



ADHD

ATTENTION DEFICIT HYPERACTIVITY DISORDER

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Eur J Hum Genet. 2009 Jul;17:958-66.

Suggestive linkage of ADHD to chromosome 18q22 in a young genetically isolated Dutch population.

Amin N, Aulchenko YS, Dekker MC, et al.

Attention deficit/hyperactivity disorder (ADHD) is a common, highly heritable, neuropsychiatric disorder among children. Linkage studies in isolated populations have proved powerful to detect variants for complex diseases, such as ADHD. We performed a genome-wide linkage scan for ADHD in nine patients from a genetically isolated population in the Netherlands, who were linked to each other within 10 generations through multiple lines of descent. The genome-wide scan was performed with a set of 400 microsatellite markers with an average spacing of +/-10-12 cM. We performed multipoint parametric linkage analyses using both recessive and dominant models. Our genome scan pointed to several chromosomal regions that may harbour ADHD susceptibility genes. None exceeded the empirical genome-wide significance threshold, but the Log of odds (LOD) scores were >1.5 for regions 6p22 (Heterogenetic log of odds (HLOD)=1.67) and 18q21-22 (HLOD=2.13) under a recessive model. We followed up these two regions in a larger sample of ADHD patients (n=21, 9 initial and 12 extra patients). The LOD scores did not increase after increasing the sample size (6p22 (HLOD=1.51), 18q21-22 (HLOD=1.83)). However, the LOD score on 6p22 increased to 2 when a separate analysis was performed for the inattentive type ADHD children. The linkage region on chromosome 18q overlaps with the findings of association of rs2311120 (P=10(-5)) and rs4149601 (P=10(-4)) in the genome-wide association analysis for ADHD performed by the Genetic Association Information Network consortium. Furthermore, there was an excess of regions harbouring serotonin receptors (HTR1B, HTR1E, HTR4, HTR1D, and HTR6) that showed a LOD score >1 in our genome-wide scan.

Dev Psychopathol. 2009;21:373-92.

Predicting behavior problems in deaf and hearing children: The influences of language, attention, and parent - Child communication.

Barker DH, Quittner AL, Fink NE, et al.

The development of language and communication may play an important role in the emergence of behavioral problems in young children, but they are rarely included in predictive models of behavioral development. In this study, cross-sectional relationships between language, attention, and behavior problems were examined using parent report, videotaped observations, and performance measures in a sample of 116 severely and profoundly deaf and 69 normally hearing children ages 1.5 to 5 years. Secondary analyses were performed on data collected as part of the Childhood Development After Cochlear Implantation Study, funded by the National Institutes of Health. Hearing-impaired children showed more language, attention, and behavioral difficulties, and spent less time communicating with their parents than normally hearing children. Structural equation modeling indicated there were significant relationships between language, attention, and child behavior problems. Language was associated with behavior problems both directly and indirectly through effects on attention. Amount of parent-child communication was not related to behavior problems.

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Epilepsy Behav. 2009;15:294-98.

Decreased fractional anisotropy in the middle cerebellar peduncle in children with epilepsy and/or attention deficit/hyperactivity disorder: A preliminary study.

Bechtel N, Kobel M, Penner IK, et al.

Children with epilepsy are at increased risk for attention deficit/hyperactivity disorder (ADHD). It has been shown that the cerebellum plays a major role in the pathophysiology of ADHD. We aimed to clarify whether children with combined epilepsy/ADHD have the same neurocerebellar pathophysiology as children with developmental ADHD. Eight boys with combined epilepsy/ADHD, 14 boys with developmental ADHD, and 12 healthy boys were investigated using diffusion tensor imaging generating fractional anisotropy (FA) maps. Healthy controls exhibited more FA in the left and in the right middle cerebellar peduncle compared with children with combined epilepsy/ADHD, and more FA in the right middle cerebellar peduncle compared with children with developmental ADHD. Our data show deficient cerebellar connections in both patient groups and endorse the crucial role of the cerebellum in the pathophysiology of ADHD. Our results suggest that ADHD seen in epilepsy might have the same cerebellar pathology as in developmental ADHD.

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J Adolesc Health. 2009;45:142-48.

Parsing the Associations Between Prenatal Exposure to Nicotine and Offspring Psychopathology in a Nonreferred Sample.

Biederman J, Monuteaux MC, Faraone SV, et al.

Purpose: Several studies have suggested an association between maternal smoking during pregnancy and both attention-deficit/hyperactivity disorder (ADHD) and conduct disorder (CD) in the offspring of women who smoke during pregnancy. However, it is unclear whether one or both of the documented links are spurious, given the considerable comorbidity between these disorders. The main aim of this study was to disentangle the association between maternal smoking during pregnancy with psychopathological outcomes, adjusting for possible confounders.

Methods: Two large, identically designed, longitudinal, case-control family studies of male and female probands with and without ADHD were combined. We used data from the nonreferred siblings of the probands from both studies (n=536). All subjects were blindly assessed with structured diagnostic interviews. Logistic regression analysis was used to determine the adjusted effect of exposure to maternal smoking during pregnancy.

Results: Among all siblings, maternal smoking during pregnancy was significantly associated with ADHD, independent of CD and other covariates. In contrast, maternal smoking during pregnancy was a risk factor for CD only in siblings of control probands, after adjusting for covariates.

Conclusions: These results support the hypothesis that maternal smoking during pregnancy is a risk factor for both ADHD and CD, independently of each other. However, the risk for CD appears to be conditional on family risk status.

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J Gen Psychol. 2009 Jul;136:243-58.

A preliminary study of lateralized processing in attention-deficit/hyperactivity disorder.

Boles DB, Adair LP, Joubert AM.

Attention-deficit/hyperactivity disorder (ADHD) is associated with deficits in spatial and sustained attention processes normally linked to the right parietal and frontal lobes. However, data on lateralization changes in attention processes are sparse. Little research has addressed whether the problems may reflect a more widespread lateralization disorder or whether there are lateralization changes over time. To address these issues, the authors examined several tasks, each using a lateralized process largely localized to a particular lobe and 2 age ranges (11-14 and 18-26 years) of unmedicated ADHD participants and control participants. ADHD children bisected lines significantly more rightward compared with control children, indicating an altered spatial attention process normally localized to the right parietal lobe. This problem was absent in young adults, suggesting a developmental resolution. The authors observed sustained attention decrements at both ages appearing earlier in the left hemisphere during a vigil. Finally, in these preliminary data, ADHD-related problems appeared specific to attention processes.

Pediatrics. 2009 Aug;124:580-89.

Parental angst making and revisiting decisions about treatment of attention-deficit/hyperactivity disorder.

Brinkman WB, Sherman SN, Zmitrovich AR, et al.

BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurobehavioral conditions of childhood and adolescence. Despite availability of effective treatment options, initiation of treatment is variable and persistence with therapeutic regimens is poor.

OBJECTIVE: We sought to better understand how parents make decisions about treatment for their child or adolescent with ADHD.

METHODS: We conducted a qualitative study among parents of children and adolescents; 52 parents participated in 1 of 12 focus groups. Parents answered questions about decision-making, information sharing, and sources of conflict and uncertainty. Sessions were audiotaped and transcribed verbatim. Themes were coded independently by 4 of the investigators, who then agreed on common themes.

RESULTS: Parents in our study made decisions about treatment for their child with ADHD in the midst of experiencing a variety of emotions as they witnessed child functional impairments at home and at school. In addition, parents felt stress as a result of their daily efforts to manage their child's struggles. Multiple factors influenced the decision to initiate medication. Subsequently, revisiting the decision to give their child medicine for ADHD was common. Many parents contrasted time on and off medicine to help inform management decisions. Trials stopping medication were almost always parent- or child-initiated.

CONCLUSIONS: Decisions about medication use for children and adolescents with ADHD are made and frequently revisited by their parents. Choices are often made under stressful conditions and influenced by a variety of factors. Striking a balance between benefits and concerns is an ongoing process that is often informed by contrasting time on and off medication. Development of strategies to support families across the continuum of decisions faced while managing ADHD is warranted.

Environ Health Perspect. 2009;117:A286.

Attention deficit hyperactivity disorder and blood lead levels in Chinese children.

Bronendum J.

Neurology. 2009;72:1526-27.

Altered anandamide degradation in attention-deficit/hyperactivity disorder.

Centonze D, Bari M, Di Michele B, et al.

Psychiatr Serv. 2009;60:950-57.

Children's beliefs about causes of childhood depression and ADHD: A study of stigmatization.

Coleman D, Walker JS, Lee J, et al.

Objective: Children's causal attributions about childhood mental health problems were examined in a national sample for prevalence; relative stigmatization; variation by age, race and ethnicity, and gender; and self-report of a diagnosis of depression or attention-deficit hyperactivity disorder (ADHD).

Methods: A national sample of 1,091 children were randomly assigned to read vignettes about a peer with depression, ADHD, or asthma and respond to an online survey. Causal attributions and social distance were assessed, and correlations were examined. Logistic regression models for each causal item tested main effects and interaction terms for conditions, demographic characteristics, and self-reported diagnosis.

Results: The beliefs that parenting, substance abuse, and low effort caused the condition were all strongly intercorrelated and were moderately correlated with social distance. The depression condition was the strongest predictor of endorsement of the most stigmatizing causal beliefs. Stigmatizing causal beliefs were evident for ADHD, but with more modest effects. Children who reported a diagnosis were more likely to endorse parenting and substance abuse as causes (attenuated for ADHD). Modest to moderate effects were found for variation in causal beliefs across ethnic groups.

Conclusions: This study demonstrated a consistent presence of stigmatization in children's beliefs about the causes of childhood mental health problems. Low effort, parenting, and substance abuse together tapped a moralistic and blaming view of mental health problems. The results reinforce the need to address

stigmatization of mental disorders and the relative stigmatization of different causal beliefs. The findings of variation by ethnicity and diagnosis can inform and target antistigmatization efforts.

Revista Brasileira de Psiquiatria. 2009;31:141-44.

Neuropsychological differences between attention deficit hyperactivity disorder and control children and adolescents referred for academic impairment.

Coutinho G, Mattos P, Malloy-Diniz LF.

Objective: To compare the performances of children and adolescents with attention deficit hyperactivity disorder with a group of control comparison subjects, both taken from a large clinical sample, using some of the most widely employed attention-based Brazilian tests.

Method: The performances of 186 children and adolescents with attention deficit hyperactivity disorder were compared to that of 80 control individuals based on attention and working memory scores. Both groups had been referred due to academic impairment. All individuals were submitted to the TAVIS-3 sustained, shifted and focused attention tests, as well as to the working memory tests that make up the WISC-III Freedom from Distractibility Index (Digit Span and Arithmetic).

Results: The control group was slightly older than the attention deficit hyperactivity disorder group ($p=0.07$); IQ and schooling did not differ between groups ($p=0.34$ and $p=0.38$, respectively). While performing a test requiring sustained attention for a longer period of time, the attention deficit hyperactivity disorder group showed a significantly higher number of commission errors compared to the controls, thus presenting sustained attention deficits ($p=0.003$); when the influence of IQ, age and schooling was reduced, the attention deficit hyperactivity disorder group also made more omission errors during a sustained attention task in comparison to the control group, thus achieving a borderline significance level ($p=0.08$); the attention deficit hyperactivity disorder group also performed worse in Digit Span forward and backward ($p=0.013$ and $p=0.01$, respectively) and in Arithmetic ($p=0.008$). Other scores did not achieve significance.

Conclusion: Our findings suggest that some of the most commonly used Brazilian attention-based tests - especially the sustained attention and working memory tests - may be useful to help distinguish subjects with attention deficit hyperactivity disorder from control subjects.

International Journal of Language & Communication Disorders. 2009 Jul;44:440-65.

Auditory processing disorder in relation to developmental disorders of language, communication and attention: a review and critique.

Dawes P, Bishop D.

Background: Auditory Processing Disorder (APD) does not feature in mainstream diagnostic classifications such as the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), but is frequently diagnosed in the United States, Australia and New Zealand, and is becoming more frequently diagnosed in the United Kingdom.

Aims: To familiarize readers with current controversies surrounding APD, with an emphasis on how APD might be conceptualized in relation to language and reading problems, attentional problems and autistic spectrum disorders.

Methods & Procedures: Different conceptual and diagnostic approaches adopted by audiologists and psychologists can lead to a confusing picture whereby the child who is regarded as having a specific learning disability by one group of experts may be given an APD diagnosis by another. While this could be indicative of co-morbidity, there are concerns that different professional groups are using different labels for the same symptoms.

Conclusions & Implications: APD, as currently diagnosed, is not a coherent category, but that rather than abandoning the construct, we need to develop improved methods for assessment and diagnosis, with a focus on interdisciplinary evaluation.

Neurosci Lett. 2009;462:179-81.

Replication of an association of a promoter polymorphism of the dopamine transporter gene and Attention Deficit Hyperactivity Disorder.

Doyle C, Brookes K, Simpson J, et al.

Genetic associations for Attention Deficit Hyperactivity Disorder (ADHD), a common highly heritable childhood behavioural disorder, require replication in order to establish whether they are true positive findings. The current study aims to replicate recent association findings from the International Multi-centre ADHD Genetics (IMAGE) project in one of the most studied genes related to ADHD, the dopamine transporter (DAT1) gene. In a family-based sample of 450 ADHD probands, three Single Nucleotide Polymorphism (SNP) markers have been genotyped using TaqMan assays. Transmission Disequilibrium Test analysis demonstrates that one of three SNP markers (rs11564750) in the 5' promoter region of the gene is significantly associated with ADHD ($P=0.02$). This provides further evidence that in addition to the well-known and investigated 3'UTR polymorphism associated with ADHD, there is potentially a further association signal emanating from the 5' promoter region of the gene. Further replication and functional studies are now required to fully understand the consequence of polymorphisms present at both the 5' and 3' ends of the DAT1 gene and their role in ADHD pathophysiology.

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J Pediatr. 2009;155:239-44.

Nocturnal Enuresis: A Suggestive Endophenotype Marker for a Subgroup of Inattentive Attention-Deficit/Hyperactivity Disorder.

Elia J, Takeda T, Deberardinis R, et al.

Objective: Attention-deficit/hyperactivity disorder (ADHD) and enuresis co-occur at a higher rate than expected; the cause for this is unclear.

Study design: Diagnostic and demographic variables were compared in 344 children ages 6 to 12 years, with and without enuresis, recruited in an ADHD genetic study. Sleep variables were investigated in a subgroup of 44 enuretic children with age- and sex-matched nonenuretic controls. The association of enuresis with single nucleotide polymorphisms located in regions reported in linkage with enuresis was explored.

Results: The prevalence rate of nocturnal enuresis was 16.9% for the entire cohort. There were no differences in sex, age, socioeconomic status, intelligence quotient, medication treatment, or comorbidities. The enuresis group had a higher likelihood of inattentive symptoms than the nonenuretic group. Night wakings and ability of children to wake themselves in the morning were both significantly decreased in children with enuresis compared with control children in the Child Sleep Habits Questionnaire Night Wakings subscale. No significant association was found with chromosomal regions previously reported in linkage with enuresis.

Conclusions: Deficits in arousal may contribute to both enuresis and inattentive ADHD. Nocturnal enuresis may be a useful clinical marker in identifying a subgroup of the inattentive phenotype in ADHD genetic studies.

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Dev Psychopathol. 2009;21:539-54.

Inhibitory deficits in children with attention-deficit/hyperactivity disorder: Intentional versus automatic mechanisms of attention.

Fillmore MT, Milich R, Lorch EP.

Application of theoretically based tasks to the study of the development of selective attention has led to intriguing new findings concerning the role of inhibitory mechanisms. This study examined inhibitory mechanisms using a countermanding task and an inhibition of return task to compare deficits in intentionally, versus reflexively, controlled inhibition of attention in children with attention deficit hyperactivity disorder. Fifty children with attention-deficit/hyperactivity disorder (ADHD) were classified into one of three subtypes: predominantly inattentive (ADHD/PI), combined (ADHD/C), and those children with ADHD/C who also met criteria for comorbid oppositional defiant disorder (ADHD/C+ODD). The groups were compared to a comparison group of children ($n = 21$). The countermanding task showed that the ADHD groups required more time to inhibit responses and this impairment did not differ among subtypes. With respect to reflexively controlled inhibition, compared with controls ADHD/C and ADHD/C+ODD groups showed impaired reflexive

inhibition, whereas the ADHD/PI group was considerably less impaired. The findings highlight a dissociation between the two forms of inhibitory deficits among children with the inattentive subtype, and raise the possibility that the efficient operation of reflexive inhibitory mechanisms might be necessary for the development of effective intentional control of inhibition.

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Psychoneuroendocrinology. 2009 Aug;34:1019-28.

Cortisol awakening response in healthy children and children with ADHD: Impact of comorbid disorders and psychosocial risk factors.

Freitag CM, Häning S, Palmason H, Meyer J, Wüst S, Seitz C.

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common child psychiatric disorders. Previous studies have reported a blunted cortisol response to challenging situations and a decreased cortisol awakening response (CAR) in children with ADHD. As ADHD often is comorbid with oppositional defiant disorder (ODD), conduct disorder (CD), or anxiety disorder (AnxD), and changes in hypothalamic-pituitary-adrenal (HPA) axis activity have also been reported for these disorders, the present study aimed to compare the CAR in children with ADHD with and without comorbid disorders. Data on the CAR were obtained in 128 children with ADHD (aged 6-13 years) and in 96 control children (aged 6-12 years). Children with ADHD+ODD showed an attenuated CAR (area under the curve, AUC) compared to children with ADHD without ODD/CD and control children. Findings point towards either disinhibition or pervasive underarousal in children with ADHD+ODD, and seem to be specific for children with ADHD+ODD, as the attenuated CAR-AUC was not observed in children with ADHD without comorbid disorders or children with ADHD+CD or ADHD+AnxD. In addition, current adverse parenting conditions, family conflicts, and acute life events were associated with mean increase in CAR, emphasizing the role of psychosocial risk factors in mediating HPA axis activity in children with ADHD.

Child Psychiatry & Human Development. 2009 Jun;40:257-68.

Objective Sleep Measurement in Typically and Atypically Developing Preschool Children with ADHD-Like Profiles.

Goodlin-Jones BL, Waters S, Anders TF.

OBJECTIVE: This study investigated the association between preschool children's sleep patterns measured by actigraphy and parent-reported hyperactivity symptoms. Many previous studies have reported sleep problems in children with attention deficit hyperactivity disorder (ADHD)-like symptoms.

METHODS: This study examined a cross-sectional sample of 186 preschoolers age 2-5 years in three groups: children with autism, children with developmental delay without autism, and typically developing children recruited from the general population. One week of actigraphic sleep data plus a parent report of the presence or absence of a current sleep problem were collected. Parents completed the child behavior checklist; a subset of children in preschool had teachers who completed the caregiver-teacher report form. Sleep behavior was compared for those children with and without clinical levels of attention-deficit/hyperactivity symptoms (T scores > or = 65).

RESULTS: The prevalence of a parent-defined sleep problem across the entire sample was 36.1%. Thirty-four percent of the sample had a parent-reported ADHD composite in the clinical range. Those children with a clinical ADHD profile were more likely to be described by parents as having a sleep problem. However, no significant differences in actigraphic sleep patterns or night-to-night sleep-wake variability were found for children with an ADHD profile in the clinical range.

CONCLUSIONS: In this non-clinical sample of preschool age children, parental reports of clinical ADHD profiles were significantly associated with parental reports of sleep problems but not with actigraphically recorded sleep-wake data.

Biol Psychol. 2009;82:45-53.

Methylphenidate improves diminished error and feedback sensitivity in ADHD: An Evoked Heart Rate analysis.

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

Attention Deficit Hyperactivity Disorder (ADHD) is a developmental disorder that has previously been related to a decreased sensitivity to errors and feedback. Supplementary to the traditional performance measures, this study uses autonomic measures to study this decreased sensitivity in ADHD and the modulating effects of medication. Children with ADHD, on and off Methylphenidate (Mph), and typically developing (TD) children performed a selective attention task with three feedback conditions: reward, punishment and no feedback. Evoked Heart Rate (EHR) responses were computed for correct and error trials. All groups performed more efficiently with performance feedback than without. EHR analyses, however, showed that enhanced EHR decelerations on error trials seen in TD children, were absent in the medication-free ADHD group for all feedback conditions. The Mph-treated ADHD group showed 'normalised' EHR decelerations to errors and error feedback, depending on the feedback condition. This study provides further evidence for a decreased physiological responsiveness to errors and error feedback in children with ADHD and for a modulating effect of Mph. (copyright) 2009 Elsevier B.V. All rights reserved

J Pediatr. 2009;155:84-89.

Cardiovascular Effects of Longer-Term, High-Dose OROS Methylphenidate in Adolescents with Attention Deficit Hyperactivity Disorder.

Hamerness P, Wilens T, Mick E, et al.

Objective: To examine the effects of high doses of extended-release methylphenidate (OROS MPH) on cardiovascular variables in adolescents with attention deficit hyperactivity disorder (ADHD).

Study design: ECG indices plus systolic blood pressure (SBP), diastolic BP (DBP) and heart rate (HR) were assessed during an open-label study of OROS MPH in 114 adolescents with ADHD (doses up to 1.5 mg/kg/d). Cardiovascular parameters were assessed at 6 weeks and 6 months.

Results: Small but statistically significant changes in DBP and HR were observed at 6 weeks, without further increases up to 6 months' follow-up. A small but statistically significant increase in SBP was observed over time. Twenty-nine percent of patients had isolated elevations in BP readings prior to study entry, and 14% had >3 consecutive visits at which elevated BP were observed during OROS MPH treatment. No clinically significant changes in ECG parameters were observed. No serious cardiovascular adverse events occurred.

Conclusions: Treatment with relatively high doses of OROS MPH was associated with small but statistically significant mean increases in BP and HR, primarily during the first 6 weeks of treatment, without clinically meaningful changes in ECG. These observations are consistent with previous reports using lower doses.

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Journal of Pineal Research. 2009 Aug;47:1-7.

Long-term follow-up of melatonin treatment in children with ADHD and chronic sleep onset insomnia.

Hoebert M, Van der Heijden KB, Geijlswijk IM, et al.

We conducted this study to assess long-term melatonin treatment course, effectiveness and safety in children with attention-deficit/hyperactivity disorder (ADHD) and chronic sleep onset insomnia (CSOI). This was conducted by means of a structured questionnaire for the parents. The subjects of this study consisted of participants who previously participated in a randomised clinical trial on melatonin efficacy. The response rate was 93% (94/101). The mean time to follow up was 3.7 yr. No serious adverse events or treatment related co-morbidities were reported. Sixty-five percent of the children still used melatonin daily and 12% occasionally. Temporal discontinuation of treatment resulted in a delay of sleep onset in 92% of the children. Nine percent of the children could discontinue melatonin completely because of improvement of sleep onset insomnia. Long-term melatonin treatment was judged to be effective against sleep onset problems in 88% of the cases. Improvement of behaviour and mood was reported in 71% and 61% respectively. We conclude that melatonin remains an effective therapy on the long term for the treatment of CSOI in children with ADHD and has no safety concerns regarding serious adverse events or treatment related co-morbidity. Discontinuation of melatonin treatment usually leads to a relapse of sleep onset insomnia and in resuming melatonin treatment, even after several years of treatment.

J Abnorm Child Psychol. 2009;37:679-81.

Can executive functions explain the relationship between attention deficit hyperactivity disorder and social adjustment?

Huang-Pollock CL, Mikami AY, Pfiffner L, et al.

This study examined the ability of executive functions (EF) to account for the relationship between Attention Deficit Hyperactivity Disorder (ADHD) status and social adjustment as indexed by parent and teacher report and by performance on a standardized observational "chat room" task. Children with the Combined subtype (ADHD-C; 23), the Primarily Inattentive Subtype (ADHD-I33), and non-ADHD controls (36) participated. EF did not mediate the relationship between ADHD status and parent or teacher report of social adjustment. EF accounted for about 40-50% of the variance between ADHD status and the ability of children to detect subtle verbal cues as well as memory for the conversation in the chat room task, but did not mediate the relationship between ADHD and the number of prosocial, hostile, or on-topic statements that were made. Results are consistent with other recent reports, and suggest that the role of EF deficits in the production of social skill deficits in ADHD may not be as prominent as is typically assumed. The implications for the development of intervention programs designed to target core cognitive etiologic factors are discussed.

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Cogn Behav Neurol. 2008;21:176-78.

Asymmetrical visual-spatial attention in college students diagnosed with ADD/ADHD .

Jones KE, Craver-Lemley C, Barrett AM.

OBJECTIVE: Research indicates that individuals with attention deficit disorder (ADD)/attention deficit hyperactivity disorder (ADHD) may exhibit left-right asymmetric spatial attention, with deficient processing of stimuli in the left visual hemispace. However, there is controversy as to when this phenomenon can be observed.

BACKGROUND: People with ADD/ADHD do not have obvious spatial bias when performing everyday tasks. Visual cancellation tasks have demonstrated behavioral asymmetry in ADD/ADHD, but results have not been consistent across studies. Children and older adults with ADD or ADHD have been assessed, but previous studies of college students with ADD/ADHD are not available.

METHOD: We tested 24 students with ADD or ADHD and 24 control students on a verbal and nonverbal cancellation task.

RESULTS: The ADD/ADHD group made significantly more left-sided omission errors than controls on a letter cancellation task. This group difference was not observed for a shape cancellation task, however.

CONCLUSIONS: These results support possible left visual inattention in college students with ADD/ADHD. Studies of functional correlates of these attentional phenomena are needed.

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Psychiatry Res. 2009;168:234-37.

A randomized, double-blind and placebo-controlled trial of modafinil in children and adolescents with attention deficit and hyperactivity disorder.

Kahbazi M, Ghoreishi A, Rahiminejad F, et al.

Attention-deficit/hyperactivity disorder (ADHD) is the most common behavioral disorder in childhood, with an estimated prevalence worldwide of 7%-17% among school-aged children. Modafinil is a centrally acting agent that is structurally and pharmacologically different from stimulants such as amphetamine and methylphenidate. It has been reported that modafinil is effective in diminishing the symptoms of ADHD. The aim of the present study was to further evaluate, under double-blind and placebo-controlled conditions, the efficacy of modafinil for ADHD in children and adolescents. Patients were 46 outpatients, children (35 boys and 11 girls) between the ages of 6 and 15 who clearly met the DSM-IV-TR diagnostic criteria for ADHD. All study subjects were randomly assigned to receive treatment with modafinil in a film-coated tablet, 200-300 mg/day, depending on weight (200 mg/day for < 30 kg and 300 mg/day for >30 kg) (group 1) or placebo (group 2) for a 6-week double-blind, randomized clinical trial. The principal outcome measure was the Teacher and Parent ADHD Rating Scale-IV. Patients were assessed by a psychiatrist at baseline, 14, 28 and 42 days after the medication started. At 6 weeks, modafinil produced a significantly better outcome on the Parent and Teacher Rating Scale scores than placebo. Decreased appetite was observed more often in the modafinil group. The results of this study indicate that modafinil significantly improved symptoms of ADHD, was well tolerated, and may open a new window in the treatment of children with ADHD.

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Neuropsychology. 2009;23:445-59.

Incidental and Intentional Sequence Learning in Youth-Onset Psychosis and Attention-Deficit/Hyperactivity Disorder (ADHD).

Karatekin C, White T, Bingham C.

The goal was to compare incidental and intentional spatial sequence learning in youth-onset psychosis and ADHD. The authors tested 8- to 19-year-olds with psychosis or ADHD and healthy controls on a serial reaction time (RT) task and used manual and oculomotor measures to examine learning. Participants were also administered a block in which they were explicitly instructed to learn a sequence. As in our previous studies with healthy adults and children, oculomotor anticipations and RTs showed learning effects similar to those in the manual modality. Results showed intact sequence-specific learning but fewer oculomotor anticipations in both clinical groups during incidental learning. In intentional learning, only the psychosis group showed impairments compared to controls. There were no interactions between age and diagnosis. Thus, the psychosis group showed relatively preserved incidental learning despite impairments in intentional learning. Additionally, both clinical groups showed impairments in the ability to search for, extract, and anticipate regularities (whether the regularities were there or not), but not in the ability to respond to these regularities when they were there.

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Pharmacol Biochem Behav. 2009;93:313-21.

Genetic and environmental influences on externalizing behavior and alcohol problems in adolescence: A female twin study.

Knopik VS, Heath AC, Bucholz KK, et al.

Genetic and environmental contributions to the observed correlations among DSM-IV ADHD problems [inattentive (INATT) and hyperactive/impulsive (HYP/IMP) behaviors], conduct problems (CDP) and alcohol problems (AlcProb) were examined by fitting multivariate structural equation models to data from the Missouri Adolescent Female Twin Study [N = 2892 twins (831 monozygotic pairs, 615 dizygotic pairs)]. Based on results of preliminary regression models, we modified the structural model to jointly estimate (i) the regression of each phenotype on significant familial/prenatal predictors, and (ii) genetic and environmental contributions to the residual variance and covariance. Results suggested that (i) parental risk factors, such as parental alcohol dependence and regular smoking, increase risk for externalizing behavior; (ii) prenatal exposures predicted increased symptomatology for HYP/IMP (smoking during pregnancy), INATT and CDP (prenatal alcohol exposure); (iii) after adjusting for measured familial/prenatal risk factors, genetic influences were significant for HYP/IMP, INATT, and CDP; however, similar to earlier reports, genetic effects on alcohol dependence symptoms were negligible; and (iv) in adolescence, correlated liabilities for conduct and alcohol problems are found in environmental factors common to both phenotypes, while covariation among impulsivity, inattention, and conduct problems is primarily due to genetic influences common to these three behaviors. Thus, while a variety of adolescent problem behaviors are significantly correlated, the structure of that association may differ as a function of phenotype (e.g., comorbid HYP/IMP and CDP vs. comorbid CDP and AlcProb), a finding that could inform different approaches to treatment and prevention.

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J Abnorm Child Psychol. 2009;37:591-609.

Community vs. clinic-based modular treatment of children with early-onset ODD or CD: A clinical trial with 3-year follow-up.

Kolko DJ, Dorn LD, Bukstein OG, et al.

This study examines the treatment outcomes of 139, 6-11 year-old, clinically referred boys and girls diagnosed with Oppositional Defiant Disorder (ODD) or Conduct Disorder (CD) who were randomly assigned to a modular-based treatment protocol that was applied by research study clinicians either in the community (COMM) or a clinic office (CLINIC). To examine normative comparisons, a matched sample of 69 healthy control children was included. Multiple informants completed diagnostic interviews and self-reports at six assessment timepoints (pretreatment to 3-year follow-up) to evaluate changes in the child's behavioral and emotional problems, psychopathic features, functional impairment, diagnostic status, and service involvement. Using HLM and logistic regression models, COMM and CLINIC showed significant and comparable improvements on all outcomes. By 3-year follow-up, 36% of COMM and 47% of CLINIC patients no longer met criteria for either ODD or CD, and 48% and 57% of the children in these two respective

conditions had levels of parent-rated externalizing behavior problems in the normal range. We discuss the nature and implications of these novel findings regarding the role of treatment context or setting for the treatment and long-term outcome of behavior disorders.

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Hum Mov Sci. 2009;28:529-42.

Can Attention Deficit Hyperactivity Disorder and Fetal Alcohol Spectrum Disorder be differentiated by motor and balance deficits?

Kooistra L, Ramage B, Crawford S, et al.

There is an ongoing debate regarding the diagnostic overlap between Attention Deficit Hyperactivity Disorder (ADHD) and Fetal Alcohol Spectrum Disorder (FASD). Differential diagnosis is important because of treatment implications. Children aged 7-10 years (47 ADHD, 30 FASD, 39 controls) participated. The Movement Assessment Battery for Children (M-ABC) and the Clinical Observations of Motor and Postural Skills (COMPS) were used. Force plate and electromyography data were collected during static balance and balance perturbation. On the M-ABC both children with ADHD and FASD had more motor problems than controls. The ADHD-Combined and the ADHD-Predominantly Inattentive subgroups were similarly affected in their fine motor skills. On the COMPS, the majority of children in both groups performed in the normal range, but for those children clinically affected, it was the children with ADHD who were more likely to be severely impaired. The children with ADHD were characterized by early onset latencies of the tibialis anterior muscles and increased amplitudes of the gastrocnemius muscles. Difficulty scaling muscle force reflecting medial cerebellar involvement may be the key problem in ADHD. Cerebellar involvement in the postural instability in FASD awaits further study.

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Neuropsychologia. 2009 Jul;47:1873-82.

Electrophysiological correlates of semantic processing during encoding of neutral and emotional pictures in patients with ADHD.

Krauel K, Duzel E, Hinrichs H, et al.

The current study investigated the relevance of semantic processing and stimulus salience for memory performance in young ADHD patients and healthy control participants. 18 male ADHD patients and 15 healthy control children and adolescents participated in an ERP study during a visual memory paradigm with two different encoding tasks requiring either perceptual or semantic processing of neutral and emotional pictures. ADHD patients and healthy controls both showed a more negative slow-wave in response to task cues signalling semantic as compared to perceptual stimulus processing. In contrast to ADHD patients, healthy control children showed a larger increase in memory performance for deeply processed neutral pictures which was accompanied by a more positive mid-latency ERP component (so-called P300) after stimulus onset. Our results demonstrate that ADHD patients succeeded in allocating neural resources in preparation of different task demands. However, this increase in preparatory activation to the semantic task cue did not suffice to support successful processing and encoding of neutral stimuli to the same extent as in healthy controls. These findings provide evidence that ADHD patients show deficits in translating pre-stimulus mobilization of neural resources to successful memory formation in the absence of salient stimulus material.

Journal of Clinical Nursing. 2009 Jun;18:1693-702.

The experiences of primary caregivers raising school-aged children with attention-deficit hyperactivity disorder.

Lin MJ, Huang XY, Hung BJ.

AIMS AND OBJECTIVES: To understand the experiences of primary caregivers who are bringing up school-aged children with attention-deficit hyperactivity disorder. The research findings will help address the problems related to caring for school-aged children with attention-deficit hyperactivity disorder.

BACKGROUND: In Taiwan, the rate of school-aged children diagnosed with attention-deficit hyperactivity disorder ranges from 7.9-11.7%. This study is the first, which tries to understand the experiences of primary

caregivers who are bringing up school-aged children with attention-deficit hyperactivity disorder in Taiwan.
DESIGN: The study used a qualitative phenomenological approach to explore the experiences of caregivers raising school-aged children with attention-deficit hyperactivity disorder.

METHODS: Purposive sampling and in-depth, face-to-face interviews were used to collect data. The unstructured interview guide allowed the major caregivers to express their experiences of raising school-aged children with attention-deficit hyperactivity disorder. When data saturation was reached, the sample size comprised 12 major caregivers. Narratives were analysed according to Colaizzi's seven-step method.

RESULTS: Three themes and seven sub-themes emerged from this study: the burdens of caring (parenting burdens, emotional burdens and family conflicts), the lack of adequate support systems (lack of support from professionals, spouses and other family members) and the mechanisms of coping (cognitive coping strategies and social coping strategies). Furthermore, several other factors that affected the caregivers of children with attention-deficit hyperactivity disorder are also revealed in the study.

CONCLUSION: The findings of the study demonstrate the importance of understanding the experiences of primary caregivers, bringing up school-aged children with attention-deficit hyperactivity disorder. Improving professional services in family care should be a major concern for all healthcare professionals.

RELEVANCE TO CLINICAL PRACTICE: The recommendations that have been made based on the findings of this research can be used as a guide to improve the delivery of caring by people who have school-aged children with attention-deficit hyperactivity disorder and by the wider family.

Pediatr Neurol. 2009;41:88-94.

Dexmedetomidine for Procedural Sedation in Children With Autism and Other Behavior Disorders.

Lubisch N, Roskos R, Berkenbosch JW.

Dexmedetomidine has been increasingly in use for pediatric noninvasive procedural sedation. This retrospective study examined experience in children with autism and other neurobehavioral disorders, populations often difficult to sedate. Records of children with autism or neurobehavioral disorders sedated with dexmedetomidine at Chris Evert Children's Hospital and Kosair Children's Hospital were reviewed. Demographic and sedation-related data were collected, including sedative doses, time to sedation, efficacy, and complications. Comparisons of sedative doses, efficacy between autism and neurobehavioral patients, and analysis of age-related factors were performed. In all, 315 patients were sedated, most commonly for magnetic resonance imaging. Mean induction and total dexmedetomidine doses were 1.4 (plus or minus) 0.6 and 2.6 (plus or minus) 1.6 (μ g/kg, respectively, with no differences between autism and neurobehavior patients. Most patients (90%) received concomitant midazolam. There was an age-related decrease in dexmedetomidine dose, independent of midazolam use. Seven patients required intervention for hypotension, bradycardia, or both, and only one adverse respiratory event (obstruction requiring nasopharyngeal airway placement) occurred. There were two episodes of overt recovery-related agitation. All but four procedures were successfully completed (4/315, or 98.7%). Dexmedetomidine with or without midazolam was an effective sedative in this population. The regimen appeared to be well tolerated with few adverse events, including recovery-related agitation, and appears to be an attractive option for this population.

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Psychiatry Res. 2009;168:222-29.

Does reward frequency or magnitude drive reinforcement-learning in attention-deficit/hyperactivity disorder?

Luman M, Van Meel CS, Oosterlaan J, et al.

Children with attention-deficit/hyperactivity disorder (ADHD) show an impaired ability to use feedback in the context of learning. A stimulus-response learning task was used to investigate whether (1) children with ADHD displayed flatter learning curves, (2) reinforcement-learning in ADHD was sensitive to either reward frequency, magnitude, or both, and (3) altered sensitivity to reward was specific to ADHD or would co-occur in a group of children with autism spectrum disorder (ASD). Performance of 23 boys with ADHD was compared with that of 30 normal controls (NCs) and 21 boys with ASD, all aged 8-12. Rewards were delivered contingent on performance and varied both in frequency (low, high) and magnitude (small, large). The findings showed that, although learning rates were comparable across groups, both clinical groups committed more errors than NCs. In contrast to the NC boys, boys with ADHD were unaffected by frequency and magnitude of reward. The NC group and, to some extent, the ASD group showed improved

performance, when rewards were delivered infrequently versus frequently. Children with ADHD as well as children with ASD displayed difficulties in stimulus-response coupling that were independent of motivational modulations. Possibly, these deficits are related to abnormal reinforcement expectancy.

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Pediatr Integr. 2009;13:150-56.

Adolescence. School problems.

Magana M.

It can be stated that an adolescent has scholar problems when his pedagogic results are lower than expected according to his intellectual capacity. They are intellectually normal subjects that have the ability to make an effort for completing a normal behavior and however, they do not actually have a satisfactory capacity for assimilating concepts. Etiology of scholar problems can be multimodal. However the most influencing for getting to set up the diagnosis and value the prognosis are: genetics, psico-social characteristics and evolution, family and school environment, culture and adaptive elements. Treatment shall always be inter-disciplinary and prevention measures shall only be applied after an exhaustive review of every associated parameter. Special attention should be paid on the knowledge of risk factors, situations and behaviors, as well as on the vulnerability level of the adolescent in trouble and on his adverse situations response capacity, i.e. on his "resilience".

Int J Psychophysiol. 2009;73:170-77.

Similarities and differences between learning abilities, "Pure" learning disabilities, "Pure" ADHD and comorbid ADHD with learning disabilities.

Mangina CA, Beuzeron-Mangina H.

This research pursues the crucial question of the differentiation of preadolescents with "Pure" ADHD, comorbid ADHD with learning disabilities, "Pure" learning disabilities and age-matched normal controls. For this purpose, Topographic Mapping of Event-Related Brain Potentials (ERPs) to a Memory Workload Paradigm with visually presented words, Bilateral Electrodermal Activity during cognitive workload and Mangina-Test performance were used. The analysis of Topographic distribution of amplitudes revealed that normal preadolescents were significantly different from "Pure" ADHD ($P<0.0001$), "Pure" learning disabilities ($P<0.0001$), and comorbid ADHD with learning disabilities ($P<0.0009$), by displaying enhanced prefrontal and frontal negativities (N450). In contrast, preadolescents with "Pure" ADHD and comorbid ADHD with learning disabilities have shown a marked reduction of prefrontal and frontal negativities (N450). As for the "Pure" Learning Disabled preadolescents, very small positivities (P450) in prefrontal and frontal regions were obtained as compared to the other pathological groups. Bilateral Electrodermal Activity during cognitive workload revealed a significant main effect for groups ($P<0.00001$), Left versus Right ($P=0.0029$) and sessions ($P=0.0136$). A significant main effect for the Mangina-Test performance which separated the four groups was found ($P<0.000001$). Overall, these data support the existence of clear differences and similarities between the pathological preadolescent groups as opposed to age-matched normal controls. The psychophysiological differentiation of these groups, provides distinct biological markers which integrate central, autonomic and neuropsychometric variables by targeting the key features of these pathologies for diagnosis and intervention strategies and by providing knowledge for the understanding of normal neurocognitive processes and functions.

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J Dev Behav Pediatr. 2008;29:206-12.

Nonsignificance of sleep relative to IQ and neuropsychological scores in predicting academic achievement.

Mayes SD, Calhoun SL, Bixler EO, et al.

OBJECTIVE: The goal of the study was to determine the relative importance of sleep, IQ, neuropsychological, and attention-deficit/hyperactivity disorder (ADHD) scores in predicting academic achievement.

METHOD: Objective overnight polysomnograph sleep scores, parent ratings of sleep problems, IQ, neuropsychological test scores, and parent ratings of ADHD were used to predict academic achievement in a general population sample of 412 elementary schoolchildren, 6 to 12 years of age with IQs of 71 to 147.

RESULTS: Using stepwise linear regression analysis, IQ was the best single predictor of reading and math achievement test scores. The most powerful combined predictors of achievement were IQ and some of the neuropsychological test scores. Subjective parent-reported sleep problems and objective polysomnograph scores (apnea-hypopnea index, mean oxygen saturation and lowest saturation percentage during sleep, snoring frequency and severity, sleep latency, minutes to rapid eye movement (REM) sleep, arousal index, number of awakenings, sleep efficiency, and percentage of stage 1, 2, 3, 4, and REM sleep) did not contribute significantly more to the prediction of achievement. Children with and without sleep problems did not differ from each other in achievement. IQ, neuropsychological test scores, and ADHD ratings were all significantly related to achievement, but correlations between achievement and objective and subjective sleep scores were all nonsignificant.

CONCLUSIONS: There may be individual children for whom sleep problems affect achievement, but for a large group of community children, sleep was not significantly related to academic functioning. In contrast, IQ and neuropsychological test scores were powerful predictors of achievement.

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Mutation Research: Fundamental & Molecular Mechanisms of Mutagenesis. 2009 Jun;666:44-49.

Absence of cytogenetic effects in children and adults with attention-deficit/hyperactivity disorder treated with methylphenidate.

Ponsa I, Ramos-Quiroga JA, Ribasés M, et al.

Attention-deficit/hyperactivity disorder (ADHD) is the most common psychiatric condition with onset in childhood, and in more than 50% of cases it persists into adulthood as a chronic disorder. Over five million methylphenidate (MPH) prescriptions were issued in the USA in 2003, mostly for children. A previous report [R.A. El-Zein, S.Z. Abdel-Rahman, M.J. Hay, M.S. Lopez, M.L. Bondy, D.L. Morris and M.S. Legator Cytogenetic effects in children treated with methylphenidate, Cancer Lett. 230 (2005) 284-291.] described the induction of chromosome abnormalities by MPH in children treated for three months, contrary to most of the in vitro and in vivo studies reported since then. We present new relevant information concerning the cytogenetic effects of MPH in children and adults. We include a prospective sample of 12 children and 7 adults with a new diagnosis of ADHD and naive to MPH. We analyzed the cytogenetic effects on peripheral lymphocytes before and three months after starting MPH therapy. The cytogenetic analyses included a cytokinesis-block micronucleus (CBMN) assay, a sister chromatid exchange (SCE) analysis and the determination of chromosome aberrations (CA). Following the same strategy and analyzing the same cytogenetic endpoints that were investigated in the original report [R.A. El-Zein, S.Z. Abdel-Rahman, M.J. Hay, M.S. Lopez, M.L. Bondy, D.L. Morris and M.S. Legator Cytogenetic effects in children treated with methylphenidate, Cancer Lett. 230 (2005) 284-291.], we found no evidence of increased frequency of micronuclei, sister chromatid exchanges or chromosome aberrations induced by MPH in children and adult populations. MPH treatment of children and adults with ADHD resulted in no significant genomic damage (as suggested by the three endpoints studied), results that do not support a potential increased risk of cancer after exposure to MPH.

Journal of Learning Disabilities. 2009 May;42:240-49.

The Role of Multidimensional Attentional Abilities in Academic Skills of Children With ADHD.

Preston AS, Heaton SC, McCann SJ, et al.

Despite reports of academic difficulties in children with attention-deficit/hyperactivity disorder (ADHD), little is known about the relationship between performance on tests of academic achievement and measures of attention. The current study assessed intellectual ability, parent-reported inattention, academic achievement, and attention in 45 children (ages 7-15) diagnosed with ADHD. Hierarchical regressions were performed with selective, sustained, and attentional control/switching domains of the Test of Everyday Attention for Children as predictor variables and with performance on the Wechsler Individual Achievement Test-Second Edition as dependent variables. It was hypothesized that sustained attention and attentional control/switching would predict performance on achievement tests. Results demonstrate that attentional control/ switching accounted for a significant amount of variance in all academic areas (reading, math, and spelling), even after accounting for verbal IQ and parent-reported inattention. Sustained attention predicted variance only in math,

whereas selective attention did not account for variance in any achievement domain. Therefore, attentional control/switching, which involves components of executive functions, plays an important role in academic performance.

J Dev Behav Pediatr. 2009;30:115-21.

Prenatal and perinatal morbidity in children with Tourette syndrome and attention-deficit hyperactivity disorder.

Pringsheim T, Sandor P, Lang A, et al.

OBJECTIVE: Tourette syndrome (TS) and attention-deficit hyperactivity disorder (ADHD) are frequently seen in combination, though the cause of comorbidity is uncertain. Low birth weight is a known risk factor for ADHD. The objective of the study was to assess the association between pre- and perinatal morbidity and the comorbid diagnosis of ADHD in children with TS.

METHOD: A nested case-control study of children evaluated for TS at a subspecialty clinic was performed. Cases were defined as children with TS and ADHD; controls had TS without ADHD. Exposure to pre- and perinatal morbidity was assessed using demographic information booklets completed by parents before the diagnostic interview.

RESULTS: Three hundred fifty-three children were included, 181 cases and 172 controls. Children with TS and ADHD had a greater odds of exposure to low birth weight status, prematurity, breathing problems, and maternal smoking compared with children with TS only. A multivariable logistic regression model found adjusted odds ratios for the comorbid diagnosis of TS and ADHD of 2.74 (95% CI 1.03-7.29, p=.04) in children born low birth weight, and of 2.43 (95% CI 1.23-4.82, p=.01) for children exposed to maternal smoking.

CONCLUSION: In children with TS, there is a greater odds of comorbid ADHD in children born with low birth weight or with exposure to maternal smoking. The commonality of risk factors for ADHD only and tic-related ADHD supports a common underlying neurobiology. Women with fetuses at risk for TS should avoid smoking and preventable causes of low birth weight to minimize the risk of comorbid ADHD.

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Aust New Zealand J Psychiatry. 2009;43:340-47.

Changes in use of psychostimulant medication for ADHD in South Australia (1990-2006).

Prosser B, Reid R.

Objective: The aim of the present study was to undertake a retrospective analysis of archival data on psychostimulant prescriptions from South Australia for the periods 1990-2000 and 2001-2006 for 7849 youths aged from birth to 18 years.

Method: A person-based data set was used to assess: (i) rate of new prescriptions by age group; (ii) demographic characteristics (age of psychostimulant start, male: female ratio); (iii) duration of psychostimulant use; and (iv) geographic variation in psychostimulant prescription.

Results: Four major findings were observed: (i) the rate of new prescriptions was highly variable both for 1990-2000 and 2000-2006; (ii) demographic characteristics such as start age and male:female ratio declined over both periods; (iii) the duration of psychostimulant use was approximately 2.5 years for 1990-2000 and 2.0 years for 2000-2006; and (iv) there was geographic variation in both periods with a significant correlation between socioeconomic status and prescription rate per region.

Conclusions: The patterns of psychostimulant use in Australia closely parallel the USA. Physicians' prescribing practice may be extremely volatile. Duration of psychostimulant treatment should receive increased attention. There is pronounced geographic variability in prescription rates, which may be related to socioeconomic status.

Psychiatry Research: Neuroimaging Section. 2009 May;172:147-54.

Manual MRI parcellation of the frontal lobe.

Ranta ME, Crocetti D, Clauss JA, et al.

The ability to examine associations between neuropsychiatric conditions and functionally relevant frontal lobe sub-regions is a fundamental goal in neuropsychiatry, but methods for identifying frontal sub-regions in

MR (magnetic resonance) images are not well established. Prior published techniques have principally defined gyral regions that do not necessarily correspond to known functional divisions. We present a method in which sulcal-gyral landmarks are used to manually delimit functionally relevant regions within the frontal lobe: primary motor cortex, anterior cingulate, deep white matter, premotor cortex regions (supplementary motor complex (SMC), frontal eye field and lateral premotor cortex) and prefrontal cortex (PFC) regions (medial PFC, dorsolateral PFC (DLPFC), inferior PFC, lateral orbitofrontal cortex (OFC) and medial OFC). Feasibility was tested by applying the protocol to brain MR data from 15 boys with attention-deficit/hyperactivity disorder (ADHD) and 15 typically developing controls, 8-12 years old. Intra- and inter-rater intraclass correlation coefficients were calculated using parcellation volumes from a subset of that group. Inter-rater results for the 22 hemisphere specific sub-regions ranged from 0.724 to 0.997, with all but seven values above 0.9. Boys with ADHD showed significantly smaller left hemisphere SMC and DLPFC volumes after normalization for total cerebral volume. These findings support the method as a reliable and valid technique for parcellating the frontal lobe into functionally relevant sub-regions.

Journal of Clinical Psychology in Medical Settings. 2009 Jun;16:148-60.

Assessing ADHD-related Family Stressors with the Disruptive Behavior Stress Inventory (DBSI): A Replication and Extension.

Reader SK, Stewart LM, Johnson JH.

The Disruptive Behavior Stress Inventory (DBSI) was developed to provide information related to the occurrence and severity of stressors that result from having a child with ADHD. Data provided in the initial 2002 study by Johnson and Reader (Journal of Clinical Psychology in Medical Settings, 9, 51–62) provided good preliminary support for the reliability of the DBSI, as well the ability of the scale scores to differentiate primary caregivers of children with and without a history of ADHD. The present study was an attempt to replicate major findings of the 2002 study using an additional larger sample and extend it by conducting item-level analyses to determine the degree to which individual DBSI items differentiate primary caregivers of children with and without a history of ADHD. Results provided additional support for the reliability and validity of the DBSI by replicating major findings from the 2002 study and further suggesting that a large majority of the 40 items individually differentiate between primary caregivers of children with and without a history of ADHD.

Accident Analysis & Prevention. 2009 Jul;41:670-75.

The role of risk-taking and errors in children's liability to unintentional injury.

Rowe R, Maughan B.

There is likely to be heterogeneity in the processes putting children at risk of injury. This paper examines whether errors may form a dissociable process from risk-taking. We further examine whether these constructs mediate the links between emotional and behavioural problems and unintentional injury. We designed the parent-report Children's Injury Related Behaviour (CIRB) questionnaire to measure errors and risk-taking in everyday activities. The sample consisted of 499 children aged 4-11 years recruited from the community. Principal components analysis showed that a two factor solution was appropriate and provided scales to measure risk and error with good psychometric properties. Both risk and error scales were independently related to injury history. Errors were associated with conduct problems, emotional problems and hyperactivity. Risk-taking was associated with conduct problems and hyperactivity only. Risk-taking and errors accounted for the links of conduct problems and hyperactivity with injury involvement. The distinction between risk and error has implications for research and interventions to reduce childhood injuries.

J Neurol. 2009;256:1103-08.

A preliminary study of the frequency of anti-basal ganglia antibodies and streptococcal infection in attention deficit/hyperactivity disorder.

Sanchez-Carpintero R, Albesa SA, Crespo N, et al.

Attention deficit/hyperactivity disorder (ADHD) is often present in patients with post-streptococcal neuropsychiatric disorders such as Sydenham's chorea and PANDAS, in which anti-basal ganglia antibodies (ABGA) have been frequently found. Our study investigates the hypothesis that pharyngeal group A (beta)-

hemolytic streptococcus (GABHS) infections and serum ABGA are more frequent in children with ADHD non-comorbid (nc-ADHD) with obsessive-compulsive disorder or tics than in controls. We compared 22 children with nc-ADHD (DSM-IV-TR) and 22 healthy controls matched by age, gender and season of sample collection, for the frequency of recent GABHS infection and the presence of ABGA. Eleven out of 22 children (51%) with nc-ADHD showed evidence of GABHS infection compared to three out of 22 (14%) controls ($P=0.007$). We found positive ABGA in one ADHD subject (4%) and in one control (4%). This preliminary study indicates that frequency of ABGA in children with nc-ADHD does not differ from that in matched controls, despite the fact that our ADHD patients had had more recent GABHS infections than the controls. This suggests that ABGA do not have a role in the pathogenesis of nc-ADHD.

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Pediatrics. 2009 May;123:1273-79.

Positive Association Between Attention-Deficit/Hyperactivity Disorder Medication Use and Academic Achievement During Elementary School.

Scheffler RM, Brown TT, Fulton BD, et al.

OBJECTIVE. Approximately 4.4 million (7.8%) children in the United States have been diagnosed with attention-deficit/hyperactivity disorder, and 56% of affected children take prescription medications to treat the disorder. Attention-deficit/hyperactivity disorder is strongly linked with low academic achievement, but the association between medication use and academic achievement in school settings is largely unknown. Our objective was to determine if reported medication use for attention-deficit/hyperactivity disorder is positively associated with academic achievement during elementary school.

METHOD. To estimate the association between reported medication use and standardized mathematics and reading achievement scores for a US sample of 594 children with attention-deficit/hyperactivity disorder, we used 5 survey waves between kindergarten and fifth grade from the nationally representative Early Childhood Longitudinal Study--Kindergarten Class of 1998--1999 to estimate a first-differentiated regression model, which controlled for time invariant confounding variables.

RESULTS. Medicated children had a mean mathematical score that was 2.9 points higher than the mean score of unmedicated peers with attention-deficit/hyperactivity disorder. Children who were medicated for a longer duration (at >2 waves) had a mean reading score that was 5.4 points higher than the mean score of unmedicated peers with attention-deficit/hyperactivity disorder. The medication-reading association was lower for children who had an individualized education program than for those without such educational accommodation.

CONCLUSIONS. The finding of a positive association between medication use and standardized mathematics and reading test scores is important, given the high prevalence of attention-deficit/hyperactivity disorder and its association with low academic achievement. The 2.9-point mathematics and 5.4-point reading score differences are comparable with score gains of 0.19 and 0.29 school years, respectively, but these gains are insufficient to eliminate the test-score gap between children with attention-deficit/hyperactivity disorder and those without the disorder. Long-term trials are needed to better understand the relationship between medication use and academic achievement.

Discourse & Society. 2009 Jul;20:499-516.

'ADHD patient' or 'illicit drug user'? Managing medico-moral membership categories in drug dependence services.

Schubert SJ, Hansen S, Dyer KR, et al.

Amphetamine-dependent patients seeking treatment are diagnosed with ADHD at a significantly higher rate than members of the general population. To study this relationship as it is constructed in everyday life, we draw on membership categorization analysis to examine how individuals account for their candidate memberships in two social categories - 'illicit amphetamine user' and 'ADHD patient'. We analyse interviews with four drug-dependent individuals, diagnosed with adult ADHD, undergoing detoxification treatment in Perth, Western Australia. Participants formulated their problematic behaviour via membership in the morally neutral category 'ADHD patient' and methodically constructed symptoms as predicates of this category, despite the availability of the equally valid alternative category 'illicit amphetamine user'. The category 'ADHD patient' is shown to be functional: it absolves drug users from responsibility for troublesome conduct, and provides continued access to amphetamines as 'medication'. In such cases, the diagnosis of ADHD arguably

affords the conditions of possibility for an iatrogenic disorder in that the prescription of ATS medication provides for a morally and legally sanctioned form of drug dependence.

Arch Gen Psychiatry. 2009 Aug;66:888-96.

Development of cortical asymmetry in typically developing children and its disruption in attention-deficit/hyperactivity disorder.

Shaw P, Lalonde F, Lepage C, et al.

CONTEXT: Just as typical development of anatomical asymmetries in the human brain has been linked with normal lateralization of motor and cognitive functions, disruption of asymmetry has been implicated in the pathogenesis of neurodevelopmental disorders such as attention-deficit/hyperactivity disorder (ADHD). No study has examined the development of cortical asymmetry using longitudinal neuroanatomical data.

OBJECTIVE: To delineate the development of cortical asymmetry in children with and without ADHD.

DESIGN: Longitudinal study.

SETTING: Government Clinical Research Institute.

PARTICIPANTS: A total of 218 children with ADHD and 358 typically developing children, from whom 1133 neuroanatomical magnetic resonance images were acquired prospectively.

MAIN OUTCOME MEASURES: Cortical thickness was estimated at 40 962 homologous points in the left and right hemispheres, and the trajectory of change in asymmetry was defined using mixed-model regression.

RESULTS: In right-handed typically developing individuals, a mean (SE) increase in the relative thickness of the right orbitofrontal and inferior frontal cortex with age of 0.011 (0.0018) mm per year ($t(337) = 6.2$, $P < .001$) was balanced against a relative left-hemispheric increase in the occipital cortical regions of 0.013 (0.0015) mm per year ($t(337) = 8.1$, $P < .001$). Age-related change in asymmetry in non-right-handed typically developing individuals was less extensive and was localized to different cortical regions. In ADHD, the posterior component of this evolving asymmetry was intact, but the prefrontal component was lost.

CONCLUSIONS: These findings explain the way that, in typical development, the increased dimensions of the right frontal and left occipital cortical regions emerge in adulthood from the reversed pattern of childhood cortical asymmetries. Loss of the prefrontal component of this evolving asymmetry in ADHD is compatible with disruption of prefrontal function in the disorder and demonstrates the way that disruption of typical processes of asymmetry can inform our understanding of neurodevelopmental disorders.

J Pediatr. 2009;155:245-49.

Children with Attention Deficit Hyperactivity Disorder Have Impaired Balance Function: Involvement of Somatosensory, Visual, and Vestibular Systems.

Shum SBM, Pang MYC.

Objectives: To compare standing balance performance and sensory organization of balance control in children with attention deficit hyperactivity disorder (combined type) (ADHD-C) and typically developing children.

Study design: School-aged children ($n=43$) with ADHD-C and 50 age- and sex-matched typically developing children participated in the study. Sensory organization of standing balance was evaluated using the Sensory Organization Test (SOT). In addition to the composite equilibrium score, somatosensory, vestibular, and visual ratios, which were indicators of the ability of the child to use information from the respective sensory systems to maintain balance, were computed. Multivariate analysis of covariance (MANCOVA) was used to compare the outcome variables between the 2 groups while controlling for physical activity level.

Results: MANCOVA revealed that children with ADHD-C had significantly lower composite equilibrium scores ($P < .001$) and somatosensory ($P = .029$), vestibular ($P = .037$), and visual ratios ($P = .001$) than control children, by 10.3%, 2.1%, 15.6%, and 16.0%, respectively.

Conclusions: Children with ADHD-C had significant deficits in standing balance performance in all conditions that included a disruption of sensory signals. The visual system tends to be more involved in contributing to the balance deficits in children with ADHD-C than the somatosensory and vestibular systems.

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J Neuroimaging. 2009;19:205-12.

Event-Related fMRI of inhibitory control in the predominantly inattentive and combined subtypes of adhd: Clinical investigative study.

Solanto MV, Schulz KP, Fan J, et al.

BACKGROUND AND PURPOSE To examine the neurophysiological basis for the pronounced differences in hyperactivity and impulsiveness that distinguish the predominantly inattentive type of attention-deficit/hyperactivity disorder (ADHD-PI) from the combined type of the disorder (ADHD-C).

METHODS Event-related brain responses to a go/no-go test of inhibitory control were measured with functional magnetic resonance imaging (fMRI) in 11 children with ADHD-C and 9 children with ADHD-PI, aged 7 to 13 years, who were matched for age, sex, and intelligence.

RESULTS There were no significant group differences in task performance. Children with ADHD-C and ADHD-PI activated overlapping regions of right inferior frontal gyrus, right superior temporal lobe, and left inferior parietal lobe during inhibitory control. However, the magnitude of the activation in the temporal and parietal regions, as well as in the bilateral middle frontal gyrus, was greater in children with ADHD-PI than those with ADHD-C. Conversely, children with ADHD-C activated bilateral medial occipital lobe to a greater extent than children with ADHD-PI.

CONCLUSIONS The results provide preliminary evidence that phenotypic differences between the ADHD-C and ADHD-PI subtypes are associated with differential activation of regions that have previously been implicated in the pathophysiology of ADHD and are thought to mediate executive and attentional processes.

J Neuroimaging 2009;19:205-212.

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J Clin Psychiatry. 2009 Jul;70:950-51.

The prefrontal cortex is out of tune in attention-deficit/hyperactivity disorder.

Stahl SM.

J Clin Rheumatol. 2008;14:30-33.

Methylphenidate and dextroamphetamine-induced peripheral vasculopathy.

Syed RH, Moore TL.

Methylphenidate and dextroamphetamine are central nervous system stimulants used in the treatment of attention deficit hyperactivity disorders in children. These medications have been associated with cerebral arteritis, renal necrotizing vasculitis, and systemic and pulmonary hypertension. We report 4 patients, 2 on methylphenidate and 2 on dextroamphetamine who presented with acral cyanosis, livedo reticularis, or Raynaud phenomenon. Two patients were found to have a positive ANA at low titers, 1 of whom had histopathologic evidence of stratum malpighian necrosis with perivascular lymphocytic infiltration on skin biopsy. Two had positive antihistone antibodies. One patient improved after withdrawal of dextroamphetamine; others had worsening of their symptoms on higher doses of medications. These cases indicate the potential for development of acral cyanosis, livedo reticularis, or Raynaud symptoms with these medications and their potential contribution to a vasculopathy.

Neuropsychologia. 2009;47:2436-45.

Different behavioral and eye movement patterns of dyslexic readers with and without attentional deficits during single word reading.

Thaler V, Urton K, Heine A, et al.

Comorbidity of learning disabilities is a very common phenomenon which is intensively studied in genetics, neuropsychology, prevalence studies and causal deficit research. In studies on the behavioral manifestation of learning disabilities, however, comorbidity is often neglected. In the present study, we systematically examined the reading behavior of German-speaking children with dyslexia, of children with attentional problems, of children with comorbid dyslexia and attentional problems and of normally developing children by measuring their reading accuracy, naming latencies and eye movement patterns during single word reading. We manipulated word difficulty by contrasting (1) short vs. long words with (2) either low or high sublexical complexity (indexed by consonant cluster density). Children with dyslexia only (DYS) showed the

expected reading fluency impairment of poor readers in regular orthographies but no accuracy problem. In contrast, comorbid children (DYS + AD) had significantly higher error rates than all other groups, but less of a problem with reading fluency than DYS. Concurrently recorded eye movement measures revealed that DYS made the highest number of fixations, but exhibited shorter mean single fixations than DYS + AD. Word length had the strongest effect on dyslexic children, whereas consonant cluster density affected all groups equally. Theoretical implications of these behavioral and eye movement patterns are discussed and the necessity for controlling for comorbid attentional deficits in children with reading deficits is highlighted.

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Cytogenetic assessment of methylphenidate treatment in pediatric patients treated for attention deficit hyperactivity disorder.

Tucker JD, Suter W, Petibone DM, et al.

Methylphenidate (MPH, Ritalin), has been prescribed to treat attention deficit/hyperactivity disorder (ADHD) since its approval by the FDA over 50 years ago. Diagnoses of pediatric patients with ADHD and the administration of MPH to treat the symptoms have increased in prevalence in recent years. A 2005 study by El-Zein et al. reported statistically significant increases in cytogenetic anomalies including chromosomal aberrations (CA), micronuclei (MN) and sister chromatid exchanges (SCEs) in peripheral blood lymphocytes cultured from pediatric patients treated for 3 months with MPH. These findings led to wide-spread concern regarding the potential for genotoxic risks associated with prolonged administration of MPH. The study described in the present paper was designed to repeat the El-Zein effort with a much larger sample size. The subjects (N = 109) were randomized into two groups: one treated with MPH as well as behavior therapy, the other was a control group that received behavior therapy only. We evaluated CAs, MN, and SCEs in peripheral blood lymphocytes in samples obtained prior to therapy and after 3 months of treatment with MPH. The data were analyzed using a Poisson regression model with a generalized estimating equation method adjusted for several covariates including time, treatment-by-time interaction, sex, and age group. The log(e) rate ratios of the MPH plus behavior therapy and behavior therapy groups were compared. The frequencies of CAs, MN, and SCEs were not increased in the MPH plus behavior therapy group when compared to the behavior therapy group only ($p = 0.53, 0.28, 0.81$, respectively). These results provide evidence in a large cohort that MPH does not induce cytogenetic anomalies in children, in contrast to the findings of the El-Zein study.

Neuropsychologia. 2009;47:2389-96.

Increased intra-individual reaction time variability in attention-deficit/hyperactivity disorder across response inhibition tasks with different cognitive demands.

Vaurio RG, Simmonds DJ, Mostofsky SH.

One of the most consistent findings in children with ADHD is increased moment-to-moment variability in reaction time (RT). The source of increased RT variability can be examined using ex-Gaussian analyses that divide variability into normal and exponential components and Fast Fourier transform (FFT) that allow for detailed examination of the frequency of responses in the exponential distribution. Prior studies of ADHD using these methods have produced variable results, potentially related to differences in task demand. The present study sought to examine the profile of RT variability in ADHD using two Go/No-go tasks with differing levels of cognitive demand. A total of 140 children (57 with ADHD and 83 typically developing controls), ages 8-13 years, completed both a "simple" Go/No-go task and a more "complex" Go/No-go task with increased working memory load. Repeated measures ANOVA of ex-Gaussian functions revealed for both tasks children with ADHD demonstrated increased variability in both the normal/Gaussian (significantly elevated sigma) and the exponential (significantly elevated tau) components. In contrast, FFT analysis of the exponential component revealed a significant task null diagnosis interaction, such that infrequent slow responses in ADHD differed depending on task demand (i.e., for the simple task, increased power in the 0.027-0.074 Hz frequency band; for the complex task, decreased power in the 0.074-0.202 Hz band). The ex-Gaussian findings revealing increased variability in both the normal (sigma) and exponential (tau) components for the ADHD group, suggest that both impaired response preparation and infrequent "lapses in attention" contribute to increased variability in ADHD. FFT analyses reveal that the periodicity of intermittent lapses of attention in ADHD varies with task demand. The findings provide further support for intra-individual variability as a candidate intermediate endophenotype of ADHD. (copyright) 2009 Elsevier Ltd. All rights reserved

Cerebrospinal Fluid Res. 2009;6.

Neuropsychological assessment of attention in children with spina bifida.

Vinck A, Mullaart R, Rotteveel J, et al.

Background: Children with the severe form of spina bifida (SBM: spina bifida with myelomeningocele with accompanying hydrocephalus) may manifest attention deficits, and have a similar psychological profile to children with hydrocephalus due to other etiologies. It is unclear to what extent tests to assess attention in SBM are confounded by the accompanying cognitive or visual-motor impairments. The aim of this study was to analyse attention functions by administering two different types of attention tests, one with high and the other with low cognitive and motor requirements. This enabled the possible interaction between attention and cognitive and motor impairment to be assessed.

Methods: The study group comprised 31 children with SBM with shunted hydrocephalus. Twenty children with SB-only formed a closely matched comparison group. Of these, 19 children with SBM and 18 with SB had a full-scale IQ (FSIQ) higher than 70. All had undergone spinal surgery and all children with SBM had been shunted within the first months of life. Between 6 and 15 years of age, the children were assessed on focused and sustained attention, encoding, and distractibility/ impulsivity, using both traditional tests and computerized attention tests.

Results: Compared to the SB group, attention scores of children with SBM were lower on the traditional tests, but when interfering cognitive and visual-motor requirements were eliminated using the computerised tasks, most differences disappeared. Furthermore, in contrast to traditional attention tasks, computerized tests showed no significant correlations with IQ-scores and visual-motor skills.

Conclusion: Assessment of attention functions in children with SBM by traditional tests may be misleading, because this paediatric population with complex cerebral malformations has difficulty with the cognitive and visual-motor requirements. To control for these interactions, the use of both traditional and computerized attention tests is recommended.

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A 13-hour laboratory school study of lisdexamfetamine dimesylate in school-aged children with attention-deficit/hyperactivity disorder.

Wigal SB, Kollins SH, Childress AC, et al.

Background: Lisdexamfetamine dimesylate (LDX) is indicated for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children 6 to 12 years of age and in adults. In a previous laboratory school study, LDX demonstrated efficacy 2 hours postdose with duration of efficacy through 12 hours. The current study further characterizes the time course of effect of LDX.

Methods: Children aged 6 to 12 years with ADHD were enrolled in a laboratory school study. The multicenter study consisted of open-label, dose-optimization of LDX (30, 50, 70 mg/d, 4 weeks) followed by a randomized, placebo-controlled, 2-way crossover phase (1 week each). Efficacy measures included the SKAMP (deportment [primary] and attention [secondary]) and PERMP (attempted/correct) scales (secondary) measured at predose and at 1.5, 2.5, 5, 7.5, 10, 12, and 13 hours postdose. Safety measures included treatment-emergent adverse events (AEs), physical examination, vital signs, and ECGs.

Results: A total of 117 subjects were randomized and 111 completed the study. Compared with placebo, LDX demonstrated significantly greater efficacy at each postdose time point (1.5 hours to 13.0 hours), as measured by SKAMP deportment and attention scales and PERMP ($P < .005$). The most common treatment-emergent AEs during dose optimization were decreased appetite (47%), insomnia (27%), headache (17%), irritability (16%), upper abdominal pain (16%), and affect lability (10%), which were less frequent in the crossover phase (6%, 4%, 5%, 1%, 2%, and 0% respectively).

Conclusion: In school-aged children (6 to 12 years) with ADHD, efficacy of LDX was maintained from the first time point (1.5 hours) up to the last time point assessed (13.0 hours). LDX was generally well tolerated, resulting in typical stimulant AEs.

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Factors Contributing to Attentional Impairments After Traumatic Brain Injury.

Willmott C, Ponsford J, Hocking C, et al.

The aim of the present study was to investigate the contribution of impaired information processing speed and strategic control of attention to performance on attentional tasks after traumatic brain injury (TBI). Forty moderately to severely injured rehabilitation inpatients and 40 healthy controls completed a selection of attentional tasks. Slowed processing speed in the TBI group was identified on the Symbol Digit Modalities Test (SDMT), 2&7 Selective Attention Test (2&7), Selective Attention (SAT), and Four Choice Reaction Time (4CRT) tasks. Impaired working memory was evident on the Letter Number Sequencing (LNS) task. Structural equation modeling revealed that the group difference in RT on the complex SAT was accounted for by slowed speed of processing on the simple SAT, and not working memory. TBI participants made more errors and missed responses on the complex version of the SAT, suggesting impairment in some aspects of strategic control of attention, and appeared unable to benefit from the automatic condition of the 2&7 Test. There was little evidence of deficit on the Sustained Attention to Response Task (SART). The present study provides evidence for a significant contribution of slowed processing speed to impaired performance on attentional tasks after TBI.

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