**EEG phenotypes predict treatment outcome to stimulants in children with ADHD.**  
This study demonstrates that the EEG phenotypes as described by Johnstone, Gunkelman & Lunt are identifiable EEG patterns with good inter-rater reliability. Furthermore, it was also demonstrated that these EEG phenotypes occurred in both ADHD subjects as well as healthy control subjects. The Frontal Slow and Slowed Alpha Peak Frequency and the Low Voltage EEG phenotype discriminated ADHD subjects best from controls (however the difference was not significant). The Frontal Slow group responded to a stimulant with a clinically relevant decreased number of false negative errors on the CPT. The Frontal Slow and Slowed Alpha Peak Frequency phenotypes have different etiologies as evidenced by the treatment response to stimulants. In previous research Slowed Alpha Peak Frequency has most likely erroneously shown up as a frontal theta sub-group. This implies that future research employing EEG measures in ADHD should avoid using traditional frequency bands, but dissociate Slowed Alpha Peak Frequency from frontal theta by taking the individual alpha peak frequency into account. Furthermore, the divergence from normal of the frequency bands pertaining to the various phenotypes is greater in the clinical group than in the controls. Investigating EEG phenotypes provides a promising new way to approach EEG data, explaining much of the variance in EEGs and thereby potentially leading to more specific prospective treatment outcomes.  
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**Mental disorders in children.**  
*Berg C.*  

**Children with ADHD in residential care.**  
Little is known about the characteristics or functioning of children with ADHD in residential care as compared to their non-ADHD peers. This study evaluated data on 538 children with (n = 125) and without (n = 413) ADHD in residential care to determine demographic, mental health, behavioral, and treatment (i.e., medication use) characteristics. Results revealed that both groups presented elevated risks, however, scores for children with ADHD indicated even greater levels of need. Specifically, differences were found between the two groups on demographics (e.g., family reunification status, restrictiveness of prior out-of-home placements), behavior (e.g., attention problems, rule-breaking and aggressive behaviors) and medication status. Findings suggest there is a need for aftercare services to help support families as children transition from care, interventions to address behavior, and medication management through assessment and monitoring.  
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St. John's Wort does not show benefit for ADHD in short trial.
Chan E.

Depression Anxiety. 2008;25:E142-E146.

Associations between symptoms of attention deficit hyperactivity disorder, depression, and suicide in Korean female adolescents.
The objective of this study was to examine the associations between symptoms of attention-deficit/hyperactivity disorder (ADHD), depression, and suicide in Korean female adolescents. It was hypothesized that the relationship between ADHD symptoms and suicidal ideation would be mediated by the level of depressive symptoms. Seven hundred and eighty-eight high school girls completed the Conners/Wells Adolescent Self-Report Scale: Short Form, Children's Depression Inventory, and Reynolds Suicidal Ideation Questionnaire. Path analyses were conducted using the statistical program, AMOS version 4.0, to determine the best fitting model. The conduct, cognitive, and hyperactivity problems of the ADHD symptoms in each domain were associated positively with the depressive symptoms, with the depressive symptoms being associated with suicidal ideation. This initially proposed model represented an acceptable fit to the data (root mean square error of approximation, RMSEA = 0.077; normed fit index, NFI = 0.998; non-NFI, NNFI = 0.990; comparative fit index, CFI = 0.998). The inclusion of a direct path from the conduct problems of ADHD symptoms to suicidal ideation significantly improved the model fit (RMSEA = 0, NFI = 1, NNFI = 1, CFI = 1). The results of our study suggest that depressive symptoms partially mediate the relationship between ADHD symptoms and suicidal ideation, and that the conduct problems of ADHD symptoms are associated with suicidal ideation both directly and indirectly via the depressive symptoms in Korean female adolescents.


Impact of attention-deficit/hyperactivity disorder on the patient and family: Results from a European survey.
Background: Children with attention-deficit/hyperactivity disorder (ADHD) often experience problems with education, interaction with others and emotional disturbances. Families of ADHD children also suffer a significant burden, in terms of strain on relationships and reduced work productivity. This parent survey assessed daily life for children with ADHD and their families.
Method: This pan-European survey involved the completion of an on-line questionnaire by parents of children (6-18 years) with ADHD (ADHD sample) and without ADHD (normative population sample). Parents were questioned about the impact of their child's ADHD on everyday activities, general behaviour and family relationships.
Results: The ADHD sample comprised 910 parents and the normative population sample 995 parents. 62% of ADHD children were not currently receiving medication; 15% were receiving 6-8 hour stimulant medication and 23% 12-hour stimulant medication. Compared with the normative population sample, parents reported that ADHD children consistently displayed more demanding, noisy, disruptive, disorganised and impulsive behaviour. Significantly more parents reported that ADHD children experienced challenges throughout the day, from morning until bedtime, compared with the normative population sample. Parents reported that children with ADHD receiving 12-hour stimulant medication experienced fewer challenges during early afternoon and late afternoon/early evening than children receiving 6-8 hour stimulant medication; by late evening and bedtime however, this difference was not apparent. ADHD was reported to impact most significantly on activities such as homework, family routines and playing with other children. All relationships between ADHD children and others were also negatively affected, especially those between parent and child (72% of respondents). Parents reported that more children with ADHD experienced a personal injury in the preceding 12 months, including those requiring the attention of healthcare professionals. Although 68% of parents were satisfied with their child's current treatment, 35-40% stated that their child's ADHD symptoms needed to be more effectively treated during the afternoon and evening.
Conclusion: This parent survey highlights the breadth of problems experienced by ADHD children and the impact throughout the day on both activities and relationships. Therefore, there is a need for treatment
approaches that take into account the 24-hour impact of the disorder and include all-day coverage with effective medication.

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Deficit in response inhibition in children with attention deficit/hyperactivity disorder (ADHD): Impact of motivation?

Desman C, Petermann F, Hampel P

To date, neuropsychological and psycho-physiological studies have revealed inconsistent results regarding an executive or motivational deficit explaining the response inhibition deficit in children with attention deficit/hyperactivity disorder (ADHD). Research on differentiating neuropsychological processes in ADHD subtypes is still scarce. Therefore, the motivational impact on response inhibition among boys with ADHD was examined in this study. In the first study, 19 boys with ADHD-combined type (ADHD-C) and 19 age-matched healthy control subjects performed a modified Go/No-Go task with the following experimental conditions: neutral, auditory feedback, reward, response cost, and reward/response cost. Performance and physiological data (heart rate and skin conductance responses) were recorded. In a second study with the modified Go/No-Go task, data for six children with ADHD-C, six with ADHD-inattentive subtype (ADHD-I), and six healthy control subjects were compared. Neither of the two studies revealed group by condition interactions. In study 1, boys with ADHD-C generally made more commissions and omissions compared to the control group. However, feedback significantly improved the response inhibition in all children. The heart rate of all children was increased in the two conditions of reward and reward/response cost. Study 2 revealed that children with ADHD-I responded more slowly and showed increased reaction time variability compared to both other groups. The present study supports an executive rather than a motivational deficit in the response inhibition among children with ADHD-C, though further results also indicate the role of auditory feedback on response inhibition. Additionally, the findings support the differentiation of ADHD-C and ADHD-I, suggesting that ADHD-I children are characterized by a sluggish cognitive tempo.

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EEG coherence in girls with Attention-Deficit/Hyperactivity Disorder: Stimulant effects in good responders.

Dupuy FE, Clarke AR, Barry RJ, et al.

This study investigated the effects of stimulants on EEG coherence in girls with Attention-Deficit/Hyperactivity Disorder (AD/HD). Twenty girls with AD/HD (aged 7-12) and 20 age- and sex-matched controls had an eyes-closed resting electroencephalogram (EEG) recorded from 21 electrode sites. Coherence was calculated from eight intrahemispheric electrode pairs (four in each hemisphere), and eight interhemispheric electrode pairs, for the delta, theta, alpha and beta frequency bands. AD/HD participants were tested twice: first, prior to medication being prescribed, and second, six months later on a therapeutic dose of a stimulant. With intrahemispheric coherences at short-medium inter-electrode distances, AD/HD girls off-medication had reduced lateralisation in the delta, theta and alpha bands. They also had reduced lateralisation in the theta band for longer inter-electrode distances, and increased frontal interhemispheric coherences in all frequency bands. Medication had no impact on the laterality anomalies, but produced novel increases in intrahemispheric coherences at short-medium inter-electrode distances, which reached significance in the delta band and approached significance in the alpha band. However, these increased coherences remained indistinguishable from control levels. Reduced hemispheric lateralisations found in these AD/HD participants illustrate cortical abnormalities consistent with maturational lag explanations. The widespread elevated frontal interhemispheric coherences found in these AD/HD girls could reflect the narrow profile of female medication responders identified in clinical settings. The lack of substantial coherence medication effects in good clinical responders supports a previous medication study with AD/HD boys, and suggests that these coherence anomalies reflect structural, rather than solely functional, differences in brain development in AD/HD.

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**Association of ADHD, tics, and anxiety with dopamine transporter (DAT1) genotype in autism spectrum disorder.**

**Gadow KD, Roohi J, DevVincent CJ, et al.**

**Background:** Autism spectrum disorder (ASD) is associated with high rates of psychiatric disturbance to include attention-deficit/hyperactivity disorder (ADHD), tic disorder, and anxiety disorders. The aim of the present study was to examine the association between a variable number tandem repeat (VNTR) functional polymorphism located in the 3'-untranslated region of the dopamine transporter gene (DAT1) and the severity of these symptoms as well as the association between the DAT1 DdeI polymorphism and severity of tics.

**Methods:** Parents (n = 62) and teachers (n = 57) completed a DSM-IV-referenced rating scale for 67 children with ASD.

**Results:** According to parent ratings, children with the 10-10 repeat allele (versus a combined group of all other genotypes) exhibited less severe symptoms of hyperactivity and impulsivity as well as less severe language deficits. Teacher ratings indicated that social anxiety and tic symptoms were more severe for children with the 10-10 genotype versus all others. Exploratory analyses provided preliminary support for the notion that heterozygosity (9-10 repeat genotype) may be a risk/protective factor. There were no associations of tic severity with the DAT1 DdeI polymorphism.

**Conclusion:** Collectively, these results suggest that the extraordinary variability in ASD clinical phenotypes may be explained in part by the same genes that are implicated in a host of other psychiatric disorders in non-ASD populations. Nevertheless, replication with independent samples is necessary to confirm this preliminary finding.

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**Hyperactivity-inattention symptoms in childhood and suicidal behaviors in adolescence: The Youth Gazel Cohort.**

**Galera C, Bouvard MP, Encrenaz G, et al.**

**Objective:** Although a link has been suggested between attention deficit/hyperactivity disorder (ADHD) and completed suicide, little is known about the association with suicidal behaviors in community settings. This study addresses the relationship between childhood hyperactivity-inattention symptoms (HI-s) and subsequent suicidal behaviors.

**Method:** Nine hundred sixteen subjects aged 7-18 were recruited from the general population and surveyed in 1991 and 1999. Parent and adolescent self-reports provided psychopathology and suicidal behavior pattern measures. Multivariate modeling was used to evaluate the effects of childhood HI-s and other risk factors on adolescent suicidal behaviors.

**Results:** In males, HI-s independently accounted for the risk of lifetime suicide plans/attempts (OR=3.25, P = 0.02) and adolescent 12-month prevalence rates of suicide plans/attempts (OR=5.46, P = 0.03). In females, HI-s did not independently heighten the likelihood of suicidal behaviors.

**Conclusion:** This survey suggests a possible specific link between HI-s and suicide plans/attempts in males.

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**Neuroanatomical abnormalities in adolescents with attention-deficit/ hyperactivity disorder.**

**Garrett A, Penniman L, Epstein JN, et al.**

**Objective:** Several neuroanatomic abnormalities have been reported in patients with attention-deficit/hyperactivity disorder (ADHD). However, findings are not always consistent, perhaps because of heterogeneous subject samples. Studying youths with documented familial ADHD provides an opportunity to examine a more homogeneous population.

**Method:** Twenty-four youths with a confirmed history of familial ADHD and 10 control youths underwent high-resolution structural magnetic resonance imaging examinations. Archived magnetic resonance imaging scan data from 12 control youths were included in the analysis to increase statistical power. Individually drawn region-of-interest methods were used to examine the frontal lobe gyri and caudate.

**Results:** Cerebral total tissue was similar between groups. The volumes of the right caudate and right inferior frontal lobe were larger in the ADHD youths compared with the control youths. Data from a subgroup
of the ADHD youths suggest that increasing left caudate volume is associated with decreasing functional activation of this region.

**Conclusions:** Because previous studies have focused primarily on younger subjects or used an extended age range, the present results may reflect neurodevelopmental changes specific to late adolescence in familial ADHD.

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**Observational study with atomoxetine for the treatment of children and adolescents with Asperger's syndrome and ADS.**

**Gehrmann J.**

Atomoxetine is approved for use as a selective noradrenaline reuptake inhibitor for the treatment of ADHD/ADS in children aged six years and older. Asperger's syndrome is a pervasive developmental disorder. As clinical experience has shown, comorbid attention deficit disorder is not uncommon. Here we report on experience with clinical application in the treatment of children and adolescents with high functioning Asperger's syndrome as well as attention deficit syndrome (ADS) (i.e. the so called inattentive subtype of ADHD). Atomoxetine gradually introduced, titrating to a target dose of between 1.2 and 1.4 mg/kg body weight was found to be well tolerated, with a gradual, but stable long-term effect on the main symptoms of ADS as well as improving psychosocial integration. However, these initial positive clinical trials need to be verified by a prospective, placebo-controlled treatment study.

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**Language profiles in ASD, SLI, and ADHD.**

**Geurts HM, Embrechts M.**

Developmental disorders might differ in their language profiles when using parent reports. The first study indicated that school aged children with ASD have similar language profiles as children with ADHD. Both groups had relatively more difficulties with pragmatics than with structural language aspects. The second study indicated that both preschoolers with ASD and those with SLI show the opposite pattern, thus having relatively more difficulties with structural language aspects than with pragmatics. Finally, an increase in the presence of ADHD characteristics of impulsivity in these preschoolers is associated with an increase in language difficulties, while there is no such relation with inattention. It seems useful to evaluate the communication abilities of children regularly in the course of development and take ADHD characteristics into account. Finally recommendations on clinical use of the Children's Communication Checklist-2 (CCC-2, Bishop 2003) are discussed.

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**Reduced white matter integrity in attention-deficit hyperactivity disorder.**

**Hamilton LS, Levitt JG, O'Neill J, et al.**

We used diffusion tensor imaging to investigate fractional anisotropy (FA), a measure of fiber tract integrity, in attention-deficit hyperactivity disorder (ADHD). Using a tract-based atlasing approach on six-direction diffusion tensor imaging data, we examined FA within the cingulum, corpus callosum, corticospinal tract, fornix, optic radiations, superior longitudinal fasciculus, uncinate fasciculus, and the superior and inferior occipitofrontal fasciculi in an all-male sample of 17 children and adolescents with ADHD and 16 age-matched controls. ADHD patients had significantly lower FA in the corticospinal tract (P=0.02) and the superior longitudinal fasciculus (P=0.017) compared with controls. Results support that disruptions in motor and attentional networks may contribute toward ADHD pathophysiology. Future research may clarify how ADHD subtype and psychiatric comorbidities affect diffusion measures.

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**Impaired conflict resolution and alerting in children with ADHD: Evidence from the Attention Network Task (ANT).**

**Johnson KA, Robertson IH, Barry E, et al.**

**Background:** An important theory of attention suggests that there are three separate networks that execute discrete cognitive functions. The ‘alerting’ network acquires and maintains an alert state, the ‘orienting’ network selects information from sensory input and the ‘conflict’ network resolves conflict that arises between potential responses. This theory holds promise for dissociating discrete patterns of cognitive impairment in disorders where attentional deficits may often be subtle, such as in attention deficit hyperactivity disorder (ADHD).

**Methods:** The Attentional Network Test (ANT), a behavioural assay of the functional integrity of attention networks, was used to examine the performance of 73 children with ADHD and 73 controls.

**Results:** Performance on the ANT clearly differentiated the children with and without ADHD in terms of mean and standard deviation (SD) of reaction time (RT), the number of incorrect responses made and the number of omission errors made. The ADHD group demonstrated deficits in the conflict network in terms of slower RT and a higher number of incorrect responses. The ADHD group showed deficits in the alerting network in terms of the number of omission errors made. There was no demonstration of a deficit in the orienting network in ADHD on this task.

**Conclusions:** The children with ADHD demonstrated deficits in the alerting and conflict attention networks but normal functioning of the orienting network.

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**Memory functioning in children with reading disabilities and/or attention deficit/hyperactivity disorder: A clinical investigation of their working memory and long-term memory functioning.**

**Kibby MY, Cohen MJ.**

We examined memory functioning in children with reading disabilities (RD), Attention deficit/hyperactivity disorder (ADHD), and RD/ADHD using a clinic sample with a clinical instrument: the Children's Memory Scale, enhancing its generalizability. Participants included 23 children with RD, 30 with ADHD, 30 with RD/ADHD, and 30 controls. Children with RD presented with reduced verbal short-term memory (STM) but intact visual STM, central executive (CE), and long-term memory (LTM) functioning. Their deficit in STM appeared specific to tasks requiring phonetic coding of material. Children with ADHD displayed intact CE and LTM functioning but reduced visual-spatial STM, especially when off stimulant medication. Children with RD/ADHD had deficits consistent with both disorders.

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**Methylphenidate in attention deficit hyperactivity disorder and bipolar disorder.**

**Kummer A, Teixeira A.**

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Behav Brain Funct. 2008;4.

**The influence of serotonin- and other genes on impulsive behavioral aggression and cognitive impulsivity in children with attention-deficit hyperactivity disorder (ADHD): Findings from a family-based association test (FBAT) analysis.**

**Oades RD, Lasky-Su J, Christiansen H, et al.**

**Background:** Low serotonergic (5-HT) activity correlates with increased impulsive-aggressive behavior, while the opposite association may apply to cognitive impulsiveness. Both types of impulsivity are associated with attention-deficit/hyperactivity disorder (ADHD), and genes of functional significance for the 5-HT system are implicated in this disorder. Here we demonstrate the separation of aggressive and cognitive components of impulsivity from symptom ratings and test their association with 5-HT and functionally related genes using a family-based association test (FBAT-PC).
Methods: Our sample consisted of 1180 offspring from 607 families from the International Multicenter ADHD Genetics (IMAGE) study. Impulsive symptoms were assessed using the long forms of the Conners and the Strengths and Difficulties parent and teacher questionnaires. Factor analysis showed that the symptoms aggregated into parent- and teacher-rated behavioral and cognitive impulsivity. We then selected 582 single nucleotide polymorphisms (SNPs) from 14 genes directly or indirectly related to 5-HT function. Associations between these SNPs and the behavioral/cognitive groupings of impulsive symptoms were evaluated using the FBAT-PC approach.

Results: In the FBAT-PC analysis for cognitive impulsivity 2 SNPs from the gene encoding phenylethanolamine N-methyltransferase (PNMT, the rate-limiting enzyme for adrenalin synthesis) attained corrected gene-wide significance. Nominal significance was shown for 12 SNPs from BDNF, DRD1, HTR1E, HTR2A, HTR3B, DAT1/SLC6A3, and TPH2 genes replicating reported associations with ADHD. For overt aggressive impulsivity nominal significance was shown for 6 SNPs from BDNF, DRD4, HTR1E, PNMT, and TPH2 genes that have also been reported to be associated with ADHD. Associations for cognitive impulsivity with a SERT/SLC6A4 variant (STin2: 12 repeats) and aggressive behavioral impulsivity with a DRD4 variant (exon 3: 3 repeats) are also described.

Discussion: A genetic influence on monoaminergic involvement in impulsivity shown by children with ADHD was found. There were trends for separate and overlapping influences on impulsive-aggressive behavior and cognitive impulsivity, where an association with PNMT (and arousal mechanisms affected by its activity) was more clearly involved in the latter. Serotonergic and dopaminergic mechanisms were implicated in both forms of impulsivity with a wider range of serotonergic mechanisms (each with a small effect) potentially influencing cognitive impulsivity. These preliminary results should be followed up with an examination of environmental influences and associations with performance on tests of impulsivity in the laboratory.

Comorbidity as a predictor and moderator of treatment outcome in youth with anxiety, affective, attention deficit/hyperactivity disorder, and oppositional/conduct disorders. Ollendick TH, Jarrett MA, Grills-Taquechel AE, et al.

In the present review, we examine one of the critical issues that have been raised about evidence-based treatments and their portability to real-world clinical settings: namely, the presence of comorbidity in the participants who have been treated in these studies and whether the presence of comorbidity predicts or moderates treatment outcomes. In doing so, we examine treatment outcomes for the four most commonly occurring childhood psychiatric disorders: Anxiety disorders, affective disorders, attention deficit/hyperactivity disorder (ADHD), and oppositional defiant disorder (ODD)/conduct disorder (CD). For each of these disorders, we first review briefly the prevalence of comorbidity in epidemiological and clinical samples and then highlight the evidence-based treatments for these disorders. We next determine the effects of comorbidity on treatment outcomes for these disorders. For the most part, comorbidity in the treated samples is the rule, not the exception. However, the majority of studies have not explored whether comorbidity predicts or moderates treatment outcomes. For the not insignificant number of studies that have examined this issue, comorbidity has not been found to affect treatment outcomes. Notable exceptions are highlighted and recommendations for future research are presented.


This study investigates the spatial bias of visual attention measured by a temporal order judgement (TOJ) task and the influence of a high attentional load condition in a group of dyslexic children compared to a control group with normal reading skills (each group N = 10). The TOJ task (T2) was placed after a shape discrimination task (T1). In a low attentional load block participants worked only on T2, whereas in the high attentional load block they were required to process both T1 and T2. Several t-tests were executed to compare performance between conditions and groups. In the low attentional load conditions, results in dyslexic children were significantly impaired for the right visual field compared to a control group. The high attentional load conditions did not enhance these effects and seems to provoke the same leftward bias in the control group.
Comorbid psychiatric and substance abuse disorders: recent treatment research.
Riggs P, Levin F, Green AI, et al.
Psychiatric comorbidity is defined as the co-occurrence of a psychiatric disorder in a patient with a substance use disorder. Psychiatric disorders in substance abuse patients can antedate the substance use disorder or be a consequence of the substance abuse. There is emerging evidence that drug use in adolescence may alter the onset of certain psychiatric disorders in vulnerable individuals. Patients with concurrent comorbid disorders present special challenges for the substance abuse treatment system in terms of diagnosis and management because each disorder has the capability of exacerbating the other. This manuscript is a summary of an ISAM symposium that featured three speakers who discussed the following topics: 1. Etiology and treatment of comorbid psychiatric and substance use disorders in adolescents; 2. Treatment of ADHD and substance use disorders in adults; 3. Effects of substance abuse on the onset, severity, and treatment of schizophrenia. Recommendations for further research will be presented.

Improved Odor Sensitivity in Attention-Deficit/Hyperactivity Disorder.
Background: Deficits in olfactory function are common features in neurodegenerative and neuropsychiatric disorders. In Parkinson's disease, olfactory deficits were found in up to 90% of patients, and there is evidence for dopaminergic dysfunction underlying these deficits. Because of the involvement of the dopamine system in the pathophysiology of attention-deficit/hyperactivity disorder (ADHD), olfactory function was investigated in children with the disorder.
Methods: We assessed odor threshold, identification, and discrimination in 20 children and adolescents with ADHD without medication, 20 patients with ADHD treated with methylphenidate, and 20 healthy control subjects matched for IQ, age, and sex.
Results: Odor sensitivity was higher (lower threshold) in ADHD patients without medication than in healthy control subjects (p < .004; Cohen’s d = 1.273), whereas medicated patients did not differ significantly from healthy control subjects. No significant differences between groups with regard to odor discrimination or identification were detected.
Conclusions: Selectively improved odor sensitivity in children with ADHD is reported for the first time, whereas odor discrimination and identification were unaffected. Stimulant medication normalized the odor sensitivity threshold. It is proposed that dopaminergic dysregulation is involved in this phenomenon.

Hypericum perforatum (St John's wort) is not effective for treatment of attention deficit/hyperactivity disorder in children and adolescents. Commentary.
Savovic J.

Neuropsychopharmacology. 2008;33:3069-77.
COMT Val108/158Met polymorphism and the modulation of task-oriented behavior in children with ADHD.
It has been suggested that the symptoms of attention-deficit/hyperactivity disorder (ADHD), including inattention and/or hyperactivity/impulsivity, translate into deficits in task-oriented behavior or problem-focused activity. The frontosubcortical dopamine pathway has been implicated in ADHD. One of the key modulators of extracellular dopamine levels in the prefrontal cortex is catechol-O-methyltransferase (COMT). The objective of this study was to examine the association of the COMT Val108/158Met polymorphism with (1) task-oriented behavior in children with ADHD, and (2) response of this behavior given methylphenidate (MPH) treatment. Children of Caucasian ethnicity, having ADHD (n=188), were assessed using the Restricted Academic Situation Scale (RASS). The RASS uses a simulated academic environment within the research clinic, to assess the child's ability for independent, sustained orientation to an assignment of math
problems. Each child was administered placebo and MPH (0.5 mg/kg in a divided b.i.d. dose), each for a 1-week period, in a randomized, double-blind, crossover trial. On day 3 of the respective treatment week, the child was administered placebo/MPH in the clinic, and the acute change in behavior (before and 1 h after treatment) was evaluated on the RASS. Analysis was carried out using mixed model analysis of variance. Significant main effects of COMT genotype (F2,184=5.12, p=0.007) and treatment (F 1,184=44.26, p<0.001) on task-oriented behavior were observed. However, no genotype by treatment interaction was observed. These results suggest that the COMT Val108/158Met polymorphism modulates task-oriented behavior, but it does not modulate the response of this behavior with MPH treatment.

Response inhibition and attention processing in 5- to 7-year-old children with and without symptoms of ADHD: An ERP study.

Spronk M, Jonkman LM, Kemner C.

Objective: Response inhibition and attention processing in 5- to 7-year-old children with or without symptoms of attention-deficit hyperactivity disorder (ADHD) were examined.

Methods: Twelve children with ADHD symptoms and 15 control children performed a CPT-AX task. Behavioral measures of inattention and impulsivity and ERP measures of conflict monitoring and inhibition (Nogo-N2 and Nogo-P3), cue-orientation and prestimulus target expectation (Cue-P2 and P3) and response preparation (CNV) were collected.

Results: ADHD children detected fewer targets and had higher Inattention scores accompanied by reduced centro-parietal Cue- and Go-P3 activity. Occipital CNV amplitude was larger in ADHD children. At fronto-central leads, strong and comparable fronto-parietal Nogo-N2 effects were found in both groups, whereas the Nogo-P3 was only marginally significant in both groups.

Conclusions: The attenuated Cue- and Go-P3 effects in the ADHD-symptom group are interpreted as early signs of delayed attention development, resulting in less preparation and less alertness to detect significant events. Whereas the Nogo-N2 effects were interpreted as signs of comparable levels of conflict processing in both groups, the small Nogo-P3 suggests that inhibitory processing is still immature at this age.

Significance: The present study shows that specific attention problems can already be detected in the behavior and brain activity of 5- to 7-year-old children with symptoms of ADHD performing a CPT-AX task, and might be better indicators for the risk of developing ADHD than impulsivity measures.

Evidence of developmental alterations in cortical and subcortical regions of children with attention-deficit/hyperactivity disorder: a multivoxel in vivo phosphorus 31 spectroscopy study.

Stanley JA, Kipp H, Greisenegger E, et al.

CONTEXT: There is mounting evidence of neurodevelopmental alterations implicating the prefrontal cortex (PFC) and basal ganglia in children with attention-deficit/hyperactivity disorder (ADHD). The brain undergoes substantive structural and functional changes with a differential timing between brain regions during development from childhood to adolescence. In vivo phosphorus 31 magnetic resonance spectroscopy ([31]P MRS) is a noninvasive neuroimaging approach that is sensitive in assessing developmental changes of overproducing/pruning of synapses.

OBJECTIVE: To provide support for a developmental mechanism targeting a bottom-up dysfunction of the basal ganglia impairing the fine-tuning of prefrontal functions in ADHD.

DESIGN: Cross-sectional study.

SETTING: Pittsburgh, Pennsylvania, and the surrounding areas.

PARTICIPANTS: Thirty-one psychostimulant-naive children with ADHD (mean [SD] age, 8.1 [1.2] years; range, 6.1-10.0 years) and 36 healthy control subjects (mean [SD] age, 8.1 [1.3] years; range, 6.1-10.4 years).

MAIN OUTCOME MEASURE: Membrane phospholipid (MPL) precursor levels (ie, phosphomonoesters that are anabolic metabolites of MPL) were assessed in the PFC and basal ganglia as well as in 4 other brain regions using in vivo [31]P MRS.

RESULTS: Lower bilateral MPL precursor levels in the basal ganglia and higher MPL precursor levels in the inferior parietal region (primarily right side) were noted in the children with ADHD as compared with healthy
control children. There was a group x age interaction in the PFC and inferior parietal region, with relatively older psychostimulant-naive children with ADHD showing significantly lower PFC and higher inferior parietal MPL precursor levels. No differences between groups were noted in the superior temporal, posterior white matter, or occipital regions.

**CONCLUSION:** Though based on cross-sectional data, these results are suggestive of possible progressive, nonlinear, and sequential alterations implicating a bottom-up developmental dysfunction in parts of the cortico-striato-thalamo-cortical network in ADHD.

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**High proportion of single CYP2D6 gene deletion in Chinese attention-deficit-hyperactivity disorder children and its risk in oppositional defiant disorder.**


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**Am J Addict. 2008;17:491-96.**

**Concordance between cigarette smoking and the modified Fagerstrom tolerance questionnaire in controlled studies of ADHD.**


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Our objective was to compare scores on a smoking questionnaire to a diagnosis of cigarette smoking. As part of follow-ups in studies of ADHD, we assessed for cigarette smoking using structured interviews and the modified Fagerstrom Tolerance Questionnaire (mFTQ). Data were obtained from 162 subjects (mean = 19.2 yrs). ROC analysis and kappa coefficients revealed that a cutoff score of 3 on the mFTQ showed the strongest agreement with a full diagnosis of cigarette smoking (kappa = 0.68). Clinicians and researchers using the mFTQ in adolescents and young adults should consider a cutoff score of 3 to be indicative of cigarette smoking.

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**Parent-reported attention-deficit/hyperactivity disorder symptomatology and sleep problems in a preschool-age pediatric clinic sample.**

*Willoughby MT, Angold A, Egger HL.*

**Objective:** To examine the association between attention-deficit/ hyperactivity disorder symptomatology and parent-reported sleep problems among preschoolers ages 2 to 5 years.

**Method:** A total of 1,073 parents of preschoolers ages 2 to 5 years attending a large pediatric clinic completed the Child Behavior Checklist 11/2-5 years. A stratified probability sample of 193 parents of high scorers and 114 parents of low scorers were interviewed with the Preschool Age Psychiatric Assessment. Poisson regression was used to test the association between parent-reported sleep problems and attention-deficit/ hyperactivity disorder symptomatology, as well as psychiatric and demographic covariates.

**Results:** When considered without reference to other psychiatric disorders, elevated hyperactive-impulsive symptomatology was positively associated with parent reported problems including sleep assistance, parasomnias, and dyssomnias; however, all of these effects were attenuated to nonsignificance once psychiatric comorbidity was controlled. In contrast, elevated inattentive symptomatology (especially at lower levels of hyperactive-impulsive symptoms) was positively associated with daytime sleepiness even after psychiatric comorbidity was controlled.

**Conclusions:** Neither hyperactive-impulsive nor inattentive attention-deficit/hyperactivity disorder symptomatology was uniquely related to parent-reported problems involving sleep assistance, parasomnias, or dyssomnias. However, inattentive symptomatology was uniquely related to daytime sleepiness above and beyond commonly occurring patterns of psychiatric comorbidity, sleep duration, and demographic factors.

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**Designing a brain-computer interface device for neurofeedback using virtual environments.**

From continuous feedback of electroencephalogram (EEG), people can learn how to change their brain electrical activity by a certain guideline. This technique is known as EEG biofeedback, or neurofeedback. It is a main application of brain-computer interface (BCI) systems in assistive technology, which has been widely used in research and clinical applications. However, there are two major limitations of current neurofeedback systems. One is that monotonous feedback methods cannot attract subjects to focus on them. The other one is that the area of EEG collection is limited in central areas. In response to these problems, a neurofeedback (NFB) system was established in this study, which utilized virtual reality (VR) to create appropriate feedback information in certain scenarios. This system collected three-channel EEG signals from frontal and central areas, and translated spontaneous EEG into "commands" signal which provided communication and control capabilities by virtual environment. This paper describes the system's configuration, hardware and software implementation and signal processing methodology. In addition, a pertinent experiment was performed with successful neurofeedback training sessions in order to test the feasibility and effectiveness of this system. Integrated visual and auditory-continuous performance test (IVA-CPT) results suggested that the attention of subjects had been strengthened after 20 training sessions. It showed that the NFB system could provide an effective therapy for treating children with attention deficit hyperactivity disorder (ADHD). Further research should be focused on mobile and wireless integration of our instrument, for providing mean more powerful and convenient application to clinical therapy.

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