







# **NEWSLETTER**

N. 26 anno III - Febbraio 2010

Turk J Pediatr. 2009 Sep;51:478-84.

Pregnancy and delivery complications and treatment approach in attention deficit hyperactivity disorder.

#### Aktepe E, Ozkorumak E, Tanriover-Kandil S.

Pregnancy, delivery complications and treatment approach were evaluated in 153 cases diagnosed with attention deficit hyperactivity disorder in the State Hospital of Antalya in the Child and Adolescent Psychiatry Polyclinic. Most of the cases had been delivered vaginally (74.5%). The most frequent delivery complication was asphyxia/hypoxia (15.6%). The agent most frequently preferred in the treatment regimen was methylphenidate (82.4%), which is a psychostimulant. The other drugs used were risperidone (29.4%), selective serotonin reuptake inhibitors (16.4%) and imipramine (4.6%). The most frequent side effect resulting from methylphenidate use was a decrease in appetite (34.9%). Attention deficit hyperactivity disorder often presents with comorbid disorders; in these cases, nonstimulant agents had to be added to methylphenidate for better treatment outcomes. Use of selective serotonin reuptake inhibitors in combined treatment and in cases with comorbidities is in agreement with the literature. Further studies of combined treatment regimens in attention deficit hyperactivity disorder are needed.

Int J Lang Commun Disord. 2010;45:61-71.

Reading comprehension, word decoding and spelling in girls with autism spectrum disorders (ASD) or attention-deficit/hyperactivity disorder (AD/HD): Performance and predictors.

#### Asberg J, Kopp S, Berg-Kelly K, et al.

**Background**: Difficulties with aspects of literacy are often seen in children with autism spectrum disorders (ASD) and attention-deficit/ hyperactivity disorder (AD/HD). The bases of the connections between these disorders and literacy difficulties are poorly understood. Furthermore, it is not clear if existing research is representative for girls.

**Aims**: There were three aims: (1) to compare performance in reading comprehension, word decoding, and spelling in girls with ASD (n = 20), AD/ HD (n = 36), and community girls with typical developing (girls; n = 54); (2) to assess rates of reading and writing disorders within groups; and (3) to examine the predictive value of measures of autistic and AD/HD symptomatology to reading comprehension in the whole girl sample.

**Methods & Procedures**: Participants were aged between 8 and 17 years, and had a full scale IQ >70. Standardized tests of literacy, oral vocabulary, and non-verbal ability were administered. Parent ratings of

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.

degree of autistic symptomatology and both parent and teacher ratings of AD/HD symptomatology were collected for all girls.

**Outcomes & Results**: Girls with diagnosed ASD could not be separated significantly from typically developing girls or girls with AD/HD on average performance on any literacy test. However, among girls with ASD, 40% had at least one reading and writing disorder. Girls with AD/HD performed lower than typically developing girls in reading comprehension, word decoding, and spelling, and 56% had at least one reading and writing disorder. In regression analysis, using the total sample, both degrees of autistic and AD/HD symptomatology negatively contributed to the variance in reading comprehension after controlling for oral vocabulary, word decoding, and non-verbal ability. Whereas AD/HD contributed to the variance in reading comprehension once autistic symptomatology was controlled for, the opposite was not true. However, a large bivariate correlation between autistic and AD/HD symptomatology somewhat complicates the interpretation of that result.

**Conclusions & Implications**: The findings highlight the importance of monitoring and supporting the literacy development in girls with ASD or AD/HD. Results from regression analyses suggested that word decoding and/or oral vocabulary training may not be sufficient for the girls fully to overcome difficulties in the important skill of reading comprehension.

Am J Psychiatry. 2010;167:61-69.

Amygdala activation during emotion processing of neutral faces in children with severe mood dysregulation versus ADHD or bipolar disorder.

Brotman MA, Rich BA, Guyer AE, et al.

**Objective**: To understand disorder-unique and common pathophysiology, studies in multiple patient groups with overlapping symptoms are needed. Deficits in emotion processing and hyperarousal symptoms are prominent features of bipolar disorder, attention deficit hyperactivity disorder (ADHD), and severe mood dysregulation. The authors compared amygdala response during emotional and nonemotional ratings of neutral faces in youths with these disorders as well as a group of healthy comparison youths.

**Method**: Blood-oxygen-level-dependent (BOLD) signal in the amygdala was examined in children with bipolar disorder (N=43), ADHD (N=18), and severe mood dysregulation (N=29) and healthy comparison subjects (N=37). During functional magnetic resonance imaging (fMRI), participants attended to emotional and nonemotional aspects of neutral faces.

**Results**: While rating subjective fear of neutral faces, youths with ADHD demonstrated left amygdala hyperactivity relative to the other three groups, whereas youths with severe mood dysregulation demonstrated hypoactivity.

**Conclusions**: These findings support the role of unique neural correlates in face-emotion processing among youths with bipolar disorder, ADHD, and severe mood dysregulation.

Child Adolesc Psychiatry Ment Health. 2009;3.

Does switching from oral extended-release methylphenidate to the methylphenidate transdermal system affect health-related quality-of-life and medication satisfaction for children with attention-deficit/hyperactivity disorder?

Bukstein OG, Arnold LE, Landgraf JM, et al.

**Background**: To evaluate health-related quality of life (HRQL) and medication satisfaction after switching from a stable dose of oral extended-release methylphenidate (ER-MPH) to methylphenidate transdermal system (MTS) via a dose-transition schedule in children with attention-deficit/hyperactivity disorder (ADHD).

**Methods**: In a 4-week, multisite, open-label study, 171 children (164 in the intent-to-treat [ITT] population) aged 6-12 years diagnosed with ADHD abruptly switched from a stable dose of oral ER-MPH to MTS nominal dosages of 10, 15, 20, and 30 mg using a predefined dose-transition schedule. Subjects remained on the scheduled dose for the first week, after which the dose was then titrated to an optimal effect. The ADHD Impact Module-Children (AIM-C), a disease-specific validated HRQL survey instrument measuring child and family impact, was used to assess the impact of ADHD symptoms on the lives of children and their families at baseline and study endpoint. Satisfaction with MTS use was assessed via a Medication Satisfaction Survey (MSS) at study endpoint. Both the AIM-C and MSS were completed by a caregiver (parent/legally authorized representative). Tolerability was monitored by spontaneous adverse event (AE) reporting.

**Results**: AIM-C child and family HRQL mean scores were above the median possible score at baseline and were further improved at endpoint across all MTS doses. Similar improvements were noted for behavior, missed doses, worry, and economic impact AIM-C item scores. Overall, 93.8% of caregivers indicated a high level of satisfaction with their child's use of the study medication. The majority of treatment-emergent AEs (> 98%) were mild to moderate in intensity, and the most commonly reported AEs included headache, decreased appetite, insomnia, and abdominal pain. Seven subjects discontinued the study due to intolerable AEs (n = 3) and application site reactions (n = 4).

**Conclusion**: This study demonstrates that MTS, when carefully titrated to optimal dose, may further improve child and family HRQL, as well as behavioral, medication worry, and economic impact item scores, as measured by the AIM-C in subjects switching to MTS from a stable dose of routinely prescribed oral ER-MPH after a short treatment period. Furthermore, following the abrupt conversion from oral ER-MPH to MTS, the majority of caregivers reported being highly satisfied with MTS as a treatment option for their children with ADHD.

Brain Res. 2010;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 (plus or minus) 1.5 years) and 27 age- and gender- matched controls (13.2 (plus or minus) 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.

Autism Res. 2009;2:312-21.

Relative clinical utility of three Child Symptom Inventory-4 scoring algorithms for differentiating children with autism spectrum disorder vs. attention-deficit hyperactivity disorder.

DeVincent CJ, Gadow KD.

**Objective**: The present study compared three separate Child Symptom Inventory-4 (CSI-4) scoring algorithms for differentiating children with autism spectrum disorder (ASD) from youngsters with attention-deficit/hyperactivity disorder (ADHD).

**Method**: Parents/teachers completed the CSI-4, a DSM-IV-referenced rating scale, for 6 to 12-year-old clinical referrals with ASD (N=186) and ADHD (N=251). Algorithms were based on either all CSI-4 items (forward logistic regressions) or the 12 DSM-IV symptoms of pervasive developmental disorder (PDD) included in the CSI-4.

**Results**: ROC analyses indicated generally good to excellent values for area under the curve, sensitivity, specificity, and positive predictive power. Algorithms for parent ratings were superior to teacher ratings. The algorithm based solely on PDD symptoms evidenced the greatest generalizability.

**Conclusion**: Although algorithms generated from regression analyses produced greater clinical utility for specific samples, the PDD-based algorithm resulted in greater stability across samples.

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Acta Med Croat, 2009:63:307-13.

The role of zinc in the treatment of hyperactivity disorder in children.

# Dodig-Curkovic K, Dovhanj J, Curkovic M, et al.

Zinc is an essential cofactor of more than 100 enzymes, including metalloenzymes and metalloenzyme complexes, which are necessary in the metabolism of carbohydrates, fatty acids, proteins and nucleic acids. It is an important factor in the metabolism of neurotrans-mitters, prostaglandins, and for maintaining brain structure and function. Dopamine is one of the most important factors in the patho-physiology of hyperactivity disorder, and the hormone melatonin has an important role in the regulation of dopamine. Because zinc is necessary in the metabolism of melatonin, it can be assumed that zinc is a very important factor in the treatment of attention deficit and hyperactivity disorder (ADHD). It is known that deficit of some minerals and vitamins is connected with hyperkinetic disorder. Preliminary investigations in humans show that many children with ADHD have lower zinc concentration in relation to healthy children. Zinc sulfate as an adjunct to methylphenidate has favorable effects in the treatment of ADHD children, pointing to the possible association of zinc deficit and ADHD pathophysiology. Zinc concentration can only point to some other factors (malnutrition) that can lead to ADHD, but is not a factor that has a causative role in ADHD. Therefore, zinc supplementation to nutrition or to ADHD therapy may be of great benefit in ADHD children with zinc deficit or low plasma zinc concentration. ADHD occurs in different cultures, mostly before seven years of age. In children younger than five years it is difficult to make an accurate diagnosis because their behavior is more variable than in older chil-dren. Hyperactive disorder is mostly observed in younger age, i.e. in childhood and adolescence. The majority of the main characteristics are less pronounced or completely lost in adult age. In the 1960s, the disorder was named "minimal cerebral dysfunction" and was most often the consequence of head trauma or low birth weight. Later, the term was changed as hyperactive reaction in childhood. Recent studies estimate its prevalence to three of ten hyperactive children, and there are data that about 4% of children have the complete frame of the disorder. The condition is more common in boys than in girls. The reason probably lies in the fact that girls primarily develop attention disorder and cognitive problems (concentration, memory, thinking), and less often have symptoms of aggressive and impulsive behavior, thus boys being earlier referred for examination. There are many theories about the possible origin of hyperactive disorder, and one of the most widely studied is the theory of the role of dopamine, which is supported by the results of treatment in these children with dopamine agonists like methylphenidate and amphetamines. Recent studies do not neglect the influence of maternal intake of food and drink additives, alcohol consumption and smoking during pregnancy, soil contamination, and low birth weight. Zinc is a coenzyme of the enzyme delta-6 desaturase, which is important in the anabolism of polyunsaturated long chain fatty acids, linolic and linolenic acids that constitute neuronal membrane. Studies point to the possible association of zinc deficiency and ADHD pathophysiology. In ADHD children with zinc deficiency or low plasma zinc concentration, zinc dietary supplementation or during therapy for ADHD may be of great benefit. A study of ADHD treatment with zinc sulfate as a supplement to methylphenidate showed beneficial effects of zinc supplementation in the treatment of children with ADHD. The dose of zinc sulfate used was 55 mg/day, which is equivalent to 15 mg zinc. The improvement achieved in ADHD children with the use of zinc sulfate appears to confirm the role of zinc deficiency in the etiopathogenesis of ADHD. Additional studies are needed to identify the real and efficient dose of zinc.

Arch Pediatr Adolesc Med. 2010;164:160-65.

Attention-deficit/hyperactivity disorder outcomes for children treated in community-based pediatric settings.

Epstein JN, Langberg JM, Lichtenstein PK, et al.

**Objective**: To determine if children treated by community physicians who participated in an attention-deficit/hyperactivity disorder (ADHD) quality improvement intervention demonstrate symptom and impairment improvements comparable with those achieved in university-based clinical trials.

Design: Case series.

**Setting**: Rural, suburban, and urban practices, with 28% of the 47 practices serving primarily (>50% of patients) Medicaid-receiving populations.

**Participants**: A total of 785 children aged between 7 and 11 years were treated for ADHD by community physicians participating in the study.

**Intervention**: A total of 158 community physicians from 47 separate practices participated in a quality improvement intervention, the ADHD Collaborative, designed to improve physician adherence to evidence-based ADHD treatment guidelines. The intervention included mapping and redesign of practice office flow to facilitate adherence to American Academy of Pediatrics ADHD guidelines as well as didactic sessions

related to diagnosis and treatment of ADHD. Medical record reviews were completed at the initial assessment and every 3 months for 1 year to evaluate treatment outcome.

**Outcome Measures**: Improvement in parent-and teacher-rated ADHD symptoms and functional impairment. **Results**: Children showed large improvements in parent-and teacher-rated ADHD symptoms, similar to some clinical trials, but made no significant improvements in functional impairment.

**Conclusions**: Large improvements in ADHD symptoms can be achieved in primary care settings when physicians provide evidence-based ADHD care using medication. Because many children with ADHD continued to have significant functional impairment despite symptom improvement, collaboration with other mental health or educational services in additional to medication appears warranted.

Rev Neurol. 2009:49:502-03.

Efficacy of levetiracetam in a patient with chronic motor tic, rolandic epilepsy and attention and behavioral disorder.

Fernandez-Mayoralas DM, Fernandez-Jaen A, Munoz-Jareno N, et al.

Educational and Psychological Measurement. 2010 Feb;70:161-73.

Factor invariance assessment of the Dean–Woodcock Sensory–Motor Battery for patients with ADHD versus nonclinical subjects.

# Finch H, Davis A, Dean RS.

The current study examined the measurement invariance of the Dean–Woodcock Sensory–Motor Battery (DWSMB) for children diagnosed with attention deficit hyperactivity disorder (ADHD) and an age- and gender-matched nonclinical sample. The DWSMB is a promising new instrument for assessing a wide range of cortical and subcortical sensory and motor skills and has been shown to conform to a three-factor latent structure for the nonclinical population. Because this instrument is used with a broad spectrum of individuals, including those with ADHD, it is important to verify that it does indeed measure the same constructs in the same way. The results of the invariance analyses showed that there were specific indicators on the DWSMB that were not invariant between the two groups, though the majority of the measurement model was found to be invariant. Specifically, several tasks that required sustained attention were not as effective for individuals with ADHD as they were for nonclinical subjects. In addition, certain measures of motor coordination were not as strongly associated with the latent variables for those with ADHD as compared with the nonclinical individuals. A number of clinical implications from these findings are discussed in detail.

Clin Ther. 2009;31:1844-55.

Long-term tolerability of the methylphenidate transdermal system in pediatric attention-deficit/hyperactivity disorder: A multicenter, prospective, 12-month, open-label, uncontrolled, phase III extension of four clinical trials.

Findling RL, Wigal SB, Bukstein OG, et al.

**Background**: Short-term treatment with the meth-ylphenidate transdermal system (MTS) has been well tolerated in several clinical trials in children with attention-deficit/hyperactivity disorder (ADHD). However, the effects of long-term use have not been systematically evaluated.

**Objectives**: The primary objective of this study was to assess the 12-month tolerability of MTS in children with ADHD. Effectiveness was a secondary objective.

**Methods**: This Phase III study was a multicenter, 12-month, open-label, flexible-dose extension of 4 previous trials. In those studies, children aged 6 to 12 years with a diagnosis of ADHD (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision criteria) received MTS, osmotic-release oral system methylphenidate, or placebo. At entry into the present study, the children either continued to receive their optimal dose of MTS (10, 15, 20, or 30 mg per 9-hour patch wear time) or underwent dose titration over 4 weeks to an optimal MTS dose, which was continued for the remainder of the study. Tolerability was evaluated based on adverse events (AEs), physical examinations, vital signs, electrocardiograms, laboratory tests, the Children's Sleep Habits Questionnaire, and the occurrence of application-site reactions.

Results: Of 327 enrolled subjects, 326 received treatment and 157 completed the study. The majority of enrolled subjects were male (64.8%) and white (73.7%), with a mean (SD) age of 9.2 (1.9) years. Two hundred sixty-five (81.3%) of the 326 subjects who received MTS reported AEs. AEs led to study discontinuation in 29 subjects (8.9%). The majority (98.3%) of treatment-emergent AEs were of mild or moderate severity. The most common AEs were decreased appetite (24.8%), headache (16.6%), upper respiratory tract infection (12.3%), cough (11.7%), pyrexia (10.1%), and decreased weight (10.1%). Of the 1118 AEs, 40.8% were considered possibly or probably related to study treatment. Three serious AEs (facial contusion, ankle fracture, and syncope) occurred and were considered unrelated to study treatment. Based on data collected across all study visits, application-site reactions generally consisted of mild erythema associated with mild discomfort at the patch site. Application-site reactions accounted for 22 (6.7%) study discontinuations.

**Conclusions**: Slightly less than half (48.0%) of subjects completed this 12-month, open-label extension study of MTS. Most AEs were mild to moderate in severity and, with the exception of application-site reactions, were typical of those previously observed with methylphenidate.

Child Adolesc Ment Health. 2010 Feb;15:12-17.

# The impact of governmental guidance on the time taken to receive a prescription for medication for ADHD in England.

#### Foreman DM.

The National Health Service in England has deployed guidance from the National Institute of Clinical Excellence (NICE) to assist practitioners in the diagnosis and treatment of Attention Deficit Hyperactivity Disorder (ADHD) but, though the number of prescriptions has risen since its introduction, the impact of the quidance on prescribing practice has not been studied. Clinic records of all open ADHD cases (296) in three English Child and Adolescent Mental Health Services were examined. The time from referral to either prescription or data collection was extracted for a survival analysis. It was hypothesised that NICE guidance, clinic, patient and referral characteristics would all influence the speed and likelihood of prescription. Following the introduction of NICE guidance, the median time to start prescribing medication fell from 1262 to 526 days: the minimum realistic time to complete a routine assessment was approximately 70 days. Overall, 70% were prescribed medication. Most of the wait was after face-to-face appointments at the clinic had been initiated. Waiting times differed between clinics and shorter waits were likely for older children and those referred from an educational source. While the introduction of NICE guidance has increased the rate of prescription, the time taken before prescription suggests that the tendency in England is still to postpone treatment by medication. The reasons for this require further research. Key Practitioner Message: 1. The introduction of NICE guidance has halved the average time taken for a child with ADHD to receive a prescription for medication to around 526 days after referral, with a minimum realistic routine assessment time of 70 days 2. Five hundred and twenty-six days is longer than can be accounted for either by waiting time or prior trials of psychological therapy 3. Educational referral, the child being older, and greater clinic resourcing also shorten time from referral to treatment.

Z Kinder- Jugendpsychiatr Psychother. 2010;38:7-20.

Algorithms for the medical treatment of attention-deficit/hyperactivity disorder with specific comorbidities.

#### Frolich J, Lehmkuhl G, Dopfner M.

**Background**: In clinical practice Attention Deficit Hyperactivity Disorder (ADHD) is a challenge for diagnostic and therapeutic effort due to a number of co-morbidities, e.g., depression, anxiety disorders, Tourette Syndrome and impulsive aggression that can be a complication or a result of the core symptoms or evolve parallel to the basic disorder. The therapeutic strategies incorporate a multimodal access with a combination of psychosocial, psychotherapeutic and medical measures. The combination of various medical substances for an effective treatment of these co-morbidities, especially Serotonin-Reuptake Inhibitors (SSRIs) and atypical neuroleptics with psychostimulants has substantially reduced the occurrence of the main symptoms of the disorder in many cases and thus can also lead to a decrease in the occurrence of co-morbidities. Where this strategy fails to suffice, it is recommended to consider medical treatment strategies in combination with other substances that alternatively or in combination with psychostimulants increasingly positively influence co-morbid symptoms.

**Objective and method**: Based on a Medline literature search we report the results of combined medical approaches for an effective medical treatment of the ADHD core symptoms accompanied by serious comorbid symptoms. Hereby we focused on the above cited disorders. Combined treatment options that include psychostimulants are considered in particular. Moreover, recommendations for medical treatment strategies oriented to the clinical cardinal symptoms are presented in the form of algorithms. Evidence-based literature and practical experience are critically reviewed.

**Results**: In most cases it will be sufficient to begin the treatment with a psychostimulant because co-morbid symptoms also will be significantly reduced. However, if the latter are in the foreground of the clinical picture, antidepressants or neuroleptics are to be considered as primary or equivalent treatment options.

**Conclusions**: Since in Germany most of the substances discussed are not licensed for use in paediatric treatment, proofs of efficacy in children are lacking. One also must reckon with the frequent occurrence of side effects. Finally, little data exist on treatments that include the use of psychostimulants.

Eur Child Adolesc Psychiatry. 2010;19:75-81.

Risk factors of abuse of parents by their ADHD children.

#### Ghanizadeh A, Jafari P.

It is interesting that there is scant research of abuse of parents by their children and no study was found on the abuse of parents by their attention deficit hyperactivity disorder (ADHD) children. Seventy-four children and adolescents suffering from ADHD and their parents were interviewed. The diagnoses were made according to DSM-IV diagnostic criteria. A questionnaire was developed to assess the children's abuse toward parents. More than half of the parents are suffering from at least one of the forms of abuse by their ADHD children. Scores of parental abuse were not related to gender. Different types of abuse correlated with oppositional defiant disorder (ODD), tic, and separation anxiety disorder (SAD). Fathers' and mothers' age, the level of education, and type of occupation were not risk factors of the abuse scores. ODD and mother's major depressive disorder were predictors of the abuse. There was a very disturbing high rate of abuse by children against parents. There is an interrelation of different forms of abuse. This study contributes to increasing awareness on the abuse of parents by their ADHD children.

J Neural Transm. 2009 Dec;116:1675-80.

Further evidence for the association between attention deficit/hyperactivity disorder and the serotonin receptor 1B gene.

#### Guimarães AP, Schmitz M, Polanczyk GV, et al.

Several evidences suggested that the serotonin 5-HT1B receptor gene (HRT1B) might be involved in the susceptibility to attention deficit/hyperactivity disorder (ADHD). Prior studies reported excess transmissions of the HRT1B gene 861G allele to affected ADHD children and of a haplotype block containing this variant and two functional promoter SNPs to probands with ADHD-inattentive subtype. However, some investigations did not replicate these findings. Therefore, we tested for biased transmissions of haplotypes derived from the 861G > C, -161A > T, and -261T > G SNPs from parents to 343 families with ADHD children. We also sought to replicate findings from the literature that the association between HTR1B is preferentially with ADHD-Inattentive subtype. Using a transmission disequilibrium test we found evidence for an excess transmission of haplotype. -261G/-161T/861G (P = 0.014) for affected children in the total sample. When the analysis was repeated with 143 families with ADHD-Inattentive subtype no significant associations were observed. Our results provide additional evidence that HRT1B gene may be an important risk factor for the development of ADHD, but this effect seems not to be attributable to inattentive cases.

An Psicol. 2009;40:211-22.

The assessment of attention deficit hyperactivity disorder in children using continous performance tasks in virtual environments.

#### Gutierrez-Maldonado J, Letosa-Porta A, Rus-Calafell M, et al.

The assessment of Attention-Deficit/Hyperactivity Disorder (ADHD) involves the use of different instruments, and one of the most frequently used is the Continuous Performance Test (CPT). Virtual reality allows for the achieving of the presentation of stimuli with high levels of control. In addition, it facilitates the presentation of

distracters with a high level of resemblance to elements which in fact can be found in the real world by placing them in a similar context. Thus, it is possible to assume that a higher ecological validity can be found in CPT tests performed in this manner as compared to the traditional CPT test. During the last years Rizzo developed a virtual reality based CPT called "the Virtual Classroom". Several studies show that "Virtual Classroom" is an effective measure to identify attention difficulties in children with ADHD. Our research team developed a virtual CPT, similar to the Virtual Classroom", that allows to execute four different tasks: an auditory task with non-distractive stimuli, an auditory task with distractive stimuli, a visual task with non-distractive stimuli and a visual task with distractive stimuli. In this study, we offer additional data supporting the validity of using this type of technology for the assessment of ADHD.

J Can Acad Child Adolesc Psychiatry. 2009;18:349-55.

Cardiac risk assessment before the use of stimulant medications in children and youth: A joint position statement by the Canadian Paediatric Society, the Canadian Cardiovascular Society and the Canadian Academy of Child and Adolescent Psychiatry.

### Hamilton R, Gray C, Belanger SA, et al.

Regulatory decisions and scientific statements regarding the management of Attention Deficit and Hyperactivity Disorder (ADHD) raise questions about the safety of medications and the appropriate pretreatment evaluation to determine suitability for treatment with medication. This is particularly true in the setting of known structural or functional heart disease. The present paper reviews the available data, including peer reviewed literature, data from the United States Food and Drug Administration website on reported adverse reactions in children using stimulant medication, and Health Canada data on the same problem. A consensus-based guideline on appropriate assessment is provided, based on input from members of the Canadian Pediatric Society, Canadian Cardiovascular Society and the Canadian Academy of Child and Adolescent Psychiatry with specific expertise and knowledge in the areas of both ADHD and pediatric cardiology. The present statement advocates a thorough history and physical examination before starting stimulant medications, with an emphasis on the identification of risk factors for sudden death, but does not routinely recommend electrocardiographic screening or cardiac subspecialist consultation unless indicated by history or physical examination findings. A checklist for identification of children who are potentially at risk of sudden death (independent of ADHD or medications used to treat it) is provided. Although recommendations are based on the best evidence currently available, the committee further agrees that more research on this subject is necessary in order to optimize the approach to this common clinical scenario.

Am J Med Genet Part B Neuropsychiatr Genet. 2010;153:97-102.

ADHD and DAT1: Further evidence of paternal over-transmission of risk alleles and haplotype. Hawi Z, Kent L, Hill M, et al.

We [Hawi et al. (2005); Am J Hum Genet 77:958-965] reported paternal over-transmission of risk alleles in some ADHD-associated genes. This was particularly clear in the case of the DAT1 30-UTR VNTR. In the current investigation, we analyzed three new sample comprising of 1,248 ADHD nuclear families to examine the allelic over-transmission of DAT1 in ADHD. The IMAGE sample, the largest of the three-replication samples, provides strong support for a parent of origin effect for allele 6 and the 10 repeat allele (intron 8 and 3'-UTR VNTR, respectively) of DAT1. In addition, a similar pattern of overtransmission of paternal risk haplotypes (constructed from the above alleles) was also observed. Some support is also derived from the two smaller samples although neither is independently significant. Although the mechanism driving the paternal over-transmission of the DAT risk alleles is not known, these finding provide further support for this phenomenon.

Child Adolesc Ment Health, 2010 Feb:15:37-43.

The diagnostic utility of executive function assessments in the identification of ADHD in children.

Holmes J, Gathercole SE, Place M, et al.

**Background**: Deficits in executive functions have been widely reported to characterise individuals with ADHD. The aim of this study was to evaluate the utility of a range of executive function measures for identifying children with ADHD.

**Method**: Eighty-three children with ADHD and 50 normally-developing children without ADHD were assessed on measures of inhibition, set-shifting, planning, problem-solving, response inhibition, sustained attention and working memory. Measures of sensitivity, specificity, likelihood ratios and diagnostic odds ratios were calculated.

**Results**: Executive function tasks effectively discriminated between children with and without ADHD. Measures of response inhibition and working memory contributed the most to the discriminant function.

Conclusions: Cognitive measures of executive function can be used to help identify children with ADHD and could be useful as additional diagnostic tools for clinical practitioners. Key Practitioner Message: 1. ADHD diagnoses are often based heavily upon symptoms assessed by behavioural checklists. These can lack diagnostic utility. 2. It is possible to enhance clinical diagnoses of ADHD by employing neuropsychological/cognitive tests of executive functioning; 3. Where there is little opportunity to undertake a full range of cognitive measures, brief tests of response inhibition and working memory can provide high levels of discrimination between individuals with and without ADHD. 4. Guidance from clinicians about the difficulties in executive functioning experienced by children with ADHD may prove helpful to teachers and parents.

J Abnorm Psychol. 2010 Feb;119:174-85.

Working memory demands impair skill acquisition in children with ADHD.

# Huang-Pollock CL, Karalunas SL.

This study examined the process of cognitive skill acquisition under differential working memory (WM) load conditions in children with the primarily inattentive (n = 21) and the combined (n = 32) subtypes of childhood attention-deficit/hyperactivity disorder (ADHD) and compared the results with those of non-ADHD controls (n = 48). Children completed 2 tasks of cognitive skill acquisition: alphabet arithmetic and finger math. The tasks differed in the amount of WM required for execution (alphabet arithmetic required more) but were otherwise matched with respect to logical structure, design, and discriminatory power. As would be predicted if the WM of the to-be-learned task affected the ability of children with ADHD to develop automaticity for a complex cognitive skill, ADHD-related impairments in the development of automaticity were seen for alphabet arithmetic but not for finger math. Results not only are relevant to ongoing debate regarding the presence of effortful versus automatic cognitive deficits in ADHD but also have implications for the development of new psychoeducational interventions for children with ADHD.

Journal of Attention Disorders. 2009 Nov;13:310-14.

# Test and product review: Pediatric Attention Disorders Diagnostic Screener. *Huang LV.*

The Pediatric Attention Disorders Diagnostic Screener was developed as a computer-based assessment system to screen for attention and executive function disorders in children aged 6 through 12 years. The PADDS integrates parent and teacher rating scales with three measures of executive functioning. The data collected from these components result in a computer generated report, including a narrative and nomographic display with the chief purpose of strengthening the predictive power of clinicians to determine the probability of an ADHD diagnosis. A comprehensive evaluation of the PADDS indicated that it can be a useful and efficient instrument. It attempts to integrate parent and teacher ratings and three executive functioning tasks together to strengthen the diagnosis of ADHD. This tool exhibits potential for the field, though psychometric studies and analyses need to be completed to further establish its effectiveness and accuracy in the identification of children with ADHD.

Journal of Psychoeducational Assessment. 2009 Dec;27:452-64.

Relationship between parenting stress and ratings of executive functioning in children with ADHD. Joyner KB, Silver CH, Stavinoha PL.

Executive functioning is important to assess in children with attention deficit/hyperactivity disorder (ADHD). Parent report is used to obtain information about a child's executive functioning; however, parent report can be influenced by many factors. This study's hypothesis was that higher ratings of children's executive dysfunction are associated with parenting stress. Parents of 32 children (ages 8-12 years) with ADHD completed the Parenting Stress Index and two executive function rating scales, the BRIEF and CEFS. Stress produced by child and family system characteristics was significantly correlated with composite scores and subscales from the executive function rating scales. Findings suggest that parent ratings of their children's executive functioning appear related to the stress they experience being parents, particularly with regard to their children's challenging behaviors.

Journal of Attention Disorders. 2009 Nov;13:277-83.

Diagnosing attention-deficit hyperactivity disorder in college students: An investigation of the impact of informant ratings on diagnosis and subjective impairment.

Katz N, Petscher Y, Welles T.

**Objective**: Formal criteria for the use informant-ratings of adult ADHD symptoms have not been established yet they are commonplace in standard assessment batteries.

**Method**: The current study explores the relationship between self- and informant-ratings and the impact of requiring interrater agreement in a sample comprised of 190 self-referred college students.

**Results**: Participants self-reported higher childhood and current symptoms scores and current impairment scores than informants. Similarities were evident between diagnostic groups who met ADHD criteria by self-report only and by both sources when considering the number of self-reported settings of impairment. Diagnostic groups who met criteria by informant-report only and by both sources were similar when considering informant-reported settings of impairment.

**Conclusion**: Participants who meet criteria for ADHD based on one source endorse a similar number of settings of impairment as participants who meet criteria for ADHD by both sources. The implications for the use of informant-ratings are presented.

Psychiatr Invest. 2009;6:278-85.

Perinatal and familial risk factors are associated with full syndrome and subthreshold attention-deficit hyperactivity disorder in a Korean community sample.

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

**Objective**: The objective of this study was to examine the effect of perinatal and familial risk factors on full syndrome and subthreshold attention-deficit/hyperactivity disorder (ADHD) among Korean children and adolescents.

**Methods**: A sample of 2,673 students was randomly selected from 19 representative schools in Seoul, Korea. The parents of the students completed the Diagnostic Interview Schedule for Children-version IV (DISC-IV), as well as guestionnaires on perinatal and familial risk factors.

**Results**: Maternal stress and alcohol use during pregnancy, parental marital discord, parental separation or divorce, changes in primary caregivers, and notbreastfeeding were significantly associated with full syndrome ADHD; however, maternal stress during pregnancy was the only variable that differentiated subthreshold ADHD from non-ADHD.

**Conclusion**: Our results provide evidence the perinatal and familial risk factors contribute to the development of ADHD in Korea children and adolescents, and suggest that these perinatal and familial risk factors are more closely related to full syndrome than to subthreshold ADHD.

J Occup Environ Med. 2009;51:1247-55.

Incremental employee health benefit costs, absence days, and turnover among employees with ADHD and among employees with children with ADHD.

Kleinman NL, Durkin M, Melkonian A, et al.

**Objective**: To assess employer economic burden of attention-deficit/ hyperactivity disorder (ADHD) for employees with ADHD and employee caregivers of children with ADHD.

**Methods**: A large multi-employer database was used to compare: 1) employees diagnosed with ADHD versus employees without ADHD and 2) employee caregivers of children with ADHD versus employee caregivers of children without ADHD. Regression modeling compared many employer-relevant outcomes.

**Results**: The study found significantly higher annual health benefit costs (\$6885 versus \$4242), absence days (8.86 versus 7.16), and turnover (8.99% versus 5.26%) for employees with ADHD (n = 539) versus employees without ADHD (n = 93,722), respectively (all P < 0.01). Similar results were found for employee caregivers of children with ADHD.

**Conclusions**: Employees with ADHD and those caring for children with ADHD are associated with a significantly higher burden in employer-relevant outcomes such as health benefit costs, absences, and terminations.

Am J Med Genet Part B Neuropsychiatr Genet. 2010;153:148-58.

Familiality and molecular genetics of attention networks in ADHD.

### Konrad K, Dempfle A, Friedel S, et al.

Indices from amore elementary neuropsychological level might be useful in the search for genes for complex psychiatric disorders, such as ADHD. In this study we investigated systematically whether attentional performance as measured with the Attention Network Test (ANT) is suited for the identification of endophenotypes of ADHD. Attentional performance in affected sib pairs with ADHD(n=181) was compared to unaffected control siblings (n=121). Intrafamilial correlation patterns were calculated. In addition, linkage and association analyses were conducted between quantitative scores of attentional functions and dopamine receptor D4 (DRD4) and dopamine transporter (DAT1 or SLC6A3) gene variants. Only the executive attention network was significantly impaired in subjects with ADHDcompared to controls (P<0.05) and showed evidence for familiality in both affected and unaffected families. Linkage analyses revealed the highest LOD score for a severity score based on DSM-IV inattentive symptoms in the DAT1 chromosomal region (LOD score 2.6 at 15 cM). However, a SNP (rs6350) at the DAT1 locus showed a tendency for association with both alerting performance (P=0.02) and executive attention (P=0.01) although it did not survive alpha adjustment for multiple testing. No evidence was found for association of any of the investigated phenotypes with the VNTR in the DRD4. Thus, our data suggest that the quantitative behavioral ratings of inattentive symptoms might be more useful when searching for new genes associated with ADHD. however, among the ANT measures the executive attention network seems to be best suited for further endophenotype analyses.

Yonsei Med J. 2009;50:650-55.

Variability of response time as a predictor of methylphenidate treatment response in Korean children with attention deficit hyperactivity disorder.

Lee SH, Song DH, Kim BN, et al.

**Purpose**: Methylphenidate (MPH) is an effective medication for the treatment of attention deficit hyperactivity disorder (ADHD). However, about 30% of patients do not respond to or are unable to tolerate MPH. Based on previous findings, we hypothesized that great variability in response time (RT) among Korean children with ADHD on a computerized continuous performance attention test would be related to poor MPH treatment response.

Materials and Methods: Children (ages 6-18 years) with ADHD were recruited for a prospective 12-week, open-labeled, multicenter study to examine optimal dosage of OROS methylphenidate. Of the 144 subjects selected, 28 dropped out due to adverse events, medication noncompliance, or follow-up loss, and an additional 26 subjects with comorbid disorders were excluded from statistical analyses. We defined 'responders' as subjects who received a score of less than 18 on the attention deficit hyperactivity disorder rating scale (ARS; Korean version, K-ARS) and a score of 1 or 2 on the Clinical Global Impression-Improvement scale (CGI-I). RT variability was assessed with the ADHD diagnostic system (ADS).

**Results**: Fifty-nine (67%) subjects responded to MPH treatment. The non-responders showed greater RT variability at baseline (Mann Whitney U = 577.0, p < 0.01). Baseline RT variability was a significant predictor of MPH response (Nagelkerke R2 = 0.136, p < 0.01). It predicted 94.9% of responder, 17.2% of non-responder and 69.3% of overall group.

Conclusion: High RT variability may predict poor response to MPH treatment in children with ADHD.

Eur Child Adolesc Psychiatry. 2010;19:37-44.

ADHD in international adoptees: A national cohort study.

Lindblad F, Ringback Weitoft G, Hjern A.

Several investigators have reported an increased frequency of attention/hyperactivity symptoms in international adoptees, though population-based studies are lacking. In this national cohort study, we aimed to determine the prevalence of ADHD medication in international adoptees in Sweden, in comparison to the general population. A further purpose was to study gender, age at adoption and region of origin as predictors of ADHD medication in international adoptees. The study population consisted of all Swedish residents born in 1985-2000 with Swedish-born parents, divided into 16,134 adoptees, and a comparison population of 1,326,090. ADHD medications were identified in the Swedish Prescribed Drug Register during 2006. Logistic regression was used to calculate the odds ratios. The rates of ADHD medication were higher in international adoptees than in the comparison population for both boys (5.3 vs. 1.5% for 10-15-year olds) and girls (2.1 vs. 0.3% for 10-15-year olds). International adoptees from all regions of birth more often consumed ADHD medication compared with the majority population, but the age and sex adjusted odds ratios were particularly high for adoptees from Eastern Europe, Middle East/Africa and Latin America. Adjusting for maternal education and single parenthood increased the odds ratios even further. The risk also increased with higher age at adoption. Adoptees from Eastern Europe have a very high risk for ADHD medication. A structured identification and support programme should be tailored for this group. Adoptees from other regions have a more moderately increased risk, which should be communicated to adoptive parents and to professionals who care for adoptees in their clinical practice.

J Abnorm Psychol. 2010 Feb;119:186-96.

A person-centered personality approach to heterogeneity in attention-deficit/hyperactivity disorder (ADHD).

#### Martel MM, Goth-Owens T, Martinez-Torteya C, et al.

Person-centered personality approaches are an underused means of illuminating clinical heterogeneity of attention-deficit/hyperactivity disorder (ADHD). In the present study, latent profile analysis was conducted with personality traits to identify homogeneous profiles within the ADHD population. Participants were 548 children ages 6–18 years (302 with ADHD). Personality traits were measured via parent report on the California Q-Sort (A. Caspi et al., 1992). Latent profile analysis was conducted on the Big 5 factors. A 6-profile solution best fit the data. Resulting groups were characterized as "disagreeable," "introverted," "poor control," "well adjusted," "extraverted," and "perfectionistic." External validation of this model using ADHD diagnosis, subtypes, and comorbid psychopathology suggested that children with ADHD could be parsed into 4 groups: (a) an introverted group with high rates of the ADHD-inattentive type, (b) a group characterized by poor control, with high rates of ADHD-combined type (ADHD-C) and comorbid disruptive behavior disorders, (c) an extraverted group, with ADHD-C and few associated comorbid disorders, and (c) possibly, a very rare "perfectionistic" group, exhibiting obsessive traits. A person-centered personality approach may be one promising way to capture homogeneous subgroups within the ADHD population.

Eur Child Adolesc Psychiatry. 2010;19:57-66.

Atomoxetine in children and adolescents with attention-deficit/ hyperactivity disorder: A 6-week, randomized, placebo-controlled, double-blind trial in Russia.

Martenyi F, Zavadenko NN, Jarkova NB, et al.

The objective of the study was to compare the efficacy and tolerability of once-daily atomoxetine ((less-than or equal to)1.8 mg/(kg day) with those of placebo in children and adolescents (aged 6-16 years) with attention-deficit/hyperactivity disorder [ADHD (DSM-IV)]. This randomized, placebo-controlled, double-blind

trial was conducted in Russia. The primary efficacy measure was baseline-to-end point changes in Attention-Deficit/Hyperactivity Disorder Rating Scale-IV-Parent Version: Investigator-Administered and Scored (ADHDRS-IV-Parent:Inv) total score. Tolerability measures included treatment-emergent signs and symptoms (TESS), laboratory values and weight. Compared with patients in the placebo group (n = 33), patients treated with atomoxetine (n = 72) with a mean final dose of 1.4 mg/kg showed significantly greater improvement in ADHDRS-IV-Parent:Inv total score (least-squares mean: atomoxetine, -15.8; placebo, -11.4; p = 0.013). The most common TESS in the atomoxetine group included anorexia [atomoxetine, n = 13 (18.1%); placebo, n = 2 (6.1%)], somnolence, n = 11 versus n = 3 (15.3% vs. 9.1%, respectively), abdominal pain n = 9 versus n = 1 (12.5% vs. 3.0%, respectively) and nausea, n = 8 versus n = 1 (11.1% vs. 3.0%, respectively). Seven patients in the atomoxetine group and two in the placebo group experienced clinically important weight loss during the study ((greater-than or equal to)7% from baseline; mean change, kg: atomoxetine, -0.6; placebo, 0.1; p = 0.032). Atomoxetine is efficacious in improving ADHD symptoms in children and adolescents. Atomoxetine treatment may be associated with a numerically higher incidence of anorexia, somnolence, abdominal pain and nausea, as well as statistically greater losses in body weight.

Drugs. 2010;70:15-40.

# Attention-deficit hyperactivity disorder: Recent advances in paediatric pharmacotherapy. *May DE, Kratochvil CJ.*

Throughout this decade, there has been significant research into pharmacotherapies for attention-deficit hyperactivity disorder (ADHD). This article considers the efficacy and safety of five of the more novel longacting pharmacological treatments recently approved by the FDA for marketing in the US for paediatric ADHD, along with an (alpha)2-adrenoceptor agonist in preparation. Reviewed treatments include the nonstimulant atomoxetine, three novel extended-release (XR) stimulant preparations: dexmethylphenidate, lisdexamfetamine dimesylate and the methylphenidate transdermal system (TDS), and the recently approved XR (alpha)2-adrenoceptor agonist, guanfacine. Dexmethylphenidate XR is a stimulant treatment in a single isomer form, and has an efficacy and tolerability similar to two doses of immediate-release (IR) dexmethylphenidate when taken 4 hours apart, but is dosed at half of the usual d,l-methylphenidate dose. Dexmethylphenidate XR utilizes a beaded bimodal release, with 50 initially released and another 50 released 4 hours later to provide benefit lasting up to 1012 hours.Lisdexamfetamine was the first stimulant treatment approved as a prodrug, whereby the single isomer d-amfetamine remains pharmacologically inactive until activated by cleaving the lysine. Its efficacy and tolerability are generally consistent with that of XR mixed amfetamine salts, with this activation method and more consistent absorption generally resulting in up to an 11- to 13-hour benefit. The methylphenidate TDS patch utilizes skin absorption to provide predictable and uniform delivery of methylphenidate when worn for 9 hoursday. The efficacy and tolerability of the methylphenidate TDS patch is generally consistent with that of osmotic-controlled release oral system (OROS(registered trademark)) methylphenidate, providing benefit for about 1112 hours. Because of their formulation, lisdexamfetamine and methylphenidate each have an onset of effect at about 2 hours after administration. An adjustable wear time for the methylphenidate TDS patch accommodates related adverse effects, but its disadvantages are frequent skin irritation and the need to remember to take the patch off.Atomoxetine is the first non-stimulant treatment approved by the FDA and employs weight-based dosing up to 1.4mgkgday. Benefit is generally observed within 28 weeks of initiation and is considered to have a lesser therapeutic effect than that of stimulants. A recent parallel-group controlled study found that atomoxetine (up to 1.8mgkgday) and OROS(registered trademark) methylphenidate both improved ADHD symptoms, although subjects receiving OROS(registered trademark) methylphenidate had a significantly better response. Interestingly, treatment-naive children had a similar beneficial response to atomoxetine as those receiving OROS(registered trademark) methylphenidate. Subsequent crossover treatment revealed a subgroup of youths who did not respond well to OROS(registered trademark) methylphenidate but did respond to atomoxetine. Also identified was a larger than expected subgroup who did not respond well to either active treatment, confirming the need to continue the pursuit of novel treatments. As of September of 2009, guanfacine in XR form is the first (alpha)2-adrenoceptor agonist to gain approval to treat ADHD, approved for the treatment of 6- to 17-year olds. A second (alpha)2-adrenoceptor agonist, clonidine, is in development as a potential XR treatment for paediatric ADHD. IR clonidine has a fast onset and short halflife, with its use historically limited by somnolence. Although early formulations did not improve inattention well, recent evidence suggests that clonidine XR may have potential use as monotherapy or in extending benefit when taken with a stimulant. Guanfacine has a more specific neuronal action and a longer action than that of clonidine. The approved dosing of guanfacine XR 1 to 4mg daily generally provides symptom benefit lasting 814 hours, and up to 24 hours in some children and adolescents receiving a higher dose. Such

recent developments and ongoing study of additional potential pharmacological interventions may lead to additional future treatment options for children with ADHD.

Psychiatry Res. 2010;175:252-55.

Platelet monoamine oxidase activity in children with attention-deficit/hyperactivity disorder.

### Nedic G, Pivac N, Hercigonja DK, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a highly heritable developmental disorder characterized by symptoms of impulsivity, hyperactivity and/or inattention, and associated with structural and biochemical abnormalities in cortical and limbic structures innervated by dopamine, noradrenalin and serotonin. The enzyme monoamine oxidase, type B (MAO-B), is expressed in platelets, and metabolizes endogenous amines. Its activity has been proposed to represent a peripheral marker of various traits and forms of psychopathology. This study evaluated platelet MAO activity with a spectrofluorimetric method in 72 boys and 12 girls with predominantly hyperactive, predominantly inattentive, and combined subtype of ADHD (DSM-IV criteria), and in 64 control children. The results showed significantly lower platelet MAO activity in children with hyperactive, inattentive, and combined subtype of ADHD than in control children. There was no significant association between platelet MAO activity and gender or age. The limitation of the study was in the small sample of girls with ADHD (N = 12), and in the determination of only one peripheral marker. In line with hypotheses of lower platelet MAO activity in different types of psychopathology, children with different subtypes of ADHD had significantly lower platelet MAO-B activity than control children.

Br J Nutr. 2009;102:1635-41.

Dietary PUFA intakes in children with attention-deficit/hyperactivity disorder symptoms.

Ng KH, Meyer BJ, Reece L, et al.

Research has shown associations between attention-deficit/hyperactivity disorder (ADHD) and erythrocyte long-chain n-3 PUFA (LC n-3 PUFA) levels, with limited evidence for dietary LC n-3 PUFA intake and ADHD. The aims of the present study were to assess dietary PUFA intakes and food sources in children with ADHD, to compare these intakes to previously published Australian National Nutrition Survey (NNS) data and determine any relationships between intakes and ADHD symptoms. Eighty-six 3-d-weighed food records (FR) were analysed from children with ADHD. The median (interquartile range) daily intakes of fatty acids (mg/d) were: linoleic acid (18:2n-6), 7797 (6240-12 333); arachidonic acid (20:4n-6), 55 (27.0-93); total n-6 PUFA, 7818 (6286-10 662); (alpha)-linolenic acid (18:3n-3), 1039 (779-1461); EPA (20:5n-3), 18 (6.0-32.0); docosapentaenoic acid (22:5n-3), 17 (6.3-39.3); DHA (22:6n-3), 16 (8.5-445); total LC n-3 PUFA (addition of 20:5n-3, 22:5n-3 and 22:6n-3), 65 (28.3-120.1); total n-3 PUFA, 1151 (876-1592). In comparison to the NNS data, 18:3n-3 intakes were higher and 20:4n-6 were lower (P<0.05). Children with ADHD consumed half the amount of fish/seafood, meat and eggs when compared to the NNS (P<0.05). No significant correlations were found between fatty acids and ADHD symptoms. Children with ADHD met the adequate intake for LC n-3 PUFA, but fell short of other recommendations.

Phytother Res. 2010;24:26-27.

Ginkgo biloba treating patients with attention-deficit disorder.

#### Niederhofer H.

Various medications such as clonidine facilitate calming, enhance frustration tolerance and reduce aggression in attention-deficit disorder (ADD) patients. The use of Ginkgo biloba was studied as an herbal alternative. Six psychiatric outpatients diagnosed with ADD were rated at baseline and while taking Ginkgo biloba to determine its efficacy as a treatment for ADD. Comparisons of Wender Utah ratings within subject were used to measure behavioral changes in the subjects. During Ginkgo biloba treatment, the patients' mean scores improved significantly overall and in hyperactivity, inattention, and immaturity factors. This preliminary study indicates that Ginkgo biloba might be a beneficial and useful treatment of ADD, with minimal side effects.

Psychiatry Res Neuroimaging. 2010;181:36-43.

Neural correlates of response inhibition in pediatric bipolar disorder and attention deficit hyperactivity disorder.

Passarotti AM, Sweeney JA, Pavuluri MN.

Impulsivity, inattention and poor behavioral inhibition are common deficits in pediatric bipolar disorder (PBD) and attention deficit hyperactivity disorder (ADHD). This study aimed to identify similarities and differences in the neural substrate of response inhibition deficits that are associated with these disorders. A functional magnetic resonance imaging (fMRI) study was conducted on 15 unmedicated PBD patients (Type I, manic/mixed), 11 unmedicated ADHD patients, and 15 healthy controls (HC) (mean age = 13.5 years; S.D. = 3.5). A response inhibition task examined the ability to inhibit a motor response to a target when a stop cue appeared shortly after. The PBD and ADHD groups did not differ on behavioral performance, although both groups were less accurate than the HC group. fMRI findings showed that for trials requiring response inhibition, the ADHD group, relative to the PBD and HC groups, demonstrated reduced activation in both ventrolateral (VLPFC) and dorsolateral (DLPFC) prefrontal cortex, and increased bilateral caudate activation compared with HC. The PBD group, relative to HC, showed decreased activation in the left VLPFC, at the junction of the inferior and middle frontal gyri, and in the right anterior cingulate cortex (ACC). Prefrontal dysfunction was observed in both the ADHD and PBD groups relative to HC, although it was more extensive and accompanied by subcortical overactivity in ADHD.

Swiss Journal of Psychology/Schweizerische Zeitschrift für Psychologie/Revue Suisse de Psychologie. 2010 Jan;69:7-14.

# Sense of time in children with attention-deficit/hyperactivity disorder (ADHD): A comparative study. *Quartier V, Zimmermann G, Nashat S.*

Parents of children with attention-deficit/hyperactivity disorder (ADHD) frequently report that their children have a poor sense of time. Several studies looking at the perception of time mentioned a form of temporal myopia. The present study investigates the sense of time in children with ADHD. Twenty-two French-speaking Swiss children with ADHD and 22 controls between the ages of 6 and 13 years were tested using a conventional time knowledge questionnaire and two Piagetian time conservation tasks. Parents were asked to complete the "It's about time" questionnaire. Better performance was observed in matched control group children than in children with ADHD on a conventional time knowledge questionnaire. For children under 10 years of age, the two Piagetian time conservation tasks were able to differentiate children with and without ADHD. Parents of ADHD children reported more frequently that their children had time-related difficulties in daily activities. This study suggests that children with ADHD take longer to develop several time-related abilities.

Pediatrics, 2010:125:e340-e348.

Mixed-handedness is linked to mental health problems in children and adolescents.

Rodriguez A, Kaakinen M, Moilanen I, et al.

**OBJECTIVE**: Problems with language and symptoms of attention-deficit/ hyperactivity disorder (ADHD) in childhood and adolescence are often strongly linked to low scholastic performance. Early recognition of children who are at increased risk is necessary. Our objective was to determine whether mixed-handedness, which is associated with atypical cerebral laterality, is associated with language, scholastic, and ADHD symptoms in childhood and adolescence.

**METHODS**: Prospective data come from the Northern Finland Birth Cohort 1986, a longitudinal, population-based birth cohort with assessments when children were 7 to 8 and 16 years of age (N = 7871). Teacher, parent, and/or adolescent reports were used to assess language difficulties, scholastic performance, and mental health, including ADHD symptoms.

**RESULTS**: Mixed-handed children, relative to right-handed, had approximately a twofold increase in odds of having difficulties with language and scholastic performance at the age of 8 years. Eight years later, as 16-year-olds, adolescents had twofold increase in odds concerning difficulties in school with language and with ADHD symptoms. Mixed-handed children were more likely to have scores indicating probable psychiatric disturbance, including ADHD symptoms. As adolescents, mixed-handed children with previous behavioral problems were at considerably higher risk for scoring within the range of probable ADHD-inattention or

ADHD-combined case. Mixed-handedness was associated with greater symptom severity in children and adolescents (P = .01) concerning psychiatric disturbance and ADHD inattention but not ADHD hyperactivity. **CONCLUSIONS**: The results indicate that mixed-handed children have a greater likelihood of having language, scholastic, and mental health problems in childhood and that these persist into adolescence. Thus, these results suggest that mixed-handedness, particularly in the presence of difficulties, could aid in the recognition of children who are at risk for stable problems. Additional research is needed to understand the connections between neural substrates related to atypical cerebral asymmetry, mixed-handedness, and mental health problems including ADHD symptoms.

J Psychiatry Neurosci. 2010;35:55-58.

Structural abnormality of the substantia nigra in children with attention-deficit hyperactivity disorder. *Romanos M, Weise D, Schliesser M, et al.* 

**Background**: Structural abnormality of the substantia nigra can be detected by transcranial sonography in neuropsychiatric disorders such as Parkinson disease and restless legs syndrome. We investigated echogenicity of the substantia nigra as a potential structural marker for dysfunction of the nigrostriatal dopamine system in children with attention-deficit hyperactivity disorder (ADHD).

**Methods**: We used a blinded design and determined echogenicity of the substantia nigra by use of transcranial sonography in 22 children with ADHD and 22 healthy controls matched for age and sex.

**Results**: The echogenic substantia nigra area was significantly larger in ADHD patients than in healthy controls (F1,42 = 9.298, p = 0.004, effect size = 0.92). We found no effects of age or sex. Limitations: Owing to a lack of dimensional assessment, we could not analyze the correlation between echogenicity and clinical symptoms.

**Conclusion**: Our results support the hypothesis that the nigrostriatal dopaminergic system is abnormal in children with ADHD.

Hum Brain Mapp. 2010;31:287-99.

Disorder-specific dysfunction in right inferior prefrontal cortex during two inhibition tasks in boys with attention-deficit hyperactivity disorder compared to boys with obsessive-compulsive disorder. *Rubia K, Cubillo A, Smith AB, et al.* 

**Background**: Inhibitory dysfunction is a key behavioral and cognitive phenotype of attention-deficit hyperactivity disorder (ADHD) and obsessive-compulsive disorder (OCD). Both disorders show neuropsychological deficits and fronto-striatal dysfunction during tasks of motor response inhibition and cognitive flexibility. This study investigates differences and commonalities in functional neural networks mediating inhibitory control between adolescents with ADHD and those with OCD to identify disorder-specific neurofunctional markers that distinguish these two inhibitory disorders.

**Methods**: Event-related fMRI was used to compare brain activation between 20 healthy boys, 18 (Stop task) or 12 boys (Switch task) with ADHD, and 10 boys with OCD during a tracking Stop task that measures inhibition and stopping failure and during a visual-spatial switching task measuring cognitive flexibility.

**Results**: Both patient groups shared brain dysfunction compared to healthy controls in right orbitofrontal (successful inhibition) and left dorsolateral prefrontal cortices (failed inhibition). Right inferior prefrontal dysfunction, however, was disorder-specific to ADHD during both tasks. Left inferior prefrontal dysfunction during the Switch task was significant in children with ADHD relative to controls, but only reached a trend in patients with OCD. Patients with ADHD furthermore showed disorder-specific dysfunction in left basal ganglia and cingulate gyrus during the Switch task.

**Conclusions**: Patients with ADHD compared to those with OCD have both common and distinct dysfunctions during inhibitory control. The most consistently reported functional abnormality in children with ADHD in right inferior prefrontal cortex during inhibitory control appears to be disorder-specific when compared to patients with OCD and may be a specific neurofunctional biomarker of ADHD.

Prog Neuro-Psychopharmacol Biol Psychiatry. 2010;34:76-80.

Ginkgo biloba for Attention-Deficit/Hyperactivity Disorder in children and adolescents: A double blind, randomized controlled trial.

#### Salehi B. Imani R. Mohammadi MR. et al.

**Background**: Although stimulants are highly effective in controlling the symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD), some children will not respond to, or are intolerant of stimulants. Thus, the desire for safe and effective nonstimulant medications has risen during the past several years. Ginkgo biloba has been suggested in the treatment of dementia and memory impairment. We hypothesized that G. biloba would be beneficial for treatment of ADHD, and this could be evaluated in a double blind, randomized, parallel group comparison of G. biloba (Ginko T.D.(trademark) Tolidaru, Iran) and methylphenidate.

**Methods**: Fifty outpatients (39 boys and 11 girls) with a DSM-IV-TR diagnosis of ADHD were study population of this trial. Subjects were recruited from an outpatient child and adolescent clinic for a 6 week double blind, randomized clinical trial. All study subjects were randomly assigned to receive treatment using tablet of Ginko T.D.(trademark) at a dose of 80-120 mg/day depending on weight (80 mg/day for < 30 kg and 120 mg/day for > 30 kg) (group 1) or methylphenidate at a dose of 20-30 mg/day depending on weight (20 mg/day for < 30 kg and 30 mg/day for > 30 kg (group 2) for a 6 week double blind, randomized clinical trial. The principal measure of outcome was the Teacher and Parent ADHD Rating Scale- IV. Patients were assessed at baseline and at 21 and 42 days after the medication started.

Results: Significant differences were observed between the two groups on the Parent and Teacher Rating Scale scores. The changes at the endpoint compared to baseline were: - 6.52 (plus or minus) 11.43 (mean (plus or minus) S.D.) and - 15.92 (plus or minus) 11.44 (mean (plus or minus) S.D.) for Ginko T.D.(trademark) and methyphenidate, respectively for Parent ADHD Rating Scale. The changes at the endpoint compared to baseline were: - 0.84 (plus or minus) 6.79 (mean (plus or minus) S.D.) and - 14.04 (plus or minus) 8.67 (mean (plus or minus) S.D.) for Ginko T.D.(trademark) and methyphenidate, respectively for Teacher ADHD Rating Scale. The difference between the Ginko T.D.(trademark) and methylphenidate groups in the frequency of side effects was not significant except for decreased appetite, headache and insomnia that were observed more frequently in the methylphenidate group.

**Conclusion**: The results of this study suggest that administration of G. biloba was less effective than methylphenidate in the treatment of ADHD.

Acad Pediatr. 2010;10:56-63.

Comparing Medical Homes for Children with ADHD and Asthma.

Toomey SL, Homer CJ, Finkelstein JA.

**Objective**: The aims of our study were, among children with attention-deficit/hyperactivity disorder (ADHD) compared with children with asthma: 1) to assess characteristics associated with parent report of having a medical home for children with either of these 2 conditions; 2) to determine whether, controlling for these characteristics, the likelihood of having a medical home differs between children with ADHD and asthma; and 3) to identify the specific components of a medical home that are lacking for children with these 2 conditions.

**Methods**: Cross-sectional analysis of the National Survey of Children with Special Health Care Needs, 2005-2006 (NS-CSHCN) was used. The outcome variable was parent report of their child's practice having specific attributes of the medical home. We used multivariate logistic regression to test whether the likelihood of having a medical home and its components differed for children with ADHD in comparison to children with asthma.

**Results**: The NS-CSHCN interviewed parents of 11 674 children with ADHD and 13 517 children with asthma aged between 4 to 17 years. Significantly fewer children with ADHD compared with children with asthma have a medical home (OR [odds ratio] 0.68; P < .001). Specifically, parents reported differences in receiving family-centered (OR 0.79; P < .001) and coordinated care (OR 0.59; P < .001).

**Conclusion**: Parents of children with ADHD report worse performance across key dimensions of primary care compared with parents of children with asthma. For primary care to be optimally effective in addressing the needs of children with ADHD, efforts to significantly strengthen these key dimensions are needed.

Journal of Child Psychology and Psychiatry. 2010 Feb;51:210-18.

Performance variability, impulsivity errors and the impact of incentives as gender-independent endophenotypes for ADHD.

Uebel H, Albrecht B, Asherson P, et al.

**Background**: Attention-deficit hyperactivity disorder (ADHD) is one of the most common and highly heritable child psychiatric disorders. There is strong evidence that children with ADHD show slower and more variable responses in tasks such as Go/Nogo tapping aspects of executive functions like sustained attention and response control which may be modulated by motivational factors and or state-regulation processes. The aim of this study was (1) to determine if these executive functions may constitute an endophenotype for ADHD; (2) to investigate for the first time whether known modulators of these executive functions may also be familial; and (3) to explore whether gender has an impact on these measures.

**Methods**: Two hundred and five children with ADHD combined type, 173 nonaffected biological siblings and 53 controls with no known family history of ADHD were examined using a Go/Nogo task in the framework of a multi-centre study. Performance-measures and modulating effects of event-rate and incentives were examined. Shared familial effects on these measures were assessed, and the influence of gender was tested.

**Results**: Children with ADHD responded more slowly and variably than nonaffected siblings or controls. Nonaffected siblings showed intermediate scores for reaction-time variability, false alarms and omission errors under fast and slow event-rates. A slower event-rate did not lead to reduced performance specific to ADHD. In the incentive condition, mean reaction-times speeded up and became less variable only in children with ADHD and their nonaffected siblings, while accuracy was improved in all groups. Males responded faster, but also committed more false alarms. There were no interactions of group by gender.

**Conclusions**: Reaction-time variability and accuracy parameters could be useful neuropsychological endophenotypes for ADHD. Performance-modulating effects of incentives suggested a familially driven motivational dysfunction which may play an important role on etiologic pathways and treatment approaches for ADHD. The effects of gender were independent of familial effects or ADHD-status, which in turn suggests that the proposed endophenotypes are independent of gender.

Child Neuropsychol. 2009 Dec;15:554-66.

Methylphenidate, interstimulus interval, and reaction time performance of children with attention deficit/hyperactivity disorder: A pilot study.

Van Der Meere JJ, Shalev RS, Borger N, et al.

Thirteen children with attention deficit/hyperactivity disorder (ADHD: DSM-IV-TR) participated in the pilot study. They carried out a Go/No-Go test with a short (2 seconds) and long (6 seconds) interstimulus interval (ISI) when on placebo and a therapeutic dose of methylphenidate (MPH). For the long-ISI placebo condition the responses were slow and inaccurate. This pattern of response may be due to underactivation of the readiness-to-respond state that is not fully controlled by effort allocation. Speed of response and accuracy were enhanced during the short-ISI placebo condition and the long-ISI MPH condition. However, the combined effect (short ISI and MPH) resulted in a fast but inaccurate response style. This pattern of response may be due to overactivation of the readiness-to-respond state. The data of the pilot study support the stimulus shift hypothesis: MPH administration result in deterioration on tests on which children had previously done well (short ISI plus placebo versus short ISI plus MPH). In addition, the data support the idea that ADHD is associated with poor state regulation rather than motivational (delay aversion) theories or temporal-processing/time-estimation theories of ADHD. The pilot study defined empirically an issue for further study with the larger controlled sample.

Child Neuropsychol. 2009 Dec;15:605-18.

Very low birth weight and attention deficit/hyperactivity disorder.

van der Meere J, Börger NA, Potgieter ST, et al.

It is well recognized that reaction time performance of term-born children with a normal birth weight (NBW > 2500 g) who fulfill the DSM-IV criteria for attention deficit/hyperactivity disorder (ADHD) in the primary school age is sensitive for the presentation rate of stimuli. They have been found to perform more poorly in conditions of relatively slow event rates as compared with fast event rates. The purpose of the current study was to explore whether reaction time performance of children with very low birth weight (VLBW < 1500 g) with or without ADHD showed the same sensitivity for the factor presentation rate of stimuli compared to

children with a normal birth weight plus ADHD. To this end, reaction time performance of four groups of children was compared on a Go/No-Go test with a fast presentation rate of 1 second and a slow presentation rate of 6 seconds. Groups were: children with VLBW plus ADHD, children with VLBW only, children born full term with normal birth weight (NBW >2500 g) plus ADHD, and children born full term without ADHD (the control group). Findings indicated that, compared to the non-ADHD groups, the groups with ADHD (NBW and VLBW) showed a more dramatic decline in their reaction time performance in the slow condition: a state regulation deficit. In addition, both groups showed a response inhibition deficit. No difference was found in reaction time performance between the groups of children with VLBW only and the control group.

Eur J Hum Genet. 2010;18:206-11.

# Genome-wide linkage analysis in a Dutch multigenerational family with attention deficit hyperactivity disorder.

### Vegt R, Bertoli-Avella AM, Tulen JHM, et al.

Attention deficit hyperactivity disorder (ADHD) is a common neuropsychiatric disorder. Genetics has an important role in the aetiology of this disease. In this study, we describe the clinical findings in a Dutch family with eight patients suffering from ADHD, in whom five had at least one other psychiatric disorder. We performed a genome-wide (parametric and nonparametric) affected-only linkage analysis. Two genomic regions on chromosomes 7 and 14 showed an excess of allele sharing among the definitely affected members of the family with suggestive LOD scores (2.1 and 2.08). Nonparametric linkage analyses (NPL) yielded a maxNPL of 2.92 (P0.001) for marker D7S502 and a maxNPL score of 2.56 (P0.003) for marker D14S275. We confirmed that all patients share the same haplotype in each region of 7p15.1-q31.33 and 14q11.2-q22.3. Interestingly, both loci have been reported before in Dutch (affected sib pairs) and German (extended families) ADHD linkage studies. Hopefully, the genome-wide association studies in ADHD will help to highlight specific polymorphisms and genes within the broad areas detected by our, as well as other, linkage studies.

Pediatr Neurol. 2010:42:118-26.

# Using Brain-Based Cognitive Measures to Support Clinical Decisions in ADHD. Williams LM, Hermens DF, Thein T, et al.

Measures of cognition support diagnostic and treatment decisions in attention deficit hyperactivity disorder. We used an integrative neuroscience framework to assess cognition and associated brain-function correlates in large attention deficit hyperactivity disorder and healthy groups. Matched groups of 175 attention deficit hyperactivity disorder children/adolescents and 175 healthy control subjects were assessed clinically, with the touch screen-based cognitive assessment battery "IntegNeuro" (Brain Resource Ltd., Sydney, Australia) and the "LabNeuro" (Brain Resource Ltd., Sydney, Australia) platform for psychophysiologic recordings of brain function and body arousal. IntegNeuro continuous performance task measures of sustained attention classified 68% of attention deficit hyperactivity disorder patients with 76% specificity, consistent with previous reports. Our additional cognitive measures of impulsivity, intrusive errors, inhibition, and response variability improved sensitivity to 88%, and specificity to 91%. Positive predictive power was 96%, and negative predictive power, 88%. These metrics were stable across attention deficit hyperactivity disorder subtypes and age. Consistent with their brain-based validity, cognitive measures were correlated with corresponding brain-function and body-arousal measures. We propose a combination of candidate cognitive "markers" that define a signature for attention deficit hyperactivity disorder: "sustained attention," "impulsivity," "inhibition," "intrusions," and "response variability." These markers offer a frame of reference to support diagnostic and treatment decisions, and an objective benchmark for monitoring outcomes of interventions.

Brain Dev. 2010:32:115-22.

Short-term effect of American summer treatment program for Japanese children with attention deficit hyperactivity disorder.

### Yamashita Y, Mukasa A, Honda Y, et al.

We reported the results of the 3-week summer treatment program (STP) for children with attention deficit hyperactivity disorder (ADHD) in 2006. The STP was based on methods established by Professor Pelham in Buffalo, NY and has been used in a number of studies and at a number of sites in the U.S. This is the first STP outside North America. Thirty-six children age 6-12 years with ADHD participated. The collection of evidence-based behavioral modification techniques that comprises the STP's behavioral program (e.g., point system, daily report card, positive reinforcement, time out) was used. Most children showed positive behavioral changes in multiple domains of functioning, demonstrated by significant improvement in points earned daily, which reflect behavior frequencies. Only one child with ADHD co-morbid with pervasive developmental disorder required an individualized program for excessive time outs. The ADHD rating scale, symptoms of oppositional defiant disorder, and hyperactivity/inattention in Strength and Difficulties Questionnaires evaluated by parents significantly improved after STP. Although the 3-week STP was much shorter than most STPs run in the U.S., the program is more intensive than typical outpatient treatment, providing 105 h of intervenion in 3 weeks. The short-term effect of the STP was demonstrated for Japanese children with ADHD.

Autism Res. 2009;2:322-33.

Attention deficit/hyperactivity disorder symptoms moderate cognition and behavior in children with autism spectrum disorders.

### Yerys BE, Wallace GL, Sokoloff JL, et al.

Recent estimates suggest that 31% of children with autism spectrum disorders (ASD) meet diagnostic criteria for attention deficit/hyperactivity disorder (ADHD), and another 24% of children with ASD exhibit subthreshold clinical ADHD symptoms. Presence of ADHD symptoms in the context of ASD could have a variety of effects on cognition, autistic traits, and adaptive/maladaptive behaviors including: exacerbating core ASD impairments; adding unique impairments specific to ADHD; producing new problems unreported in ASD or ADHD; having no clear impact; or producing some combination of these scenarios. Children with ASD and co-morbid ADHD symptoms (ASD+ADHD; n=121), children with ASD without ADHD (ASD; n=28), and a typically developing control group (n=21) were included in the study; all groups were matched on age, gender-ratio, IQ, and socioeconomic status. Data were collected on verbal and spatial working memory, response inhibition, global executive control (EC), autistic traits, adaptive functioning, and maladaptive behavior problems. In this sample, the presence of ADHD symptoms in ASD exacerbated impairments in EC and adaptive behavior and resulted in higher autistic trait, and externalizing behavior ratings. ADHD symptoms were also associated with greater impairments on a lab measure of verbal working memory. These findings suggest that children with ASD+ADHD symptoms present with exacerbated impairments in some but not all domains of functioning relative to children with ASD, most notably in adaptive behavior and working memory. Therefore, ADHD may moderate the expression of components of the ASD cognitive and behavioral phenotype, but ASD+ADHD may not represent an etiologically distinct phenotype from ASD alone.

Journal of Child Psychology and Psychiatry. 2010 Feb;51:116-33.

Practitioner review: Non-pharmacological treatments for ADHD: A lifespan approach.

Young S. Amarasinghe JM.

**Background**: Attention-deficit hyperactivity disorder (ADHD) is a chronic and pervasive developmental disorder that is not restricted to the childhood years.

**Methods**: This paper reviews non-pharmacological interventions that are available at present for preschoolers, school-age children, adolescents and adults.

Results: The most appropriate intervention for preschoolers is parent training. For school-age children with moderate impairments there is some evidence to suggest that group parent training programmes and classroom behavioural interventions may suffice as a first-line treatment. For school-age children with severe impairments, interventions are more appropriate when combined with stimulant medication (i.e., integrated treatment packages are likely to be more successful than standalone treatments). Multimodal interventions seem to be best suited for middle school adolescent children, which most likely reflects that these

interventions usually integrate home and school treatment strategies and often include an element of social skills training. Stimulant medication is generally the first line of treatment for adults but CBT has also been found to be effective at addressing the complex needs of this population.

**Conclusion**: Current research has largely ignored that ADHD is a developmental disorder that spans the preschool to adult years. Most studies focus on young school-age children and outside of this age group there is a dearth of controlled trials that provide conclusive evidence. As children mature the mode and agent of intervention will shift to reflect the developmental needs and circumstances of the individual.

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