



ADHD

ATTENTION DEFICIT HYPERACTIVITY DISORDER


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Tunis Med. 2009;87:645-50.

Attentional impairment in children with attention deficit/hyperactivity.

Abbes Z, Bouden A, Amado I, et al.

Background: Attention-deficit hyperactivity disorder (ADHD) is a heterogeneous disorder currently defined by clinical history and behavioral report of impairment. The Attention Network test (ANT) gives measures of different aspects of the complex process of attention.

Aims: We ask if children with Attention Deficit Hyperactivity Disorder (ADHD) will show a characteristic pattern of deficits on this test.

Methods: The sample included 40 children (M = 9 years) who performed the "Attention network test". Children with an ADHD diagnosis (N = 20) were compared to a control group (N= 20).

Results: The group of children with ADHD showed slower reaction times in all conditions (mean RT= 866ms; SD= 234, 063). Children with ADHD showed a significant impairment in their executive control system compared to healthy subjects, with slower reaction times in incongruent conditions and lower accuracy scores (RT =1064 ms; $F(1.38) p= 0.02$). Our results showed that spatial orienting and alerting in ADHD was no different than controls ($p= 0, 68$). ADHD group showed a greater variable response ($p= 0, 0001$).

Conclusion: The present study showed that impairment in executive control system and variability measures are the characteristic pattern of deficits in children with ADHD.

Clin EEG Neurosci. 2010;41:1-10.

Wavelet-synchronization methodology: A new approach for EEG-based diagnosis of ADHD .

Ahmadlou M, Adeli H.

A multi-paradigm methodology is presented for electroencephalogram (EEG) based diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD) through adroit integration of nonlinear science; wavelets, a signal processing technique; and neural networks, a pattern recognition technique. The selected nonlinear features are generalized synchronizations known as synchronization likelihoods (SL), both among all electrodes and among electrode pairs. The methodology consists of three parts: first detecting the more synchronized loci (group 1) and loci with more discriminative deficit connections (group 2). Using SLs among all electrodes, discriminative SLs in certain sub-bands are extracted. In part two, SLs are computed, not among all electrodes, but between loci of group 1 and loci of group 2 in all sub-bands and the band-limited EEG. This part leads to more accurate detection of deficit connections, and not just deficit areas, but more discriminative SLs in sub-bands with finer resolutions. In part three, a classification technique, radial basis function neural network, is used to distinguish ADHD from normal subjects. The methodology was applied to EEG data obtained from 47 ADHD and 7 control individuals with eyes closed. The Radial Basis Function (RBF) neural network classifier yielded a high accuracy of 95.6% for diagnosis of the ADHD in the feature space discovered in this research with a variance of 0.7%.

Per la ricerca degli articoli pubblicati nella letteratura scientifica nel mese in esame sono state consultate le banche dati Medline, Embase, PsycINFO e PsycArticle utilizzando le seguenti parole chiave (o i loro sinonimi): 'Attention deficit disorder', 'Attention deficit hyperactivity disorder', 'Infant', 'Child', 'Adolescent', 'Human'. Sono qui riportate le referenze considerate rilevanti e pertinenti.

Focus Altern Complement Ther. 2010;15:28-29.

Does Ginkgo biloba help children with attention deficit hyperactivity disorder?

Akhondzadeh S.

J Child Adolesc Psychopharmacol. 2009;19:673-81.

Predictive factors for persistent use and compliance of immediate-release methylphenidate: A 36-month naturalistic study.

Atzori P, Usala T, Carucci S, et al.

Aim: The objective of this study was to evaluate predictors of long-term adherence to treatment with methylphenidate (MPH).

Methods: A total of 134 children (ages 4-16) with a diagnosis of attention-deficit/hyperactivity disorder (ADHD) determined by specific protocols, including a semistructured parent interview, Conners' Teacher/Parent Rating Scales, cognitive and learning evaluation, and child self-reports for anxiety and depression, were assessed monthly for up to 36 months. At the end of the study (36 months), three outcomes were evaluated (continuing medication, medication withdrawn due to functional remission, and medication withdrawn for other reasons including poor compliance). Outcomes were first analyzed by mean of the chi-squared test, Mann-Whitney-U test, or t-test, and predictive models were subsequently generated using Cox proportional hazards model analysis. Age, ADHD subtype, co-morbidity, cognitive functioning, side effects, and family and social characteristics were considered as independent variables.

Results: Thirty-six months after starting MPH, 62 children (46%) were still on treatment, 32 (24%) had stopped MPH due to functional remission, and 40 (30%) had suspended MPH for other reasons. Within the last group, 20 suspended for poor compliance, 10 for decrease of efficacy, 5 for side effects, and 5 because they entered in an atomoxetine clinical trial. The presence of associated disorders, younger age, female gender, and not living with both parents were predictors for continuing medication until end of the study (36 months); absence of associated disorders and older age were predictors of discontinuation medication due to functional remission before the end of study, older age, and hyperactive subtype were predictors of discontinuing medication for other reasons.

Conclusion: Clinical outcome of ADHD treatment is heterogeneous: Specific clinical and social predictive parameters for long-term MPH use and compliance can be identified. An accurate tailoring of clinical intervention to the individual child appears crucial for good outcome.

J Pediatr. 2010;156:798-803.

From Regulatory Problems in Infancy to Attention-Deficit/Hyperactivity Disorder in Childhood: A Moderating Role for the Dopamine D4 Receptor Gene?

Becker K, Blomeyer D, El-Faddagh M, et al.

Objective: To examine whether the dopamine receptor D4 gene (DRD4) exon III VNTR moderates the risk of infants with regulatory disorders for developing attention-deficit/hyperactivity disorder (ADHD) later in childhood.

Study design: In a prospective longitudinal study of children at risk for later psychopathology, 300 participants were assessed for regulatory problems in infancy, DRD4 genotype, and ADHD symptoms and diagnoses from childhood to adolescence. To examine a potential moderating effect on ADHD measures, linear and logistic regressions were computed. Models were fit for the main effects of the DRD4 genotype (presence or absence of the 7r allele) and regulatory problems (presence or absence), with the addition of the interaction term. All models were controlled for sex, family adversity, and obstetric risk status.

Results: In children without the DRD4-7r allele, a history of regulatory problems in infancy was unrelated to later ADHD. But in children with regulatory problems in infancy, the additional presence of the DRD4-7r allele increased the risk for ADHD in childhood.

Conclusions: The DRD4 genotype seems to moderate the association between regulatory problems in infancy and later ADHD. A replication study is needed before further conclusions can be drawn, however.

Br J Nutr. 2010 Apr;103:1160-67.

The fatty acid compositions of erythrocyte and plasma polar lipids in children with autism, developmental delay or typically developing controls and the effect of fish oil intake.

Bell JG, Miller D, MacDonald DJ, et al.

The erythrocyte and plasma fatty acid compositions of children with autism were compared in a case-control study with typically developing (TD) children and with children showing developmental delay (DD). Forty-five autism subjects were age-matched with TD controls and thirty-eight with DD controls. Fatty acid data were compared using paired t tests. In addition, blood fatty acids from treatment-naive autism subjects were compared with autism subjects who had consumed fish oil supplements by two-sample t tests. Relatively few differences were seen between erythrocyte fatty acids in autism and TD subjects although the former had an increased arachidonic acid (ARA):EPA ratio. This ratio was also increased in plasma samples from the same children. No changes in n-3 fatty acids or ARA:EPA ratio were seen when comparing autism with DD subjects but some SFA and MUFA were decreased in the DD subjects, most notably 24 : 0 and 24 : 1, which are essential components of axonal myelin sheaths. However, if multiple comparisons are taken into account, and a stricter level of significance applied, most of these values would not be significant. Autism subjects consuming fish oil showed reduced erythrocyte ARA, 22 : 4n-6, 22 : 5n-6 and total n-6 fatty acids and increased EPA, 22 : 5n-3, 22 : 6n-3 and total n-3 fatty acids along with reduced n-6:n-3 and ARA:EPA ratios. Collectively, the autism subjects did not have an underlying phospholipid disorder, based on erythrocyte fatty acid compositions, although the increased ARA:EPA ratio observed suggested that an imbalance of essential highly unsaturated fatty acids may be present in a cohort of autism subjects.

Am J Psychiatry. 2010 Apr;167:409-17.

Adult psychiatric outcomes of girls with attention deficit hyperactivity disorder: 11-year follow-up in a longitudinal case-control study.

Biederman J, Petty CR, Monuteaux MC, et al.

OBJECTIVE: Few follow-up studies have been conducted of girls with ADHD, and none have followed girls into adulthood. The authors sought to estimate the prevalence of psychopathology in girls with and without ADHD followed into young adulthood.

METHOD: The authors conducted a longitudinal case-control study of 6- to 18-year-old girls with (N=140) and without (N=122) ADHD ascertained from psychiatric and pediatric sources. At the 11-year follow-up, 96 (69%) of the girls with ADHD and 91 (75%) of the comparison girls were reassessed (mean age=22 years). Participants were blindly assessed by structured diagnostic interviews.

RESULTS: Lifetime and 1-year risks for all composite categories of psychopathology were significantly greater in girls with ADHD grown up relative to comparison girls; lifetime hazard ratios were 7.2 (95% CI=4.0-12.7) for antisocial disorders, 6.8 (95% CI=3.7-12.6) for mood disorders, 2.1 (95% CI=1.6-2.9) for anxiety disorders, 3.2 (95% CI=2.0-5.3) for developmental disorders, 2.7 (95% CI=1.6-4.3) for addictive disorders, and 3.5 (95% CI=1.6-7.3) for eating disorders. For lifetime psychopathology, all six composite categories remained statistically significant after controlling for other baseline psychopathology. Except for addictive disorders, significant 1-year findings remained significant after controlling for baseline psychopathology. The 1-year prevalences of composite disorders were not associated with lifetime or 1-year use of ADHD medication.

CONCLUSION: By young adulthood, girls with ADHD were at high risk for antisocial, addictive, mood, anxiety, and eating disorders. These prospective findings, previously documented in boys with ADHD, provide further evidence for the high morbidity associated with ADHD across the life cycle.

PLoS ONE. 2010;5.

Hotspots of large rare deletions in the human genome.

Bradley WEC, Raelson JV, Dubois DY, et al.

Background: We have examined the genomic distribution of large rare autosomal deletions in a sample of 440 parent-parent-child trios from the Quebec founder population (QFP) which was recruited for a study of Attention Deficit Hyperactivity Disorder.

Methodology/Principal Findings: DNA isolated from blood was genotyped on Illumina Hap300 arrays. PennCNV combined with visual evaluation of images generated by the Beadstudio program was used to determine deletion boundary definition of sufficient precision to discern independent events, with near-perfect concordance between parent and child in about 98% of the 399 events detected in the offspring; the

remaining 7 deletions were considered de novo. We defined several genomic regions of very high deletion frequency ('hotspots'), usually of 0.4-0.6 Mb in length where independent rare deletions were found at frequencies of up to 100 fold higher than the average for the genome as a whole. Five of the 7 de novo deletions were in these hotspots. The same hotspots were also observed in three other studies on members of the QFP, those with schizophrenia, with endometriosis and those from a longevity cohort.

Conclusions/Significance: Nine of the 13 hotspots carry one gene (7 of which are very long), while the rest contain no known genes. All nine genes have been implicated in disease. The patterns of exon deletions support the proposed roles for some of these genes in human disease, such as NRXN1 and PARKIN, and suggest limited roles or no role at all, for others, including MACROD2 and CTNNA3. Our results also offer an alternative interpretation for the observations of deletions in tumors which have been proposed as reflecting tumor-suppressive activity of genes in these hotspots. (copyright) 2010 Bradley et al

European Journal of Developmental Psychology. 2010 Mar;7:178-97.

CPT performance, motor activity, and continuous relations to ADHD symptom domains: A developmental study.

Brocki KC, Tillman CM, Bohlin G.

Using a population-based sample consisting of 401 6- to 12-year-olds, this study examined normative age and sex distributions on motor activity as measured in an actigraphic-based motion tracking system (MTS) and on attention-related functions derived from a Continuous Performance Test (CPT). Specific objectives were to present new knowledge on age-related change in motor activity and to study age effects on changes in motor activity and CPT performance as a function of time on task. Further, continuous relations between the two ADHD symptom domains and CPT performance and motor activity, and importantly, age effects in these relations were examined. CPT performance improved, and level of motor activity decreased with age. Linear associations between the two ADHD symptom domains and several of the CPT and MTS parameters support available research describing the nature of ADHD as a continuous dimension with variable expression throughout the general population. Further, our study is one of the first to provide developmental data using a time on task design, particularly with regard to motor activity. Imperative for ADHD future research are our results showing that age-matters in the relation between ADHD behaviours and neuropsychological function.

Brain Res. 2010 Jan;1310:172-80.

The macrostructural and microstructural abnormalities of corpus callosum in children with attention deficit/hyperactivity disorder: A combined morphometric and diffusion tensor MRI study.

Cao Q, Sun L, Gong G, et al.

The corpus callosum (CC) is one of focused target areas which may play an important role in the pathophysiology of attention deficit hyperactivity disorder (ADHD). Conventional structural magnetic resonance imaging (MRI) studies have revealed the macrostructural abnormalities of CC and its subdivisions in ADHD compared with controls. However, no study has examined the macrostructural and microstructural characteristics of the CC in the same ADHD group. In this study, MRI morphometric and diffusion tensor imaging (DTI) techniques were combined to explore the area and measure fractional anisotropy (FA) abnormality of CC and its seven subdivisions in children with ADHD. Twenty-eight boys with ADHD (13.3±1.5 years) and 27 age- and gender- matched controls (13.2±0.9 years) were included. We co-registered individual structural MRI and DTI images manually and subdivided the midsagittal CC into seven subdivisions. The area and FA of the CC and its subdivisions were then compared between the patients and the matched controls. Results showed that ADHD had decreased area of entire CC, anterior middle-body, and isthmus. Meanwhile, reduced FA value of the isthmus was found in the ADHD group compared with the controls. Our study indicated that not only macrostructural abnormalities but also microstructural alterations in CC, especially in isthmus occurred in ADHD. The abnormality of the isthmus, the subdivision that contains the fibers connecting posterior regions of brain, may play an important role in the pathophysiology of ADHD and may be implicated in the disorders of attention.

Chin J Contemp Pediatr. 2009;11:992-95.

Function of the hypothalamus-pituitary-adrenal axis in children with attention deficit hyperactivity disorder.

Chen YH, Chen H, Liu YY, et al.

Objective: To study the function of the hypothalamus-pituitary-adrenal (HPA) axis in children with attention deficit hyperactivity disorder (ADHD).

Methods: One hundred and twenty-eight boys with ADHD at ages of 6 to 14 years were enrolled. The diagnosis and grouping of ADHD were based on the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV): ADHD-predominantly inattention type (ADHD-I, n = 44), ADHD-predominantly hyperactive impulsivetype (ADHD-HI, n = 32) and ADHD-combined type (ADHD-C, n = 52). Thirty healthy boys served as the control group. Plasma levels of cortisol and adrenocorticotrophic hormone (ACTH) were measured by automatic particle enzyme immunoassay and electrochemiluminescence respectively at 8:00 am. The intelligence level was tested by Raven's standard progressive matrices.

Results: The children with ADHD had lower IQ score (84.5 (plus or minus) 11.3) than the control group (94.6 (plus or minus) 12.4) ($P < 0.01$). There were significant differences in the IQ score among the three ADHD subgroups ($P < 0.01$). The IQ score in the ADHD-I and the ADHD-C groups was significantly lower than that in the control group. The mean plasma cortisol level in the ADHD group (226.5 (plus or minus) 129.1 nmol/L) was significantly lower than that in the control group (384.5 (plus or minus) 141.4 nmol/L) ($P < 0.01$). The three ADHD subgroups showed significantly decreased plasma cortisol level compared with the control group ($P < 0.01$). The plasma level of cortisol was the lowest in the ADHD-HI group (154.4 (plus or minus) 71.6 nmol/L), followed by the ADHD-I group (219.4 (plus or minus) 117.7 nmol/L) and the ADHD-C group (258.3 (plus or minus) 136.4 nmol/L). There were no significant differences in plasma concentration of ACTH between ADHD and control children.

Conclusions: In the non-stress state, the HPA axis may be dysfunctional in children with ADHD, which may be attributed to the under reactivity of the HPA axis. Lower plasma cortisol has fewer impacts on the cognitive-behavior function, but it may closely be related to attention deficit, hyperactivity and impulsive behaviors.

Curr Med Res Opin. 2010;26:977-89.

Pharmacological treatment patterns among patients with attention-deficit/ hyperactivity disorder: Retrospective claims-based analysis of a managed care population.

Christensen L, Sasane R, Hodgkins P, et al.

Objective: To develop a descriptive profile of attention-deficit/ hyperactivity disorder (ADHD) pharmacological treatment patterns in terms of persistence, adherence, augmentation, switching, and dosing changes; and to assess differences in treatment patterns with regard to ADHD medication type, class, and duration of action.

Methods: This retrospective claims database analysis used medical data, pharmacy data, and enrollment information to examine treatment patterns among patients with at least one claim with a diagnosis code for ADHD and a filled prescription for ADHD medication (index therapy) during the period 01 January 2004 through 30 September 2006. Treatment persistence and adherence (days supplied/days persistent) were calculated. Dose changes, medication switching, and augmentation were analyzed at three levels of comparison: class (stimulant vs nonstimulant [atomoxetine]), drug type (amphetamine vs methylphenidate), and duration of action (short, intermediate, long). Statistical comparisons were made using the chi-square test for proportions and Students t-test or the F-test from one-way ANOVA for means.

Results: Of 60,010 patients meeting eligibility criteria, 58.4 were younger than age 18. Most (78.4) were prescribed a stimulant as their index therapy. Persistence and adherence were greater for patients on stimulants (vs the nonstimulant), for patients on amphetamines (vs methylphenidates), and for patients on long-acting medications (vs short-and intermediate-acting medications; all $p < 0.0001$). Index drug dose changes were least likely among individuals taking the nonstimulant (vs stimulants), methylphenidates (vs amphetamines), or intermediate-acting drugs (vs short-and long-acting drugs; all $p < 0.0001$), and medication switches were more frequent among those on nonstimulants, methylphenidates, or short-acting drugs (all $p < 0.0001$). Subjects taking long-acting medication were less likely to augment with a drug with a different duration of action than those taking intermediate-or short-acting medication ($p < 0.0001$). This claims-based study is limited by possible discrepancies between claims and patient behaviors (i.e., a claim for a prescription does not necessarily indicate that the medication was taken as prescribed).

Conclusions: Patients were more stable on treatment compared with their respective comparator groups if their index therapy was a stimulant, long-acting drug, or amphetamine.

Rev Neurol. 2010;50:S119-S123.

Population-based diagnostic study to compare the DSM-IV and the questionnaire for screening latin American schoolchildren and adolescents for attention deficit hyperactivity disorder.

Cornelio-Nieto JO, Borbolla-Sala ME, Garcia-Valdovinos S.

Aim. To detect attention deficit hyperactivity disorder (ADHD) in children between 4 and 14 years of age by means of the Questionnaire for screening Latin American schoolchildren and adolescents for ADHD (QLSA-ADHD) and the criteria of the Diagnostic and statistical manual of mental disorders, fourth edition, ADHD version (DSM-IV ADHD).

Patients and methods. A prospective, cross-sectional, analytical study was conducted to detect ADHD in the child population that visited the outpatient department at the Rodolfo Nieto Padron Children's Hospital. These children were administered two surveys: the DSM-IV ADHD and the QLSA-ADHD. The results were analysed using graphs and test statistics from the SPSS package, such as the correlation coefficient and chi squared.

Results. The questionnaires were analysed by finding the overall sum of the criteria of the 200 children included in the DSM-IV ADHD and the average score values were found to be 64 'yes' (32%) and 137 'no' (68%). The QLSA-ADHD was evaluated in the same way and the average was 50 'yes' (25%) and 149 'no' (75%). The chi squared test was then performed for the two, the result being 1.762, with 1 degree of freedom and $p > 0.05$; that is to say, there was no significant difference between the scores obtained in both surveys. With the QLSA-ADHD, 25% of children with ADHD were detected, whereas the figure rose slightly to 25.5% (51 patients) with the DSM-IV. The chi squared test was conducted between the results from the two surveys, the value being 3.405, with 1 degree of freedom and $p > 0.05$.

Conclusions. Our findings show that, in our population, there is no difference between the QLSA-ADHD and the DSM-IV for detecting ADHD.

Ther Clin Risk Manage. 2009;5:943-48.

Update on the management of attention-deficit/hyperactivity disorder in children and adults: Patient considerations and the role of lisdexamfetamine.

Cowles BJ.

Attention-deficit/hyperactivity disorder (ADHD) is a behavioral disorder characterized by atypical levels of inattention, hyperactivity, and impulsivity that impair daily living activities. Although commonly associated with children and adolescents, current literature and practice now demonstrate the impairment the disorder may impose on adults as well. Central nervous system (CNS) stimulant medications are the first-line therapy for ADHD. CNS stimulants include methylphenidate and amphetamine derivatives. Longer-acting formulations used once daily are often preferred to avoid medication administration during school or work as well as to avoid side effects associated with rapid fluctuations in serum concentrations associated with multiple daily dosing. Lisdexamfetamine, a new, novel amphetamine product, has been shown to provide efficacy upwards of 12 hours in children and adults with a side effect profile similar to those of other longer-acting amphetamine products. Owing to its unique prodrug composition and the need for oral administration to activate the medication, lisdexamfetamine may offer advantages in clinical situations where stimulant abuse is a concern.

Arch Clin Neuropsychol. 2009;24:273-86.

The canonical relationship between sensory-motor functioning and cognitive processing in children with attention-deficit/hyperactivity disorder.

Davis AS, Pass LA, Finch WH, et al.

Children with Attention-Deficit/Hyperactivity Disorder (ADHD) typically exhibits a pattern of behavioral deficits, impairment in academic achievement, and cognitive processing, and presents with sensory-motor deficits. This study examined the relationships between sensory-motor tasks, cognitive processing, and academic achievement for a group of 67 children with ADHD. Strong canonical correlations emerged

between sensory-motor functioning and academic achievement (.93) and sensory-motor functioning and cognitive processing (.98). An analysis of the redundancy coefficient showed that sensory-motor skills accounted for 65% of the variance in the achievement variables and 31% of the variance in the cognitive processing variables. The strong relationship between sensory-motor skills and higher order cognitive processes indicates that early assessment of sensory-motor skills may be useful in the identification of subsequent deficits in academic performance. Neuropsychologists should carefully consider the contribution of sensory-motor functioning to the more widely studied and assessed constructs of academic, behavioral, and emotional problems in children with ADHD.

J Child Adolesc Psychopharmacol. 2009;19:699-707.

Differential effects of atomoxetine on executive functioning and lexical decision in attention-deficit/hyperactivity disorder and reading disorder.

De Jong CGW, Van De Voorde S, Roeyers H, et al.

Objective: The effects of a promising pharmacological treatment for attention-deficit/hyperactivity disorder (ADHD), atomoxetine, were studied on executive functions in both ADHD and reading disorder (RD) because earlier research demonstrated an overlap in executive functioning deficits in both disorders. In addition, the effects of atomoxetine were explored on lexical decision.

Methods: Sixteen children with ADHD, 20 children with ADHD + RD, 21 children with RD, and 26 normal controls were enrolled in a randomized placebo-controlled crossover study. Children were measured on visuospatial working memory, inhibition, and lexical decision on the day of randomization and following two 28-day medication periods.

Results: Children with ADHD + RD showed improved visuospatial working memory performance and, to a lesser extent, improved inhibition following atomoxetine treatment compared to placebo. No differential effects of atomoxetine were found for lexical decision in comparison to placebo. In addition, no effects of atomoxetine were demonstrated in the ADHD and RD groups.

Conclusion: Atomoxetine improved visuospatial working memory and to a lesser degree inhibition in children with ADHD + RD, which suggests differential developmental pathways for co-morbid ADHD + RD as compared to ADHD and RD alone.

Child Psychiatry Hum Dev. 2010 Apr;41:168-92.

A systematic review of parenting in relation to the development of comorbidities and functional impairments in children with attention-deficit/hyperactivity disorder (ADHD).

Deault LC.

This review synthesizes recent research evidence regarding the parenting characteristics associated with families with children with Attention-Deficit/Hyperactivity Disorder (ADHD). ADHD is a complex, heterogeneous disorder with a range of genetic and environmental factors that contribute to its behavioral expression and different developmental trajectories. The current review adopts a developmental psychopathology perspective to conceptualize the risk and protective factors that might shape the developmental pathways of the disorder across different domains. Following from Johnston and Mash's review (Johnston and Mash, Clin Child Fam Psychol Rev 4:183–207, 2001), the present review systematically examines empirical studies from 2000–2008 that investigate parenting variables in relation to the development of children with ADHD, with a particular focus on the development of externalizing and internalizing comorbidities, as well as functional impairments in academic and social contexts. The most recent research evidence uses correlational designs to show that ADHD is associated with problematic family functioning, including greater stress within the family, higher rates of parental psychopathology and conflicted parent–child relationships, which appears to be exacerbated in children with comorbid oppositional and conduct problems. However, there is an absence of literature that considers the role that parents play in contributing to children's development in areas such as academic achievement and peer competence, as well as the development of internalizing difficulties. Future research should examine family factors that are associated with resilience in children with ADHD, using longitudinal designs that reflect the dynamic changes associated with a developmental psychopathology framework.

Circulation. 2010;121:1329-37.

Modeled economic evaluation of alternative strategies to reduce sudden cardiac death among children treated for attention deficit/hyperactivity disorder.

Denchev P, Kaltman JR, Schoenbaum M, et al.

Background: Stimulants are widely used to treat children with attention deficit/hyperactivity disorder and may increase the risk for sudden cardiac death (SCD). We examined the cost-effectiveness of pretreatment screening with ECG for reducing SCD risk in children diagnosed with attention deficit/hyperactivity disorder who are candidates for stimulant medication.

METHOD AND RESULTS: We constructed a state-transition Markov model with 10 annual cycles spanning 7 to 17 years of age. Taking a societal perspective, we compared the cost-effectiveness of 3 screening strategies: (1) performing a history and physical examination with cardiology referral if abnormal (current standard of care); (2) performing a history and physical examination plus ECG after negative history and physical examination, with cardiology referral if either is abnormal; and (3) performing a history and physical examination plus ECG, with cardiology referral only if ECG is abnormal. Children identified with SCD-associated cardiac abnormalities would be restricted from stimulants and from playing competitive sports. The expected incremental cost-effectiveness over strategy 1 was \$39 300 and \$27 200 per quality-adjusted life-year for strategies 2 and 3, respectively. Monte Carlo simulation found that the chance of incremental cost-effectiveness was 55% for strategy 2 and 71% for strategy 3 (willingness to pay (less-than or equal to)\$50 000 per quality-adjusted life-year). Both strategies 2 and 3 would avert 13 SCDs per 400 000 children seeking stimulant treatment for ADHD, for a cost of \$1.6 million per life for strategy 2 and \$1.2 million per life for strategy 3.

Conclusions: Relative to current practice, adding ECG screening to history and physical examination pretreatment screening for children with attention deficit/hyperactivity disorder has borderline cost-effectiveness for preventing SCD. Relative cost-effectiveness may be improved by basing cardiology referral on ECG alone. Benefits of ECG screening arise primarily by restricting children identified with SCD risk from competitive sports.

J Child Adolesc Psychopharmacol. 2009;19:377-83.

The meaning of attention-deficit/hyperactivity disorder medication and parents' initiation and continuity of treatment for their child.

DosReis S, Mychailyszyn MP, Evans-Lacko SE, et al.

Objective: The aim of this study was to examine parents' early understanding of medication for attention-deficit/hyperactivity disorder (ADHD) in relation to decisions to initiate and continue treatment for their child.

Methods: Qualitative, semistructured telephone interviews were conducted with 48 parents of children newly diagnosed with ADHD. Parents were recruited from inner city, outpatient primary care, and mental health clinics affiliated with a large university hospital. Data were analyzed using grounded theory.

Results: Parents' initial perspectives of the appropriateness, anticipated effects, and symbolic meaning of medication were classified by four typologies (illness oriented, problem oriented, generally acceptable, unacceptable). In this sample, 29% of parents believed medication was required to treat the illness and 20% believed medication was unacceptable. Except for the unacceptable group, nearly all of the parents in the other groups initiated medication shortly after diagnosis. More than 80% of the illness- and problem-oriented groups used medication at 6 months; this fell to 64% and 78%, respectively, at 12 months. Only half of the unacceptable group ever used medication for their child.

Conclusions: Parents' views of ADHD medication may be predictive of continuity of treatment. Increasing physician awareness of parent preferences for managing their child's ADHD problems may lead to care management plans that maximize continuity.

Turk Pediatr Ars. 2010;45:37-40.

Attention deficit and hyperactivity symptoms in children with monosymptomatic nocturnal enuresis.

Ertan P, Gonulal D, Sogut A, et al.

Aim: Monosymptomatic nocturnal enuresis in children may cause psychological and behavioral problems. The aim of this study was to assess symptoms of attention deficit and hyperactivity in children with monosymptomatic nocturnal enuresis.

Material and Method: Fifty-seven children (23 male, 34 female) with monosymptomatic nocturnal enuresis and 57 healthy controls (25 male, 32 female) aged 6 to 12 years participated in the study. Conners' Parent

Rating Scale-48 (CPRS), a 48-item multiple-choice questionnaire, was completed by the mothers to identify the attention deficit and hyperactivity symptoms in children.

Results: Mean age of the children with enuresis was 8.54 (plus or minus) 2.18 years and that of the control group 9.12 (plus or minus) 2.13 years. Attention deficit score in the enuretic group was significantly higher than that in the control group ($p=0.02$). Hyperactivity scores were not significantly different between the groups ($p=0.36$). Bedwetting frequencies were not different between enuretic children with and without attention deficit or hyperactivity symptoms ($p=0.06$).

Conclusions: Psychological and behavioral assessment may be indicated in children with monosymptomatic nocturnal enuresis since the results of this study demonstrate increased attention deficit symptomatology.

J Child Adolesc Psychopharmacol. 2009;19:649-62.

Effectiveness, safety, and tolerability of lisdexamfetamine dimesylate in children with attention-deficit/hyperactivity disorder: An open-label, dose-optimization study.

Findling RL, Ginsberg LD, Jain R, et al.

Objective: The aim of this study was to assess the effectiveness and safety of lisdexamfetamine dimesylate (LDX) in children with attention-deficit/hyperactivity disorder (ADHD).

Method: This was a 7-week, open-label study evaluating 20, 30, 40, 50, 60, or 70 mg/day LDX in 318 children aged 6-12 years with ADHD. The ADHD Rating Scale IV (ADHD-RS-IV) was the primary efficacy assessment. Secondary measures included the Clinical Global Impressions-Improvement (CGI-I), Expression and Emotion Scale for Children (EESC), and Behavior Rating Inventory of Executive Function (BRIEF). Safety assessments included treatment-emergent adverse events (TEAEs), vital signs, and electrocardiograms.

Results: At end point, mean (standard deviation [SD]) improvement from baseline in ADHD-RS-IV total score was 28.6 (10.9) ($p < 0.0001$). Most subjects (89.9%) were rated "improved" (i.e., CGI-I 1 or 2). Improvements from baseline were observed in the EESC total and subscale scores (p (less-than or equal to) 0.0002). LDX treatment resulted in significant improvement on the Global Executive Composite, Behavioral Regulation, and Metacognition indices of the BRIEF ($p < 0.0001$). TEAEs (incidences (greater-than or equal to) 10%) were decreased appetite, decreased weight, irritability, insomnia, headache, upper abdominal pain, and initial insomnia.

Conclusions: LDX was effective and generally well tolerated with a safety profile consistent with long-acting stimulant use. There was overall improvement in ADHD symptoms and executive function measures and no worsening of emotional expression measures.

Neuroendocrinol Lett. 2010;31:47-55.

Placenta and umbilical cord blood deserve attention.

Foltinova J, Foltin V, Morvova M, et al.

OBJECTIVES: This work follows up with our already published results concerning consequences of lead on prenatal and postnatal development of child in connection with the rise of hyperkinetic syndrome (ADHD). This disease has in children increasing tendency all over the world.

METHODS: In our work we used a set of histological and histochemical methods, method of scanning electron microscopy, infrared spectroscopy and statistical evaluation.

RESULTS: Our new method for proof of lead in placenta enabled us to show how lead is cumulated in syncytiotrophoblast. We have found release of lead from mother's erythrocytes in the intervillous space and receipt of lead by erythrocytes of fetus in the vessels of the villi of placenta. This finding enriches knowledge about relation between mother's erythrocytes, lead, calcium that is lead carrier, syncytiotrophoblast, and erythrocytes of fetus in the vessels of placental villi. We have proved that syncytiotrophoblast is the most frequent place for cumulation of lead deposits. We verified our ecomorphologic results by means of infrared spectroscopy in cooperation with physicists and statistically evaluated occurrence of ADHD in particular age categories what helps to fill gaps in knowledge of ADHD etiology.

CONCLUSIONS: Our finding of lead in umbilical cord blood immediately after the child birth is forewarning against the possible rise of the ADHD. This finding facilitates early diagnostics and means preventing step against the rise, development and consequences of this disease. The obtained results give evidence about

the serious influence of mothers dwelling in environment polluted with neurotoxic metal - lead on the prenatal and postnatal development of child.

Exp Brain Res. 2010;201:167-76.

Timing of conditioned eyeblink responses is impaired in children with attention-deficit/hyperactivity disorder.

Frings M, Gaertner K, Buderath P, et al.

Structural changes of the cerebellum have been reported in several psychiatric diseases like schizophrenia, autism and attention-deficit/ hyperactivity disorder (ADHD). Beside behavioral deficits children with ADHD often show slight motor abnormalities. Cerebellar malfunction may contribute. The cerebellum is a structure essential for motor coordination, various forms of motor learning and timing of motor responses. In the present study, eyeblink conditioning was applied to investigate learning and timing of motor responses both in children with ADHD and children with cerebellar lesions. Acquisition, timing and extinction of conditioned eyeblink responses were investigated in children with ADHD, children with chronic surgical cerebellar lesions and controls using a standard delay paradigm with two different interstimulus intervals. Timing of conditioned eyeblink responses was significantly impaired in children with ADHD in the long interstimulus interval condition. Also in children with cerebellar lesions conditioned responses (CR) tended to occur earlier than in controls. Incidences of CRs were significantly reduced in children with cerebellar lesions and tended to be less in children with ADHD than in controls. Extinction of the CRs was impaired in children with cerebellar lesions in both interstimulus interval conditions and in children with ADHD in the long interstimulus interval condition. Cerebellar malfunction may contribute to disordered eyeblink conditioning in ADHD. However, because CR abnormalities differed between ADHD and cerebellar subjects, dysfunction of non-cerebellar structures cannot be excluded.

Somnologie. 2009;13:176-81.

Coherency of attention deficit/hyperactivity and sleep-related problems: Results from a cross-sectional study in elementary school children.

Frolich J, Lehmkuhl G, Fricke L, et al.

In the process of the Cologne Children's Sleep Study, we assessed whether the occurrence of symptoms indicative of sleep onset and maintenance problems, daytime sleepiness, sleep disordered breathing (SDB), and restless legs syndrome (RLS) is related to an increased risk for the presence of symptoms of hyperactivity (ADHD). A total of 8,599 parents and 4th grade public school children were surveyed in a cross-sectional study concerning sleep habits, sleep problems, and environmental factors with a parental sleep questionnaire. Relative risks were calculated to examine the relationship between various sleep problems and ADHD symptoms. Frequent snoring was reported in 3.7% of the children, apneas in 0.6% and restless legs in 1.0%. Of the children, 8.9% were reported to be frequently hyperactive. Symptoms of sleep onset and maintenance problems were related to an increased risk of hyperactivity in contrast to daytime sleepiness that was not related to hyperactivity. Moreover, a significantly elevated risk for the symptom hyperactivity could be calculated for children presenting restless legs, snoring, and apneas. For apneas, however, this relationship only existed in children with moderate symptoms of hyperactivity but not in children with frequent hyperactivity. Our results clearly demonstrate that symptoms of hyperactivity are related to sleep onset and maintenance problems. In contrast, no indication was found for hyperactivity in children presenting increased daytime sleepiness. Our study results further support the hypothesis of significant correlations between ADHD, RLS, and SDB.

Psychiatr Serv. 2009;60:1075-83.

National variation of ADHD diagnostic prevalence and medication use: Health care providers and education policies.

Fulton BD, Scheffler RM, Hinshaw SP, et al.

Objectives: Attention-deficit hyperactivity disorder (ADHD) diagnostic prevalence and medication use vary across U.S. census regions, but little is known about state-level variation. The purpose of this study was to

estimate this variation across states and examine whether a state's health care provider characteristics and education policies are associated with this variation.

Methods: Logistic regression models were estimated with 69,505 children aged four to 17 from the state-stratified and nationally representative 2003 National Survey of Children's Health, conducted by the Centers for Disease Control and Prevention.

Results: Diagnostic prevalence was higher in the South (odds ratio [OR]=1.42, $p<.001$) than in the West; among children with ADHD diagnoses, medication use was higher in the South (OR=1.60, $p<.01$) and the Midwest (OR=1.53, $p<.01$) versus the West. On these measures, several states differed from the U.S. averages, including some states that, on the basis of the regional patterns found above, would not be expected to differ: Michigan had a high diagnostic prevalence; Vermont, South Dakota, and Nebraska had low diagnostic prevalences; and Connecticut, New Jersey, and Kentucky had low medication rates. Both diagnosis and medication status were associated with the number, age, and type of physicians within a state, particularly pediatricians. However, state education policies were not significantly associated with either diagnostic prevalence or medication rates.

Conclusions: To better understand the association between a state's health care provider characteristics and both diagnostic prevalence and medication use, it may be fruitful to examine the content of provider continuing education programs, including the recommendations of major health professional organization guidelines to treat ADHD.

Int J Neuropsychopharmacol. 2010;13:243-56.

Improvement of executive functions in boys with attention deficit hyperactivity disorder: An open-label follow-up study with once-daily atomoxetine.

Gau SSF, Shang CY.

Atomoxetine is efficacious in reducing symptoms of attention deficit hyperactivity disorder (ADHD) but its effect on executive functions needs more investigation. We examined the effect of atomoxetine on a wide range of non-verbal executive functions among 30 drug-naïve male patients with DSM-IV ADHD, aged 8-16 yr, in an open-label 12-wk atomoxetine treatment trial. Before administration of atomoxetine, the participants were assessed by psychiatric interviews, the WISC-III, and the tasks involving executive functions of the Cambridge Neuropsychological Test Automated Battery (CANTAB): Intra-dimensional/Extra-dimensional Shifts (IED), Rapid Visual Information Processing (RVIP), Spatial Span (SSP), Spatial Working Memory (SWM), and Stockings of Cambridge (SOC); and reassessed at weeks 4 and 12. All the raw scores of the CANTAB were transformed to z scores based on a normative sample of 180 children aged 8-16 yr. Results showed significant improvement in executive functions after treatment with atomoxetine for 4 wk or 12 wk including improved shifting and flexibility of attention in the IED; improved spatial short-term memory in the SSP; improved sustained attention and increased response inhibition in the RVIP; improved spatial working memory in the SWM; and improved spatial planning and problem solving in the SOC. Our findings suggested that atomoxetine was associated with significant improvement in various non-verbal executive functions among boys with ADHD, in addition to its well-known efficacy in ADHD-related symptom reductions. However, owing to lack of a placebo-controlled trial design, the findings should be interpreted with caution that changes in performance may be due to practice effects.

Psychiatry (GBR). 2009;6:40-43.

Can behavioral sensory processing problems guide us to a better pharmacological management of children with attention deficit hyperactivity disorder? A case report.

Ghanizadeh A.

Sensory processing problems in children with attention deficit hyperactivity disorder have been the focus of many studies in recent years. It is obvious that different aspects of sensory problems such as with tactile sensory are involved in attention deficit hyperactivity disorder. However, whether the sensory information process problems can be factors in decision making regarding pharmacological management of children with attention deficit hyperactivity disorder has not been researched. This case report presents two children with attention deficit hyperactivity disorder. The mother of the first patient reported that her child's ability for detecting, identifying, and discriminating smells was very high and more than the other children at this age. As she reported, the child also liked to touch everything and everybody. He experienced nail biting after taking 20mg methylphenidate in single dosage. By decreasing of the dosage, nail biting disappeared in the three trials. The other patient started lip biting about half an hour after taking the first dosage of the

medication. It continued for four hours. This report suggests that there is an association between methylphenidate and tactile sensory problems in children with attention deficit hyperactivity disorder. It is possible that methylphenidate induces or exacerbates tactile hyposensitivity. If this assumption is supported in controlled clinical trials, then tactile sensory assessment might help to make decisions for the pharmacological management of children with attention deficit hyperactivity disorder. Further studies should investigate whether attention deficit hyperactivity disorder with sensory processing problems is a phenotype with an overlap between autistic disorders and attention deficit hyperactivity disorder in which stimulants may exacerbate some sensory processing problems. Also, if this is the case, the diagnosis of attention deficit hyperactivity disorder as an exclusionary criterion for pervasive developmental disorder needs to be revised.

Pharmacopsychiatry. 2009;42:35-36.

Excessive talking triggered by methylphenidate in a boy with ADHD.

Ghanizadeh A.

There has previously been no report of provocation of excessive talking as an adverse effect of methylphenidate (MPH) in children with ADHD. This is a report of excessive talking after taking methylphenidate in a child with ADHD, diagnosed according to DSM-IV diagnostic criteria using the bFarsi version of KSADS. His mother and nursery teacher reported a significant increase of talking about 45 min after taking medication. They scored hypertalking as 7-9 on a 1 - 10 visual analogue scale. There were no symptoms of affective or anxiety disorder. Re-challenge was conducted many times and hypertalking reoccurred after every time he took the medication. It is possible that MPH increases verbal output in some ADHD children.

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2010 Apr;38:303-14.

Equivalency for father and mother ratings of the ADHD symptoms.

Gomez R.

The study used multiple-group confirmatory factor analysis (CFA) and multiple indicators multiple causes (MIMIC) procedures to examine the measurement and construct equivalencies for father and mother ratings of ADHD symptoms, recoded as binary scores. Fathers (N = 387) and mothers (N = 411) rated their primary school-aged children on the Disruptive Behavior Rating Scale (Barkley & Murphy, 1998). For the multiple-group CFA analyses, the results involving differences in practical fit indices supported full measurement and construct equivalencies, whereas the chi-square difference test showed lack of equivalency in five symptoms for factor loadings, four symptoms for error variance, and the variance and mean scores for the hyperactivity-impulsivity factor. For the MIMIC analyses, six symptoms lacked equivalency for thresholds. These findings extend existing data in this area. The theoretical, psychometric and clinical implications of the findings are discussed.

Prim Psychiatry. 2010;17:44-52.

Interpreting ADHD rating scale scores: Linking ADHD rating scale scores and CGI levels in two randomized controlled trials of lisdexamfetamine dimesylate in ADHD.

Goodman D, Faraone SV, Adler LA, et al.

Objective: To provide additional understanding of the clinical significance of Attention-Deficit/Hyperactivity Disorder Rating Scale, Version IV (ADHD-RS-IV) total and change scores in relation to Clinical Global Impressions-Severity or -Improvement (CGI-S/-I) levels.

Methods: Using two similarly designed pivotal trials of lisdexamfetamine dimesylate (Vyvanse, Shire US Inc), equipercenile linking was used to identify scores on the ADHD-RS-IV and CGI that have the same percentile rank.

Results: As assessed by CGI-S levels, moderately, markedly, severely, and extremely ill adults had mean (SD) baseline ADHD-RS-IV scores of 36.2 (4.9), 42.1 (6.1), 45.4 (5.1), and 53.0, respectively. A similar relationship was observed in children. At endpoint, children categorized as minimally, much, or very much improved by CGI-I demonstrated mean (SD) ADHD-RS-IV changes from baseline of -9.9 (6.8), -25.5 (7.2), and -33.2 (9.3), respectively. Adults demonstrated a similar relationship between ADHD-RS-IV change

scores and CGI-I ratings. Based on equipercentile link function, a change from baseline in ADHD-RS-IV total score of ~10-15 points or 25% to 30% corresponded to a change of 1 level in CGI-I score.

Conclusion: This analysis makes possible the establishment of a clinical impression of severity of illness from total ADHD-RS-IV scores and may facilitate the clinical interpretation of improvement of ADHD-RS-IV change scores.

Brain Dev. 2010;32:347-55.

Saccade eye movements as a quantitative measure of frontostriatal network in children with ADHD.

Goto Y, Hatakeyama K, Kitama T, et al.

Background: Evidence of poor inhibition in attention deficit hyperactivity disorder (ADHD) comes primarily from neuropsychological tasks and neuroimaging studies, many of which have revealed structural/functional abnormalities of the frontostriatal network with opposing functions of disinhibition and inhibition. Studies of saccades have therefore contributed to the understanding of the pathophysiological basis of ADHD.

Object: To investigate the development of reflexive/voluntary control of saccades in normal children, compare saccade parameters between ADHD and control groups, and clarify dysfunctional nervous systems in ADHD.

Methods: Subjects comprised 50 normal subjects (6-35. years), 19 ADHD patients (6-11. years) and four patients with frontal lesions (13-15. years). Saccade latency and accuracy were computed in all saccade tasks, while percentage of anticipatory errors (PAE) was determined in memory-guided saccade task, and percentage of direction errors (PDE) was determined in antisaccade task.

Results: In normal controls, significant correlations were observed between saccade latency, saccade accuracy, error rates and age. Significant differences existed between ADHD and 6- to 8-year-old controls in saccade latency and accuracy. The ADHD group showed significantly higher PAE and PDE rates than controls. Patients with frontal lesions showed significantly higher PAE and PDE.

Conclusions: These results suggest that saccade eye movements do not fully mature until adolescence, and that ADHD patients show dysfunction in "response inhibition", which is modulated by the frontal lobe, particularly the prefrontal cortex, cingulate cortex and basal ganglia.

Personality and Individual Differences. 2010 Apr;48:601-06.

The relationship between ADHD symptoms in college students and core components of maladaptive personality.

Gudjonsson GH, Sigurdsson JF, Guðmundsdóttir HB, et al.

The main purpose of this study was to investigate the relationship between symptoms of Attention Deficit Hyperactivity Disorder (ADHD) and core maladaptive personality problems (i.e., functional impairment). The participants were 397 college students in Iceland, who were screened for childhood and current ADHD symptoms (DSM-IV Checklist) and completed the Reasoning and Rehabilitation (R&R) ADHD Training Evaluation Scale (RATE) and the Severity Indices of Personality Problems (SIPP). There was a significant overlap between some of the SIPP and RATE domains. ADHD symptoms correlated significantly with the SIPP domains. Multiple regressions showed that ADHD symptoms were associated with SIPP Responsibility beyond Self-Control. In addition, inattention was a much better predictor of the Responsibility domain than hyperactivity/impulsivity. The findings show that ADHD symptoms are significantly related to core components of maladaptive personality, but salient differences exist between the attentional and hyperactivity/impulsivity symptoms. The findings clearly link inattention in adults primarily to impaired capacity to set and achieve aspired goals as a core personality problem. This adds to the growing evidence that functional impairment is significantly associated with adult ADHD.

Brain Res. 2010;1322:134-43.

Altered spontaneous low frequency brain activity in Attention Deficit/Hyperactivity Disorder.

Helps SK, Broyd SJ, James CJ, et al.

Background: Resting brain activity appears altered in Attention Deficit/Hyperactivity Disorder (ADHD). The default mode interference hypothesis (Sonuga-Barke and Castellanos, 2007) postulates that patterns of spontaneous very low frequency brain activity, typical of the resting brain, cause attention lapses in ADHD

when they remain unattenuated following the transition from rest to active task performance. Here we test this hypothesis using DC-EEG.

Methods: DC-EEG recordings of very low frequency brain activity (< 1.5 Hz) were compared for 16 male children with ADHD and 16 healthy controls during both rest and active task performance (two choice reaction time task).

Results: A previously identified very low frequency resting network of electrodes was replicated. At rest ADHD children showed less EEG power in very low frequency bands (i.e., .02-.2 Hz). They also showed less attenuation of power at these frequency bands during rest-to-task transition. Reduced attenuation was associated with a number of measures of performance.

Discussion: We confirmed the existence of altered very low frequency brain activity in ADHD. ADHD children may have deficits both in maintaining a resting brain when needed and 'protecting' an active brain from the intrusion of resting state brain activity.

Genes Brain Behav. 2010;9:296-304.

A genetic study of ADHD and activity level in infancy.

Ilott N, Saudino KJ, Wood A, et al.

It is well known that there are strong genetic influences on attention-deficit hyperactivity disorder (ADHD), with genetic association studies providing good evidence for the involvement of the dopamine neurotransmitter system in its aetiology. Developmental origins of ADHD represent an interesting area of research to understand the genetics that underlie early appearing individual differences. However, understanding the molecular basis of ADHD requires accurate, unbiased, heritable measures that can be used for molecular genetic association analyses. We take two approaches to examine the genetics of ADHD behaviours in infancy. Using quantitative genetic techniques, we explore the relationship between objective measures of activity level (AL) in both home and laboratory environments as well as with parent ratings of ADHD symptoms in a population sample of 2-year-old twins. Molecular association analyses of these measures examine candidate genes previously associated with ADHD. We find that ADHD symptoms, AL in the home and AL in the lab represent heritable phenotypes in 2-year-old infants. AL measured in the home has a strong genetic correlation with symptoms of ADHD, whereas AL in the lab correlates only modestly with the same ADHD measure. Genetic correlations suggest that AL in the home is more comparable than AL in the lab to ADHD behaviour and support the separation of all three for molecular analyses. There was modest evidence for association between DAT1, NET1 and ADHD symptom scores, as well as between DAT1 and AL in the lab.

Am J Psychiatry. 2010 Apr;167:397-408.

Morphological abnormalities of the thalamus in youths with attention deficit hyperactivity disorder.

Ivanov I, Bansal R, Hao X, et al.

OBJECTIVE: The role of the thalamus in the genesis of attention deficit hyperactivity disorder (ADHD) remains poorly understood. The authors used anatomical MRI to examine the morphology of the thalamus in youths with ADHD and healthy comparison youths.

METHOD: The authors examined 46 youths with ADHD and 59 comparison youths 8-18 years of age in a cross-sectional case-control study. Conventional volumes and measures of surface morphology of the thalamus served as the main outcome measures.

RESULTS: A mixed-effects model comparing whole thalamic volumes revealed no significant differences between groups. Maps of the thalamic surface revealed significantly smaller regional volumes bilaterally in the pulvinar in youths with ADHD relative to comparison subjects. Post hoc analyses showed that ADHD patients who received stimulants (N=31) had larger conventional thalamic volumes than untreated youths with ADHD, and maps of the thalamic surface showed enlargement over the pulvinar in those receiving stimulants. Smaller regional volumes in the right lateral and left posterior thalamic surfaces were associated with more severe hyperactivity symptoms, whereas larger regional volumes in the right medial thalamic surfaces were associated with more severe symptoms of inattention.

CONCLUSION: These findings demonstrate reduced pulvinar volumes in youths with ADHD and indicate that this same area is relatively enlarged in patients treated with stimulants compared to those untreated. Associations of hyperactivity scores with smaller regional volumes on the lateral thalamic surface and

inattention scores with larger regional volumes on the medial thalamic surface suggest the differential involvement of thalamic subcircuits in the pathogenesis of differing ADHD symptoms

J Child Neurol. 2010;25:284-86.

Assessment of the QT interval in the electroencephalography (EEG) of children with syncope, epilepsy, and attention-deficit hyperactivity disorder (ADHD).

Jha OP, Khurana DS, Carvalho KS, et al.

The interpretation of QT interval is often neglected during electroencephalography (EEG) reading. We compared the incidence of prolonged QT interval, as seen in the electrocardiography (ECG) recording lead of the EEG, in children presenting with seizure, syncope, or attention-deficit hyperactivity disorder (ADHD). Abnormal QT was defined as >460 ms. The incidence of prolonged QT in the seizure, syncope, and ADHD groups was 1/50 (2%), 7/50 (14%), and 2/50 (4%), respectively ($P = .036$, chi-square). The mean (plus or minus) SD of QT were 405 (plus or minus) 34, 424 (plus or minus) 39, and 414 (plus or minus) 36, respectively ($P = .035$, analysis of variance [ANOVA], syncope group, compared with seizure group). The incidence of prolonged QT as measured in the EEG was unexpectedly high in children presenting with seizure, syncope, or ADHD. These data support the concept that QT evaluation should be emphasized during routine EEG reading, as it may aid in identifying cases of undiagnosed cardiac conduction abnormalities. Prospective studies comparing EEG-ECG tracings with 12-lead ECG are warranted.

Neuropsychologia. 2010;48:1255-64.

Right-sided spatial difficulties in ADHD demonstrated in continuous movement control.

Johnson KA, Daibhis A, Tobin CT, et al.

Children with Attention Deficit Hyperactivity Disorder (ADHD) often show spatial attentional deficits, exhibiting a subtle rightwards bias, possibly due to dysfunction within the right hemisphere fronto-parietal network. Approximately 50% of children with ADHD also show signs of movement dysfunction. The nature of this movement dysfunction and possible interactions with spatial attention difficulties has not been clearly described. This study compared 31 children with and 31 children without ADHD on a movement kinematic task that tested hand-drawing movement precision. Participants used an electronic pen on a digitizing tablet. The pen tip position was sampled as X and Y coordinates at 200. Hz. The task was to join targets of either 10 or 20. mm diameter that were separated by a distance of 62.5 or 125. mm. Constant error in the X and Y planes, peak absolute velocity and acceleration, movement time, the number of pauses and pause time were analysed. Apart from a significantly increased rate of acceleration across all conditions, the children with ADHD demonstrated no temporal difficulties with the task; rather they showed subtle spatial difficulties, possibly suggestive of cerebellar involvement. The children with ADHD showed difficulties in accuracy of movement towards the right. They were less accurate in the X plane when moving towards the right-sided targets over the long distance. Greater variability in target accuracy was shown when moving towards the small target on the right side. The children with ADHD made significantly more pauses on the left target, when preparing the right movement, than the control group. These results suggest that the subtle spatial bias towards the right that has been demonstrated in ADHD in spatial attention also extends into the continuous movement domain.

Progress in Neuro-Psychopharmacology & Biological Psychiatry. 2010 Feb;34:219-24.

Effect of a[_{2A}]-adrenoceptor C-1291G genotype and maltreatment on hyperactivity and inattention in adolescents.

Kiive E, Kurrikoff T, Mäestu J, et al.

The C-1291G polymorphism (rs1800544) in the promoter region of the a[_{2A}]-adrenoceptor gene (ADRA2A) has been associated with attention deficit and hyperactivity in clinical samples. We have examined the effect of ADRA2A C-1291G on inattentive, hyperactive and aggressive behaviour in a population representative cohort of healthy schoolchildren, and possible interaction of genotype with family relations. Ratings on aggressiveness, motor restlessness and concentration difficulties were obtained from the class teachers by using the Hyperactivity Scale of af Klinteberg, and the teacher-report version of SNAP-IV. The relations in the family were reported by children. Symptom scores, self-reports and genotype data of

429 15-years old children (196 boys, 233 girls) were available for analysis. There was a significant interaction effect of maltreatment and the ADRA2A genotype on behavioural functioning in 15 years old boys. Boys with CC genotype and higher score of maltreatment demonstrated more overactive behaviour and concentration difficulties than boys with CC genotype and low maltreatment score. They also had more inattentive symptoms measured by SNAP-IV. Among boys with low maltreatment score, subjects with CC genotype demonstrated less overactivity than G allele carriers. In girls, the G allele carriers did not differ from the CC genotype, but in maltreated girls with GG genotype aggression and inattention symptoms were reduced, and the score of aggressive behaviour was also lower compared to maltreated girls with CC genotype. Our data suggest that family environmental factors may act together with the α_2A -adrenoceptor genotype to increase the expression of hyperactive and inattentive symptoms in adolescents.

J Child Adolesc Psychopharmacol. 2010;20:63-67.

Report of an initial pilot study on the feasibility of using the MacArthur Competence Assessment Tool for Clinical Research in children and adolescents with attention-deficit/hyperactivity disorder.

Koelch M, Prestel A, Singer H, et al.

Introduction: The MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR) was used in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) and co-morbid oppositional defiant disorder (ODD) and in their parents. The aims were to test feasibility and to determine children's understanding of the elements of disclosure for a clinical drug trial and their competence to assent.

Method: The contents and language of MacCAT-CR were adapted to be age appropriate for the children. Twelve children (mean age, 9.87 [7.7-12.2]; mean intelligence quotient [IQ], 97 [72-122]) and either the mother or father of each child were interviewed. Psychologists rated the interviews and, in addition to MacCAT-CR, competence was assessed by trained clinicians.

Results: The MacCAT-CR was practicable, and the time required was acceptable. Interrater reliability was excellent in children. Children performed less well than parents on this test (children's vs. parents' scores: Understanding 5.86 vs. 9.08, appreciation 2.64 vs. 4.96, reasoning 3.05 vs. 4.63, respectively). Whereas clinicians assessed all children as competent, lack of competence became apparent in the MacCAT-CR.

Conclusions: The practicability and the interrater reliability suggest that the MacCAT-CR is feasible in children, but the question of whether competence is assessed validly remains unsolved in the absence of external validation. The differences between assessment by clinicians and the low scores obtained in the MacCAT-CR suggest that children may give assent even if they do not understand completely. The results of this initial pilot study may help in the planning of further investigations intended to improve information about studies and assessment of assent/consent.

Journal of Emotional and Behavioral Disorders. 2010 Mar;18:41-50.

Parent agreement on ratings of children's Attention Deficit/Hyperactivity Disorder and broadband externalizing behaviors.

Langberg JM, Epstein JN, Simon JO, et al.

Mothers and fathers often disagree in their ratings of child behavior, as evidenced clinically and as supported by a substantial literature examining parental agreement on broadband rating scales. The present study examined mother–father agreement on Diagnostic and Statistical Manual–based symptom-specific ratings of Attention-Deficit/Hyperactivity Disorder (ADHD), as compared to agreement on broadband ratings of externalizing behavior. Based on mother and father ratings of 324 children who participated in the Multimodal Treatment Study of Children with ADHD (MTA), parental agreement was computed and patterns of disagreement examined. Mother–father ratings were significantly correlated; however, a clear pattern of higher ratings by mothers was present. Agreement on attention-deficit/hyperactivity disorder symptom-specific ratings was significantly lower than that for broadband externalizing behaviors and oppositional defiant disorder symptoms. Of several moderator variables tested, parental stress was the only one that predicted the discrepancy in ratings. Disagreement between parents is clinically significant and may pose complications to the diagnostic process.

Neuropsychologia.

Altered evoked gamma-band responses reveal impaired early visual processing in ADHD children.

Lenz D, Krauel K, Flechtner HH, et al.

Neurophysiological studies yield contrary results whether attentional problems of patients with attention-deficit/hyperactivity disorder (ADHD) are related to early visual processing deficits or not. Evoked gamma-band responses (GBRs), being among the first cortical responses occurring as early as 90 ms after visual stimulation in human EEG, have been assigned a pivotal role in early visual processing. In particular, they are involved in memory matching processes and are enhanced when known stimuli are processed. The current study examined whether evoked GBR patterns during early memory matching processes could be indicative of an early visual processing deficit in ADHD patients. EEG was recorded from 13 young ADHD patients as well as 13 age-matched healthy participants. Both groups performed a simple forced choice reaction task employing line drawings of either known real-world items with representations in long-term memory or physically similar unknown items without such representations. Evoked GBRs of ADHD patients did not differentiate between known and unknown items. However, in healthy children, evoked GBRs were enhanced when stimuli matched a representation stored in memory. This finding indicates disadvantages at early visual processing stages in ADHD patients: In contrast to healthy participants, ADHD children lack an early memory based classification, possibly resulting in an impaired ability to rapidly reallocate attentional resources to relevant stimuli. These findings suggest that impaired early automatic stimulus classification in ADHD patients could be involved in deficits of selective and sustained attention.

J Am Acad Child Adolesc Psychiatry. 2010;49:368-77.

Familial Clustering and DRD4 Effects on Electroencephalogram Measures in Multiplex Families With Attention Deficit/Hyperactivity Disorder.

Loo SK, Hale TS, Hanada G, et al.

Objective: The current study tests electroencephalogram (EEG) measures as a potential endophenotype for attention deficit/hyperactivity disorder (ADHD) by examining sibling and parent-offspring similarity, familial clustering with the disorder, and association with the dopamine receptor D4 (DRD4) candidate gene.

Method: The sample consists of 531 participants (191 parents and 340 children) from 132 multiplex families with ADHD who participated in a larger genetics study. All members of the families underwent extensive assessment including semi-structured diagnostic interviews and EEG recording.

Results: Strong sibling similarity and parent-offspring correlations in EEG power emerged, suggesting high trait heritability. Increased theta power was observed among children with ADHD when compared with unaffected children, and there were no differences according to ADHD subtype. Within the parent sample, ADHD diagnostic status and ADHD subtype group differences emerged in the theta, alpha, and beta frequency bands. DRD4 effects for both parents and children were apparent in the beta frequency band and for children only in the theta frequency band.

Conclusions: This study suggests that EEG measures are a promising avenue of study in the search for putative endophenotypes for ADHD, and that variability at the DRD4 gene may contribute to this endophenotype.

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2010 Apr;38:291-301.

A developmental examination of story recall and coherence among children with ADHD.

Lorch EP, Milich R, Flake RA, et al.

This study investigated developmental differences in story recall in children with attention-deficit/hyperactivity disorder (ADHD), N = 57 (77.2% male) and their comparison peers, N = 98 (61.2% male). Children at the ages of 4–6 or 7–9 completed a free recall immediately after viewing each of two televised stories, once in the presence of toys during viewing and once in their absence. This procedure was repeated with new stories 21 months later. Comparison children recalled more story events and showed a greater sensitivity to the thematic importance of the story events than did children with ADHD, a pattern that remained stable over time. Older comparison children showed a dramatic increase over time in the global coherence of their

narrations, whereas the older children with ADHD showed limited improvement over time. The implications of these findings for academic performance and the possible need for remediation are discussed.

Eur Psychiatry. 2010;25:146-50.

Possible association between attention deficit hyperactivity disorder and attempted suicide in adolescents - A pilot study.

Manor I, Gutnik I, Ben-Dor DH, et al.

Objective: Both adolescent suicide and attention deficit hyperactivity disorder (ADHD) are troubling phenomena with high comorbidity, including impulsivity, depression and personality disorders (PD). Studies on the association between these two phenomena are relatively rare. This pilot study's aim was to estimate the rate of ADHD in adolescents attempting suicide.

Method: Subjects constituted consecutive admissions to the psychiatric emergency room (ER) who were admitted as a result of attempting suicide. Assessment included the use of the Kiddie-SADS, Strengths and Difficulties Questionnaire (SDQ) and the Conners' Rating Scale (CRS). Those diagnosed as suffering from ADHD were assessed by a standardized Continuous Performance Test (Test of Variables of Attention [TOVA]) that included methylphenidate (MPH) challenge. Twenty-three (23) adolescents completed the study. M:F ratio was 5:18, respectively.

Results: Of the 23 participants who completed the study, 65% were diagnosed with ADHD, 43.5% with depression and 39% with cluster. B PD. ADD/ADHD ratio was 66%:34%. Only five of the patients were formerly diagnosed as ADHD, only three had been medicated and 14 out of 15 adolescents responded well to MPH challenge.

Conclusion: These preliminary results suggest a significant association between ADHD and suicidal behavior in adolescents. Further study is needed to establish this association and assess the causality.

J Child Adolesc Psychopharmacol. 2009;19:709-18.

Atomoxetine and neuropsychological function in children with attention-deficit/hyperactivity disorder: Results of a pilot study.

Maziade M, Rouleau N, Lee B, et al.

This pilot longitudinal study using measures from parents and teachers evaluated the effects of flexible doses of atomoxetine (ATX) on neuropsychological and functional outcomes in 21 children with attention-deficit/hyperactivity disorder (ADHD) (mean age, 8.0 (plus or minus) 1.3 years; inattentive subtype, 71.4%; combined subtype, 28.6%). Among 16 children completing 6 months of ATX treatment, neuropsychological function measured by the NEPSY instrument found significant improvement from baseline in the memory and learning domain ($p = 0.01$); this change was also seen in an age- and sex-matched healthy control group ($p = 0.011$). The patient group showed significant improvement on the Test of Everyday Attention (TEA-Ch) and parent and teacher versions of the Behavior Rating Inventory of Executive Function (BRIEF), which assess attentional and executive processes, respectively. Functional improvement was also observed on the Weiss Functional Impairment Rating Scale-Parent Report (WFIRS-P) and parent and teacher versions of the ADHD Rating Scale (ADHDRS-IV), and the investigator-rated Clinical Global Impressions-Severity (CGI-S) scale evidenced reductions in ADHD symptoms. These findings suggest that potential benefits of ATX treatment may extend beyond reduction of core ADHD symptoms to amelioration of some neuropsychological and functional deficits.

Psychiatry (GBR). 2009;6:21-29.

Estimating the size of treatment effects: Moving beyond P values.

McGough JJ, Faraone SV.

Objective: To increase understanding of effect size calculations among clinicians who over-rely on interpretations of P values in their assessment of the medical literature.

Design: We review five methods of calculating effect sizes: Cohen's d (also known as the standardized mean difference) - used in studies that report efficacy in terms of a continuous measurement and calculated from two mean values and their standard deviations; relative risk - the ratio of patients responding to treatment divided by the ratio of patients responding to a different treatment (or placebo), which is

particularly useful in prospective clinical trials to assess differences between treatments; odds ratio - used to interpret results of retrospective case-control studies and provide estimates of the risk of side effects by comparing the probability (odds) of an outcome occurring in the presence or absence of a specified condition; number needed to treat - the number of subjects one would expect to treat with agent A to have one more success (or one less failure) than if the same number were treated with agent B; and area under the curve (also known as the drug-placebo response curve) - a six-step process that can be used to assess the effects of medication on both worsening and improvement and the probability that a medication-treated subject will have a better outcome than a placebo-treated subject.

Conclusion: Effect size statistics provide a better estimate of treatment effects than P values alone

Int J Eating Disord. 2010;43:248-59.

Bulimia nervosa symptoms in the multimodal treatment study of children with ADHD.

Mikami AY, Hinshaw SP, Arnold LE, et al.

Objective: We investigated body image dissatisfaction and bingeing/purging characteristics of bulimia nervosa (BN) in the ongoing prospective follow-up of the Multimodal Treatment Study of Children with attention-deficit/hyperactivity disorder (ADHD).

Method: Participants were 337 boys and 95 girls with ADHD and 211 boys and 53 girls forming a local normative comparison group (LNCG), reassessed in midadolescence (mean age, 16.4), 8 years after original recruitment.

Results: Youth with childhood ADHD showed more BN symptoms in midadolescence than did LNCG youth, and girls demonstrated more BN symptoms than did boys, with effect sizes between small and medium. Childhood impulsivity, as opposed to hyperactivity or inattention, best predicted adolescent BN symptoms, particularly for girls. Among youth with ADHD, treatment received during the follow-up period was not associated with BN pathology.

Discussion: Both boys and girls with ADHD may be at risk for BN symptoms in adolescence because of the impulsivity central to both disorders.

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2010 Apr;38:315-26.

Does childhood executive function predict adolescent functional outcomes in girls with ADHD?

Miller M, Hinshaw SP.

We prospectively followed an ethnically and socioeconomically diverse sample of preadolescent girls with ADHD (n = 140) and matched comparison girls (n = 88) over a period of 5 years, from middle childhood through early/mid-adolescence. Our aim was to examine the ability of measures of childhood executive function (EF) to predict functional outcomes in adolescence. Measures of neuropsychological functioning comprised the childhood predictors, with academic, social, and global functioning serving as adolescent criterion measures. Results indicated that childhood EF predicted (a) academic achievement and social functioning across our entire sample (independent of diagnostic group status) and (b) global functioning only in girls with ADHD (independent of IQ). These results highlight the non-specificity of EF deficits and suggest the importance of assessing and developing interventions that target EF impairments, particularly in those at high-risk for negative outcomes, in order to prevent long-term difficulties across a range of important functional domains.

Rev Neurol. 2010;50:S135-S142.

Reading comprehension of students with attention deficit hyperactivity disorder: What is the role of executive functions?

Miranda-Casas A, Fernandez MI, Robledo P, et al.

Introduction. Deficits in reading comprehension of children with attention deficit hyperactivity disorder (ADHD) have received scarce attention. However, to establish the underlying cognitive processes of ADHD and deficits in reading comprehension association could be essential for deeply understanding neurobiological bases of reading comprehension.

Aim. To examine the contribution of verbal fluency, reading fluency, and executive functions (working memory, attention and suppression mechanism) in predicting mental processes of texts comprehension. Patients and methods. The participants in the study were 42 students, 12 to 16 year old, with a clinical diagnosis of ADHD. A battery of tests was administered to measure cognitive processes and reading processes.

Results and conclusions. Stepwise regression analysis carried out showed that the score in verbal fluency was the best single predictor of reading comprehension. Furthermore executive functions, but not reading fluency, made a significant contribution to reading comprehension. These findings underline the need for consideration of the role of executive functions in assessment and treatment of reading comprehension deficits of students with ADHD.

J Child Adolesc Psychopharmacol. 2009;19:731-35.

Early repolarization in young children with attention-deficit/hyperactivity disorder versus normal controls: A retrospective preliminary chart review study.

Nahshoni E, Sclarovsky S, Spitzer S, et al.

Objective and background: Early repolarization (ER), considered a common and benign electrocardiographic pattern on the surface 12-lead electrocardiogram (ECG), was recently found to be prevalent among patients with idiopathic ventricular fibrillation. It is also highly predominant in physically active young males. Reports on sudden cardiac death (SCD) of children and adolescents treated with psychotropic agents have raised concerns regarding the need for cardiovascular monitoring and risk stratification schedules. The rate of ER pattern has not been estimated in children with attention deficit/hyperactivity disorder (ADHD). Thus, in the present retrospective chart review study, we estimated the rate of ER pattern, as well as RR, QT, and QTc intervals, from ECG tracings of physically healthy children with ADHD versus physically and mentally healthy controls.

Methods: The ECG tracings of 50 children (aged 8.7 (plus or minus) 1.4 years; 12 girls, 44 boys) diagnosed as suffering from ADHD were compared to 55 physically and mentally healthy controls (aged 8.25 (plus or minus) 2.1 years; 20 girls, 35 boys). ER was defined as an elevation of the QRS-ST junction (J point) of at least 0.1 mV from baseline with slurring or notching of the QRS complex, and assessed separately by two senior cardiologists who were blind to all other data relating to the study participants.

Results: The rate of ER pattern was significantly higher in ADHD children compared to normal controls (32% vs. 13%, respectively, $P = 0.012$; relative risk [RR] = 1.68, 95% confidence interval [CI] 1.16-2.44), irrespective of stimulant treatment or gender. All other standard ECG measures (heart rate, QT and QTc intervals) were within normal range.

Conclusion: The rate of ER in children with ADHD is significantly higher than in normal controls. Its clinical significance awaits further research.

Child Psychiatry Hum Dev. 2010 Apr;41:193-203.

Prefrontal dysfunction in attention-deficit/hyperactivity disorder as measured by near-infrared spectroscopy.

Negoro H, Sawada M, Iida J, et al.

Recent developments in near-infrared spectroscopy (NIRS) have enabled non-invasive clarification of brain functions in psychiatric disorders with measurement of hemoglobin concentrations as cerebral blood volume. Twenty medication-naïve children with attention-deficit/hyperactivity disorder (ADHD) and 20 age- and sex-matched healthy control subjects participated in the present study after giving consent. The relative concentrations of oxyhemoglobin (oxy-Hb) were measured with frontal probes every 0.1 s during the Stroop color-word task, using 24-channel NIRS machines. During the Stroop color-word task, the oxy-Hb changes in the control group were significantly larger than that in the ADHD group in the inferior prefrontal cortex, especially in the inferior lateral prefrontal cortex bilaterally. The Stroop color-word task used with NIRS may be one useful measurement to assess prefrontal brain dysfunction in ADHD children.

Arch Gen Psychiatry. 2010 Apr;67:388-96.

Unraveling the nature of hyperactivity in children with attention-deficit/hyperactivity disorder.

Ohashi K, Vitaliano G, Polcari A, et al.

CONTEXT: Seated hyperactivity is a defining feature of the combined and predominantly hyperactive-impulsive subtypes of attention-deficit/hyperactivity disorder (ADHD), but its underlying nature is unknown.

OBJECTIVE: To determine whether hyperactivity is a consequence of an impaired ability to inhibit activity to low levels or to maintain positional stability.

DESIGN: Case-control study.

SETTING: Academic research center and school.

PARTICIPANTS: Sixty-two boys 9 to 12 years of age (of 73 screened), recruited from the community by advertisement, who met DSM-IV criteria for ADHD combined subtype on structured interview. Sixty-two controls were selected by matching for age and sex from a community sample of 1168 subjects in 3 participating school districts. Pupils with Conners' Teacher Rating Scores Revised within ± 1 SD of the mean for age were eligible for randomized matching. Intervention Infrared motion analysis of head-marker movements (50 Hz) during performance of a 15-minute cognitive control task. Subjects with ADHD were tested at least 18 hours following their last dose of methylphenidate and again 120 minutes after a 0.4-mg/kg probe dose.

MAIN OUTCOME MEASURES: Inhibitory control (spike and basal amplitude) and head-marker stability (approximate entropy, Lyapunov, and spectral exponents).

RESULTS: Inhibitory control measures were 2-fold higher in subjects with ADHD ($d' = 0.63-0.95$). Group differences in head-marker stability were even greater ($d' = 2.20-4.71$; receiver operating characteristic area = 0.956-1.0). Methylphenidate restored inhibitory ability to control levels but only partially corrected stability deficits, which still distinguished subjects with ADHD from controls (receiver operating characteristic area = 0.722-0.995).

CONCLUSIONS: Children with ADHD have a deficient ability to inhibit activity to low levels and unstable control of head-marker position characterized by deterministic chaos (sensitivity to initial conditions). These deficits differed in degree of correctability by methylphenidate, suggesting that they may be mediated by different neural circuits (eg, corticostriatal vs cerebrotvestibular).

Neuroendocrinol Lett. 2010;31:131-36.

The association between TaqI A polymorphism of ANKK1 (DRD2) gene and ADHD in the Czech boys aged between 6 and 13 years.

Pacit I, Drtilkova I, Kopeckova M, et al.

OBJECTIVE: The purpose of this study was the correlation of the combined type of ADHD in children and Taq IA polymorphism DRD2 gene. We hypothesized a positive correlation of DRD2 polymorphisms in the combined type of ADHD patients without co-morbidity.

PATIENTS AND METHODS: Our research sample included 586 unrelated boys of the Czech origin aged between 6 and 13 years. The ADHD group consisted of 269 boys and the control group consisted of 317 boys. PCR detection of the DRD2 polymorphism was carried out by using primers, described by Grandy (Grandy et al. 1989).

RESULTS: The comparison of genotype frequencies showed statistically highly significant difference between the studied groups ($p < 0.0001$). A statistically significant difference was also found when the allelic frequencies between the two groups were compared ($p < 0.0001$), with the A1 allele having a 4.359 fold higher risk of ADHD (Risk Ratio=4.359, 95% CI of RR=3.5753 to 5.3144, Odds Ratio= 7.7824; 95% CI of OR=10.315 to 13.6719).

CONCLUSIONS: Our results presented a highly positive correlation between the combined type of ADHD without co-morbidity and ANKK1 (DRD2) polymorphism.

Adverse Drug React Bull. 2010;999-1002.

Safety of psychotropic drug prescribed for attention-deficit/hyperactivity disorder in Italy.

Pane P, Arcieri R, Bonati M, et al.

The drugs prescribed to treat attention-deficit/hyperactivity disorder, one of the most prevalent psychiatric disease affecting children and adolescents, may risk causing harm. Recently, the U.S. Food and Drug Administration (FDA) has warned about liver and cardiovascular risks, and the European Medicines Agency (EMA) had performed an assessment of risk-benefit ratio of psychostimulants. Pharmacovigilance in an

Italian population aged 6-17 years suggests that atomoxetine is more likely to be reported as causing harm than methylphenidate.

Prog Neuro-Psychopharmacol Biol Psychiatry.

Evidence that genetic variation in the oxytocin receptor (OXTR) gene influences social cognition in ADHD.

Park J, Willmott M, Vetuz G, et al.

Some children with ADHD also have social and communication difficulties similar to those seen in children with autistic spectrum disorders and this may be due to shared genetic liability. As the oxytocin receptor (OXTR) gene has been implicated in social cognition and autistic spectrum disorders, this study investigated whether OXTR polymorphisms previously implicated in autism were associated with ADHD and whether they influenced OXTR mRNA expression in 27 normal human amygdala brain samples. The family-based association sample consisted of 450 DSM-IV diagnosed ADHD probands and their parents. Although there was no association with the ADHD phenotype, an association with social cognitive impairments in a subset of the ADHD probands (N = 112) was found for SNP rs53576 (F = 5.24, p = 0.007) with post-hoc tests demonstrating that the AA genotype was associated with better social ability compared to the AG genotype. Additionally, significant association was also found for rs13316193 (F = 3.09, p = 0.05) with post-hoc tests demonstrating that the CC genotype was significantly associated with poorer social ability than the TT genotype. No significant association between genotype and OXTR mRNA expression was found. This study supports previous evidence that the OXTR gene is implicated in social cognition.

Arq Neuro-Psiquiatr. 2010;68:103-06.

Frequency of symptoms of attention deficit and hyperactivity disorder in autistic children.

Ponde MP, Novaes CM, Losapio MF.

Background: Both DSM-IV and the ICD-10 exclude diagnosis of attention deficit/hyperactivity disorder (ADHD) when autism diagnostic is present. Some authors suggest, however, that autism can be associated to other comorbidity amongst which the ADHD.

Objective: To estimate prevalence of ADHD in children with autism.

Method: Children were selected from a specialized school, all of them had previous diagnosis or diagnostic suspicion of autism. The Brazilian version of the KIDDIE-SADS PL was applied to parents for diagnostic of ADHD. DSM-IV diagnostic of autism was based on parents' interview and child observation.

Results: 32 children were included in the study. Results show that 53.1% of the ASD child had ADHD symptoms enough to fulfill DSM-IV diagnostic criteria, whereas 56.9% did not fulfill DSM-IV criteria for ADHD.

Conclusion: Results suggest a high frequency of ADHD symptoms in ASD patients. Elucidating if we are facing a comorbidity or an autism distinct phenotype can contribute for a more adjusted pharmacotherapy approach for these children.

Med Sci Monit. 2009;15:CR595-CR599.

ADHD and growth: Anthropometric changes in medicated and non-medicated ADHD boys .

Ptacek R, Kuzelova H, Paclt I, et al.

Background: ADHD children can show changes in growth and development. Many studies describe these changes as a side effect of stimulant medication. However, changes in somatic development can also appear in non-medicated children. This suggests that the changes could be a manifestation of the disorder itself and not just a side effect of the treatment.

Material/Methods: This study compared anthropometric characteristics in medicated and non-medicated ADHD boys (n=104, age 4-16 years) with the normal non-clinical population. In contrast to most previous studies, complex anthropometrical measurements were used.

Results: The results showed significant differences between children with ADHD and those without the diagnosis, the differences found to be statistically significant (p<0.01) being signs of nutrition (percentage of fat, abdominal circumference) and growth suppression (lower body height, smaller head circumference).

Differences between the medicated and non-medicated groups corresponded only to a lower value of body fat in the medicated children.

Conclusions: These results suggest that growth changes in ADHD children may be more specific to the disorder itself than to stimulant treatment.

Conscious Cogn. 2010;19:341-51.

ADHD children outperform normal children in an artificial grammar implicit learning task: ERP and RT evidence.

Rosas R, Ceric F, Tenorio M, et al.

This study focuses on Implicit learning (IL) in children. One of the main debates in this field concerns the occurrence of IL indicators in experimental settings and its manifestation in different populations. In this research, we are looking for evidence of the occurrence of IL in normal children and in children with Attention Deficit Hyperactive Disorder (ADHD), based on the relationship between accuracy, reaction time and event-related potentials (ERPs). Our results show differences between the analyzed groups with respect to markers for electrophysiological activity and reaction time, but not for accuracy. In consequence, we suggest that research in IL should explore different indicators and their relationship with the cognitive processing levels involved. In addition, IL might involve different forms of information processing in normal children and children with ADHD. We discuss the possible impact of these findings for future research.

J Int Neuropsychol Soc. 2010 Mar;16:388-93.

Interstimulus jitter facilitates response control in children with ADHD.

Ryan M, Martin R, Denckla MB, et al.

Interstimulus "jitter" involves randomization of intervals between successive stimulus events, and can facilitate performance on go/no-go tests among healthy adults, though its effect in clinical populations is unclear. Children with Attention-deficit/Hyperactivity Disorder (ADHD) commonly exhibit deficient response control, leading to increased intra-subject variability (ISV), which has been linked to anomalous functioning within frontal circuits, as well as their interaction with posterior "default mode" regions. We examined effects of interstimulus jitter on response variability in 39 children, ages 9-14 years (25 ADHD, 14 controls). Participants completed 2 computerized go/no-go tests: one with fixed interstimulus interval (ISI) and one with jittered ISI. Repeated measures analysis of variance (ANOVA) revealed a significant group-by test interaction, such that introduction of jitter produced a significant decrease in ISV among children with ADHD, but not among controls. Whereas children with ADHD were significantly more variable than controls on the go/no-go test with fixed ISI, their performance with jittered ISI was equivalent to that of controls. Jittering stimulus presentation provides a nonpharmacologic mechanism for improving response control in ADHD. This bottom-up approach may be mediated by increases in vigilance through noradrenergic circuits that facilitate maintenance of frontal circuits critical to response control.

Rev Neurol. 2010;50:283-90.

Validation of the attention deficit hyperactivity disorder adult assessment scale (EDAH) in a teenage population.

Sanchez CR, Ramos C, Diaz F, et al.

Aim. To validate the attention deficit hyperactivity disorder assessment scale (EDAH) for a teenage population. **Subjects and methods.** Out of an initial sample of 3400 participants, a final sample of 2382 boys and girls was selected. This reduction in the number of participants was mainly due to parents' failing to sign the informed consent document (948 cases) and to incomplete questionnaires (70 cases). Finally, we extracted a sub-sample of those who presented scores above the 75 centile on the total EDAH factor of the questionnaire. This sub-sample consisted of 637 pupils, 258 of whom were girls (40.5%) and the remaining 379 were boys (59.5%), with ages between 11 and 17 years old.

Results and conclusions. The original test has proved to be useful in screening for attention deficit hyperactivity disorder in childhood. The main result of the factorial analysis with Varimax rotation performed on a sample of teenagers was the appearance of a new factor ('social interaction disorders'); the three factors of the original test were maintained, although with slight differences in their composition. High internal

consistency was also observed by means of Cronbach's alpha coefficient (0.85), which confirmed the reliability of the scale. The sociodemographic variables sex and number of failed subjects account for a significant part of the variance of the total EDAH score (28%); in 'attention deficit', gender, age and number of failed subjects are the variables that exert the greatest influence; in 'social interaction disorders', age and number of failed subjects are involved; in 'hyperactivity', age and gender are the variables with the most weight; and in 'behavioural disorders', none of these variables have any repercussion on the scores that are obtained.

J Child Adolesc Psychopharmacol. 2009;19:737-48.

Anxiety in boys with attention-deficit/hyperactivity disorder with and without chronic multiple tic disorder.

Schneider J, Gadow KD, Crowell JA, et al.

Objective: This study examined the psychosocial and behavioral concomitants of anxiety in clinic-referred boys with attention-deficit/hyperactivity disorder (ADHD) with and without chronic multiple tic disorder (CMTD).

Method: ADHD boys with (n = 65) and without (n = 94) CMTD were evaluated with measures of psychiatric symptoms, mental health risk factors, and academic and social performance.

Results: Boys with CMTD evidenced more severe anxiety and less social competence and were more likely to be living with only one biological parent than the ADHD Only group, but the magnitude of group differences was generally small. The severity of generalized anxiety, separation anxiety, social phobia, and obsessive-compulsive symptoms were uniquely associated with a different pattern of risk factors, and there was some evidence that these patterns differed for the two groups of boys.

Conclusion: Boys with CMTD had a relatively more severe and complex pattern of anxiety that was associated with different clinical features, all of which suggests that ADHD plus CMTD might better be conceptualized as a distinct clinical entity from ADHD Only. However, findings from the extant literature are mixed, and therefore this remains a topic for further study.

Child Psychiatry Hum Dev. 2010 Apr;41:230-38.

Dream recall and dream content in children with attention deficit/hyperactivity disorder.

Schredl M, Sartorius H.

Although sleep is widely investigated in children with ADHD, dream studies in this group are completely lacking. The continuity hypothesis of dreaming stating that waking life is reflected in dreams would predict that waking-life symptoms are reflected in the dreams of such children. 103 children with ADHD and 100 controls completed a dream questionnaire eliciting dream recall frequency and the most recent dream. The dreams of the children with ADHD did not show a heightened occurrence of activities but were more negatively toned and included more misfortunes/threats, negative endings, and physical aggression towards the dreamer. Dream recall frequency and general dream characteristics like dream length and dream bizarreness did not differ from children without ADHD. The dreams seem to reflect the inner world of the child with ADHD. From a clinical point of view, it would be very interesting to study whether the negatively toned dreams change during treatment (pharmacological and/or psychotherapeutic) in a way similar to how sleep quality improves.

Aust New Zealand J Psychiatry. 2010;44:323-32.

Psychopathology and symptom remission at adolescence among children with attention-deficit/hyperactivity disorder.

Shur-Fen Gau S, Lin YJ, Tai-Ann Cheng A, et al.

Objective: The aim of the present study was to examine changes of attention-deficit/hyperactivity disorder (ADHD) symptoms and psychiatric comorbidities at adolescence, and mother-child agreement on reports of ADHD symptoms among children with ADHD as compared to unaffected controls.

Methods: The participants included 93 patients (male, 82.8%) aged 11-16, who were clinically diagnosed with ADHD at the mean age of 7.3 (plus or minus) 2.8 years, and 93 age-, sex-, and parental education-matched school controls. The participants and their mothers were first interviewed separately for baseline

psychopathology at childhood, followed by current psychopathology using the Chinese Kiddie Epidemiologic version of the Schedule for Affective Disorders and Schizophrenia.

Results: At adolescence, 46 patients (49.5%) met full DSM-IV ADHD criteria, 31 (33.3%) had subthreshold ADHD, and 16 (17.2%) had recovered from ADHD. We found a significant progressive decline in the three ADHD core symptoms for the ADHD group: hyperactivity had the greatest effect size, followed by inattention, and then impulsivity. Children with ADHD tended to report less severe ADHD symptoms at childhood and adolescence than their mothers. They were more likely than the controls to have oppositional defiant disorder (odds ratio (OR)=18.0; 95% confidence interval (CI)=8.3-38.9), conduct disorder (OR=23.1, 95%CI=5.3-100.2), mood disorders (OR=3.8, 95%CI=1.5-9.4), bipolar disorders (Fisher's exact $p < 0.001$), and sleep disorders (OR=3.1, 95%CI=1.6-6.0) at adolescence.

Conclusions: The present findings are similar to those of Western studies, regarding the patterns of comorbidity, stability of core symptoms, and motherchild differences on symptom reports.

Brain Imaging Behav. 2008;2:123-31.

Dysfunction in the fronto-parietal network in attention deficit hyperactivity disorder (ADHD): An fMRI study.

Silk TJ, Vance A, Rinehart N, et al.

ADHD is associated with spatial working memory deficits, thought to be subserved by dysfunction of neural circuits. In this study we aimed to further examine fronto-parietal dysfunction in ADHD by examining brain activation associated with the Raven's Progressive Matrices task, a visuo-spatial pattern sequencing task involving relational reasoning and thereby placing high-demand loading on the prefrontal cortex. Functional MRI was conducted on twelve right-handed 8-12 year old boys with ADHD-combined type and 12 right-handed, age and performance IQ-matched, healthy boys as they completed items from the Raven's Progressive Matrices. Our findings further confirm striatum and parietal lobe dysfunction in ADHD. Furthermore, dysfunction in lateral prefrontal regions was found. In addition to lateral prefrontal, striatum and posterior parietal regions, the temporal lobe was also less active. These findings suggest deficits in a widespread 'functional network' in ADHD that may be fundamental for visuo-spatial information processing and relational reasoning.

J Child Adolesc Psychopharmacol. 2009;19:663-71.

Stimulant drug response in the predominantly inattentive and combined subtypes of attention-deficit/hyperactivity disorder.

Solanto M, Newcorn J, Vail L, et al.

Objective: This study compared the methylphenidate (MPH) dose-response profiles of children with the Predominantly Inattentive (PI) and Combined (CB) subtypes of attention-deficit/hyperactivity disorder (ADHD). It is the first such study to enroll a sample comprised exclusively of children, all but one of whom had no prior exposure to ADHD medications.

Method: The design was a double-blind crossover with 1-week exposures to placebo and low, medium, and high, fixed, three times daily (t.i.d.) dosage regimens of immediate-release MPH, administered in random order. Parents and teachers completed weekly behavioral questionnaires (Conners, Swanson, Kotkin, Agler, M-Flynn and Pelham Scale [SKAMP]) and a child psychiatrist provided weekly ratings of symptom severity (ADHD Rating Scale [ADHD-RS]), side effects (Side Effects Rating Scale), and a Clinical Global Impressions-Severity (CGI-S). In addition, laboratory measures of vigilance (Continuous Performance Test [CPT]) and resistance to cognitive interference (Stroop) were administered weekly.

Results: Twenty-five children (15 CB, 10 PI), who met rigorous diagnostic criteria for their ADHD subtype, completed the study. Groups did not differ on demographic variables or severity at baseline. Behavioral questionnaires and clinical ratings indicated significant improvement on MPH for both subtypes but no differences in response profiles of the two groups. Drug effects were predominantly linear for both subtypes. Effects of MPH were significant for the CPT, but not the Stroop, instrument with no differences between ADHD subtypes.

Conclusions: Results support the clinical utility of MPH in the treatment of the PI subtype and provide no evidence of differences in response between the subtypes.

J Am Acad Child Adolesc Psychiatry. 2010;49:345-55.

Beyond the Dual Pathway Model: Evidence for the Dissociation of Timing, Inhibitory, and Delay-Related Impairments in Attention-Deficit/Hyperactivity Disorder.

Sonuga-Barke E, Bitsakou P, Thompson M.

Objective: The dual pathway model explains neuro-psychological heterogeneity in Attention Deficit/Hyperactivity Disorder (ADHD) in terms of dissociable cognitive and motivational deficits each affecting some but not other patients. We explore whether deficits in temporal processing might constitute a third dissociable neuropsychological component of ADHD.

Method: Nine tasks designed to tap three domains (inhibitory control, delay aversion and temporal processing) were administered to ADHD probands (n=71; ages 6 to 17 years), their siblings (n=71; 65 unaffected by ADHD) and a group of non-ADHD controls (n=50). IQ and working memory were measured.

Results: Temporal processing, inhibitory control and delay-related deficits represented independent neuropsychological components. ADHD children differed from controls on all factors. For ADHD patients, the co-occurrence of inhibitory, temporal processing and delay-related deficits was no greater than expected by chance with substantial groups of patients showing only one problem. Domain-specific patterns of familial co-segregation provided evidence for the validity of neuropsychological subgroupings.

Conclusion: The current results illustrate the neuropsychological heterogeneity in ADHD and initial support for a triple pathway model. The findings need to be replicated in larger samples.

J Child Adolesc Psychopharmacol. 2009;19:683-90.

Adverse reactions to methylphenidate treatment for attention-deficit/ hyperactivity disorder: Structure and associations with clinical characteristics and symptom control.

Sonuga-Barke EJS, Coghill D, Wigal T, et al.

Background: Methylphenidate (MPH)-related adverse events are well characterized. Their predictors and their relationship with therapeutic effects are less well understood. Here we examine these issues in relation to two long-acting formulations.

Method: Comparison of Methylphenidates in the Analog Classroom Setting (COMACS) was made in a large (n = 184) placebo-controlled trial comparing Equasym XL(registered trademark)/Metadate CD(registered trademark), Concerta(registered trademark), and placebo (PLA) using a Laboratory School protocol. Therapeutic effects were measured using direct observation, scores on a simple math productivity task and parent ratings. Parents also completed the Barkley Stimulant Side Effect Rating Scale (BSSERS).

Results: The BSSERS had six factors: Emotionality, sleep/appetite, disengaged, dizzy, uninterested, and aches. Treatment effects were seen only for emotionality (which improved) and sleep and appetite (which worsened). Adverse events were not predictable from personal and clinical characteristics of patients. Sleep/appetite adverse events were not associated with therapeutic effects. Improvements in attention-deficit/hyperactivity disorder (ADHD) and emotionality were correlated.

Discussion: The results support a narrow conceptualization of MPH adverse events with problems restricted to appetite and sleep. These effects were not predictable on the basis of available information and may be due to an underlying mechanism rather distinct from those determining therapeutic effects.

J Child Adolesc Psychopharmacol. 2009;19:691-98.

Measuring methylphenidate response in attention-deficit/hyperactivity disorder: How are laboratory classroom-based measures related to parent ratings?

Sonuga-Barke EJS, Coghill D, Debacker M, et al.

Background: Methylphenidate (MPH) is an efficacious and normally well-tolerated treatment for attention-deficit/hyperactivity disorder (ADHD). Although treatment effects are usually assessed using parent-rating scales, these can be supplemented by more objective methods. Here we examine the associations between ratings and one such method, assessments made across the day in the laboratory classroom.

Method: Comparison of Methylphenidates in the Analog Classroom Setting (COMACS) was made in a large (n = 184) placebo-controlled trial comparing Equasym XL(registered trademark)/Metadate CD (registered trademark), Concerta(registered trademark), and placebo (PLA) using a Laboratory School protocol. Therapeutic effects were measured using direct observation, scores on a simple math productivity task and parent ratings.

Results: Treatment effects were observed on all measures. Laboratory measures were correlated with each other, most strongly between Swanson, Kotkin, Agler, M-Flynn and Pelham Scale (SKAMP) inattention and Permanent Product Measure of Performance (PERMP). Parental ratings were correlated with classroom measures during the main morning period (1.5-4.5 hours after dosing) and to a lesser extent in the afternoon (6.0-7.5 hours after dosing), but not, by and large, immediately after dosing or in the evening. The morning correlations seemed stronger for female than for male participants.

Discussion: The results suggest that parental ratings and direct observations tap different aspects of MPH response and that both may be required for comprehensive assessment.

Journal of Child Psychology and Psychiatry. 2010 Apr;51:368-89.

Developmental phenotypes and causal pathways in attention deficit hyperactivity disorder: Potential targets for early intervention?

Sonuga-Barke EJS, Halperin JM.

Early intervention approaches have rarely been implemented for the prevention of attention deficit hyperactivity disorder (ADHD). In this paper we explore whether such an approach may represent an important new direction for therapeutic innovation. We propose that such an approach is most likely to be of value when grounded in and informed by developmental models of the dynamic, complex and heterogeneous nature of the condition. First, we set out a rationale for early intervention grounded in the science of ADHD viewed through developmental models. Second, we re-examine the concept of disorder-onset from the perspective of developmental trajectories and phenotypes. Third, we examine potential causal pathways to ADHD with regard to originating risk, pathophysiological mediators, environmental moderators and developmental continuities. Finally, we explore the potential value of strategies for identifying young children at risk for ADHD, and implementing interventions in ways that can target these underlying pathogenic processes. The utility of such an approach represents an important area for future research but still requires proof of concept. Therefore prior to widespread clinical implementation, far greater knowledge is required of (i) developmental pathways into ADHD, (ii) the value of identifying neuropsychological mediators of these pathways, and (iii) the extent to which targeting mediating mechanisms will improve treatment outcomes for children with ADHD.

J Child Adolesc Psychopharmacol. 2010;20:49-54.

Plasma methylphenidate concentrations in youths treated with high-dose osmotic release oral system formulation.

Stevens JR, George RA, Fusillo S, et al.

Background: Children and adolescents are being treated increasingly for attention-deficit/hyperactivity disorder (ADHD) with a variety of stimulants in higher than Food and Drug Administration (FDA)-approved doses and in combination with other medications.

Objective: We sought to determine methylphenidate (MPH) concentrations in children and adolescents treated with high-dose, extended-release osmotic release oral system (OROS) MPH plus concomitant medications, and to examine MPH concentrations with respect to the safety and tolerability of treatment.

Methods: Plasma MPH concentrations were measured by liquid chromatography-mass spectrometry 4-5 hours after administration of medication in a sample of youths diagnosed with ADHD. These youths were treated naturalistically with higher than FDA-approved doses of OROS MPH in addition to their concomitant medications. Markers of safety and tolerability (e.g., measures of blood pressure and heart rate) were also examined.

Results: Among the 17 patients (with a mean age of 16.2 (plus or minus) 2 years and a mean number of concurrent medications of 2.23 (plus or minus) 0.94), the mean plasma MPH concentration was 28 (plus or minus) 9.1 ng/mL, despite a mean daily dose of OROS MPH of 169 (plus or minus) 5 mg (3.0 (plus or minus) 0.8 mg/kg per day). No patient had a plasma MPH level (greater-than or equal to) 50 ng/mL or clinical signs of stimulant toxicity. No correlation was found between plasma MPH concentrations and OROS MPH dose or changes in vital signs.

Conclusions: High-dose OROS MPH, used in combination with other medications, was not associated with either unusually elevated plasma MPH concentrations or with clinically meaningful changes in vital signs.

Study limitations include a single time-point sampling of MPH concentrations, a small sample size, and a lack of outcome measures to address treatment effectiveness.

Paediatr Anaesth. 2010;20:323-29.

Anesthesia induction, emergence, and postoperative behaviors in children with attention-deficit/hyperactivity disorders.

Tait AR, Voepel-Lewis T, Burke C, et al.

Background/Aim: Given the increasing prevalence of attention-deficit and attention-deficit hyperactivity disorders (ADHD), anesthesiologists are now presented with a greater number of children who are diagnosed with these conditions. This prospective, observational study was designed to compare anesthesia induction, emergence, and postoperative behaviors in children with and without ADHD.

Methods/Materials: The sample included 268 children, 4-17 years of age undergoing elective surgery with a confirmed diagnosis of ADHD. A cohort of children without ADHD, matched for age, gender, and procedure served as controls. Preoperative cooperation, induction, and emergence behaviors were measured using established scales. Postoperative maladaptive behaviors were measured using a modified Post-Hospital Behavioral Questionnaire that was administered via telephone 1 week after surgery.

Results: Children with ADHD were significantly less cooperative at induction of anesthesia compared with controls (20.9% vs 10.6% respectively, $P = 0.001$). Although some control children exhibited an increase in maladaptive behaviors postoperatively, these behaviors were significantly greater among children with ADHD. In particular, relative to their normal behaviors, children with ADHD had greater difficulties in concentration and decision-making; were more disobedient, impulsive, fidgety, had poor appetite; were difficult to talk to; and exhibited an increase in temper tantrums following surgery.

Conclusions: This is the first prospective study to our knowledge that has examined the perioperative and postoperative behaviors of children with ADHD compared to those without this disorder. These results are important in alerting anesthesiologists, parents, and teachers to the potential for difficulties during induction of anesthesia and postoperative behavioral problems at home and in school, respectively.

Kaohsiung J Med Sci. 2009;25:530-36.

Behavior Problems and Subtypes of Attention-deficit Hyperactivity Disorder With Comorbidities.

Tzang RF, Chang YC.

This study investigated the relationship between Child Behavior Checklist (CBCL) symptoms and attention-deficit hyperactivity disorder (ADHD) subtypes [inattentive (ADHD-I) and combined (ADHD-C)] with or without comorbidities. Overall, 116 ADHD children were interviewed using the Mini-International Neuropsychiatric Interview to assess ADHD subtypes and comorbidities, and were then divided into four groups according to their subtypes and comorbidities. The CBCL was completed by the parents of the ADHD children. The association between behavioral symptom severity and groups was examined by comparing the CBCL scales of the four groups. The scores for the Aggressive Behavior ($p = 0.014$) and Anxiety/Depression scales ($p = 0.033$) were higher in patients with ADHD-I with comorbidities than with ADHD-I without comorbidities. In addition, the score for the Aggressive Behavior scale was higher in patients with ADHD-C without comorbidities than in patients with ADHD-I without comorbidities ($p = 0.011$). The scores for the six CBCL scales were all higher in patients with ADHD-C with comorbidities than in patients with ADHD-I without comorbidities. Our findings suggest a synergistic effect of the co-occurrence of comorbidities and the ADHD-C subtype on behavioral symptom severity. Physicians could use the CBCL scales to distinguish patients with more severe symptoms from patients with less severe symptoms.

J Child Adolesc Psychopharmacol. 2010;20:55-61.

Trends in incidence and characteristics of children, adolescents, and adults initiating immediate- or extended-release methylphenidate or atomoxetine in The Netherlands during 2001-2006.

Van Den Ban E, Souverein P, Swaab H, et al.

Background: Previous Dutch studies showed increasing psychostimulant use, especially methylphenidate immediate-release (MPH-IR), between 1995 and 2003. In 2003 the extended-release (ER) formulation of

MPH and in 2005 atomoxetine (ATX) were introduced in The Netherlands, which increased treatment options.

Objective: The aim of this study was to describe the change in incidence of attention-deficit/hyperactivity disorder (ADHD) drugs and the prescription profiles of patients younger than 45 years starting treatment with these medicines between 2001 and 2006.

Methods: Data were obtained from Dutch community pharmacies as collected by the Foundation for Pharmaceutical Statistics, covering 97% of all dispenses for prescription medicines to outpatients in The Netherlands.

Results: The overall incidence of ADHD drugs use increased 6.5-fold from 2001 to 2006 in men as well as in women. The absolute incidence was highest among 6- to 11-year-old boys. The percentage of first-time MPH-IR users decreased from 98.3% in 2001 to 75.9% in 2006. Likewise, MPH-ER use increased from 0% in 2001 to 18.9% in 2006, and ATX use increased from 0% in 2001 to 3.9% in 2006. The new nonstimulant drug ATX was prescribed more often to adults if they had been previously treated with selective serotonin reuptake inhibitors (SSRIs), benzodiazepines, or antipsychotics. Youngsters <17 years initiated on ATX were often previously treated with antipsychotics or clonidine/guanfacine.

Conclusion: These findings demonstrate an increase in incidence in use of ADHD drugs between 2001 and 2006 in The Netherlands. The major proportion of all treated patients comprised boys, 6-11 years old; most of them were treated with MPH-IR. In a few years time, the use of extended-release drugs as part of all ADHD drug prescriptions increased considerably, despite the lack of full reimbursement of these extended-release drugs. Psychostimulants and atomoxetine in children, adolescents, and adults are probably used to address different treatment needs.

Rev Neurol. 2009;49:69-75.

Psychomotor profile of children between 5 and 12 years of age, clinically diagnosed with attention deficit hyperactivity disorder in Colombia.

Vidarte JA, Ezquerro M, Giraldez MA.

Introduction. One of the comorbid alterations of attention deficit hyperactivity disorder (ADHD) affects motricity, to the point where the quality of motor performance during the first 5-6 years of life could constitute a predictor of the later appearance of symptoms of the disorder. Moreover, the association between motor clumsiness and ADHD results in a poorer prognosis of the condition. Nevertheless, few studies have examined the evolution of motricity in children affected with this pathology.

Aim. To characterise the psychomotor profile of children between 5 and 12 years of age who were clinically diagnosed with ADHD in the town of Manizales (Colombia) and to compare it with healthy children of the same age. **Subjects and methods.** A cross-sectional descriptive study was conducted with a sample of 846 children (422 diagnosed with ADHD and 424 healthy controls).

Results. Although the values for all the motricity factors were within ranges that are considered to be normal, they were significantly poorer ($p < 0.000$) in diagnosed children at all ages.

Conclusions. The psychomotor profile of children diagnosed with ADHD was eupractic and is classified within the same category as the healthy children, although quantitatively it was lower.

J Am Acad Child Adolesc Psychiatry. 2010;49:356-67.

Neural Mechanisms of Interference Control and Time Discrimination in Attention-Deficit/Hyperactivity Disorder.

Vloet TD, Gilsbach S, Neufang S, et al.

Objective: Both executive functions and time perception are typically impaired in subjects with attention-deficit/hyperactivity disorder (ADHD). However, the exact neural mechanisms underlying these deficits remain to be investigated.

Method: Fourteen subjects with ADHD and 14 age- and IQ-matched controls (aged 9 through 15 years) were assessed with functional magnetic resonance imaging while they performed a combined spatial stimulus-response compatibility (SRC) and time duration discrimination (TD) paradigm using identical stimuli for all experimental conditions.

Results: Children with ADHD performed less accurately in the SRC but not in the TD task compared with controls. On the brain level, subjects with ADHD showed significantly reduced neural activity in the left putamen during SRC and reduced fronto-cerebellar activation during TD when compared with the baseline conditions. Compared with subjects with ADHD, control subjects had increased activation in a left-

hemispheric fronto-parietal network during the SRC task and in the right superior-frontal gyrus during the TD task. Functional connectivity analyses revealed abnormal fronto-parietal coupling during the SRC task and reduced fronto-cerebellar connectivity during the TD task in the ADHD group compared with controls.

Conclusions: Our findings suggest specific but distinct patterns of cerebral dysfunction associated with interference control and TD processing in ADHD, characterized by both reduced neural activation in regions critical for task performance and reduced co-activation of frontal cortex. Group differences on the behavioral level were controlled by several methodological approaches. Nonetheless, given the use of a block design, we cannot rule out the possibility that between-group differences in behavior confounded the neural activation patterns.

Neuropsychology Review. 2010 Mar;20:103-20.

Executive function in pediatric bipolar disorder and attention-deficit hyperactivity disorder: In search of distinct phenotypic profiles.

Walshaw PD, Alloy LB, Sabb FW.

Often, there is diagnostic confusion between bipolar disorder (BD) and attention-deficit hyperactivity disorder (ADHD) in youth due to similar behavioral presentations. Both disorders have been implicated as having abnormal functioning in the prefrontal cortex; however, there may be subtle differences in the manner in which the prefrontal cortex functions in each disorder that could assist in their differentiation. Executive function is a construct thought to be a behavioral analogy to prefrontal cortex functioning. We provide a qualitative review of the literature on performance on executive function tasks for BD and ADHD in order to determine differences in task performance and neurocognitive profile. Our review found primary differences in executive function in the areas of interference control, working memory, planning, cognitive flexibility, and fluency. These differences may begin to establish a pediatric BD profile that provides a more objective means of differential diagnosis between BD and ADHD when they are not reliably distinguished by clinical diagnostic methods.

J Adolesc Health. 2010 Mar;46:209-17.

Social and emotional impairment in children and adolescents with ADHD and the impact on quality of life.

Wehmeier PM, Schacht A, Barkley RA.

This review provides an overview as to how the social and emotional impairments involved in Attention-Deficit/Hyperactivity Disorder affect the quality of life of patients and their families. A model of three categories into which the emotional difficulties fall, and how they impair quality of life, is also presented.

Acta Psychiatr Scand. 2010;121:273-79.

The antecedents of non-affective psychosis in a birth-cohort, with a focus on measures related to cognitive ability, attentional dysfunction and speech problems.

Welham J, Scott J, Williams GM, et al.

Welham J, Scott J, Williams GM, Najman JM, Bor W, O'Callaghan M, McGrath J. The antecedents of non-affective psychosis in a birth-cohort, with a focus on measures related to cognitive ability, attentional dysfunction, and speech problems.

Objective: Adults with non-affective psychosis show subtle deviations in a range of developmental trajectories as children and adolescents.

Method: Based on a birth-cohort (n = 3801), we examined the Peabody Picture Vocabulary Test (PPVT) at age 5, and Raven's Standard Progressive Matrices (RSPM) and Wide Range Achievement Test reading scale (WRAT-R) at age 14. Items related to speech problems and attentional dysfunction were available from maternal- or self-report. At age 21, we identified 60 cohort members who were screen-positive for non-affective psychosis (SP-NAP).

Results: Impaired performance on the PPVT and RSPM (but not WRAT-R) predicted SP-NAP for males only. Male cohort members in the highest quartile for attentional dysfunction at ages 5 and 14 were about 5-8 times more likely to develop SP-NAP. SP-NAP in males was significantly associated with speech problems at age 14.

Conclusion: Males who develop non-affective psychoses have subtle impairments in cognitive capacity prior to the development of their psychotic disorder.

J Child Adolesc Psychopharmacol. 2009;19:719-30.

Atomoxetine treatment in adolescents with attention-deficit/hyperactivity disorder.

Wietecha LA, Williams DW, Herbert M, et al.

Introduction: This study compared two atomoxetine titration dosing schedules and two atomoxetine maintenance doses for treating adolescent attention-deficit/hyperactivity disorder (ADHD) inattention and hyperactivity/impulsivity.

Methods: Adolescents (N = 267) were randomized to a slow or fast titration schedule. Patients who responded continued on a 40-week maintenance treatment, randomized to either 0.8 or 1.4 mg/kg/day.

Results: During the acute period, significant benefit was demonstrated with both titration schedules on the ADHD Rating Scale total score. Although patients in both groups maintained benefit relative to week 0, statistically significant loss of benefit was found for patients maintained on 0.8 mg/kg/day but not on 1.4 mg/kg/day. A similar pattern was observed on the Clinical Global Impressions-ADHD-Severity scores and Life Participation Scale for ADHD-Child Version scores. Mean grades for most subjects improved for patients in both maintenance treatment groups although most improvements were not statistically significant.

Conclusions: In adolescents with ADHD, treatment benefit at 8 weeks was better maintained long-term with 1.4 mg/kg/day than with 0.8 mg/kg/day. Improvement in adaptive functioning and age-appropriate developmental function was also demonstrated. Atomoxetine 0.8 and 1.4 mg/kg/day were equally well tolerated.

Anadolu Psikiyatr Derg. 2010;11:44-50.

Efficiency and tolerability of OROS-methylphenidate in Turkish children and adolescents with attention-deficit/hyperactivity disorder.

Yildiz Oc O, Agaoglu B, Karakaya I, et al.

Objective: The aim of the study was to compare efficacy and tolerability of OROS-methylphenidate HCL (OROSMPH) with immediate-release methylphenidate (IR-MPH) in Turkish children with attention-deficit/hyperactivity disorder (ADHD).

Methods: This study was designed as an open label, prospective, for an 8-week period. A total of 83 subjects, between the ages of 7 and 14 with ADHD, were included in this study. The dosages of OROSMPH and IR-MPH were adjusted by the investigators based on symptoms and adverse events assessments performed (OROS-MPH doses: 18-36 mg/day-once daily, IR-MPH doses:10-20 mg/day-divided dose). The efficacy and adverse effects of the drugs were assessed due to Turgay DSM-IV-Based Child and Adolescent Behavior Disorders Screening and Rating Scale (T-DSM-IV-S), Clinical Global Impression-Global improvement Scale (CGI-GI), and Methylphenidate Side Effects Rating Form (MSERF).

Results: Both OROS-MPH and IRMPH showed definitive improvement of severity symptoms of ADHD ($p < 0.05$). No significant differences were found between two groups at 8th week in mean scores of T-DSM-IV and CGI-GI. Weight loss was found to be related with the dose increase according to parents' reports on adverse effects of OROS-MPH.

Conclusion: OROS-MPH was found to be as effective as IR-MPH in the treatment of behavioral symptoms in Turkish children with ADHD. These results demonstrated that both drugs were effective and well tolerated in the treatment of Turkish children with ADHD.

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