and -0.40 for GMO. Our data suggested that co-occurrence of ADHD and MP possibly marks a distinct subtype of ADHD, rather than signaling increased severity of disease.

Conclusions: Attention-deficit/hyperactivity disorder and MP have a common basis that may be due to genetic factors and/or shared environmental factors. Attention-deficit/hyperactivity disorder accompanied by MP may behave like a distinct subtype of ADHD, but more research will be needed to support that hypothesis.

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Br J Psychiatry. 2009 Jan;194:62-67.

Psychopathy traits in adolescents with childhood attention-deficit hyperactivity disorder.

Fowler T, Langley K, Rice F, et al.

BACKGROUND: Children with attention-deficit hyperactivity disorder (ADHD) are thought to be at higher risk of psychopathy. Early biological and social adversity may contribute to this risk. **AIMS:** To examine psychopathy traits in ADHD.

METHOD: In a sample of children with ADHD who had reached adolescence, total psychopathy and 'emotional-dysfunction' scores (e.g. callousness, lack of affect) were assessed using the Hare Psychopathy Checklist-Youth Version.

RESULTS: A total of 156 (79%) eligible families participated. Total psychopathy and emotional-dysfunction scores were elevated in comparison to published UK norms but none scored in the clinical range for psychopathy. Adjusting for associated conduct problems, total psychopathy scores were associated with maternal smoking during pregnancy, emotional-dysfunction scores were associated with birth complications, and neither was associated with family adversity.

CONCLUSIONS: Children with ADHD show psychopathy traits but are not 'psychopaths'. Early adversity, indexed by pre- or perinatal adversity but not family factors, appears to be associated

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1568-75.

A common haplotype at the dopamine transporter gene 5' region is associated with attention-deficit/hyperactivity disorder.

Genro JP, Polanczyk GV, Zeni C, et al.

The dopamine transporter (DAT) is the major site of methylphenidate action, which is one of the main drugs used to treat attention-deficit/hyperactivity disorder (ADHD). Most association studies with ADHD focused in a VNTR at the 3'-untranslated region of the gene (3'UTR) presenting conflicting results. However, the most common explanation to inconsistent results is variable linkage disequilibrium with an adjacent functional variant, just a few number of DAT1 studies have reported LD structure across the gene. In this study, we screened 16 polymorphisms across the DAT1 gene to understand LD structure in a Brazilian sample of families with ADHD probands and to verify if there were evidence for a biased transmission of alleles and haplotypes from parents to their 243 children with ADHD. In the DSM-IV combined subtype, we observed a preferential transmission of the haplotype A/C/C/C/A derived from five SNPs (rs2550948, rs11564750, rs261759, rs2652511, rs2975223) in 5' region (P corrected = 0.018) and no association with any allele/haplotype at the 3' region of the gene, including the 3' VNTR and the VNTR of intron 8. These results suggest a role for the promoter region in ADHD susceptibility and that allele heterogeneity should be highly considered in DAT1 gene association studies highlighting the importance of this gene in the genetics of the disorder.

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Arch Iran Med. 2008;11:618-24.

Distribution of symptoms of attention deficit-hyperactivity disorder in schoolchildren of Shiraz, South of Iran.

Ghanizadeh A.

Background: This study was conducted to study the prevalence rate of attention deficit hyperactivity disorder symptoms and differences between subtypes in school age children of Shiraz, south of Iran.

Methods: A random sample of 2000 school age children from both genders was selected. A parent-completed, DSM-IV-referenced rating scale of attention deficit hyperactivity symptoms was used.

Results: About 10.1% of participants obtained screening cutoff scores for attention deficit hyperactivity; 13.6% in boys and 6.5% in girls. The most common type of probable attention deficit hyperactivity in boys and girls was the hyperactive-impulsive type of attention deficit hyperactivity and the least frequent type was the combined type of attention deficit hyperactivity.

Conclusion: The rate of probable attention deficit hyperactivity in Shiraz, southern Iran is very similar to other counties and it is more common in boys than girls.

Int J Pediatr Otorhinolaryngol. 2009;73:81-87.

Screening signs of auditory processing problem: Does it distinguish attention deficit hyperactivity disorder subtypes in a clinical sample of children?

Ghanizadeh A.

Objectives: The aim of this study is to survey parental report of screening signs of auditory processing problem in attention deficit hyperactivity disorder (ADHD) children and its association with gender and comorbidity with oppositional defiant disorder (ODD) and separation anxiety (SAD).

Methods: 104 children and adolescents referrals to the child and adolescent psychiatry clinic were interviewed. The auditory processing problem checklist asked parents to indicate their child's reaction to sounds. It screens signs of two aspects of auditory processing problem including hypersensitivity to sounds (HES) (or auditory defensiveness) and hyposensitivity to sound (HOS) (under-registers).

Results: The mean age of the children was 8.5 (SD = 1.8). Children with ODD had significantly higher HES, HOS and the whole checklist mean scores. Subtypes of ADHD were not associated with the auditory processing problems.

Conclusions: ADHD children with ODD are likely to be at a significant risk for manifesting both of the auditory processing problem including defensiveness and auditory hyposensitivity to sounds. Auditory processing problems do not differentiate different subtypes of ADHD.

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J Clin Psychopharmacol. 2008 Dec;28:725-26.

Insomnia, night terror, and depression related to clonidine in attention-deficit/hyperactivity disorder.

Ghanizadeh A.

This report is about a child with attention-deficit/hyperactivity disorder (ADHD) who experienced insomnia, night terrors, and depression associated with the long-term use of clonidine. He revealed resolution of insomnia and night terror when clonidine was removed.

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J Child Adolesc Psychopharmacol. 2008 Oct;18:413-47.

Psychopharmacological and other treatments in preschool children with attention-deficit/hyperactivity disorder: Current evidence and practice.

Ghuman JK, Arnold LE, Anthony BJ.

Objective: This article reviews rational approaches to treating attention-deficit/hyperactivity disorder (ADHD) in preschool children, including pharmacological and nonpharmacological treatments. Implications for clinical practice are discussed.

Data Sources: We searched MEDLINE, PsycINFO, Cumulative Index to Nursing & Allied Health, Educational Resources Information Center, Cochrane Database of Systematic Reviews and Database of Abstracts of Reviews of Effects for relevant literature published in English from 1967 to 2007 on preschool ADHD. We also reviewed the references cited in identified reports.

Study Selection: Studies were reviewed if the sample included at least some children younger than 6 years of age or attending kindergarten, the study participants had a diagnosis of ADHD or equivalent symptoms, received intervention aimed at ADHD symptoms, and included a relevant outcome measure.

Data Extraction: Studies were reviewed for type of intervention and outcome relevant to ADHD and were rated for the level of evidence for adequacy of the data to inform clinical practice.

Conclusions: The current level of evidence for adequacy of empirical data to inform clinical practice for short-term treatment of ADHD in preschool children is Level A for methylphenidate and Level B for parent behavior training, child training, and additive-free elimination diet.

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Journal of Attention Disorders. 2009 Jan;12:386-88.

Current literature in ADHD summarized by Sam Goldstein.

Goldstein S.

A collection of abstracts focusing on children and adolescents who suffer from ADHD.
(PsycINFO Database Record (c) 2009 APA, all rights reserved)

Pediatr Neurol. 2009;40:42-46.

Sleep Study Abnormalities in Children With Attention Deficit Hyperactivity Disorder.

Gojara JS, Cruz M, Valencia I, et al.

The study objective was to describe polysomnographic findings in children with attention deficit hyperactivity disorder (ADHD) with diverse sleep problems. Polysomnographic data were retrospectively analyzed for 33 children (age 3-16 years) with ADHD who had sleep studies performed for diverse sleep complaints. Eight patients (24%) had obstructive sleep apnea, 10 (30%) had periodic limb movements of sleep, 8 (24%) had upper airway resistance syndrome, and 5 (15%) had obstructive hypoventilation. The ADHD group showed decreased sleep efficiency, increased arousal index, increased wake after sleep onset, decreased oxygen saturation nadir, and increased snoring, compared with control subjects. Compared with ADHD children without sleep disordered breathing, those who had sleep disordered breathing were significantly more obese and had more sleep architectural abnormalities (including increased sleep latency, increased rapid eye movement latency, increased wake after sleep onset, and increased arousal index with more oxygen desaturations), although total sleep time and sleep efficiency were not significantly different. Sleep disordered breathing and periodic limb movements of sleep appear to be common among children with ADHD who have symptoms of disturbed sleep.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1547-53.

Attention deficit hyperactivity disorder in obese melanocortin-4-receptor (MC4R) deficient subjects: A newly described expression of MC4R deficiency.

granat-Meged A, Ghanadri Y, Eisenberg I, et al.

Attention deficit hyperactivity disorder (ADHD) is a heterogeneous highly heritable disorder which has recently been described to be comorbid in obese subjects. This study investigated phenotype/genotype associations in a consanguineous family with genetic obesity due to the melanocortin-4-receptor (MC4R) (C271R) mutation. MC4R deficiency disrupts hunger/satiety regulation resulting in abnormal eating behaviors. To date, the behavioral/psychiatric characteristics of MC4R deficiency have not been described except for a possible association with Binge Eating Disorder. Twenty-nine subjects of a family known to carry the MC4R (C271R) mutation, were genotyped for the mutation and underwent extensive evaluations in search for physical/psychiatric phenotype characteristics. Subjects originated from proband nuclear families with morbid obese children (BMI percentile > 97%). All probands were homozygous for the MC4R (C271R) mutation. ADHD prevalence was higher than expected only in the groups carrying the homozygous or heterozygous mutation ($P = 0.00057$, 0.0028 , respectively). An obvious difference was observed between the homozygous group and the rest of the family in terms of obesity: homozygous subjects had childhood morbid obesity whereas heterozygous subjects included lean, normal weight and later onset obese subjects. A significant difference was found in ADHD prevalence between the homozygous MC4R (C271R) group (80%) and the rest of the family (22%) ($P = 0.033$) and a significant trend was found between ADHD prevalence and the number of MC4R (C271R) alleles ($P = 0.0267$). We conclude that in our sample, the MC4R (C271R) mutation causing obesity, is in association with ADHD. Identifying specific subgroups in which the comorbidity of obesity and ADHD occur may contribute to the understanding of the underlying molecular mechanisms.

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Early Hum Dev. 2009;85:1-6.

Quality of general movements and psychiatric morbidity at 9 to 12 years.

Hadders-Algra M, Bouwstra H, Groen SE.

Background: General movements (GMs) form the basic motility of young infants. The quality of GMs may predict neurological outcome, but little is known about relationships between GM-quality and behavioral problems, including those resulting in overt psychiatric morbidity.

Aim: To explore relationships between abnormal GMs and behavioral problems, in particular relationships between abnormal GMs and Attention Deficit Hyperactivity Disorder (ADHD) with or without psychiatric co-morbidity at school-age.

Methods: Twenty-five low-risk full term infants and 16 infants at high risk for neurodevelopmental disorder but without cerebral palsy were studied prospectively. GM-quality was assessed during 'writhing' age (around term till 2 months post-term) and 'fidgety' age (2-4 months post-term). GMs were classified into normal and abnormal movements. When the children were 9-12 years, parents completed the Child Behavior Checklist (CBCL) and provided information on the presence of psychiatric diagnoses; teachers completed the Teachers Report Form (TRF). Both parents and teachers completed a questionnaire on ADHD-like behavior.

Results: Abnormal GMs at 'writhing' and 'fidgety' age were related to the presence of ADHD with psychiatric co-morbidity ($p < 0.05$), but not to isolated ADHD. Abnormal GMs at 'fidgety' age were weakly related to problematic behavior at school (TRF-scores) and hyperactive behavior at home (ADHD-questionnaire).

Conclusions: This explorative study suggests that abnormal GMs in early infancy may be associated with an increased risk for behavioral problems, in particular for ADHD with psychiatric co-morbidity at school-age.

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Biol Psychiatry. 2009;65:39-45.

Task Complexity Enhances Response Inhibition Deficits in Childhood and Adolescent Attention-Deficit/Hyperactivity Disorder: A Meta-Regression Analysis.

Huizenga HM, van Bers BMCW, Plat J, et al.

Background: The ability to inhibit motor responses, as assessed by the stop-signal reaction time (SSRT), is impaired in children and adolescents with attention-deficit/hyperactivity disorder (ADHD). However, the between-study variation in effect sizes is large. The aim of this study was to investigate whether this variability can be explained by between-study variation in Go task complexity.

Method: Forty-one studies comparing children or adolescents diagnosed with ADHD to normal control subjects were incorporated in a random-effects meta-regression analysis. The independent variables were a global index of Go task complexity (i.e., mean reaction time in control subjects [RTc]) and a more specific index (i.e., spatial compatibility of the stimulus-response mapping). The dependent variable was the SSRT difference between ADHD and control subjects.

Results: The SSRT difference increased significantly with increasing RTc. Moreover, the SSRT difference was significantly increased in studies that employed a noncompatible, that is, arbitrary, mapping compared with studies that incorporated a spatially compatible stimulus-response mapping.

Conclusions: These results indicate that inhibitory dysfunction in children and adolescents with ADHD varies with task complexity: inhibitory dysfunction in ADHD is most pronounced for spatially noncompatible responses. Explanations in terms of inhibition and working memory deficits and a tentative neurobiological explanation are briefly discussed.

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Eur Addict Res. 2009;15:1-9.

Attention deficit hyperactivity disorder symptoms mediate early-onset smoking.

Huizink AC, Van Lier PAC, Crijnen AAM.

Background/Aims: Symptoms of attention deficit hyperactivity disorder (ADHD) have often been associated with early-onset smoking. We hypothesize that reductions in ADHD symptoms due to an intervention have a mediating effect on early-onset smoking.

Methods: In a universal, school-based, randomized controlled intervention trial, we examined whether intervention-induced reductions in ADHD symptoms at age 9 mediated the reduced risk of tobacco use onset among these children at age 10 or 11 years. A sample of 477 first-grade boys and girls were randomly assigned to the Good Behavior Game intervention ($n = 263$), a 2-year (grades 2 and 3) universal classroom-based intervention aimed at reducing disruptive behavior problems, or to a control condition ($n = 214$). ADHD symptoms were assessed through teacher ratings. Early onset of tobacco use was assessed through self-report.

Results: The intervention-induced reductions in ADHD symptoms fully mediated the distal effect of intervention on reductions in early-onset smoking.

Conclusions: Our results showed that programs that target ADHD symptoms may protect children from early-onset smoking as well. Further research is needed to examine pathways from ADHD symptoms to tobacco use.

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European Child & Adolescent Psychiatry. 2008 Dec;17:52-58.

How often are German children and adolescents diagnosed with ADHD? Prevalence based on the judgment of health care professionals: Results of the German health and examination survey (KiGGS).

Huss M, Hölling H, Kurth BrM, et al.

Background Attention deficit/hyperactivity disorder (ADHD) is a chronic disorder with a substantial lifelong impact on personal and social functioning, academic performance, and the health system in general. Extended knowledge regarding its epidemiology will help to optimise the distribution of health resources and support affected children and adolescents.

Objectives To report (1) the lifetime prevalence rates of ADHD in children and adolescents in Germany ages 3-17 years diagnosed by health care professionals, (2) the symptoms of hyperactivity and inattention in children and adolescents, and (3) the distributions and odds ratios for gender, age, socioeconomic status (SES), and history of migration.

Methods Data were collected from May 2003 until May 2006 in 167 representatively selected sample points in Germany. A total of 17,461 children and adolescents (7,569 boys and 7,267 girls) were medically and physically examined, and their parents completed a self-administered questionnaire. Parent-reports of a lifetime ADHD diagnosis by a medical doctor or psychologist were taken as case definitions. Additional information was obtained via the parents from the strengths and difficulties questionnaire (SDQ) and also from trained observers.

Results The overall lifetime prevalence of ADHD diagnosis was 4.8%. As expected, there was a significant gender difference between boys (7.7%) and girls (1.8%). Additionally, 4.9% of subjects had scores above threshold on the Inattention/ Hyperactivity subscale of the SDQ. As expected, a significant age effect was found for ADHD diagnosis (1.5% preschool age; 5.3% primary school; 7.1% secondary school). There were neither German east/west differences nor differences for rural versus urban areas. However, socioeconomic status was significantly associated with the prevalence of diagnosis (low SES: 6.4%, medium SES: 5.0%; high SES: 3.2%).

Conclusion The prevalence of diagnosed ADHD and the influence of its mediating factors found in our study are in line with those from other European countries, but our findings reflect a lower band of variation. (PsycINFO Database Record (c) 2009 APA, all rights reserved) (from the journal abstract)

Z Kinder- Jugendpsychiatr Psychother. 2008;36:411-17.

Attention therapy for children - Long-term effects of the ATTENTIONER.

Jacobs C, Petermann F.

A high percentage of children are affected by attention deficit disorders. For a large proportion the cardinal symptom is inattention; in particular, deficits in selective attention prevail. The ATTENTIONER offers an effective training method for the treatment of selective attention deficit. Methods: In 2007, long-term effects of therapy were already reported by Jacobs and Petermann, who examined children ten weeks after therapy on average. Results: In the current study three measurements were conducted: pre-intervention, post-intervention, and at follow-up ten to 76 months after post-intervention. Significant long-term effects on measures of selective attention were observed. At follow-up the majority of patients achieved average results which were not clinically relevant. Conclusions: For most children stable therapy effects can be achieved with the ATTENTIONER.

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Journal of the American Academy of Child & Adolescent Psychiatry. 2008 Oct;47:1158-65.

Trajectories of childhood aggression and inattention/hyperactivity: Differential effects on substance abuse in adolescence.

Jester JM, Nigg JT, Buu A, et al.

Objective: Aggression and hyperactivity/inattention each are linked to risk of alcohol use disorder (AUD), but their unique contributions remain ambiguous. The present study disaggregated these two domains developmentally and examined the relation between childhood behavior trajectories and adolescent substance use.

Method: A total of 335 children of alcoholic and nonalcoholic fathers were studied prospectively. Parallel process latent trajectory class analysis was developed with behavioral ratings by parents and teachers of aggression and inattention/hyperactivity across ages 7 to 16. Membership in the four latent classes was used as a predictor for problem adolescence alcohol use and substance onset.

Results: Youths in the four latent trajectory classes differed in number of alcohol problems at age 16: healthy class (39% of sample, mean 2.1 alcohol-related problems), inattentive/hyperactive but not aggressive (33%; mean 2.7 problems), aggressive but not inattentive/hyperactive (4%, mean 5.0 problems), and comorbid (24%; mean 4.0 problems). Survival analysis revealed that the aggressive, comorbid, and inattentive/hyperactive classes had significantly earlier onsets of drinking, drunkenness, and marijuana use than the healthy class. Illicit drug use was also significantly increased in the comorbid, aggressive, and inattentive/hyperactive classes compared to the healthy class.

Conclusions: Three levels of behavioral risk of substance abuse exist, the highest having trajectories of increased aggressive and inattentive/hyperactive problems throughout childhood, the next involving only an increased inattentive/hyperactive behavioral trajectory, and the lowest involving those with neither type of problem. Children with both inattention/hyperactivity and aggression have the greatest need for childhood intervention to prevent substance abuse in adolescence.

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J Clin Psychol. 2009 Jan;65:76-93.

Clinically significant symptom change in children with attention-deficit/hyperactivity disorder: Does it correspond with reliable improvement in functioning?

Karpenko V, Owens JS, Evangelista NM, et al.

This study examined the relation between clinically significant (CS) change in symptoms of attention-deficit/hyperactivity disorder (ADHD) and of oppositional defiant disorder (ODD), and reliable change in multiple domains of functioning in children who participated in the Multimodal Treatment Study of Children with ADHD. Children with CS change in symptoms were significantly more likely than children without CS change to have reliable change across five domains of functioning. Interestingly, however, depending on the measure of functioning, 14 to 52% of children who did not achieve CS change in symptoms showed reliable improvement in functional domains. The results have implications for the definition and measurement of CS change in child treatment-outcome studies.

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BMJ: British Medical Journal. 2008 Nov;337:1-7.

Early head injury and attention deficit hyperactivity disorder: Retrospective cohort study.

Keenan HT, Hall GC, Marshall SW.

Objective: To explore the hypothesis that medically attended head injury in young children may be causal in the later development of attention deficit hyperactivity disorder.

Design: Retrospective cohort study. Setting: Health improvement network database (1988-2003), a longitudinal UK general practice dataset.

Participants: All children registered in the database from birth until their 10th birthday.

Main outcome measures: Risk of a child with a head injury before age 2 developing attention deficit hyperactivity disorder before age 10 compared with children with a burn injury before age 2 and children with neither a burn nor a head injury.

Results: Of the 62 088 children who comprised the cohort, 2782 (4.5%) had a head injury and 1116 (1.8%) had a burn injury. The risk of diagnosis of attention deficit hyperactivity disorder before 10 years of age after adjustment for sex, prematurity, socioeconomic status, and practice identification number was similar in the head injury (relative risk 1.9, 95% confidence interval 1.5 to 2.5) and burn injury groups (1.7, 1.2 to 2.5) compared with all other children.

Discussion: Medically attended head injury before 2 years of age does not seem to be causal in the development of attention deficit hyperactivity disorder. Medically attended injury before 2 years of age may be a marker for subsequent diagnosis of attention deficit hyperactivity disorder.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1431-35.

Catechol-O-methyltransferase Val158Met polymorphism is associated with methylphenidate response in ADHD children.

Kereszturi E, Tarnok Z, Bognar E, et al.

Methylphenidate is the most frequently prescribed drug in the treatment of attention deficit hyperactivity disorder (ADHD) but it is not effective in every case. Therefore, identifying genetic and/or biological markers

predicting drug-response is increasingly important. Here we present a case-control study and pharmacogenetic association analyses in ADHD investigating three dopaminergic polymorphisms. Previous studies suggested variable number of tandem repeats (VNTR) in the dopamine D4 receptor (DRD4) and the dopamine transporter (DAT1) genes as genetic risk factors for ADHD and as possible markers of methylphenidate response. Our results did not indicate substantial involvement of these two VNTRs in ADHD, however, both the case-control and the pharmacogenetic analyses showed significant role of the high activity Val-allele of catechol-O-methyltransferase (COMT) Val158Met polymorphism in our ADHD population. The Val-allele was more frequent in the ADHD group (n = 173) compared to the healthy population (P = 0.016). The categorical analysis of 90 responders versus 32 non-responders showed an association between the Val-allele or Val/Val genotype and good methylphenidate response (P = 0.009 and P = 0.034, respectively). Analyzing symptom severity as a continuous trait, significant interaction of COMT genotype and methylphenidate was found on the Hyperactivity-Impulsivity scale (P = 0.044). Symptom severity scores of all three genotype groups decreased following methylphenidate administration (P < 0.001), however Val/Val homozygote children had significantly less severe symptoms than those with Met/Met genotype after treatment (P = 0.015). This interaction might reflect the regulatory effect of COMT dominated prefrontal dopamine transmission on subcortical dopamine systems, which are the actual site of methylphenidate action.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1580-88.

SNPs in dopamine D2 receptor gene (DRD2) and norepinephrine transporter gene (NET) are associated with continuous performance task (CPT) phenotypes in ADHD children and their families.
Kollins SH, Anastopoulos AD, Lachiewicz AM, et al.

Haplotype-tagging SNP analyses were conducted to identify molecular genetic substrates of quantitative phenotypes derived from performance on a Continuous Performance Task (CPT). Three hundred sixty-four individuals were sampled from 152 families ascertained on the basis of at least one child having ADHD. Proband, their affected and unaffected siblings, and parents were administered a CPT. Four different components of performance were analyzed and tested for association with SNPs from 10 candidate genes involved in monoaminergic function. After correcting for multiple comparisons and controlling for multiple individuals from the same family, significant associations were identified between commission errors and SNPs in the DRD2 gene (rs2075654, rs1079596), and between reaction time variability and a SNP in the NET gene (rs3785155). These findings suggest that commission errors and reaction time variability are excellent candidates as ADHD endophenotypes based on previously published criteria. Results also shed light on the molecular genetic basis of specific processes that may underlie the disorder.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1355-58.

Genome-wide association scan of the time to onset of attention deficit hyperactivity disorder.
Lasky-Su J, Anney RJL, Neale BM, et al.

A time-to-onset analysis for family-based samples was performed on the genomewide association (GWAS) data for attention deficit hyperactivity disorder (ADHD) to determine if associations exist with the age at onset of ADHD. The initial dataset consisted of 958 parent-offspring trios that were genotyped on the Perlegen 600,000 SNP array. After data cleaning procedures, 429,981 autosomal SNPs and 930 parent-offspring trios were used found suitable for use and a family-based logrank analysis was performed using that age at first ADHD symptoms as the quantitative trait of interest. No SNP achieved genome-wide significance, and the lowest P-values had a magnitude of 10⁻⁷. Several SNPs among a pre-specified list of candidate genes had nominal associations including SLC9A9, DRD1, ADRB2, SLC6A3, NFIL3, ADRB1, SYT1, HTR2A, ARRB2, and CHRNA4. Of these findings SLC9A9 stood out as a promising candidate, with nominally significant SNPs in six distinct regions of the gene.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1345-54.

Genome-wide association scan of quantitative traits for attention deficit hyperactivity disorder identifies novel associations and confirms candidate gene associations.
Lasky-Su J, Neale BM, Franke B, et al.

Attention deficit hyperactivity disorder (ADHD) is a complex condition with environmental and genetic etiologies. Up to this point, research has identified genetic associations with candidate genes from known biological pathways. In order to identify novel ADHD susceptibility genes, 600,000 SNPs were genotyped in

958 ADHD pro-band-parent trios. After applying data cleaning procedures we examined 429,981 autosomal SNPs in 909 family trios. We generated six quantitative phenotypes from 18 ADHD symptoms to be used in genome-wide association analyses. With the PBAT screening algorithm, we identified 2 SNPs, rs6565113 and rs552655 that met the criteria for significance within a specified phenotype. These SNPs are located in intronic regions of genes CDH13 and GFOD1, respectively. CDH13 has been implicated previously in substance use disorders. We also evaluated the association of SNPs from a list of 37 ADHD candidate genes that was specified a priori. These findings, along with association P-values with a magnitude less than 10⁻⁵, are discussed in this manuscript. Seventeen of these candidate genes had association P-values lower than 0.01: SLC6A1, SLC9A9, HES1, ADRB2, HTR1E, DDC, ADRA1A, DBH, DRD2, BDNF, TPH2, HTR2A, SLC6A2, PER1, CHRNA4, SNAP25, and COMT. Among the candidate genes, SLC9A9 had the strongest overall associations with 58 association test P-values lower than 0.01 and multiple association P-values at a magnitude of 10⁻⁵ in this gene. In sum, these findings identify novel genetic associations at viable ADHD candidate genes and provide confirmatory evidence for associations at previous candidate genes. Replication of these results is necessary in order to confirm the proposed genetic variants for ADHD. (copyright) 2008 Wiley-Liss, Inc

Psychiatr Invest. 2008;5:228-31.

Personality characteristics of mothers of children with attention deficit hyperactivity disorder as assessed by the Minnesota Multiphasic Personality Inventory.

Lee SJ, Kwon JH, Lee YJ.

Objective: The current study investigated the personality characteristics of mothers of children with attention deficit hyperactivity disorder (ADHD) using the Minnesota Multiphasic Personality Inventory (MMPI).

Methods: Fifty mothers (average age of 38.1 (plus or minus) 4.2 years) of children with ADHD not having comorbidity (37 boys, 13 girls; average age of 8.5 (plus or minus) 1.9 years) and 59 mothers (average age of 38.1 (plus or minus) 2.7 years) of comparison children (37 boys, 13 girls; average age of 8.1 (plus or minus) 1.5 years) completed the Korean version of the MMPI. Only mothers whose psychiatric health was verified by the Structured Clinical Interview for axis-I DSM-IV disorders (SCID-IV) were included in current study.

Results: After controlling for maternal age, maternal education level, children's gender, age, and total and verbal intelligence quotient (IQ), the MMPI scores of the mothers of children with ADHD were significantly higher on the depression (D), hysteria (Hy) and psychasthenia (Pt) scales than those of the mothers of children in the comparison group.

Conclusion: These results suggested that even psychologically healthy mothers of children with ADHD alone might be depressed, histrionic and anxious.

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Journal of Attention Disorders. 2009 Jan;12:361-71.

Parent-child joint picture-book reading among children with ADHD.

Leonard MA, Lorch EP, Milich R, et al.

Objective: Children with AD/HD exhibit two disparate areas of difficulty: disrupted interactions with parents and significant problems in story comprehension. This study links these two difficulties by examining parent-child joint picture-book reading to determine whether there were diagnostic group differences in parent and child storytelling.

Method: Parents of 25 children with ADHD and 39 comparison children (mean age = 7.5 years) told their children a story based on a wordless picture-book, and children then retold the story to an examiner from memory.

Results: Parents in both groups told stories of similar length and complexity and demonstrated similar affective and responsive quality. The length of the child's retell of the parent's story did not differ across groups but children with ADHD included fewer goal-based events.

Conclusions: Results are discussed in terms of implications for enhancing the quality and frequency of parent-child storytelling among children with ADHD.

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Acta Paediatr Int J Paediatr. 2009;98:173-79.

Coffee consumption during pregnancy and the risk of hyperkinetic disorder and ADHD: A prospective cohort study.

Linnert KM, Wisborg K, Secher NJ, et al.

Aim: Based on hypotheses from experimental studies, we studied the association between intrauterine exposure to coffee and the risk of clinically verified hyperkinetic disorder and attention-deficit hyperactivity disorder (ADHD).

Methods: A cohort study with prospectively collected data from the Aarhus Birth Cohort, Denmark. We included 24 068 singletons delivered between 1990 and 1998. Linkage was performed with three Danish longitudinal registers: The Danish Psychiatric Central Register, The Integrated Database for Labour Market Research and The Danish Civil Registration System. We identified 88 children with hyperkinetic disorder and ADHD. Information about coffee consumption during pregnancy was obtained at 16 weeks of gestation from self-administrated questionnaires. Potential confounding factors were evaluated using Cox regression analyses.

Results: We found that intrauterine exposure to 10 or more cups of coffee per day was associated with a threefold increased risk of hyperkinetic disorder and ADHD. After adjustments for a number of confounding factors, the risk decreased and became statistically insignificant (RR 2.3, 95% CI 0.9-5.9).

Conclusion: Prenatal exposure to high levels of coffee did not significantly increase the risk of clinically verified hyperkinetic disorder and ADHD in childhood.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1488-94.

Association of the cannabinoid receptor gene (CNR1) with ADHD and post-traumatic stress disorder.

Lu AT, Ogdie MN, Jarvelin MR, et al.

Attention deficit hyperactivity disorder (ADHD) is a highly heritable disorder affecting some 5-10% of children and 4-5% of adults. The cannabinoid receptor gene (CNR1) is a positional candidate gene due to its location near an identified ADHD linkage peak on chromosome 6, its role in stress and dopamine regulation, its association with other psychiatric disorders that co-occur with ADHD, and its function in learning and memory. We tested SNP variants at the CNR1 gene in two independent samples - an unselected adolescent sample from Northern Finland, and a family-based sample of trios (an ADHD child and their parents). In addition to using the trios for association study, the parents (with and without ADHD) were used as an additional case/control sample of adults for association tests. ADHD and its co-morbid psychiatric disorders were examined. A significant association was detected for a SNP haplotype (C-G) with ADHD (P = 0.008). A sex by genotype interaction was observed as well with this haplotype posing a greater risk in males than females. An association of an alternative SNP haplotype in this gene was found for post-traumatic stress disorder (PTSD) (P = 0.04 for C-A, and P = 0.01 for C-G). These observations require replication, however, they suggest that the CNR1 gene may be a risk factor for ADHD and possibly PTSD, and that this gene warrants further investigation for a role in neuropsychiatric disorders.

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Biol Psychiatry. 2009;65:84-88.

Decreased Callosal Thickness in Attention-Deficit/Hyperactivity Disorder.

Luders E, Narr KL, Hamilton LS, et al.

Background: Neuroimaging studies of attention-deficit/hyperactivity disorder (ADHD) have revealed structural abnormalities in the brains of affected individuals. One of the most replicated alterations is a significantly smaller corpus callosum (CC), for which conflicting reports exist with respect to the affected callosal segments.

Methods: We applied novel surface-based geometrical modeling methods to establish the presence, direction, and exact location of callosal alterations in ADHD at high spatial resolution. For this purpose, we calculated the thickness of the CC at 100 equidistant midsagittal points in an age-matched male sample of 19 individuals with ADHD and 19 typically developing control subjects.

Results: In close agreement with many prior observations, the CC was shown to be significantly thinner in ADHD subjects in anterior and, particularly, posterior callosal sections. Covarying for intelligence did not significantly alter the observed ADHD effects. However, group differences were no longer present in anterior sections when covarying for brain volume and after excluding ADHD subjects comorbid for oppositional defiant disorder.

Conclusions: Decreased callosal thickness may be associated with fewer fibers or a decrease in the myelination of fibers connecting the parietal and prefrontal cortices. This might affect interhemispheric communication channels that are necessary to sustain attention or motor control, thus contributing to symptoms of hyperactivity and impulsivity, or inattention, observed in ADHD. Future studies are necessary to determine whether callosal abnormalities reflect maturational delays or persist into adulthood.

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1501-08.

Association between tryptophan hydroxylase 2, performance on a continuance performance test and response to methylphenidate in ADHD participants.

Manor I, Laiba E, Eisenberg J, et al .

The main objective of this study was to examine neuropsychological mechanisms mediating the association between tryptophan hydroxylase 2 (TPH2) and attention deficit hyperactivity disorder (ADHD). A continuous performance test (T.O.V.A.) was administered to 344 participants diagnosed with DSM IV ADHD who were also genotyped for eight TPH2 intronic SNPs. Association between TPH2 (single SNPs and haplotypes), ADHD, and performance on the T.O.V.A. were tested using robust family-based association tests as implemented in two statistical genetic programs: UNPHASED and PBAT. Association was only observed between an eight locus haplotype and ADHD DSM IV combined type III (global P = 0.036). Robust association was observed between TPH2 single SNPs (and haplotypes) and performance on the T.O.V.A., especially Errors of Omission (eight locus haplotypes, global P = 0.038). Significant associations were also observed between TPH2 and improvement (before-after scores) in T.O.V.A. Total Response Variability scores following acute methylphenidate challenge (eight locus haplotypes, global P = 0.009). Using the MFBAT program, significant multivariate association was observed between single SNPs and haplotypes [eight locus haplotypes and all four T.O.V.A. variables (PBAT-GEE P = 0.013)]. The two most common TPH2 eight locus haplotypes were in a Yin Yang configuration and the Yang haplotype was the risk haplotype for both DSM IV ADHD and deficits in neuropsychological performance. The current investigation shows that risk for ADHD conferred by TPH2 variants is partially mediated by serotonergic mechanisms impacting some facets of executive function. Importantly, improvement in T.O.V.A. performance, especially on Response Time Variability, following methylphenidate was also associated with TPH2.
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Journal of the American Academy of Child & Adolescent Psychiatry. 2008 Oct;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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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1412-18.

Genome-wide association study of response to methylphenidate in 187 children with attention-deficit/hyperactivity disorder.

Mick E, Neale B, Middleton FA, et al.

We conducted a genome-wide association study of symptom response in an open-label study of a methylphenidate transdermal system (MTS). All DNA extraction and genotyping was conducted at SUNY Upstate Medical University using the Affymetrix Genome-Wide Human SNP Array 6.0. All quality control and association analyses were conducted using the software package PLINK. After data cleaning and quality control, there were 187 subjects (72% (N = 135) male) with mean age 9.2 (plus or minus) 2.0 years and 319,722 SNPs available for analysis. The most statistically significant association (rs9627183 and rs11134178; $P = 3 \times 10^{-6}$) fell short of the threshold for a genome-wide significant association. The most intriguing association among suggestive findings (rs3792452; $P = 2.6 \times 10^{-5}$) was with the metabotropic glutamate receptor 7 gene (GRM7) as it is expressed in brain structures also previously associated with ADHD. Among the 102 available SNPs covering previously studied candidate genes, two SNPs within the norepinephrine transporter gene (NET, SLC6A2) were significant at P (less-than or equal to) 1×10^{-2} . These results should be considered preliminary until replicated in larger adequately powered, controlled samples but do suggest that noradrenergic and possibly glutaminergic genes may be involved with response to methylphenidate.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1461-69.

Serotonin transporter gene and adverse life events in adult ADHD.

Muller DJ, Mandelli L, Serretti A, et al.

Childhood attention deficit hyperactivity disorder (ADHD) symptomatology persists in a substantial proportion of cases into adult life. ADHD is highly heritable but the etiology of ADHD is complex and heterogeneous, involving both genetic and non-genetic factors. In the present article we analyzed the influence of both genetics and adverse life events on severity of ADHD symptoms in 110 adult ADHD patients. Subjects were genotyped for the norepinephrine transporter (NET), the catechol-O-methyltransferase (COMT), the serotonin transporter promoter polymorphism (SERTPR) and the more rare A/G variant within SERTPR. Three main outcomes were obtained: (1) adverse events showed a small but positive correlation with current ADHD severity; (2) NET, COMT and the A/G variant within SERTPR were not associated with ADHD severity; (3) taking into account stressors, the long (L) SERTPR variant showed a mild effect on ADHD, being associated with an increased severity, particularly as regard affective dysregulations; on the other hand, in subjects exposed to early stressors, it showed a protective effect, as compared to the short (S) variant. In conclusion, our data support the role of environmental factors in adult ADHD symptomatology. SERTPR may be involved in some features of the illness and act as a moderator of environmental influences in ADHD. (copyright) 2008 Wiley-Liss, Inc

Families, Systems, & Health. 2008 Dec;26:447-58.

African American caretakers' views of ADHD and use of outpatient mental health care services for children.

Mychailyszyn MP, dosReis S, Myers M.

Despite the extensive research on childhood Attention-Deficit/Hyperactivity Disorder (ADHD), there is still much to learn about the association between the meanings parents ascribe to an ADHD diagnosis and their use of outpatient mental health services for their children. This study examined primarily African American mothers' experiences with their child's ADHD in order to develop a theory that links conceptualization of ADHD with implications for clinical outpatient mental health services. Semi-structured interviews with 34 parents of children 6 to 18 years old and recently diagnosed with ADHD probed for understanding of their child's behaviors and their treatment expectations. Using a grounded theory approach, a theoretical model emerged describing a process of how parents making sense of ADHD, either as a medical illness, a general problem, or a behavior that was not a problem. Making sense involved forming opinions, contemplating the origin, and reevaluating self-control. Stages in this process can be used by clinicians to educate and to assist families with treatment decisions that they are comfortable with. In the end, this may improve parents' adherence to their children's mental health treatment.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1337-44.

Genome-wide association scan of attention deficit hyperactivity disorder.

Neale BM, Lasky-Su J, Anney R, et al.

Results of behavioral genetic and molecular genetic studies have converged to suggest that genes substantially contribute to the development of attention deficit/hyperactivity disorder (ADHD), a common disorder with an onset in childhood. Yet, despite numerous linkage and candidate gene studies, strongly consistent and replicable association has eluded detection. To search for ADHD susceptibility genes, we genotyped approximately 600,000 SNPs in 958 ADHD affected family trios. After cleaning the data, we analyzed 438,784 SNPs in 2,803 individuals comprising 909 complete trios using ADHD diagnosis as phenotype. We present the initial TDT findings as well as considerations for cleaning family-based TDT data. None of the SNP association tests achieved genome-wide significance, indicating that larger samples may be required to identify risk loci for ADHD. We additionally identify a systemic bias in family-based association, and suggest that variable missing genotype rates may be the source of this bias.

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Journal of the American Academy of Child & Adolescent Psychiatry. 2009 Jan;48:51-59.

Stimulant dosing for children with ADHD: A medical claims analysis.

Olfson M, Marcus S, Wan G.

Objective: To evaluate stimulant dosing patterns in the community treatment of children with attention-deficit/hyperactivity disorder (ADHD).

Method: Claims data from U.S. managed care organizations (2000-2004) were analyzed for patients ages 6 to 12 years treated for ADHD with osmotically released oral system (OROS) methylphenidate (MPH; n = 3,815), immediate-release (IR) MPH (n = 1,960), mixed amphetamine salts extended-release (MAS XR; n = 1,847), or IR MAS (n = 1,937), and who filled prescriptions covering at least 72 of the first 90 days of treatment.

Results: The mean initial and maximum dosages were 23.8 and 33.4 mg/day for OROS MPH, 14.8 and 21.8 mg/day for IR MPH, 12.7 and 17.4 mg/day for MAS XR, and 11.2 and 16.5 mg/day for IR MAS. Dose titration occurred in 51.8% (MAS XR) to 61.6% (IR MPH) of patients. Lower initial dose and three or more visits for the treatment of ADHD during the first 90 days of treatment were associated with dose titration. Maximum dose was significantly related to higher initial dose and titration for all four stimulants. For children treated with OROS MPH or IR MAS, treatment by a psychiatrist was significantly related to higher maximum dose.

Conclusions: Among children with ADHD who continue stimulants through the first 3 months of treatment, dosing in the community treatment of ADHD tends to be lower than doses used in clinical trials. When titration does occur, it is linked to lower initial dosing, clinical monitoring, higher final stimulant doses, and treatment by a psychiatrist.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1442-49.

Association of the dopamine transporter gene and ADHD symptoms in a Canadian population-based sample of same-age twins.

Ouellet-Morin I, Wigg KG, Feng Y, et al.

Attention deficit hyperactivity disorder (ADHD) is the most prevalent psychiatric disorder emerging during childhood. Psychostimulant medications (e.g., methylphenidate) noticeably reduce ADHD symptoms in most children. Since methylphenidate inhibits dopamine transporter activity, the dopamine transporter gene (DAT1) was considered to be the prime candidate risk gene in ADHD. Several studies found evidence for an association between the 10-repeat allele of the variable number of tandem repeat (VNTR) located in the 3' untranslated region and ADHD and/or ADHD symptoms in clinical and population-based samples. However, this finding was not replicated in all samples. In this study, we investigated the association between the DAT1 gene and ADHD symptoms in a population-based twin sample from Quebec (Canada). We used two polymorphisms, the VNTR and rs27072, the last providing the most significant results in a clinical sample from Toronto (Ontario, Canada). No association was noted between the VNTR and ADHD symptoms in children at 6 and 7 years of age, as reported by teachers. However, a significant association was found for the rs27072 polymorphism and symptoms of inattention and hyperactivity/impulsivity. These findings indicate that the DAT1 gene contributes to ADHD symptoms in this sample and further suggest that the VNTR may not be the optimal polymorphism for study in all populations. (copyright) 2007 Wiley-Liss, Inc

J Pediatr. 2008;153:851-56.

Attention-Deficit/Hyperactivity Disorder Symptoms and Child Maltreatment: A Population-Based Study.

Ouyang L, Fang X, Mercy J, et al.

Objective: To examine whether symptoms of attention-deficit/hyperactivity disorder (ADHD) during childhood are associated with child maltreatment.

Study design: The study sample consisted of 14 322 participants in the National Longitudinal Study of Adolescent Health. We used logistic regression and propensity score matching to examine the relationship, adjusting for demographic, socioeconomic, and familial risk factors for child maltreatment.

Results: Inattentive type, by criteria of Diagnostic and Statistical Manual of Mental Disorders Fourth Edition, was significantly associated with the likelihood of supervision neglect (odds ratio [OR]: 1.6; 95% confidence interval [CI]: 1.2-2.2), physical neglect (OR: 2.1; 95% CI: 1.4-3.1), physical abuse (OR: 1.6; 95% CI: 1.1-2.3), and contact sexual abuse (OR: 2.6; 95% CI: 1.5-4.5). To a lesser extent, hyperactive type was associated with the likelihood of supervision neglect (OR: 1.5; 95% CI: 1.1-2.0) and physical abuse (OR: 1.3; 95% CI: 1.0-1.6). The association between hyperactive type and physical neglect or contact sexual abuse was not significant. The results from the propensity score matching were similar.

Conclusions: Childhood ADHD symptoms were associated with self-reported child maltreatment. Health care providers should be alert to the potential for child maltreatment among children with ADHD symptoms, especially those with inattentive symptoms

Child Neuropsychol. 2009;15:40-52.

Parent report of attention problems predicts later adaptive functioning in children with brain tumors.

Papazoglou A, King TZ, Morris RD, et al.

Children with brain tumors are at risk for psychological and behavioral difficulties. This study examined the ability of parent report of attention problems, withdrawal, anxiety, and depression, as well as IQ, to predict later adaptive functioning in 42 children treated for brain tumors. Age at diagnosis, SES, gender, and scores on the Neurological Predictor Scale (NPS) also were examined as predictors. Parent report of attention problems, SES, and NPS were significant predictors of later adaptive functioning across domains. This finding highlights the ability of parent report of attention problems to predict later adaptive functioning in children treated for brain tumors.

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J Am Acad Child Adolesc Psychiatry. 2008;47:721-22.

ADHD treatment in Latin America and the Caribbean.

Polanczyk G, Rohde LA, Szobot C, et al.

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1419-24.

The impact of individual and methodological factors in the variability of response to methylphenidate in ADHD pharmacogenetic studies from four different continents.

Polanczyk G, Faraone SV, Bau CHD, et al.

Several studies have evaluated the association between individual polymorphisms and response to methylphenidate (MPH) in subjects with attention-deficit/hyperactivity disorder (ADHD). There are few replication studies for each polymorphism of interest and results are sometimes inconsistent in this field. Although data collection from multiple international sites would allow large sample sizes, this approach has been criticized for introducing sampling variability due to differences in ethnicity and methodology between studies. To examine these issues, we aggregated nine pharmacogenetic studies from four different continents and conducted a two stage analysis: (a) we evaluated the role of methodological aspects in the variability of ADHD symptom improvement between studies using meta-regression analysis; (b) we assessed the role of individual characteristics of the subjects in the variability of ADHD symptoms improvement using multivariate regression analysis in the same data sets. At the study level, from five evaluated factors, only the design of the study (open studies vs. randomized controlled trials) was significantly associated with heterogeneity of results ($P = 0.001$). At the individual level, age (P (less-than or equal to) 0.001), comorbid oppositional defiant disorder (P (less-than or equal to) 0.001), and pre-treatment scores (P (less-than or equal to) 0.001) were associated with change of ADHD scores with treatment in the final multivariate model. Our results suggest that joint analyses of pharmacogenetic studies are feasible and promising, since fixed

variables, such as the site where the study was conducted, were not related to results. Nevertheless, stratified analyses according to the design of the study must be preferentially conducted and the role of individual factors such as demographic data and comorbid profile as confounders should be assessed.
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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1425-30.

Pharmacogenetics of methylphenidate response in attention deficit/hyperactivity disorder: Association with the dopamine transporter gene (SLC6A3).

Purper-Ouakil D, Wohl M, Orejarena S, et al.

Pharmacogenetic studies investigating the 40-bp VNTR polymorphism at SLC6A3 and methylphenidate response have shown conflicting results and large differences in study design and efficacy endpoints. Our objective was to investigate the relation between the 30-VNTR at SLC6A3 and variability in methylphenidate response in a sample of 141 ADHD children and adolescents, assessed before and after methylphenidate treatment with both clinical and neuropsychological outcome measures. 10-R homozygotes were significantly overrepresented in the low response group, but no genotype effect was shown in cognitive variables improvement. A meta-analysis of pharmacogenetic studies with comparable data (responders vs. non-responders) on a total of 475 subjects showed a significant association between the 10-10 genotype and low rates of methylphenidate response (mean Odds Ratio = 0.46; 95% CI [0.28-0.76]). Heterogeneity between these studies did not reach a significant level but, as publications with different endpoints were excluded from this meta-analysis, our results do not rule out a possible influence of study design.

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Journal of Attention Disorders. 2009 Jan;12:353-60.

Untreated ADHD in adults: Are there sex differences in symptoms, comorbidity, and impairment?

Rasmussen K, Levander S.

Objective: To analyze sex differences among adult, never-treated patients referred for central stimulant treatment of ADHD.

Method: Data for 600 consecutive patients from northern Norway referred for evaluation by an expert team during 7 years were analyzed. General background information, diagnostic and social history, and symptom profiles were compared between previously never-treated men and women. Results: The sex ratio was skewed. Of the previously untreated patients, more than 20% fell outside society's ordinary vocational activities or social benefit system. Most patients had the combined form, one third the inattentive type, and only 2% the hyperactive/impulsive subtype. Abuse and criminality were more common among men, and affective, eating, and somatization disorders were more common among women. Otherwise few sex differences were found.

Conclusion: AD/HD symptom intensity and subtypes did not differ between the sexes and was unrelated to age. Symptom intensity was linked with criminality, abuse, and other psychiatric problems, differentially for the two sexes.

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Mol Psychiatry. 2009;14:71-85.

Exploration of 19 serotonergic candidate genes in adults and children with attention-deficit/hyperactivity disorder identifies association for 5HT2A, DDC and MAOB.

Ribases M, Ramos-Quiroga JA, Hervas A, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common psychiatric disorder in which different genetic and environmental susceptibility factors are involved. Several lines of evidence support the view that at least 30% of ADHD patients diagnosed in childhood continue to suffer the disorder during adulthood and that genetic risk factors may play an essential role in the persistence of the disorder throughout lifespan. Genetic, biochemical and pharmacological studies support the idea that the serotonin system participates in the etiology of ADHD. Based on these data, we aimed to analyze single nucleotide polymorphisms across 19 genes involved in the serotonergic neurotransmission in a clinical sample of 451 ADHD patients (188 adults and 263 children) and 400 controls using a population-based association study. Several significant associations were found after correcting for multiple testing: (1) the DDC gene was strongly associated with both adulthood ($P=0.00053$; odds ratio (OR)=2.17) and childhood ADHD ($P=0.0017$; OR=1.90); (2) the MAOB gene was found specifically associated in the adult ADHD sample ($P=0.0029$; OR=1.90) and (3) the

5HT2A gene showed evidence of association only with the combined ADHD subtype both in adults ($P=0.0036$; $OR=1.63$) and children ($P=0.0084$; $OR=1.49$). Our data support the contribution of the serotonergic system in the genetic predisposition to ADHD, identifying common childhood and adulthood ADHD susceptibility factors, associations that are specific to ADHD subtypes and one variant potentially involved in the continuity of the disorder throughout lifespan.
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Arq Neuro-Psiquiatr. 2008;66:821-27.

Clinical and neuropsychological profile in a sample of children with attention deficit hyperactivity disorders.

Rizzutti S, Sinnes EG, Scaramuzza LF, et al.

The aim of this study was to evaluate clinical and neuropsychological findings in children with suspicion of attention deficit hyperactivity disorder (ADHD). The assessment involved 150 children aged 7 to 14 referred to NANI at UNIFESP. Results: 75 children (55 M and 20 F) fulfilled the criteria for ADHD, among which 35 were of the inattentive type, 28 of combined type and 12 were hyperactive/impulsive. There was negative correlation between the digit score and the Corsi test. Children with hyperactivity and impulsivity had a low performance for functional memory. Children with oppositional defiant disorder presented pattern changes in adaptability when there was a change in the rhythm the stimuli were presented and lower adaptation to time variability (Hit RT), in addition to higher rates of omission in the continuous performance test. Conclusion: This study suggests multiple interrelations between the scores of neuropsychological battery useful for detailed delimitation of the clinical profile of children with ADHD.

Allergol Immunopathol. 2008;36:303-05.

Desensitization to methylphenidate - The relevance of continued drug intake for a successful outcome.

Rodrigues J, Da Costa Botelho CM, Cadinha S, et al.

Methylphenidate is the treatment of choice in attention-deficit/ hyperactivity disorder (ADHD). The authors report the case of a 7 year old boy with ADHD and psoriasis who developed generalised erythema, pruritus and fever 5 hours after the first oral administration of methylphenidate. After 2 days of treatment the drug was discontinued with complete resolution of symptoms. Later on, the drug was re-introduced with recurrence of the same clinical symptoms. Patch tests were performed with negative results. Desensitization was proposed and performed because there is no alternative treatment for ADHD. After the therapeutic dose was achieved, the mother interrupted drug intake because of a misunderstanding of instructions, and a mild rash subsided when another pill was administered. After this event the same desensitization procedure was carefully repeated. Interruption of drug intake during desensitization and consequent recurrence of clinical symptoms highlights the importance of continued exposure to the culprit drug in this kind of procedure. This modified protocol may enable patients with cutaneous reactions to this drug, to maintain therapy without recurrent reactions.

Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1524-30.

Differential association between MAOA, ADHD and neuropsychological functioning in boys and girls.

Rommelse NNJ, Altink ME, rias-Vasquez A, et al.

Attention-deficit/hyperactivity disorder (ADHD) is more common in boys than in girls. It has been hypothesized that this sex difference might be related to genes on the X-chromosome, like Monoamine Oxidase A (MAOA). Almost all studies on the role of MAOA in ADHD have focused predominantly on boys, making it unknown whether MAOA also has an effect on ADHD in girls, and few studies have investigated the relationship between MAOA and neuropsychological functioning, yet this may provide insight into the pathways leading from genotype to phenotype. The current study set out to examine the relationship between MAOA, ADHD, and neuropsychological functioning in both boys (265 boys with ADHD and 89 male non-affected siblings) and girls (85 girls with ADHD and 106 female non-affected siblings). A haplotype was used based on three single nucleotide polymorphisms (SNPs) (rs12843268, rs3027400, and rs1137070). Two haplotypes (GGC and ATT) captured 97% of the genetic variance in the investigated MAOA SNPs. The ATT haplotype was more common in non-affected siblings ($P = 0.025$), conferring a protective effect for ADHD in both boys and girls. The target and direction of the MAOA effect on neuropsychological functioning was different in boys and girls: The ATT haplotype was associated with poorer motor control in boys ($P =$

0.002), but with better visuo-spatial working memory in girls ($P = 0.01$). These findings suggest that the genetic and neuropsychological mechanisms underlying ADHD may be different in boys and girls and underline the importance of taking into account sex effects when studying ADHD.
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J Autism Dev Disord. 2009;39:67-74.

Association of a monoamine oxidase-A gene promoter polymorphism with ADHD and anxiety in boys with autism spectrum disorder.

Roohi J, DeVincent CJ, Hatchwell E, et al.

The aim of the present study was to examine the association between a variable number tandem repeat (VNTR) functional polymorphism in the promoter region of the MAO-A gene and severity of ADHD and anxiety in boys with ASD. Parents and teachers completed a DSM-IV-referenced rating scale for 5- to 14-year-old boys with ASD ($n = 43$). Planned comparisons indicated that children with the 4- versus 3-repeat allele had significantly ($p < 0.05$) more severe parent-rated ADHD inattention and impulsivity, and more severe teacher-rated symptoms of generalized anxiety. Our results support a growing body of research indicating that concomitant behavioral disturbances in children with ASD warrant consideration as clinical phenotypes, but replication with independent samples is necessary to confirm this preliminary finding.

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Arq Neuro-Psiquiatr. 2008;66:828-31.

Inattention, hyperactivity, oppositional-defiant symptoms and school failure.

Serra-Pinheiro MA, Mattos P, Regalla MA, et al.

Background: Attention-deficit hyperactivity disorder (ADHD) is associated with school failure. Inattention has been mainly implicated for this association. Oppositional-defiant disorder's (ODD) impact on academic performance remains controversial, because of the high comorbidity between ODD and ADHD.

Objective: To understand the role of inattention (IN), hyperactivity (H/I) and ODD in school failure. Method: Parents and teachers filled out SNAP-IV questionnaires for 241 / 6th grade students. The associations of the scores of oppositional-defiant (OP), H/I and IN symptoms with school year failure were calculated.

Results: IN was strongly correlated with school failure. H/I and OP were not associated with school failure, when controlled for IN.

Conclusion: OP and H/I symptoms do not play an important role in school failure, when controlled for IN symptoms. Our study supports the cross-cultural role of IN as a major predictor of school failure.

Prog Neuro-Psychopharmacol Biol Psychiatry. 2008;32:1824-28.

Increased levels of plasma brain-derived neurotrophic factor (BDNF) in children with attention deficit-hyperactivity disorder (ADHD).

Shim SH, Hwangbo Y, Kwon YJ, et al.

Background: Recent reports have suggested a pathophysiological role of brain-derived neurotrophic factor (BDNF) in attention deficit-hyperactivity disorder (ADHD). We evaluated the plasma levels of BDNF in patients with ADHD.

Methods: Plasma BDNF levels were measured in 41 drug naive ADHD patients and 107 normal controls. The severity of ADHD symptoms was determined by patient scores on the ADHD rating scale (ARS) and the computerized ADHD diagnostic system (ADS).

Results: ANCOVA with age and gender as covariates showed that the mean plasma BDNF levels were significantly higher in ADHD patients than in normal controls ($F = 16.968$, $p < 0.001$). There were also significant differences in plasma BDNF levels of ADHD patients and those of normal controls for males and females (Mann-Whitney U-test, $p = 0.001$ and 0.041 , respectively). We also found a significant correlation between plasma BDNF levels and omission errors in ADS outcome-variable T-scores ($p < 0.001$).

Conclusions: Our study suggests that there is an increase of plasma BDNF levels in untreated ADHD patients, and that plasma BDNF levels had a significant positive correlation with the severity of inattention symptoms. Further studies are required to elucidate the source and role of circulating BDNF in ADHD.

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Journal of the American Academy of Child & Adolescent Psychiatry. 2009 Jan;48:35-41.

Prevalence of enuresis and its association with attention-deficit/hyperactivity disorder among U.S. children: Results from a nationally representative study.

Shreeram S, He JP, Kalaydjian A, et al.

Objective: There are no published nationally representative prevalence estimates of enuresis among children in the United States using standardized diagnostic criteria. This study sets out to describe the prevalence, demographic correlates, comorbidities, and service patterns for enuresis in a representative sample of U.S. children.

Method: The diagnosis of enuresis was derived from parent-reported data for "enuresis, nocturnal" collected using the computerized version of the Diagnostic Interview Schedule for Children (C-DISC 4.0) from a nationally representative sample of 8- to 11-year-old children (n = 1,136) who participated in the 2001-2004 National Health and Nutrition Examination Surveys.

Results: The overall 12-month prevalence of enuresis was 4.45%. The prevalence in boys (6.21%) was significantly greater than that in girls (2.51%). Enuresis was more common at younger ages and among black youth. Attention-deficit/hyperactivity disorder (ADHD) was strongly associated with enuresis (odds ratio 2.88; 95% confidence interval 1.26-6.57). Only 36% of the enuretic children had received health services for enuresis.

Conclusions: Enuresis is a common condition among children in the United States. Few families seek treatment for enuresis despite the potential for adverse effects on emotional health. Child health care professionals should routinely screen for enuresis and its effects on the emotional health of the child and the family. Assessment of ADHD should routinely include evaluation for enuresis and vice versa. Research on the explanations for the association between enuresis and ADHD is indicated.

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Ann N Y Acad Sci 2008;1145:199-211

Impaired serial visual search in children with developmental dyslexia.

Sireteanu R, Goebel C, Goertz R, et al.

In order to test the hypothesis of attentional deficits in dyslexia, we investigated the performance of children with developmental dyslexia on a number of visual search tasks. When tested with conjunction tasks for orientation and form using complex, letter-like material, dyslexic children showed an increased number of errors accompanied by faster reaction times in comparison to control children matched to the dyslexics on age, gender, and intelligence. On conjunction tasks for orientation and color, dyslexic children were also less accurate, but showed slower reaction times than the age-matched control children. These differences between the two groups decreased with increasing age. In contrast to these differences, the performance of dyslexic children in feature search tasks was similar to that of control children. These results suggest that children with developmental dyslexia present selective deficits in complex serial visual search tasks, implying impairment in goal-directed, sustained visual attention.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1359-68.

Does parental expressed emotion moderate genetic effects in ADHD? An exploration using a genome wide association scan.

Sonuga-Barke EJS, Lasky-Su J, Neale BM, et al.

Studies of gene x environment (G x E) interaction in ADHD have previously focused on known risk genes for ADHD and environmentally mediated biological risk. Here we use G x E analysis in the context of a genome-wide association scan to identify novel genes whose effects on ADHD symptoms and comorbid conduct disorder are moderated by high maternal expressed emotion (EE). SNPs (600,000) were genotyped in 958 ADHD proband-parent trios. After applying data cleaning procedures we examined 429,981 autosomal SNPs in 909 family trios. ADHD symptom severity and comorbid conduct disorder was measured using the Parental Account of Childhood Symptoms interview. Maternal criticism and warmth (i.e., EE) were coded by independent observers on comments made during the interview. No G x E interactions reached genome-wide significance. Nominal effects were found both with and without genetic main effects. For those with genetic main effects 36 uncorrected interaction P-values were <10⁻⁵ implicating both novel genes as well as some previously supported candidates. These were found equally often for all of the interactions being investigated. The observed interactions in SLC1A1 and NRG3 SNPs represent reasonable candidate genes for further investigation given their previous association with several psychiatric illnesses. We find evidence for the role of EE in moderating the effects of genes on ADHD severity and comorbid conduct disorder,

implicating both novel and established candidates. These findings need replicating in larger independent samples.

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Child Neuropsychol. 2009;15:53-72.

Executive functions: Performance-based measures and the behavior rating inventory of executive function (BRIEF) in adolescents with attention deficit/hyperactivity disorder (ADHD).

Toplak ME, Bucciarelli SM, Jain U, et al.

Performance-based measures and ratings of executive functions were examined in a sample of adolescents with attention deficit/hyperactivity disorder (ADHD) and comparison controls. Performance-based measures of executive function included inhibition, working memory, set shifting, and planning, and ratings of these same executive functions were completed by parents and teachers. Adolescents with ADHD demonstrated lower executive function performance than controls and displayed elevated ratings on the executive function ratings by parents and teachers. Significant associations were obtained between the performance-based measures and the parent and teacher ratings, but each measure was not uniquely associated with its respective scale on the rating scales. When performance-based measures and ratings were examined as predictors of ADHD status, the parent and teacher ratings entered as significant predictors of ADHD status. Further commonality analyses indicated that performance-based measures accounted for little unique variance in predicting ADHD status and also displayed little overlap with the behavioral ratings. These findings highlight the diagnostic utility of behavioral ratings of executive function in predicting ADHD status; however, behavioral ratings should not be assumed to be a proxy for performance on measures of executive function in clinical practice.

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J Med Assoc Thai. 2008 Dec;91:1894-98.

Clinical characteristics of ADHD in Thai children.

Trangkasombat U.

OBJECTIVE: To study the clinical characteristics of children who were diagnosed as ADHD.

MATERIAL AND METHOD: A retrospective chart review was conducted on 202 children who came to a child mental health clinic and were diagnosed as ADHD.

RESULTS: Most cases were in the 6-12 years age group and came from small families with 1-2 children. Males outnumbered females (M:F = 3.4:1). One-fifth of the sample received previous psychiatric evaluation from other health professionals but parents needed 'second opinion'. The most frequent chief complaints were academic/learning problems. Almost one-fourth of the samples came for problems not directly related to ADHD. In this group the most frequent complaints were aggressive and oppositional behavior. Comorbidity was found in 53.5%. More than half of the cases who took intelligence tests had an IQ below 90. Behavioral management was the only treatment modality in 38% of the sample. In 62% stimulants were instituted either at the beginning of treatment or as an "add-on" after behavioral management proved to be insufficient. Among cases that received stimulants, 28% needed the combination of other psychotropic medications, mostly antidepressant and anxiolytic drugs.

CONCLUSION: A study of the clinical characteristics of ADHD in Thai children revealed male preponderance and high rates of non-ADHD presentations and comorbid conditions. Awareness of varied presentations of ADHD and proper treatment of comorbid conditions is imperative in the comprehensive care of ADHD children.

S Afr Med J. 2008;98:570.

Impact of withdrawal of Ritalin LA in the Western Cape.

van Bever Donker F, Riordan G, Wilmshurst J.

Toxicol Lett. 2009;184:38-43.

No elevated genomic damage in children and adolescents with attention deficit/hyperactivity disorder after methylphenidate therapy.

Walitza S, Kampf K, Artamonov N, et al.

Background and objective: Attention-deficit/hyperactivity disorder (ADHD) is the most frequent psychiatric disorder in children and adolescents and is often treated with methylphenidate (MPH), resulting in MPH exposure in more than 1% of all children in many countries. A 2005 report on cytogenetic effects in peripheral lymphocytes from 12 ADHD children treated for 3 months with MPH raised questions about its

genetic toxicity and potential carcinogenicity. In 2007, we described no elevated micronucleus frequency in 21 children after 3 months of MPH-treatment; since the difference between the two studies could not be explained we now enlarged the overall sample size, and added a healthy control group, a new chronically treated group and positive control slides. Furthermore, micronuclei were analyzed in a second tissue, buccal mucosa.

Study participants: A healthy control group (23 individuals), a chronically MPH-treated (>12 months) group (21 patients), and a drug naive group of ADHD-affected children (26 patients), which was analyzed again after 3 months (17 patients) and 6 months (11 patients), provided samples for analysis of micronucleated lymphocytes. With inclusion of 14 previously obtained blood samples, an overall group size of 31 patients was reached for the comparison of the 3 months observation time with before for micronucleated lymphocytes. For buccal mucosa cells, an additional inclusion of 10 more chronically treated patients (no lymphocytes donated) yielded sample numbers of 22 (healthy), 17 (chronically treated), 23 (ADHD drug naive), 14 (3 months) and 11 (6 months).

Results: No significant alteration in genomic damage as seen as micronucleus frequency in peripheral lymphocytes or buccal mucosa cells was detected after MPH treatment.

Conclusions: No indication for genomic damage induced by MPH was obtained in this study, as in our previous study. Together with our previous study, our overall number of MPH-treated patients is now 68 (30 chronically treated, 38 prospectively followed), plus 23 healthy controls. Ongoing studies in the USA, as well as continuation of recently published epidemiological cancer incidence analysis should provide additional reassurance for MPH-treated ADHD patients.

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J Child Adolesc Psychopharmacol. 2008;18:573-88.

The efficacy and tolerability of methylphenidate and behavior modification in children with attention-deficit/hyperactivity disorder and severe mood dysregulation.

Waxmonsky J, Pelham WE, Gnagy E, et al.

Objectives: This study examines the tolerability and efficacy of methylphenidate (MPH) and behavior modification therapy (BMOD) in children with attention-deficit/hyperactivity disorder (ADHD) and severe mood dysregulation (SMD).

Methods: Children (ages 5-12) from a summer program for ADHD were screened for SMD and additional manic-like symptoms using structured assessments and direct clinical interview with the Young Mania Rating Scale (YMRS). The SMD group was comprised of 33 subjects with SMD and elevated YMRS scores (mean = 23.7). They underwent weekly mood assessments plus the daily ADHD measures that are part of the program. The comparison group (n = 68) was comprised of the rest of the program participants. Using a crossover design, all subjects in both groups were treated with three varying intensities of BMOD (no, low, high) each lasting 3 weeks, with MPH dose (placebo, 0.15 mg/kg t.i.d., 0.3mg/kg t.i.d., and 0.6mg/kg t.i.d.) varying daily within each behavioral treatment.

Results: Groups had comparable ADHD symptoms at baseline, with the SMD group manifesting more oppositional defiant disorder/conduct disorder (ODD/CD) symptoms ($p < 0.001$). Both groups showed robust improvement in externalizing symptoms ($p < 0.001$). There was no evidence of differential treatment efficacy or tolerability. Treatment produced a 34% reduction in YMRS ratings in SMD subjects ($p = 0.001$). However, they still exhibited elevated YMRS ratings, more ODD/CD symptoms ($p < 0.001$), and were more likely to remain significantly impaired at home than non-SMD subjects ($p < 0.05$).

Conclusions: MPH and BMOD are tolerable and effective treatments for children with ADHD and SMD, but additional treatments may be needed to optimize their functioning.

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Genes Brain Behav. 2008;7:877-86.

Association of ADHD and the Protogenin gene in the chromosome 15q21.3 reading disabilities linkage region.

Wigg KG, Feng Y, Crosbie J, et al.

Twin studies indicate genetic overlap between symptoms of attention deficit hyperactivity disorder (ADHD) and reading disabilities (RD), and linkage studies identify several chromosomal regions possibly containing common susceptibility genes, including the 15q region. Based on a translocation finding and association to two specific alleles, the candidate gene, DYX1C1, has been proposed as the susceptibility gene for RD in 15q. Previously, we tested markers in DYX1C1 for association with ADHD. Although we identified association for haplotypes across the gene, we were unable to replicate the association to the specific alleles

reported. Thus, the risk alleles for ADHD are yet to be identified. The susceptibility alleles may be in a remote regulatory element, or DYX1C1 may not be the risk gene. To continue study of 15q, we tested a coding region change in DYX1C1, followed by markers across the gene Protogenin (PRTG) in 253 ADHD nuclear families. PRTG was chosen based on its location and because it is closely related to DCC and Neogenin, two genes known to guide migratory cells and axons during development. The markers in DYX1C1 were not associated to ADHD when analyzed individually; however, six markers in PRTG showed significant association with ADHD as a categorical trait ($P = 0.025-0.005$). Haplotypes in both genes showed evidence for association. We identified association with ADHD symptoms measured as quantitative traits in PRTG, but no evidence for association with two key components of reading, word identification and decoding was observed. These findings, while preliminary, identify association of ADHD to a gene that potentially plays a role in cell migration and axon growth. (copyright) 2008 The Authors

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Varying the wear time of the methylphenidate transdermal system in children with attention-deficit/hyperactivity disorder.

Wilens TE, Boellner SW, Lopez FA, et al.

Objective: Children with attention-deficit/hyperactivity disorder often have varying needs for coverage of their symptoms throughout the day. The objectives of this study were to determine the efficacy, duration of action, and safety of methylphenidate transdermal system worn for variable times by children (ages 6-12) diagnosed with ADHO.

Method: Methylphenidate dose was optimized over 5 weeks using 10-, 15-, 20-, or 30-mg patches worn for 9 hours. The efficacy of 4- and 6-hour wear times was then assessed in an Analog Classroom setting during a randomized, placebo-controlled, double-blind, three-way crossover phase. The main efficacy measures were the Swanson, Kotkin, Agler, M-Flynn, and Pelham Rating Scale department scale and the Permanent Product Measure of Performance math test.

Results: All of the efficacy measures indicated that 4- and 6-hour wear times improved ADHD symptoms and that medication effects on the Swanson, Kotkin, Agler, M-Flynn, and Pelham Rating Scale department scale and Permanent Product Measure of Performance math test decreased between 2 and 4 hours after patch removal. The majority of adverse events were transient and mild to moderate in severity.

Conclusions: These findings suggest that the duration of medication effect is related to the wear time of the patch and may be tailored to accommodate the schedules of patients.

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J Am Acad Child Adolesc Psychiatry. 2008;47:1375-83.

Methylphenidate and amphetamine do not induce cytogenetic damage in lymphocytes of children with ADHD.

Witt KL, Shelby MD, Itchon-Ramos N, et al.

Objective: In response to previously published findings of methylphenidate-induced chromosomal changes in children, this study was designed to determine whether methylphenidate- or amphetamine-based drugs induce chromosomal damage (structural aberrations, micronuclei, and sister chromatid exchanges) in peripheral blood lymphocytes of children with attention-deficit/ hyperactivity disorder after 3 months of continuous treatment.

Method: Stimulant drug-naive subjects, 6 to 12 years of age, in good overall health, and judged to be appropriate candidates for stimulant therapy based on rigorously diagnosed ADHD using DSM-IV criteria, were randomized into two open-label treatment groups (methylphenidate or mixed amphetamine salts). Each subject provided a blood sample before initiation of treatment and after 3 months of treatment. Pretreatment and posttreatment frequencies of chromosomal aberrations, micronuclei, and sister chromatid exchanges were determined for each subject.

Results: Sixty-three subjects enrolled in the study; 47 subjects completed the full 3 months of treatment, 25 in the methylphenidate group and 22 in the amphetamine group. No significant treatment-related increases were observed in any of the three measures of cytogenetic damage in the 47 subjects who completed treatment or the 16 subjects who did not.

Conclusions: Earlier findings of methylphenidate-induced chromosomal changes in children were not replicated in this study. These results add to the accumulating evidence that therapeutic levels of methylphenidate do not induce cytogenetic damage in humans. Furthermore, our results indicate that amphetamine-based products do not pose a risk for cytogenetic damage in children.

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Am J Med Genet Part B Neuropsychiatr Genet. 2008;147:1509-10.

Lack of association of the dopamine transporter gene in a French ADHD sample.

Wohl M, Boni C, Asch M, et al.

Discrepancies in the role of the 40 bp VNTR polymorphism of the dopamine transporter gene (DAT1) in attention-deficit hyperactivity disorder (ADHD) could be due to various sources of genetic or phenotypical heterogeneity. We therefore analyzed a sample of 146 ADHD children and their parents, with a transmission disequilibrium test (TDT) design, assessing age, inattention, and hyperactivity dimensions and total score of the ADHD Rating Scale, the number of errors and the total score at Stroop Color-Word test, and the total score at the Trail Making Test. The TDT for 10-repeat (10-R) allele shows a perfect lack of transmission bias (Mc Nemar $(\chi^2 = 0)$ and PBAT analyses showed no role of this polymorphism for any of the studied endophenotypes. Lack of statistical power is always a possibility, but with a sample size above the average of the majority of previous studies, and an odds ratio (number of transmitted versus untransmitted 10-R allele) of 1.00 exactly, this possibility may be considered as not very likely.

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Chinese Journal of Clinical Psychology. 2008 Oct;16:529-30.

A study of self-concept of ADHD with and without oppositional defiant disorder.

Xiong Ji, Luo Xr, Zhang Yh.

Objective: To explore the characteristics of self-concept of children with attention in children with attention deficit hyperactivity disorder (ADHD) and oppositional defiant disorder (ODD).

Methods: A sampling survey was made of 9495 children from six regions of Hunan province together. After using the two stages epidemiologic research methods, 425 children having completed Children's Self-Concept Scale, including 146 normal controls, 109 ADHD + ODD children and 170 pure ADHD children (criteria of DSM-TV), were collected as our sample.

Results: In the Children's Self-Concept Scale, the scores of ADHD with and without ODD children were lower than those of the normal group, including total score, behavior, intelligence, anxiety, gregariousness, happiness ($P < 0.01$) and body factor ($P < 0.05$). Meanwhile, the scores of ADHD with ODD children were lower than those of the pure ADHD, including total score, behavior, intelligence, anxiety, gregariousness, and happiness, but body factor score was higher than that of the pure ADHD.

Conclusion: The level of self-concept of ADHD with or without ODD is significantly lower than that of the normal children. And the level of ADHD with ODD is lower than that of the pure ADHD.

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Replication of a rare protective allele in the noradrenaline transporter gene and ADHD.

Xu X, Hawi Z, Brookes KJ, et al.

Replication is a key to resolving whether a reported genetic association represents a false positive finding or an actual genetic risk factor. In a previous study screening 51 candidate genes for association with ADHD in a multi-centre European sample (the IMAGE project), two single nucleotide polymorphisms (SNPs) within the norepinephrine transporter (SLC6A2) gene were found to be associated with attention deficit hyperactivity disorder (ADHD). The same SNP alleles were also reported to be associated with ADHD in a separate study from the Massachusetts General Hospital in the US. Using two independent samples of ADHD DSM-IV combined subtype trios we attempted to replicate the reported associations with SNPs rs11568324 and rs3785143 in SLC6A2. Significant association of the two markers was not observed in the two independent replication samples. However, across all four datasets the overall evidence of association with ADHD was significant (for SNP rs11568324 $P = 0.0001$; average odds ratio = 0.33; for SNP rs3785143 $P = 0.008$; average odds ratio = 1.3). The data were consistent for rs11568324, suggesting the existence of a rare allele conferring protection for ADHD within the SLC6A2 gene. Further investigations should focus on identifying the mechanisms underlying the protective effect.

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Psychiatry Res Neuroimaging. 2008;164:245-53.

Absence of gender effect on children with attention-deficit/hyperactivity disorder as assessed by optimized voxel-based morphometry.

Yang P, Wang PN, Chuang KH, et al.

Brain abnormalities, as determined by structural magnetic resonance imaging (MRI), have been reported in patients with attention-deficit hyperactivity disorder (ADHD); however, female subjects have been underrepresented in previous reports. In this study, we used optimized voxel-based morphometry to compare the total and regional gray matter volumes between groups of 7- to 17-year-old ADHD and healthy children (total 114 subjects). Fifty-seven children with ADHD (n=57, 35 males and 22 females) and healthy children (n=57) received MRI scans. Segmented brain MRI images were normalized into standardized stereotactic space, modulated to allow volumetric analysis, smoothed and compared at the voxel level with statistical parametric mapping. Global volumetric comparisons between groups revealed that the total brain volumes of ADHD children were smaller than those of the control children. As for the regional brain analysis, the brain volumes of ADHD children were found to be bilaterally smaller in the following regions as compared with normal control values: the caudate nucleus and the cerebellum. There were two clusters of regional decrease in the female brain, left posterior cingulum and right precuneus, as compared with the male brain. Brain regions showing the interaction effect of diagnosis and gender were negligible. These results were consistent with the hypothesized dysfunctional systems in ADHD, and they also suggested that neuroanatomical abnormalities in ADHD were not influenced by gender.

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Genetic heterogeneity in ADHD: DAT1 gene only affects probands without CD.

Zhou K, Chen W, Buitelaar J, et al.

Previous studies have found heterogeneous association between DAT1-3'-UTR-VNTR and attention deficit hyperactivity disorder (ADHD). Various proportions of conduct disorder (CD) comorbidity in their ADHD samples may partially explain the observational discrepancies. Evidence for this comes from family and twin studies which found ADHD probands with CD (ADHD + CD) are genetically different from those without CD (ADHD - CD). Genotypes of 20 DAT1 markers were analyzed in 576 trios, consisting of 141 ADHD + CD and 435 ADHD - CD. In addition to the classical TDT test, a specific genetic heterogeneity test was performed to identify variants that have different transmission patterns in the two phenotypic subgroups. After multiple-test correction, rs40184 and rs2652511 were significant in TDT tests. Further heterogeneity test found the two SNPs had a significant transmission pattern difference between ADHD + CD and ADHD - CD children, indicating that DAT1 has a significantly greater genetic influence on ADHD without CD. Although the result needs further replications, it does highlight the importance of selecting genetically homogeneous samples for molecular genetic analyses of ADHD.

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