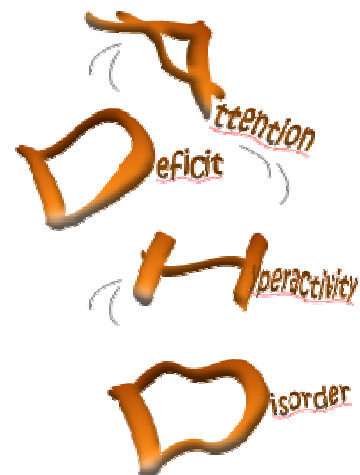
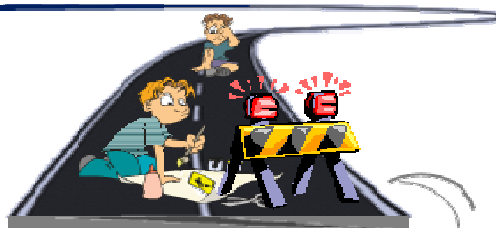


NEWSLETTER



INDICE:

1. Dalle banche dati bibliografiche

pag. 2

2. Documenti

- Fusar-Poli P, Rubia K, Rossi G, Sartori G, Balottin U.
**Striatal Dopamine Transporter Alterations in A DHD:
Pathophysiology or Adaptation to Psychostimulants?
A Meta-Analysis.**

Am J Psychiatry 2012;169:264-272.

pag. 53

BIBLIOGRAFIA ADHD APRILE 2012

Addiction. 2012 Mar;107:467-77.

THE DIVERSION AND MISUSE OF PHARMACEUTICAL STIMULANTS: WHAT DO WE KNOW AND WHY SHOULD WE CARE?
Kaye S, Darke S.

Aims: To examine the literature pertaining to the diversion and misuse of pharmaceutical stimulants.

Methods: Relevant literature was identified through comprehensive MEDLINE, EMBASE and PubMed searches.

Results: The evidence to date suggests that the prevalence of diversion and misuse of pharmaceutical stimulants varies across adolescent and young adult student populations, but is higher than that among the general population, with the highest prevalence found among adults with attention deficit hyperactive disorder (ADHD) and users of other illicit drugs. Concerns that these practices have become more prevalent as a result of increased prescribing are not supported by large-scale population surveys. Information on trends in misuse in countries where there have been recent increases in prescription and consumption rates, however, is limited. Little is known about the frequency and chronicity of misuse, or the extent of associated harms, particularly among those populations, i.e. adolescents, young adult student populations, those with ADHD and illicit drug users, where abuse may be more likely to occur.

Conclusions: Continued monitoring of the diversion and misuse of pharmaceutical stimulants is of major clinical importance. Despite recognition of the abuse liability of these medications, there is a paucity of data on the prevalence, patterns and harms of diversion and misuse among populations where problematic use and abuse may be most likely to occur (e.g. adolescents, young adults, illicit drug users). Comprehensive investigations of diversion and misuse among these populations should be a major research priority, as should the assessment of abuse and dependence criteria among those identified as regular users.

.....

Addiction Research & Theory. 2012 Feb;20:72-81.

AN EXAMINATION OF DIFFERENCES IN VARIABLES MAINTAINING SMOKING BEHAVIOR IN ADULT SMOKERS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Van Voorhees E, McClernon FJ, Fuemmeler B, et al.

Individuals with attention-deficit/hyperactivity disorder (ADHD) smoke cigarettes at higher rates and have greater difficulty quitting than their non-diagnosed peers. This study examined differences between smokers with and without ADHD on a range of smoking-related variables. Twenty-two subjects with ADHD and 22 controls completed self-report measures of withdrawal symptoms, smoking motivation, sensory experience of smoking, and positive and negative affect. Compared to control smokers, smokers with ADHD reported greater craving and negative affect; perceived smoking as providing greater enhancement of concentration and alertness, as more calming, and as providing a greater decrease in irritability; found cigarette puffs to be more enjoyable and satisfying; and rated smoking as providing greater positive and negative reinforcement and greater cognitive enhancement. Women with ADHD reported the greatest effects of smoking on improving concentration and reducing irritability. Findings support the hypothesis that smokers with ADHD may experience smoking differently than smokers without the disorder, and that they may identify different motivations for smoking.

.....

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.

ADHD Atten Deficit Hyperact Disord. 2012;4:11-23.

NEUROCOGNITIVE TRAINING FOR CHILDREN WITH AND WITHOUT AD/HD.

Johnstone SJ, Roodenrys S, Blackman R, et al.

There is accumulating evidence that computerised cognitive training of inhibitory control and/or working memory can lead to behavioural improvement in children with AD/HD. Using a randomised waitlist control design, the present study examined the effects of combined working memory and inhibitory control training, with and without passive attention monitoring via EEG, for children with and without AD/HD. One hundred and twenty-eight children (60 children with AD/HD, 68 without AD/HD) were randomly allocated to one of three training conditions (waitlist; working memory and inhibitory control with attention monitoring; working memory and inhibitory control without attention monitoring) and completed with pre- and post-training assessments of overt behaviour (from 2 sources), trained and untrained cognitive task performance, and resting EEG activity. The two active training conditions completed 25 sessions of training at home over a 4-5-week period. Results showed significant improvements in overt behaviour for children with AD/HD in both training conditions compared to the waitlist condition as rated by a parent and other adult. Post-training improvements in the areas of spatial working memory, ignoring distracting stimuli, and sustained attention were reported for children with AD/HD. Children without AD/HD showed behavioural improvements after training. The improvements for both groups were maintained over the 6-week period following training. The passive attention monitoring via EEG had a minor effect on training outcomes. Overall, the results suggest that combined WM/IC training can result in improved behavioural control for children with and without AD/HD.

Am J Epidemiol. 2011;173:S160.

STIMULANT TREATMENT AND INJURY AMONG CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): AN APPLICATION OF THE SELFCONTROLLED CASE SERIES STUDY DESIGN.

Raman SR, Marshall SW, Sturmer T, et al.

Background: Children with ADHD experience high rates of injuries and stimulant medication use is hypothesized to decrease injury risk by reducing symptoms.

Objective: To assess the association between stimulant medication use and risk of injury among children diagnosed with ADHD. **Methods:** All children ages 1 to 18 years old diagnosed with ADHD who experienced an incident medically-attended injury event and received at least 1 prescription for stimulant medication between 1993 and 2008 (n = 328) were identified from the UK-based Health Improvement Network (THIN) primary care database. A self-controlled case series method was used to estimate incident rate ratios (IRR) and 95% confidence intervals (CI) for injury comparing periods of time exposed to stimulant medication to unexposed periods.

Results: The rate of medically-attended injury was decreased during periods of stimulant medication use as compared to unexposed periods [IRR (95%CI): 0.70 (0.52, 0.93)]. The association was clearly apparent for males and did not decline with increasing time on treatment. Estimates stratified by injury type, day of injury, and period of time (pre or post 2000) were all similar to the main estimate, except for head injury (IRR = 1.18; 95%CI: 0.56, 2.48). Excluding post-diagnosis untreated time prior to medication initiation yielded a slightly higher estimate (IRR = 0.82, 95%CI: 0.58, 1.17).

Conclusions: Stimulant medication use may be associated with a decreased risk of injury among children treated for ADHD. Injury risk can be considered in the decision-making process about the use of stimulant medication for ADHD.

Am J Psychiatry. 2012;169:195-204.

GENOME-WIDE ANALYSIS OF COPY NUMBER VARIANTS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: THE ROLE OF RARE VARIANTS AND DUPLICATIONS AT 15Q13.3.

Williams NM, Franke B, Mick E, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is a common, highly heritable psychiatric disorder. Because of its multifactorial etiology, however, identifying the genes involved has been difficult. The authors followed up on recent findings suggesting that rare copy number variants (CNVs) may be important for ADHD etiology.

Method: The authors performed a genome-wide analysis of large, rare CNVs (<1% population frequency) in children with ADHD (N=896) and comparison subjects (N=2,455) from the IMAGE II Consortium.

Results: The authors observed 1,562 individually rare CNVs >100 kb in size, which segregated into 912 independent loci. Overall, the rate of rare CNVs >100 kb was 1.15 times higher in ADHD case subjects relative to comparison subjects, with duplications spanning known genes showing a 1.2-fold enrichment. In accordance with a previous study, rare CNVs >500 kb showed the greatest enrichment (1.28-fold). CNVs identified in ADHD case subjects were significantly enriched for loci implicated in autism and in schizophrenia. Duplications spanning the CHRNA7 gene at chromosome 15q13.3 were associated with ADHD in single-locus analysis. This finding was consistently replicated in an additional 2,242 ADHD case subjects and 8,552 comparison subjects from four independent cohorts from the United Kingdom, the United States, and Canada. Presence of the duplication at 15q13.3 appeared to be associated with comorbid conduct disorder.

Conclusions: These findings support the enrichment of large, rare CNVs in ADHD and implicate duplications at 15q13.3 as a novel risk factor for ADHD. With a frequency of 0.6% in the populations investigated and a relatively large effect size (odds ratio=2.22, 95% confidence interval=1.5-3.6), this locus could be an important contributor to ADHD etiology.

Am J Psychiatry. 2012;169:186-94.

INVESTIGATING THE CONTRIBUTION OF COMMON GENETIC VARIANTS TO THE RISK AND PATHOGENESIS OF ADHD.

Stergiakouli E, Hamshere M, Holmans P, et al.

Objective: A major motivation for seeking disease-associated genetic variation is to identify novel risk processes. Although rare copy number variants (CNVs) appear to contribute to attention deficit hyperactivity disorder (ADHD), common risk variants (single-nucleotide polymorphisms [SNPs]) have not yet been detected using genome-wide association studies (GWAS). This raises the concern as to whether future larger-scale, adequately powered GWAS will be worthwhile. The authors undertook a GWAS of ADHD and examined whether associated SNPs, including those below conventional levels of significance, influenced the same biological pathways affected by CNVs.

Method: The authors analyzed genomewide SNP frequencies in 727 children with ADHD and 5,081 comparison subjects. The gene sets that were enriched in a pathway analysis of the GWAS data (the top 5% of SNPs) were tested for an excess of genes spanned by large, rare CNVs in the children with ADHD.

Results: No SNP achieved genome-wide significance levels. As previously reported in a subsample of the present study, large, rare CNVs were significantly more common in case subjects than comparison subjects. Thirteen biological pathways enriched for SNP association significantly overlapped with those enriched for rare CNVs. These included cholesterol-related and CNS development pathways. At the level of individual genes, CHRNA7, which encodes a nicotinic receptor subunit previously implicated in neuropsychiatric disorders, was affected by six large duplications in case subjects (none in comparison subjects), and SNPs in the gene had a gene-wide p value of 0.0002 for association in the GWAS.

Conclusions: Both common and rare genetic variants appear to be relevant to ADHD and index-shared biological pathways.

ANN CLIN PSYCHIATRY. 2012 Feb;24:110-11.

REVIEW OF 'ADHD IN ADULTS. CHARACTERIZATION, DIAGNOSIS, AND TREATMENT'.

Balon R.

Reviews the book, "ADHD in Adults. Characterization, Diagnosis, and Treatment" edited by Jan K. Buitel, Cornells C. Kan and Philip Asherson (2011). The diagnosis and management of attention-deficit/hyperactivity disorder (ADHD) in adults have been and still remain a bit controversial for many clinicians. The book is divided into 7 sections (altogether 25 chapters) and 2 appendices. The authors bring to the reader's attention the fact that although the rate of remission from the full disorder in patients age 18 to 20 is fairly high, nearly one-third of patients still experience some symptoms past this age and the majority of ADHD patients continue to report low levels of functioning despite full symptomatic remission. Despite a lot of theoretical material (eg, genetics, imaging), this is a useful volume that would be appreciated by anybody interested in adult ADHD. Reading this volume also would help to alleviate anxiety among clinicians who are not used to prescribing stimulants and other treatment modalities to adults suffering from ADHD.

.....

ANN CLIN PSYCHIATRY. 2012 Feb;24:23-37.

THE CANADIAN NETWORK FOR MOOD AND ANXIETY TREATMENTS (CANMAT) TASK FORCE RECOMMENDATIONS FOR THE MANAGEMENT OF PATIENTS WITH MOOD DISORDERS AND COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Bond DJ, Hadjipavlou G, Lam RW, et al.

Background: Patients with bipolar disorder (BD) and major depressive disorder (MDD) experience adult attention-deficit/hyperactivity disorder (ADHD) at rates substantially greater than the general population. Nonetheless, ADHD frequently goes untreated in this population.

Methods: We reviewed the literature regarding the management of adult ADHD in patients with mood disorders. Because a limited number of studies have been conducted in adults, our treatment recommendations also are partly informed by research in children and adolescents with BD+ADHD or MDD+ADHD, adults with ADHD, and our clinical experience.

Results: In individuals with mood disorders, ADHD is best diagnosed when typical symptoms persist during periods of sustained euthymia. Individuals with BD+ADHD, particularly those with bipolar I disorder (BD I), are at risk for mood destabilization with many ADHD treatments, and should be prescribed mood-stabilizing medications before initiating ADHD therapies. Bupropion is a reasonable first-line treatment for BD+ADHD, while mixed amphetamine salts and methylphenidate also may be considered in patients determined to be at low risk for manic switch. Modafinil and cognitive-behavioral therapy (CBT) are second-line choices. In patients with MDD+ADHD and moderate to severe depression, MDD should be the treatment priority, whereas in mildly depressed or euthymic patients the order may be reversed. First-line treatments for MDD+ADHD include bupropion, an antidepressant plus a long-acting stimulant, or an antidepressant plus CBT. Desipramine, nortriptyline, and venlafaxine are second-line options.

Conclusions: Clinicians should be vigilant in screening for comorbid ADHD in mood disorder patients. ADHD symptoms can respond to appropriately chosen treatments.

.....

Arch Iran Med. 2012;15:76-78.

TOURETTE'S SYNDROME, CHRONIC TICS, AND COMORBID ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN ELEMENTARY STUDENTS.

Amiri S, Fakhari A, Golmirzaei J, et al.

Background: This study estimated the true prevalence of chronic motor and vocal tic disorders, and Tourette's syndrome in students as well as its comorbidity with attention deficit/hyperactivity disorder (ADHD).

Methods: A random clustered sample of elementary students was selected from schools in Tabriz, Iran. Students were screened by Conner's teacher rating scale for ADHD and a detailed history from parents and teachers for the presence of any type of tic was obtained. Next, a clinical interview based on the Kiddie

Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL), and an interview with parents lead to the definitive diagnosis.

Results: A total of 1658 children were evaluated. Vocal tic was observed in 3.2% ((plus or minus)SD = 0.02) students, and was more prevalent in boys. ADHD was diagnosed in 45.5% of these students. Motor tic was observed in 7.3% ((plus or minus)SD = 0.02) of students. Almost half (48.1%) of these students had ADHD. Tourette's syndrome was observed in 1.3% ((plus or minus)SD = 0.01), with a male/female ratio of 3.5:1.

Conclusion: This is the first study to provide the prevalence of chronic tics in elementary school students in Iran. ADHD is more common among students with chronic tics and Tourette's syndrome.

Arq Neuro-Psiquiatr. 2012 Feb;70:83-84.

ATTENTION DEFICIT HYPERACTIVITY DISORDER AND DYSLEXIA: A HISTORY OF OVERLAP.

de Queiroz Campos Araujo AP.

Comments on an article by M. C. Miranda et al. (see record 2012-05485-004). Attention deficit hyperactivity disorder (ADHD) is a frequent disorder like dyslexia. The ADHD worldwide-pooled prevalence is 5.29% and for dyslexia the prevalence ranges from 6 to 9%. Co-morbidity among those two disorders is found in more than a third of ADHD. Furthermore, dyslexia is much more frequent in children with ADHD, up to six times more, as it is among children without ADHD. Overlap here may be more than just the simple case of two common problems occurring by chance in the same person. Both developmental disorders arise from multiple cognitive deficits. Common underlying features may be contributing to the high co-morbidity between these disorders. There are propositions that dyslexia might be related to underlying deficits in attention shifting. Miranda et al. contributes to this field. With the aim of investigating the performance parameters of children with dyslexia (32), children with ADHD (52) and control children (475), using the Conners' Continuous Performance Test, they found some overlapping as both show failure in inhibitory control. Children with ADHD displayed specific deficits compared with the Control Group: a failure in attention (omission error), a failure in inhibitory control (commission error), inconsistency in the response rate (standard error of the reaction time), intra-participant variability, higher level of impulsiveness (perseverations), and poor vigilance (change in the inter-stimulus interval). Those with dyslexia had more errors due to failures in the inhibitory control (commission errors), more variable and anticipatory responses (perseverations), and less response consistency as the test progressed compared to the Control Group. In summary, Miranda et al. advance in understanding the differences and similarities of both disorders in children, as put forward by Dhar et al. in adults with dyslexia as compared to those with ADHD.

Behav Brain Funct. 2012 Jan;8.

CHARACTERIZING OPERANT HYPERACTIVITY IN THE SPONTANEOUSLY HYPERTENSIVE RAT.

Hill JC, Herbst K, Sanabria F.

Background: Operant hyperactivity, the emission of reinforced responses at an inordinately high rate, has been reported in children with ADHD and in the Spontaneously Hypertensive Rat (SHR), the most widely studied animal model of ADHD. The SHR emits behavior at hyperactive levels, relative to a normoactive strain, only when such behavior is seldom reinforced. Because of its dependence on rate of reinforcement, operant hyperactivity appears to be driven primarily by incentive motivation, not motoric capacity. This claim was evaluated in the present study using a novel strategy, based on the organization of behavior in bouts of reinforced responses separated by pauses.

Method: Male SHR, Wistar-Kyoto (WKY) and Wistar rats (WIS) were exposed each to a multiple variable-interval schedule of sucrose reinforcement (12, 24, 48, 96, and 192 s) between post-natal days (PND) 48 and 93. Responding in each schedule was examined in two epochs, PND 58-62 and 89-93. Parameters of response-reinforcement functions (Herrnstein hyperbola) and bout-organized behavior were estimated in each epoch.

Results: SHR emitted higher response rates than WKY and WIS, but only when rate of reinforcement was low (fewer than 2 reinforcers per minute), and particularly in the second epoch. Estimates of Herrnstein

hyperbola parameters suggested the primacy of motivational over motoric factors driving the response-rate differential. Across epochs and schedules, a more detailed analysis of response bouts by SHR revealed that these were shorter than those by WKY, but more frequent than those by WKY and WIS. Differences in bout length subsided between epochs, but differences in bout-initiation rate were exacerbated. These results were interpreted in light of robust evidence linking changes in bout-organization parameters and experimental manipulations of motivation and response-reinforcement contingency.

Conclusions: Operant hyperactivity in SHR was confirmed. Although incentive motivation appears to play an important role in operant hyperactivity and motoric capacity cannot be ruled out as a factor, response-bout patterns suggest that operant hyperactivity is primarily driven by steeper delay-of-reinforcement gradients. Convergence of this conclusion with theoretical accounts of ADHD and with free-operant performance in children with ADHD supports the use of SHR as an animal model of ADHD.

.....

Biol Psychiatry. 2012 Mar;71:443-50.

ABNORMAL FUNCTIONAL CONNECTIVITY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Tomasi D, Volkow ND.

Background: Attention-deficit/hyperactivity disorder (ADHD) is typically characterized by symptoms of inattention and hyperactivity/impulsivity, but there is increased recognition of a motivation deficit too. This neuropathology may reflect dysfunction of both attention and reward-motivation networks.

Methods: To test this hypothesis, we compared the functional connectivity density between 247 ADHD and 304 typically developing control children from a public magnetic resonance imaging database. We quantified short- and long-range functional connectivity density in the brain using an ultrafast data-driven approach.

Results: Children with ADHD had lower connectivity (short- and long-range) in regions of the dorsal attention (superior parietal cortex) and default-mode (precuneus) networks and in cerebellum and higher connectivity (short-range) in reward-motivation regions (ventral striatum and orbitofrontal cortex) than control subjects. In ADHD children, the orbitofrontal cortex (region involved in salience attribution) had higher connectivity with reward-motivation regions (striatum and anterior cingulate) and lower connectivity with superior parietal cortex (region involved in attention processing).

Conclusions: The enhanced connectivity within reward-motivation regions and their decreased connectivity with regions from the default-mode and dorsal attention networks suggest impaired interactions between control and reward pathways in ADHD that might underlie attention and motivation deficits in ADHD.

.....

Biol Psychiatry. 2012 Mar;71:467-73.

DIFFERENTIAL SENSITIVITY TO PSYCHOSTIMULANTS ACROSS PREFRONTAL COGNITIVE TASKS: DIFFERENTIAL INVOLVEMENT OF NORADRENERGIC A_1 - AND A_2 -RECEPTORS.

Berridge CW, Shumsky JS, Andrzejewski ME, et al.

BACKGROUND: Psychostimulants improve a variety of cognitive and behavioral processes in patients with attention-deficit/hyperactivity disorder (ADHD). Limited observations suggest a potentially different dose-sensitivity of prefrontal cortex (PFC)-dependent function (narrow inverted-U-shaped dose-response curves) versus classroom/overt behavior (broad inverted U) in children with ADHD. Recent work in rodents demonstrates that methylphenidate (MPH; Ritalin) elicits a narrow inverted-U-shaped improvement in performance in PFC-dependent tests of working memory. The current studies first tested the hypothesis that PFC-dependent tasks, in general, display narrow dose sensitivity to the beneficial actions of MPH.

METHODS: The effects of varying doses of MPH were examined on performance of rats in two tests of PFC-dependent cognition, sustained attention and attentional set shifting. Additionally, the effect of pretreatment with the α_1 -antagonist prazosin (.5 mg/kg) on MPH-induced improvement in sustained attention was examined.

RESULTS: MPH produced a broad inverted-U-shaped facilitation of sustained attention and attentional set shifting. Prior research indicates α_1 -receptors impair, whereas α_2 -receptors improve, working memory. In

contrast, attentional set shifting is improved with α_1 -receptor activation, whereas α_2 -receptors exert minimal effects in this task. Given the similar dose sensitivity of sustained attention and attentional set-shifting tasks, additional studies examined whether α_1 -receptors promote sustained attention, similar to attentional set shifting. In these studies, MPH-induced improvement in sustained attention was abolished by α_1 -receptor blockade.

CONCLUSIONS: PFC-dependent processes display differential sensitivity to the cognition-enhancing actions of psychostimulants that are linked to the differential involvement of α_1 - versus α_2 -receptors in these processes. These observations have significant preclinical and clinical implications.

.....
Biol Psychiatry. 2012 Mar;71:434-42.

DIMENSIONAL BRAIN-BEHAVIOR RELATIONSHIPS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Chabernaud C, Mennes M, Kelly C, et al.

Background: Emerging neuroscientific and genetic findings emphasize the dimensional rather than the categorical aspects of psychiatric disorders. However, the integration of dimensional approaches within the current categorical diagnostic framework remains unclear. Here, we used resting state functional magnetic resonance imaging to examine whether dimensional measures of psychiatric symptomatology capture brain-behavior relationships unaccounted for by categorical diagnoses. Additionally, we examined whether dimensional brain-behavior relationships are modified by the presence of a categorically defined illness, attention-deficit/hyperactivity disorder (ADHD).

Methods: Resting state functional magnetic resonance imaging scans were collected from 37 typically developing children (aged 10.2 ± 2 ; 21 female subjects) and 37 children meeting DSM-IV Text Revision criteria for ADHD (9.7 ± 2 ; 11 female subjects). Parent-rated Child Behavior Checklist Externalizing and Internalizing scores served as dimensional measures in our analyses of default network (DN) resting state functional connectivity (RSFC).

Results: Regardless of diagnosis, we observed several significant relationships between DN RSFC and both internalizing and externalizing scores. Increased internalizing scores were associated with stronger positive intra-DN RSFC, while increased externalizing scores were associated with reduced negative RSFC between DN and task-positive regions such as dorsal anterior cingulate cortex. Several of these brain-behavior relationships differed depending on the categorical presence of ADHD.

Conclusions: Our findings suggest that while categorical diagnostic boundaries provide an inadequate basis for understanding the pathophysiology of psychiatric disorders, psychiatric illness cannot be viewed simply as an extreme of typical neural or behavioral function. Efforts to understand the neural underpinnings of psychiatric illness should incorporate both categorical and dimensional clinical assessments.

.....
Biol Psychiatry. 2012 Mar;71:474-81.

PRE- AND PERINATAL RISK FACTORS IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Halmly A, Klungsoyr K, Skjerve R, et al.

Background: Attention-deficit/hyperactivity disorder (ADHD) is a prevalent and disabling lifespan disorder, but little is yet known about risk factors for ADHD persisting beyond adolescence. The present study investigates the association between pregnancy and birth complications and ADHD in adulthood.

Methods: We used data from the Medical Birth Registry of Norway to compare pre-and perinatal risk factors among 2323 adults approved for medical treatment for ADHD, with the remaining population born during the same years, 1967-1987, and surviving into adulthood ($n = 1,170,073$). Relative risks (RR) adjusted for potential confounders were calculated.

Results: Preterm (< 37 weeks of gestation) and extremely preterm birth (< 28 weeks of gestation) were associated with 1.3- and 5-fold increased risks of ADHD, respectively. Birth weights < 2500 g and < 1500 g also increased the risk of ADHD (RR: 1.5, 95% confidence interval [CI]: 1.2-1.8, and RR: 2.1, 95% CI: 1.3-3.6, respectively). Five-minute Apgar scores < 4 and < 7 were associated with 2.8- and 1.5-fold increased risks of persisting ADHD, respectively. Maternal epilepsy (RR: 1.7, 95% CI: 1.1-2.7) and offspring oral cleft

(RR: 2.8, 95% CI: 1.6-4.9) occurred more frequently among adult ADHD patients. Conclusions: This is the first population-based study of pre-and perinatal risk factors in adults with ADHD. We show that low birth weight, preterm birth, and low Apgar scores increase the risk of ADHD, persisting up to 40 years after birth. The increased risk of ADHD related to oral cleft and to maternal epilepsy warrants further investigation to explore possible causal mechanisms.

.....

Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement. 2012 Jan;44:59-69.

PRADICTEURS DES PRATIQUES PARENTALES: COGNITIONS SOCIALES PARENTALES ET COMPORTEMENT DES ENFANTS TDAH.

Beaulieu MC, Normandeau S.

The purpose of this study was to examine the association between parental social cognitions (parental causal attributions, parental self-efficacy) and the behavioural characteristics of their child (ADHD subtypes, comorbidity, oppositional and anxiety/shy symptoms). Participants were 110 families with a child with ADHD (ADHD-I: n = 31, ADHD-H: n = 11, ADHD-C: n = 68). Multiple regressions show that parental self-efficacy is associated with more use of appropriate discipline, praise and incentives, positive verbal discipline, and less use of harsh and inconsistent discipline and physical punishment. Results also show that parental causal attributions for the child's misbehaviour to their own efforts are a predictor of positive verbal discipline whereas parents' causal attributions for the child's misbehaviour to the child's lack of efforts are a predictor of harsh and inconsistent discipline. Parents' perception of their child's oppositional symptom is a predictor of appropriate discipline and positive verbal discipline. Finally, children's comorbidity is a predictor of harsh and inconsistent discipline. The findings of this study highlight the importance of parental self-efficacy, because from all the variables studied, it shows the strongest association with positive and negative parenting practices. No association between ADHD subtype and parenting practices were observed. Implications of these results are explored in the discussion.

.....

Canadian Journal of Behavioural Science/Revue canadienne des sciences du comportement. 2012 Apr;44:146-57.

EFFICACIT D'UN PROGRAMME DE CONSULTATION POUR LES ENSEIGNANTS DU PRIMAIRE VISANT FAVORISER L'INCLUSION SCOLAIRE DES ENFANTS AYANT UN TDAH.

Nadeau MF, Normandeau S, Mass L.

Classroom management interventions, such as behaviour and academic strategies, are well-established interventions for improving social behaviour and academic skills of children with ADHD (DuPaul & Eckert, 1997; Hoza et al., 2008; Pelham & Fabiano, 2008). Bridging the gap between research and practice raises the question of the practicality of interventions and the necessity to support teachers in the sustained implementation of appropriate classroom management strategies. The aim of this research is to evaluate the effectiveness of a consultation-based program for teachers (CPT) of elementary schoolchildren with ADHD, using a problem-solving and a functional assessment approaches. A total of 37 child-teacher pairs participated in the study. All children were diagnosed as ADHD and received a stimulant medication treatment. The parents of some of these children had previously participated in a parent-training program (PTP). The final group composition is: Medication (M) (n = 4); M + PTP (n = 11), M + CPT (n = 11), M + PTP + CPT (n = 11). Findings confirm the effectiveness of the CPT above and beyond M and M + PTP to avoid an intensification of inappropriate behaviours and to improve academic performance of ADHD children. Results also indicate that teachers that both integrated CPT and received prior professional development on ADHD show a significant improvement of their classroom management strategies. Overall findings offer valuable information for discussing clinical implications for the psychosocial treatment of ADHD children.

Child & Family Behavior Therapy. 2012 Jan;34:33-52.

MATERNAL ADHD: PARENT-CHILD INTERACTIONS AND RELATIONS WITH CHILD DISRUPTIVE BEHAVIOR.

Zisser AR, Eyberg SM.

This study examined how ADHD symptoms in mothers of children with ADHD relate to their behavior during parent-child interactions and to their children disruptive behavior. Findings indicated that mothers retrospective self-ratings of ADHD symptoms were related to their present negativity during parent-led play. Mothers self-ratings of current inattentive symptoms were related to their impatience during child-led play. Maternal ADHD symptoms were also related to their ratings of their children ADHD and oppositional-defiant behaviors. Identifying relations between maternal psychopathology, such as ADHD symptomatology, and behaviors during parent-child interactions may yield clues to additional parent behavioral changes that would enhance treatment outcomes for young children with ADHD.

Child Neuropsychol. 2012 Mar;18:168-81.

FACTORIAL VALIDITY OF THE BEHAVIOR RATING INVENTORY OF EXECUTIVE FUNCTION (BRIEF)-TEACHER FORM.

Peters C, Algina J, Smith SW, et al.

Deficits in executive function (self-regulatory mechanisms) have been linked with many childhood disorders including attention deficit/hyperactivity disorder (ADHD), autism spectrum disorder, and conduct disorder. Executive functioning is typically assessed by individually administering performance-based measures in a clinical setting. However, performance-based methods are inefficient for school psychologists. A more feasibly implemented measure for applied settings is the Behavior Rating Inventory of Executive Function (BRIEF), but researchers have raised questions about the internal validity and the proposed factors. In this study, we examined the factor structure of the teacher form of the BRIEF in a sample of 2,044 general education elementary students and 131 teachers in a multilevel design. Results revealed support for a model with three factors at Level 1 and one general factor at Level 2. The results of our study do not support the current two-factor model of the published BRIEF protocol.

Child Neuropsychol. 2012 Mar;18:190-207.

A COMPARISON OF WORKING MEMORY PROFILES IN SCHOOL-AGED CHILDREN WITH SPECIFIC LANGUAGE IMPAIRMENT, ATTENTION DEFICIT/HYPERACTIVITY DISORDER, COMORBID SLI AND ADHD AND THEIR TYPICALLY DEVELOPING PEERS.

Hutchinson E, Bavin E, Efron D, et al.

The association between specific language impairment (SLI), attention deficit/hyperactivity disorder (ADHD), and working memory (WM) was examined. WM has been implicated in language acquisition and models of ADHD; however, evidence for WM deficits in SLI and ADHD has been inconsistent. The components of Baddeley WM model were investigated in 18 children with SLI, 16 children with ADHD, 11 children with comorbid SLI + ADHD, and 24 typically developing (TD) children. The presence of SLI resulted in deficits in more components of WM than the presence of ADHD indicating that children with SLI are more vulnerable to WM deficits than those with ADHD.

Child Psychiatry Hum Dev. 2012 Apr;43:293-305.

GENETIC RISKS AND ADHD SYMPTOMATOLOGY: EXPLORING THE EFFECTS OF PARENTAL ANTISOCIAL BEHAVIORS IN AN ADOPTION-BASED STUDY.

Beaver KM, Nedelec JL, Rowland MW, et al.

A great deal of research has examined the etiology of attention-deficit/hyperactivity disorder (ADHD) and ADHD symptomatology. Genetic factors are consistently shown to explain a significant proportion of variance in measures of ADHD. The current study adds to this body of research by examining whether genetic liabilities for criminality and alcoholism have effects on the development of ADHD symptomatology. Analyses based on a sample of adoptees drawn from the National Longitudinal Study of Adolescent Health (Add Health) revealed that ADHD symptomatology were elevated among adoptees

who had biological mothers and fathers who had been arrested or who were alcoholics. These results suggest that part of the covariation between ADHD and antisocial behaviors may be the result of genetic factors that have general effects across a range of maladaptive outcomes.

.....
Child Psychiatry Hum Dev. 2012 Apr;43:254-70.

BULLYING AND PEER VICTIMISATION IN ADOLESCENT GIRLS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Sciberras E, Ohan J, Anderson V.

Emerging evidence suggests that adolescent girls with Attention-Deficit/Hyperactivity Disorder (ADHD) are more socially impaired compared with their peers; however, research has yet to elucidate the nature of this impairment. We investigated overt (e.g., physical, such as hitting or kicking or verbal, such as teasing and taunting) and relational (e.g., social manipulation, such as social exclusion) bullying and victimisation in adolescent girls with and without ADHD. Adolescent girls (mean age = 15.11) with (n = 22) and without (n = 20) ADHD and their primary caregivers completed measures of overt/relational bullying and victimisation and social impairment. Adolescent girls with ADHD experienced more social problems and more relational and overt victimisation than adolescent girls without ADHD. Although adolescent girls with ADHD engaged in more overt and relational bullying than adolescent girls without ADHD, this difference was not statistically significant. Oppositional Defiant Disorder symptoms appeared to be more strongly related to bullying behaviour, while victimisation appeared to be more strongly related to ADHD.

.....
Clin Child Psychol Psychiatry. 2012 Jan;17:121-39.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER, DRUG COMPANIES AND THE INTERNET.

Mitchell J, Read J.

This study investigated the influence of drug-company funding on websites about attention-deficit hyperactivity disorder (ADHD). Websites in the top 60 for either Google or Yahoo!Xtra with information about causation and treatment were analysed. Likert scales, based on those used in previous similar studies, were developed to rate aetiological explanations and recommended treatment approaches, on a dimension from psycho-social to biological. Overall, the quality of information on websites was poor with a strong bias towards bio-genetic aetiological explanations of ADHD. Twenty-one of the 57 websites (37%) were funded by drug companies. The drug-company funded (DCF) websites were significantly more likely than non-DCF websites to recommend medication rather than psycho-social treatments. The selective lack of consideration of psycho-social treatments by DCF websites is discussed in relation to the relevant research literature, including the evidence in favour of a multimodal approach. The findings, which are consistent with previous similar studies in relation to websites about adult mental health problems, confirm that the pharmaceutical industry is seeking to influence public opinion via the internet.

.....
CNS Neuroscience & Therapeutics. 2012 Feb;18:126-32.

IS RESPONSE TO OROS METHYLPHENIDATE TREATMENT MODERATED BY TREATMENT WITH ANTIDEPRESSANTS OR PSYCHIATRIC COMORBIDITY? A SECONDARY ANALYSIS FROM A LARGE RANDOMIZED DOUBLE BLIND STUDY OF ADULTS WITH ADHD.

Biederman J, Mick E, Spencer T, et al.

Aims: The main aim of this post hoc analysis was to evaluate whether response to osmotic release oral system (OROS) methylphenidate (OROS-MPH) was moderated by the concomitant use of antidepressants in attention-deficit/hyperactivity disorder (ADHD) adults stabilized on these medicines for the treatment of depression or anxiety disorders, or a history of mood, anxiety, or substance use disorders.

Methods: Two hundred and ninety-six subjects were screened for participation; 227 were randomized (112 to OROS-MPH and 115 to placebo), and 223 were analyzed (N = 109 and N = 114 for OROS-MPH and placebo, respectively). Subjects with anxiety disorders and depression treated with a stable medication regimen of non-MAOI antidepressants or benzodiazepines for at least 3 months could be enrolled in the

study. Subjects currently receiving pharmacotherapy for anxiety disorders or depression were required to have Hamilton-Depression and Hamilton-Anxiety rating scales below 15 (mild range).

Results: Concomitant antidepressant use at baseline was not associated with ADHD response, OROS-MPH dose, study completion rate, adverse effects, or exacerbation of anxiety/depression. We did find nominally significant evidence that a life-time history of mood ($P = 0.09$) or anxiety ($P = 0.04$) disorders was a moderator of ADHD symptoms and that a lifetime history of substance use disorder ($P = 0.02$) was a potential moderator of dose at endpoint.

Discussion and Conclusions: We found few moderating effects in this large clinical trial of OROS-MPH in adults with ADHD, which supports the robustness of the clinical response to OROS-MPH in adult ADHD despite variable clinical pictures.

.....

Dev Neuropsychol. 2012 Feb;37:119-33.

MULTIPLE TASK INTERFERENCE IS GREATER IN CHILDREN WITH ADHD.

Ewen JB, Moher JS, Lakshmanan BM, et al.

There is considerable lay discussion that children with attention deficit hyperactivity disorder (ADHD) have increased difficulty with multitasking, but there are few experimental data. In the current study, we examine the simultaneous processing of two stimulus-response tasks using the Psychological Refractory Period (PRP) effect. We hypothesized that children with ADHD would show a greater PRP effect, suggesting a prolonged bottleneck in stimulus response processing. A total of 19 school-aged children with ADHD showed a prolonged PRP effect compared with 25 control children, suggesting a higher cognitive cost in ADHD for multitasking.

.....

Developmental Psychology. 2012 Mar;48:567-74.

DOPAMINE TRANSPORTER GENE MODERATES RESPONSE TO BEHAVIORAL PARENT TRAINING IN CHILDREN WITH ADHD: A PILOT STUDY.

van den Hoofdakker BJ, Nauta MH, Dijck-Brouwer DAJ, et al.

There is great variability in the degree to which children with attention deficit/hyperactivity disorder (ADHD) improve through behavioral treatments. This study investigates the influence of the dopamine transporter gene (SCL6A3/DAT1) on outcome of behavioral parent training (BPT). Study subjects were a subsample ($n = 50$, for whom DAT1 genotypes were available) of a randomized controlled BPT effectiveness study ($N = 94$) comparing BPT plus ongoing routine clinical care (RCC) versus RCC alone in referred children (4-12 years old) with ADHD. Treatment outcome was based on parent-reported ADHD symptoms and behavioral problems. Presence of 2 versus no or 1 DAT1 10-repeat allele served as moderator variable. Time — Treatment — Genotype effect was analyzed with repeated-measures analysis of variance, controlling for baseline medication status. Results indicate that DAT1 moderated treatment response ($p = .009$). In children with no or 1 DAT1 10-repeat allele, superior treatment effects of BPT + RCC compared with RCC alone were present ($p = .005$), which was not the case in children with 2 DAT1 10-repeat alleles ($p = .57$). Our findings suggest that genetic differences in DAT1 in children with ADHD influence their susceptibility to a behavioral intervention directed at shaping their environment through their parents. The role of the dopamine system in motivation and learning and in the aberrant sensitivity to reinforcement in children with ADHD may explain this moderating effect, given that the management of contingencies is typically addressed in BPT.

.....

Disability & Society. 2012 Mar;27:263-75.

REFLECTING ON ATTENTION-DEFICIENT HYPERACTIVITY DISORDER AND DISABLEMENT IN EDUCATION WITH ERIC FROMM.

Veck W.

Drawing upon the thought of Eric Fromm, this paper argues that efforts to understand and counter behaviour that causes difficulties in education should begin in a critical and reflective engagement with both

the conditions of human freedom and the character of educational institutions and society as a whole. Fromm critique of dominating ideas about good mental health within capitalistic societies is examined in relation to disablement and attention-deficient hyperactivity disorder. A study of a sixth-form college in the south of England elucidates connections between Fromm insights into social psychology and disablement as a process of oppression.

.....
 Dissertation Abstracts International Section A: Humanities and Social Sciences. 2012;72.

ASSESSMENT AND INTERVENTION PRACTICES FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD): A NATIONAL SURVEY OF SCHOOL PSYCHOLOGISTS.

Borick TJ.

This study examined school psychologists' assessment and intervention practices regarding ADHD. Five hundred school psychologists who practiced in a school setting and were regular members of the National Association of School Psychologists were randomly selected to complete and return a questionnaire titled Assessment and Intervention Practices for ADHD: A National Survey of School Psychologists. The instrument, which collected data on demographics, assessment practices, diagnostic practices, and intervention practices, was developed by the author for the purpose of this study. Data were analyzed using descriptive statistics, Pearson *r* and Spearman *rho* correlation coefficients, binary logistic regression, and Mann-Whitney U tests. With a return rate of 49.2%, the main finding of this study was that the majority of school psychologists are conducting assessments and providing interventions for ADHD. Results showed that 77.2% of the respondents conduct ADHD assessments and 90.7% provide ADHD interventions, but only 26.8% reported that they provide an ADHD diagnosis. The majority of respondents indicated that they are well-trained, qualified, and confident within ADHD assessment, diagnostic, and intervention practices. The most notable correlations were between level of education, licensure, and indication of providing a diagnosis of ADHD. A relationship existed between years of experience and beliefs about being well-trained to assess for ADHD and to provide ADHD interventions. Results showed that licensure was a significant predictor in determining if school psychologists were more likely to conduct assessments for ADHD. Level of education, SES, national certification, and beliefs about being qualified to diagnose ADHD were significant in differentiating whether or not school psychologists were more likely to provide a diagnosis of ADHD when warranted. State certification and beliefs about being qualified to assess for ADHD to determine if the disorder exists were significant in differentiating whether or not school psychologists were more likely to provide interventions for ADHD. Significant differences were found for level of education, licensure, confidence to assess and diagnose ADHD, and qualifications to diagnose ADHD and assess for ADHD to determine services and if the disorder exists between the groups of school psychologists who provide and do not provide an ADHD diagnosis.

.....
 Dissertation Abstracts International Section A: Humanities and Social Sciences. 2012;72.

EXPLORING PARENT ACCULTURATION AND STUDENT CHARACTERISTICS THAT ARE RELATED TO TEACHER ACADEMIC RATINGS AMONG LATINO STUDENTS WITH SYMPTOMS OF ADHD.

Cintron J.

Given that children who have academic and/or mental health issues exhibit underachievement, measures completed by teachers become a primary source of information for school psychologists (DuPaul & Stoner, 2003; Fuchs & Fuchs, 2006; Sherman, Rasmussen, & Baydala, 2008). However, teacher measures have been called into question because of the discrepancies between teacher academic ratings and student scores on direct (Feinberg & Shapiro, 2009; Hamilton & Shinn, 2003) and norm referenced measures (Eaves et al., 1994). The objective of this study was to examine the validity of the Academic Competence Evaluation Scales (ACES; DiPerna & Elliott, 1999), a teacher academic measure, used on a Latino population referred for Attention Deficit Hyperactivity Disorder (ADHD). Further, the current study explored whether teachers' ratings of their Latino students' academic competence were related to the parents' acculturation and/or students' characteristics, such as language proficiency, grade retention and special education status, gender, socioeconomic status, and ADHD diagnosis. The current study was conducted in conjunction with a study investigating ADHD among school-age children under the auspices of Children's

Hospital of Philadelphia (CHOP). Participants included 60 parents and their children who received an evaluation for ADHD through CHOP. The study used parent acculturation scales, student standardized scores, and teacher academic ratings. Pearson correlations, analysis of variance, and independent samples t-tests were employed. Pearson correlations were used to analyze the relationship between teachers' academic ratings and students' standardized achievement scores, language proficiency, and family socioeconomic status. Results indicated that there were statistically significant correlations between teachers' academic ratings and students' standardized achievement scores. Results also indicated that student characteristics, such as language proficiency were related to the Reading/Language Arts ACES; and socioeconomic status was related to teachers' ratings of the overall ACES, Reading/Language Arts, and Mathematics, but not Critical Thinking. A one way ANOVA was employed between teachers' academic ratings and parents' acculturation level. Results indicated that there were no differences in teacher academic ratings and parent's level of acculturation. An independent samples t-test was employed to analyze the difference in teachers' academic ratings and students' grade retention and special education status, and ADHD diagnosis. Due to the restricted range of variability within the special education status variable, it was impossible to interpret this, and instead grade retention was analyzed. Results indicated that there were no significant differences detected between teacher academic ratings and students' grade retention or ADHD diagnosis. An independent samples t-test was also used to examine the difference between male and female students in their teacher academic ratings. Results indicated that teachers rated their male students slightly higher on the overall academic and Mathematics competence scales as compared with the female students, but not for the Reading/Language Arts and Critical Thinking. Findings suggest that teachers' academic ratings are consistent with standardized achievement scores of Latino students referred for ADHD. Further, Latino students' language proficiency, family SES, and gender may affect teachers' academic ratings. Implications for the major findings, limitations and suggestions for further research, and implications for school psychologists and educators are discussed.

.....

Dissertation Abstracts International Section A: Humanities and Social Sciences. 2012;72.

IDENTIFYING THE CHARACTERISTICS OF FETAL ALCOHOL SPECTRUM DISORDERS (FASD) AMONG CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Someki F.

Fetal alcohol spectrum disorder (FASD), characterized by various levels of dysmorphia and behavioral and cognitive dysfunctions, is the result of prenatal alcohol exposure. FASD characteristics can be masked by many other conditions. As a result, early identification of FASD is often difficult, leading to a delay of children with FASD receiving necessary services. However, screening children with attention-deficit/hyperactivity disorder (ADHD), which is the major comorbid disorder of FASD, may enable the identification of children with FASD earlier than screening all children in schools. Therefore, the purpose of this study was to examine the differences between children with ADHD only and children with FASD and ADHD in terms of adaptive functioning, behavioral characteristics, and academic performance that impact school outcomes and can be recognized in classrooms. This study conducted a review of the medical records of 149 individuals with single ADHD diagnosis and 189 individuals with dual diagnosis of FASD and ADHD ($M[\text{sub}]age[\text{sub}] = 11.25, SD = 2.12$). Results of analysis of covariance analysis indicated: (1) no difference in adaptive functioning between the dual diagnosis group and the single diagnosis group, (2) the dual diagnosis group exhibited significantly more externalizing behaviors than the single diagnosis group, but the difference between the two groups regarding internalizing behaviors was not significant, (3) there was no significant differences between the two groups on reading and mathematics. Differences in characteristics between the two groups and implications for future research are also discussed.

Dissertation Abstracts International Section A: Humanities and Social Sciences. 2012;72.

INTERPRETING THE RELATION OF INTERNAL BEHAVIOR, EXTERNAL BEHAVIOR, ACADEMIC BEHAVIOR, AND SOCIAL BEHAVIORS IN STUDENTS DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Hajghassemali S.

Professionals who diagnose ADHD must follow the criteria set forth by the Diagnostic and Statistical Manual of Mental Disorders. They not only base their evaluation on characteristic behaviors, but also on a series of medical, behavioral, and educational assessments. The National Institute of Mental Health's (NIMH) Multimodal Treatment Study of Children with and without Attention-Deficit/Hyperactivity Disorder was a multisite study designed to evaluate the primary treatments for ADHD. The NIMH database is composed of a large number of assessments that were given to children/adolescents, parents, and teachers. The Conners, SNAP-IV, and Harter assessments were the only measures completed by all three groups. The purpose of this study was to determine if the responses to the three assessments from adolescents, parents, and teachers resulted in four behavioral constructs: Academic Behavior, External Behavior, Internal Behavior, and Social Behavior. The results of a factor analysis identified Social Behavior in all assessments, Academic Behavior in all assessments except for the Harter teacher assessment, Internal Behavior as evident only in the adolescent assessment for Conners and SNAP-IV, and External Behavior as evident in all parent assessments as well as the adolescent assessments for Conners and SNAP-IV. The assessments of adolescents had two similar constructs (Social and Academic Behavior); those completed by parents had three similar constructs (Academic, Social, and External Behavior); and those completed by teachers had two common constructs (Academic and External Behavior). A multitrait-multimethod matrix analysis showed a lack of convergent or discriminant validity for the constructs across all assessments. Examination of the scores from the Conners and SNAP-IV adolescent assessments illustrated only moderate agreement in classifying adolescents as having ADHD and Hyperactivity. The results of the study provided another perspective in examining ADHD rating scales that may assist not only in improving psychological assessments but also in developing more accurate forms of diagnosis.

.....

Dissertation Abstracts International Section A: Humanities and Social Sciences. 2012;72.

SHE'S TOO SMART TO HAVE ADHD': FACULTY WILLINGNESS TO ACCOMMODATE STUDENTS WITH ADHD AT ELITE POSTSECONDARY INSTITUTIONS.

Rush TA.

Students with Attention Deficit Hyperactivity Disorder (ADHD) are entering college in increasing numbers. Often, these students have difficulty adjusting to the rigors of college as well as their newly found independence. Students with ADHD at elite colleges and universities face additional pressure to perform, as well as to substantiate their disability diagnosis. Faculty may have apprehensions about the students' ability to perform as well as concerns regarding the academic integrity issues they may associate with the provision of accommodations to this population of students. This study is designed to improve our understanding of faculty members' attitudes towards students with ADHD in their classroom and their willingness to provide the necessary academic accommodations for these students. In this dissertation, I use descriptive and multivariate analysis to examine faculty willingness to provide accommodations for students with ADHD and the effect that gender, rank, field of study and personal experience with ADHD may have on their actions. The results of this study will be used to identify professional development opportunities and institutional support that may best assist faculty members in creating a positive educational experience for college students with ADHD. The findings may also be used to create a program for faculty that will enhance faculty knowledge of ADHD and encourage their acceptance of students with ADHD in their classrooms.

Dissertation Abstracts International: Section B: The Sciences and Engineering. 2012;72.

INTEGRATING SEMANTIC AND EMOTIONAL INFORMATION IN BOYS WITH AND WITHOUT ADHD DURING AN AUDITORY STROOP-LIKE TASK.

Techentin C.

The present study used a word/emotion conflict task to examine interference and laterality effects in boys with and without ADHD. Eighty male participants (39 control, 41 ADHD), were presented dichotically with words ("mad", "sad", "glad", or "fad") pronounced in either congruent or incongruent emotional tones (angry, happy, sad or neutral) and asked to identify the presence of a target word or emotion. The dichotic procedure involves presenting pairs of sounds such as words or emotions (a different one in each ear) and asking the listener to identify one or both of the sounds heard. Following the sounds, a specific post cue target word or line drawing face depicting an emotional tone appeared on the screen to indicate the target on each trial. Participants also completed two binaural auditory tasks, the Waterloo Handedness Questionnaire, and the Word Reading Subtest of the WIAT-II-R. The caregiver of the participant completed the Child Behavior Checklist. The hypotheses were: 1) the ADHD group would have lower accuracy and longer reaction times on the identification of both word and emotion targets on the word/emotion conflict task than the control group; 2) interference effects would be larger in the ADHD group than in the control group 3) a right ear advantage (REA) for words and a left ear advantage (LEA) for emotions would be found for the control group; however, either no laterality effects or effects of a smaller magnitude would be found for the ADHD group. Results of the primary analysis indicated that the ADHD group showed poorer identification of both word and emotion targets on the word/emotion conflict task. For both groups, words were identified faster and more accurately than emotions. Additionally, words interfered with the identification of emotions and, although emotions also interfered with the identification of words, the effect was significantly smaller. Regarding laterality effects, no significant REA was found for the identification of words in either the ADHD or the control groups. In both groups, a significant LEA was found for the detection of emotional targets, but only when the emotional tone and word were congruent. Results are discussed in the context of the differences between the Techentin, Voyer, and Klein (in press) conflict task and other conflict tasks. The possibility that the word/emotion conflict task allows a dissociation of the role of attention and working memory processes was also discussed.

.....
Dissertation Abstracts International: Section B: The Sciences and Engineering. 2012;72.

COMPARING THE NEUROCOGNITIVE EFFECTS OF STRATTERA AND FOCALIN ON BEHAVIORAL INHIBITION: AN ERP STUDY.

Khislavsky AL.

This project examined the effects of Dexmethylphenidate and Atomoxetine on behavioral and electrophysiological brain activity associated with behavioral inhibition (BI) in ADHD adults. Method. Young adults (N=29) diagnosed with ADHD were randomly assigned to a treatment regimen of Dexmethylphenidate, Atomoxetine, or psychotherapy. All participants engaged in the Stop-Signal task pre and post-treatment. Response speed, latencies, accuracy, stop signal response times (SSRTs), and Event Related Potentials (ERP) served as outcome measures. Results: Pre-treatment weaknesses in oral language skills were observed. Exposure to overall treatment was associated with faster SSRTs and longer SOAs during successful inhibition. Post-treatment increases in right frontal N2 amplitudes, decreased parietal N2 amplitudes, and faster parietal N2 onset was observed. Post-treatment increase in frontal P2 amplitudes, and decreased central and parietal P2 amplitudes were also evident. No significant BI-related behavioral or ERP changes were observed in Atomoxetine-exposed participants. Dexmethylphenidate-exposed participants showed increased zenith N2 and P2 amplitudes, as well as right frontal N2 amplitudes during successful inhibition. Treatment with Dexmethylphenidate was associated with decreased parietal P2 amplitudes. Changes in P2 amplitudes most clearly distinguished the three treatment conditions. Conclusions. Overall treatment improved participants ability to anticipate environmental feedback and facilitated faster inhibition. Dexmethylphenidate notably affected BI-related frontal and parietal electrophysiology of ADHD adults, whereas Atomoxetine did not. Dexmethylphenidate effectively facilitated the function of fronto-parietal neural networks associated with preperceptual attentional and inhibitory processes. Dopaminergic, deep-brain basal ganglia circuits were implicated as central to BI-related deficits in young adults with ADHD.

Dissertation Abstracts International: Section B: The Sciences and Engineering. 2012;72.

NON-MEDICAL PRESCRIPTION STIMULANT USE AMONG SORORITY AND FRATERNITY COLLEGE POPULATIONS: RELATIONSHIP WITH PSYCHOLOGICAL VARIABLES.

Dussault C.

Research findings suggest that approximately 2-10% of college students display symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD) (McKee, 2008). Pharmacological interventions, such as stimulants, are most often used to treat ADHD symptoms (Conner, 2006). The non-medical use of prescription stimulants among college students has become evident in recent years (DeSantis, Noar & Webb, 2010). Preliminary studies suggest that students who are members of fraternities and sororities tend to report higher rates of non-medical stimulant use and that psychological variables may also be related to non-medical stimulant use (Weyandt et al., 2009). The present study examined non-medical stimulant use among fraternity/sorority members and non-members and explored whether psychological variables were related to non-medical stimulant use among 1,033 undergraduate students from five universities located in the northeastern, southeastern, northwestern, southwestern, and midwestern regions of the United States. It was hypothesized that sorority/fraternity members would report higher ratings of self-reported prescription stimulant use, perception of prevalence of stimulant use among peers, knowledge of atypical stimulant use among peers, and perception of safety of stimulants. It was also hypothesized that college students who reported higher ratings of depression, anxiety, and stress would also reported higher ratings of non-medical stimulant use. The final hypothesis was that college students who reported higher ratings of internal distractibility, internal restlessness, internal impulsivity, and internal disorganization would report higher ratings of non-medical stimulant use. Results revealed that fraternity and sorority members reported a higher rate of non-medical stimulant use than non-members. Regression analyses revealed that higher ratings of anxiety and stress significantly predicted non-medical stimulant use and that higher ratings of internal impulsivity and internal restlessness also significantly predicted non-medical stimulant use.

.....

Dissertation Abstracts International: Section B: The Sciences and Engineering. 2012;72.

EMPIRICALLY SUPPORTED TREATMENT STRATEGIES FOR CHILDREN DIAGNOSED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Phommarath S.

.....

Dissertation Abstracts International: Section B: The Sciences and Engineering. 2012;72.

PREDICTING PARENTING STRESS IN FAMILIES OF CHILDREN WITH ADHD.

Theule J.

This dissertation consists of two studies that investigated predictors of parenting stress as they relate to child ADHD. Two main questions were explored: what is the magnitude of the association between child ADHD and parenting stress, and what are the parent and contextual predictors of parenting stress? In Study 1, meta-analyses were conducted on the association between parenting stress and ADHD. Predictors comprising child, parent, and contextual factors, and methodological and demographic moderators of the relationship between parenting stress and ADHD were examined. Findings from 44 studies were included. In Study 2, I examined parent and contextual (parental ADHD symptoms, parental education, social support, and marital status) predictors of parent domain parenting stress (parental distress) as a function of teacher-reported child ADHD symptoms. Results confirmed that parents of children with ADHD experience more parenting stress than parents of nonclinical control children, and that severity of child ADHD symptoms are associated with parenting stress. Child oppositionality was only predictive of parental distress when reported by parents (not teachers). A post-hoc analysis in Study 2 showed that child factors did not predict parental distress over and above parent and contextual factors. In Study 1, children's co-occurring conduct problems and parental depressive symptomatology predicted parenting stress. Little difference in parenting stress was found between mothers and fathers, but lower parenting stress levels were found in samples with higher proportions of girls. Parental ADHD symptomatology was the strongest predictor of parental distress considered in Study 2. Social support was inversely related to parental distress in Study 2, whereas parental age and education were unrelated to

parental distress. In Study 2, marital status was significantly correlated with parental distress, but was not a significant predictor in the regression. Marital quality was not a significant predictor of parenting stress in Study 1. The large effects observed for parent level predictors suggests that parent factors (i.e., ADHD and depressive symptoms) are critically important in parenting stress and play a primary role in the experience of elevated parenting stress. Future research should give greater consideration to factors outside of the child in increasing parenting stress.

.....
Dissertation Abstracts International: Section B: The Sciences and Engineering. 2012;72.

SLEEP DISTURBANCE IN CHILDREN AND ADOLESCENTS WITH ADHD: UNIQUE EFFECTS OF MEDICATION, ADHD SUBTYPE, AND COMORBID STATUS.

Helwig JR.

ADHD is among the most common childhood psychiatric disorders, estimated to affect approximately 3% to 5% of elementary school-aged children, with 11% to 37% reporting sleep disturbance (American Psychiatric Association, 2000; Owens, Spirito, McGuinn, & Nobile, 2000). Disturbed sleep can result in daytime sleepiness and behavioral difficulties that affect cognitive functions in children, such as attention and memory, as well as exacerbate symptoms of ADHD (Fallone, Owens, & Deane, 1998; Owens, 2005). The primary aim of this study was to determine the prevalence of ICD-9 sleep disorders, prescribed sleep medications, and complaints of sleep problems as diagnosed by pediatric primary care providers in children and adolescents with ADHD across medication status, ADHD subtype, and comorbidity. Electronic medical records were reviewed for 5,881 patients (6-18 years) diagnosed with ADHD and 5,881 patients without ADHD matched by age, gender, and primary care practice and seen for a well-child visit in 2007. Information was collected on ICD-9 sleep diagnoses, medications potentially used to treat sleep disorders, demographic variables, medications commonly used to treat symptoms of ADHD, ICD-9 ADHD subtype, and comorbidity. A secondary analysis was conducted on 556 participants to examine parent and/or patient complaint of sleep problems. Results indicated that children and adolescents with ADHD were more likely to be diagnosed with a sleep disorder or prescribed a sleep medication compared to their pediatric counterparts with no ADHD diagnosis. The significance of medications commonly used to treat symptoms of ADHD, ICD-9 ADHD subtype, and comorbidity as risk factors of sleep disturbance was discussed. This is one of the first studies to highlight the subgroups of children and adolescents with ADHD significantly more likely to exhibit sleep disturbance across a large primary care network. These risk factors and their subsequent effects on the severity of symptoms associated with ADHD must be considered when assessing and treating children and adolescents with ADHD.

.....
Dissertation Abstracts International: Section B: The Sciences and Engineering. 2012;72.

INHIBITORY CONTROL AND REWARD PROCESSES IN CHILDREN AND ADOLESCENTS WITH TRAUMATIC BRAIN INJURY AND SECONDARY ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Sinopoli KJ.

Children with traumatic brain injury (TBI) often experience difficulties with inhibitory control (IC), manifest in both neurocognitive function (poor performance on the stop signal task, SST) and behavior (emergence of de novo attention-deficit/hyperactivity disorder, or secondary ADHD, S-ADHD). IC allows for the regulation of thought and action, and interacts with reward to modify behaviour adaptively as environments change. Children with developmental or primary ADHD (P-ADHD) exhibit poor IC and abnormalities when responding to rewards, yet the extent to which S-ADHD is similar to and different from P-ADHD in terms of these behaviours is not well-characterized. The cancellation and restraint versions of the SST were used to examine the effects of rewards on 2 distinct forms of IC in children and adolescents divided into 4 groups (control, TBI, S-ADHD, and P-ADHD). The SST requires participants to respond to a "go signal" and inhibit their responses when encountering a "stop signal". Rewards improved performance similarly across groups, ages, and cancellation and restraint IC tasks. Adolescents exhibited better IC and faster and less variable response execution relative to children. Significant IC deficits were found in both tasks in the P-ADHD group, with participants with S-ADHD exhibiting intermediate cancellation performance relative to the other groups. Participants with TBI without S-ADHD were not impaired on either task. The relationship

between neurocognitive and behavioral IC was examined by comparing multi-informant ratings of IC across groups, and examining the relationship between ratings and IC performance on the SST. Participants in the control and TBI groups were rated within the typical range, and exhibited fewer problems than either of the ADHD groups, who differed from each other (the P-ADHD group was rated as more inattentive than the S-ADHD group). Moderate to high concordance was found between parent and teacher reports, each of which was poorly concordant with self-reports. The P-ADHD and S-ADHD groups were unaware of their own deficits. Poorer IC predicted parent and teacher classification of participants into ADHD subtypes, although IC did not predict rating concordance. Despite similar clinical presentations, S-ADHD and P-ADHD differ in the phenotypic expression of behaviour and manifestation of IC across contexts.

.....

Dissertation Abstracts International: Section B: The Sciences and Engineering. 2012;72.

LECTURE NOTE-TAKING IN POSTSECONDARY STUDENTS WITH SELF-REPORTED ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Vekaria PC.

Taking and reviewing lecture notes is a prevalent activity that is related to higher test performance in higher education. Yet few studies have focused on the underlying cognitive variables related to lecture note-taking. The current study is an extension of previous studies on lecture note-taking (Peeverly & Garner, 2010; Peeverly et al., 2007; Peeverly et al., 2010) to a disability population, specifically students reporting clinically significant symptoms of ADHD. The primary purpose of this dissertation was to determine if disability differences in lecture note-taking exist, and if they do, to examine the cognitive variables that might explain them. Participants included 22 postsecondary students with self-reported ADHD and 50 postsecondary students who served as controls. Students took notes on a videotaped lecture, reviewed their notes, and took a written recall test. The independent variables included disability status (i.e., self-reported ADHD and non-ADHD), attention, transcription fluency, verbal working memory, and listening comprehension. The dependent variables were quality of notes and essay performance. All measures were group administered. Results revealed that attention and listening comprehension were the only predictors of quality of notes, and disability status, quality of notes, and listening comprehension all predicted essay performance. Students with self-reported ADHD obtained lower scores on a written recall test and a measure of transcription fluency compared to non-ADHD peers, but did not differ in terms of quality of notes, attention, verbal working memory, or listening comprehension. There were also differences between males and females in terms of notes quality and essay performance. Future research should examine the present findings in postsecondary students with confirmed ADHD to test for possible differences in outcomes due to confirmed versus self-reported diagnoses.

.....

Early Child Development and Care. 2012 Jan;182:59-69.

THE RELATIONSHIP BETWEEN FATHER RESIDENCY AND A CHILD'S ADHD SYMPTOMS.

Sulak TN, Barnard-Brak L, Frederick K.

Attention deficit hyperactivity disorder (ADHD) is a commonly diagnosed neuropsychological disorder among school-aged children. The purpose of the current study was to examine the relationship between father residency status and children symptoms of ADHD using a large, nationally representative and community-based sample. To achieve this purpose, structural equation modelling was used to examine the relationship between ADHD symptoms and father residency. The relationship was examined in the context of a sample of typically developing children and a sample of children diagnosed with ADHD. The association between father residency and symptoms of ADHD among typically developing children was significant, but the same relationship among children diagnosed with ADHD was not significant. Father residency appears to share some relationship with symptoms of ADHD, but when symptoms reach the level for a clinical diagnosis, father residency appears to share little relationship with severity of symptoms of ADHD.

Early Childhood Research Quarterly. 2012;27:329-37.

MULTI-METHOD ASSESSMENT OF ADHD CHARACTERISTICS IN PRESCHOOL CHILDREN: RELATIONS BETWEEN MEASURES.

Sims DM, Lonigan CJ.

Several forms of assessment tools, including behavioral rating scales and objective tests such as the Continuous Performance Test (CPT), can be used to measure inattentive and hyperactive/impulsive behaviors associated with Attention-Deficit/Hyperactivity Disorder (ADHD). However, research with school-age children has shown that the correlations between parent ratings, teacher ratings, and scores on objective measures of ADHD-characteristic behaviors are modest at best. In this study, we examined the relations between parent and teacher ratings of ADHD and CPT scores in a sample of 65 preschoolers ranging from 50 to 72 months of age. No significant associations between teacher and parent ratings of ADHD were found. Parent-ratings of both inattention and hyperactivity/impulsivity accounted for variance in CPT omission errors but not CPT commission errors. Teacher ratings showed evidence of convergent and discriminant validity when entered simultaneously in a hierarchical regression. These tools may be measuring different aspects of inattention and hyperactivity/impulsivity.

Emotional & Behavioural Difficulties. 2012 Mar;17:65-82.

HE'S JUST ENTHUSIASTIC. IS THAT SUCH A BAD THING?' EXPERIENCES OF PARENTS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

McIntyre R, Hennessy E.

Parenting a child with Attention Deficit Hyperactivity Disorder (ADHD) is a challenging experience. The hyperactivity, impulsivity and inattention of a child with ADHD often put parenting skills to the test. The present study thus aimed to explore the experiences of parents of children with ADHD in Ireland. Eighteen parents of 7-12-year-old boys with a diagnosis of ADHD took part in open-ended interviews. Thematic analysis was carried out on the interview content. Six major themes were identified: (1) getting your head around ADHD; (2) the child takes over; (3) emotional impact; (4) inconsistency of structural supports; (5) ignorance and discrimination; and (6) its not all bad. Results are discussed in terms of the need to implement family-centred supports for ADHD. The importance of educating the population at large about ADHD is also discussed. Finally, the need to take a more positive, strengths-based approach to ADHD is highlighted.

European Archives of Psychiatry and Clinical Neuroscience. 2012 Feb;262:79-86.

THE ESTIMATED PREVALENCE AND CORRELATES OF ADULT ADHD IN A GERMAN COMMUNITY SAMPLE.

Zwaan M, GruÅ B, MÅ¼ller A, et al.

Little research on the prevalence and correlates of adult ADHD has been conducted outside the United States. The aim of the present study was to estimate the prevalence and correlates of adult ADHD in a large representative sample of the German population aged 18-64 years (n = 1,655). Two self-rating screening instruments to assess childhood and adult ADHD symptomatology were used to estimate the prevalence of ADHD. A 4-item screening tool was used to assess probable cases of current depression and anxiety (Patient Health Questionnaire). The estimated crude prevalence rate of current ADHD was 4.7%. Adult ADHD was significantly associated with lower age, low educational level, unemployment, marital status (never married and divorced), and rural residency. No association was found with gender. Adult ADHD was strongly associated with positive screening results for depression and anxiety. ADHD is a common disorder of adulthood, is associated with significant social impairment and psychiatric co-morbidity, and should receive further research attention

European Child & Adolescent Psychiatry. 2012 Mar;21:141-47.

PRESENCE OF GAD65 AUTOANTIBODIES IN THE SERUM OF CHILDREN WITH AUTISM OR ADHD.

Rout UK, Mungan NK, Dhossche DM.

Antibodies against glutamic acid decarboxylase 65 (GAD65) have been detected in the serum of patients with several neurological disorders. The presence of antibodies against GAD65 has not yet been examined in the serum of patients with neurodevelopmental disorders such as autism or attention-deficit/hyperactivity disorder (ADHD). In this study, GAD65 antibodies and total IgG were assayed in the serum of normal subjects and patients diagnosed with autism or ADHD. GAD65 antibodies were detected in the serum of 15% of children with autism (N = 20), 27% of children with ADHD (N = 15) and of none of the controls (N = 14). The serum of 60% of autistic and 53% of ADHD patients reacted with Purkinje neurons in mouse cerebellum. Serum from 20% of ADHD patients reacted also with the cells in the molecular and granule cell layers and cells in the vicinity of the Purkinje neurons. No association was found between the titer of GAD65 antibodies and total IgG levels, and presence of seizures or mental retardation. None of the ADHD patients were diagnosed with mental retardation. Serum anti-GAD65 antibodies may be a common marker of subgroups of patients with autism and ADHD. Reactions of serum antibodies with the cells in the cerebellum in these patients suggest direct effects on brain function. The subgroup of children with autism and ADHD that tests positive for GAD65 antibodies needs further characterization in a larger study.

European Child & Adolescent Psychiatry. 2012 Mar;21:157-64.

THE BEHAVIOURAL PROFILE OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND OF THEIR SIBLINGS.

Steinhausen HC, Zalli-Weilenmann N, Brandeis D, et al.

The behavioural profiles in N= 69 index children with attention-deficit/hyperactivity disorder (ADHD), N=32 siblings with ADHD, N=35 siblings without ADHD, and N = 36 normal controls were compared by the use of standardized parent and teacher rating scales. The four groups were matched by age and IQ. The behavioural profiles of the two ADHD groups were very similar not only in the behavioural domains of ADHD, but also in scales measuring emotional and conduct problems. Siblings without ADHD shared more similarities with normal controls except for more emotional problems. These general trends were stronger in the parent compared to the teacher ratings. These findings indicate that not only ADHD-related but also other behaviours show a strong family aggregation. The informant differences may reflect context dependent differences in child behaviour and contrast effects particularly in parental ratings.

Eur Child Adolesc Psychiatry. 2012;1-8.

EFFICACY AND SAFETY OF ARIPIRAZOLE IN CHILD AND ADOLESCENT PATIENTS.

Kirino E.

Aripiprazole (APZ) has a unique pharmacological profile, as a partial agonist at the dopamine D2 and serotonin 5HT1A receptors and an antagonist at the serotonin 5HT2A receptor; this drug has few side effects (such as extrapyramidal syndrome, hyperprolactinemia, weight gain, metabolic disorders, and sedation) which are typical problems with other antipsychotic drugs. Due to its high tolerability, it is possible to safely administer it to children and adolescents. Efficacy and tolerability of APZ in children and adolescents have been well demonstrated in many clinical studies, which supported approvals granted by the US Food and Drug Administration (FDA) for schizophrenia, bipolar diseases, and irritability associated with autistic disorder in children and adolescents. APZ is expected to exert sedative, anti-depressive, and anti-anxiety effects, and stabilize emotion. APZ is an antipsychotic drug which could be useful for a wider spectrum of psychiatric disorders in children and adolescents. There is little risk of deterioration (such as disinhibition and acting out) and rapid stabilization is easy to achieve in children and adolescents without definitive diagnoses or with a combination of more than one spectrum of disorders. The effectiveness of APZ in children and adolescents is reviewed and discussed, given its pharmacological profile and the outcomes of various clinical studies. However, randomized or blind studies are still limited, and the majority of reports referenced here are open-label studies and case reports. Conclusions drawn from such studies must be evaluated with caution, and a further accumulation of controlled studies is thus needed.

European Eating Disorders Review. 2012 Jan;20:e103-e107.

ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN A PREBARIATRIC SURGERY SAMPLE.

Gruss B, Mueller A, Horbach T, et al.

Background: Research suggests that obese children, adolescents and adults frequently suffer from attention deficit/hyperactivity disorder (ADHD). The aim of the current study was to estimate the prevalence of adult ADHD in a group of patients with grade 3 obesity (body mass index 40 kg/m²) prior to bariatric surgery.

Method: We assessed 116 patients for childhood and adult ADHD, co occurring psychiatric disorders, severity of depression and daytime sleepiness.

Results: Fourteen participants (12.1%) screened positive for adult ADHD. Even though this rate is higher compared with prevalence rates in representative population samples, it was not elevated compared with a group of morbidly obese individuals in a German general population sample (14.3%). Adult ADHD was associated with greater severity of depressive symptoms and more psychotherapy contact in the past but not with binge eating disorder or daytime sleepiness.

Conclusion: As ADHD appears to be a common condition in morbidly obese individuals, the impact of adult ADHD on postsurgical weight loss needs to be examined. Besides, the causal link between obesity and ADHD in adults should be further investigated.

.....

European Eating Disorders Review. 2012 Jan;20:e91-e95.

BINGE EATING AND TEMPERAMENT IN MORBIDLY OBESE PREBARIATRIC SURGERY PATIENTS.

Maller A, Claes L, Mitchell JE, et al.

The objective of this study was to investigate the relationship between binge eating and temperament variables, controlling for depression and adult attention deficit/hyperactivity disorder (ADHD), in 90 extremely obese individuals. The participants completed questionnaires assessing eating pathology, reactive temperament, effortful control, depression and ADHD and were grouped based on the presence of regular binge eating. Patients reporting regular binge eating did not differ from patients not reporting regular binge eating with respect to BMI, age, gender, the occurrence of adult ADHD and reactive temperament. However, individuals with binge eating exhibited more pathological scores with regard to eating pathology, depression and effortful control. A logistic regression analysis revealed that only eating concerns and reduced effortful control remained significantly associated with regular binge eating. Binge eating in morbidly obese individuals appears to be associated with a lack of effortful control.

.....

Exp Clin Psychopharmacol. 2012 Apr;20:107-17.

DRINKING TO DISTRACTION: DOES ALCOHOL INCREASE ATTENTIONAL BIAS IN ADULTS WITH ADHD?

Roberts W, Fillmore MT, Milich R.

Previous research has shown that social drinkers continue to show attentional bias toward alcohol-related stimuli even after consuming a moderate dose of alcohol. In contrast, little is known about how alcohol acutely affects attentional bias in groups at risk to develop alcohol-related problems, such as adults with attention-deficit/hyperactivity disorder (ADHD). Such individuals may show increased attentional bias following alcohol relative to nonclinical controls. The present study tested this hypothesis by examining acute alcohol effects on attentional bias in 20 social drinkers with ADHD and 20 social drinkers with no history of ADHD. Participants performed a visual-probe task after receiving the following doses of alcohol: 0.64g/kg, 0.32g/kg, and 0.0g/kg (placebo). Those in the ADHD group showed increased attentional bias under active alcohol doses, whereas attentional bias was similar across doses in the control group. Attentional bias predicted ad libitum alcohol consumption during a taste-rating session. This relation was observed only in the ADHD group. These findings indicate that an acute alcohol dose increases attentional bias in adults with ADHD. Further, attentional bias appears to be a predictor of ad libitum consumption in this group.

.....

Expert Rev Neurother. 2012 Jan;12:13-26.

THE USE OF LISDEXAMFETAMINE DIMESYLATE FOR THE TREATMENT OF ADHD.

Childress AC, Sallee FR.

ADHD is a common neurobehavioral disorder characterized by significant impairment in attention, hyperactivity and impulsivity. Symptoms begin in childhood and can persist into adulthood. Current data suggest that abnormal functioning of the prefrontal cortex, cortical and subcortical regions of the brain have roles in ADHD. All currently approved drugs used to treat ADHD enhance dopamine and norepinephrine signals in these regions. Lisdexamphetamine dimesylate (LDX) is a long-acting amphetamine prodrug indicated for the treatment of ADHD and has been shown to be effective in children, adolescents and adults. The prodrug properties of LDX make it a desirable treatment because of its long duration of effect, and low intrasubject and intersubject pharmacokinetic variability, and attenuated response on measures of abuse liability when compared with immediate-release amphetamine. However, LDX is still classified as a controlled substance. In this article, the pharmacokinetic parameters and efficacy and safety of LDX are reviewed.

.....

Front Human Neurosci. 2012 Jan;5.

CAN TASK-SWITCHING TRAINING ENHANCE EXECUTIVE CONTROL FUNCTIONING IN CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER?

Kray J, Karbach J, Haenig S, et al.

The key cognitive impairments of children with attention deficit/hyperactivity disorder (ADHD) include executive control functions such as inhibitory control, task-switching, and working memory (WM). In this training study we examined whether task-switching training leads to improvements in these functions. Twenty children with combined type ADHD and stable methylphenidate medication performed a single-task and a task-switching training in a crossover training design. The children were randomly assigned to one of two groups. One group started with the single-task training and then performed the task-switching training and the other group vice versa. The effectiveness of the task-switching training was measured as performance improvements (relative to the single-task training) on a structurally similar but new switching task and on other executive control tasks measuring inhibitory control and verbal WM as well as on fluid intelligence (reasoning). The children in both groups showed improvements in task-switching, that is, a reduction of switching costs, but not in performing the single-tasks across four training sessions. Moreover, the task-switching training led to selective enhancements in task-switching performance, that is, the reduction of task-switching costs was found to be larger after task-switching than after single-task training. Similar selective improvements were observed for inhibitory control and verbal WM, but not for reasoning. Results of this study suggest that task-switching training is an effective cognitive intervention that helps to enhance executive control functioning in children with ADHD.

.....

Human Psychopharmacology: Clinical and Experimental. 2012 Mar;27:209-16.

ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER AND OTHER PSYCHIATRIC SYMPTOMS IN RECREATIONAL POLYDRUG USERS.

Parrott AC, Hatton NP, Rowe KL, et al.

Aims: Previous research has shown that recreational drug use is associated with more psychiatric symptoms and psychobiological distress. This study investigated whether symptoms of adult attention deficit hyperactivity disorder (ADHD) were also raised in polydrug users.

Methods: We assessed a non-clinical sample of 84 unpaid volunteers (mean age 27.5 years): n = 17 light novice polydrug users; n = 29 moderate polydrug users; and n = 38 non-user controls (14 non-drug users, 24 alcohol/tobacco users). They completed the Symptom Checklist 90 (SCL-90) self-rating inventory for psychiatric symptoms, the Adult ADHD Self-report Scale symptom checklist for adult ADHD, and also the questions on positive moods and sociability. Saliva samples provided a neuroendocrine cortisol measure.

Results: Moderate polydrug users reported significantly higher adult ADHD symptoms and SCL-90 psychiatric symptoms and lower sociability than non-user controls and light polydrug users. Novice light polydrug users did not differ from control groups on any measure. There were no significant group

differences in cortisol. These findings are debated using the interactive diathesis distress model. Psychoactive drugs can affect both mood and cognition. When taken regularly, the drug-induced psychobiological vacillation may exacerbate prior problems with mood stability and attentional cognitive control.

Conclusions: It is not polydrug usage per se, but rather their regular-repeated usage, that is associated with increased signs of psychiatric and attentional hyperactivity distress.

Human Psychopharmacology: Clinical and Experimental. 2012 Jan;27:76-81.

DOUBLE BLIND CONTROLLED TRIAL OF VENLAFAXINE FOR TREATMENT OF ADULTS WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Amiri S, Farhang S, Ghoreishizadeh MA, et al.

Background: Attention deficit/hyperactivity disorder (ADHD) is one of the most common mental disorders beginning in childhood that may continue to adulthood. The purpose of this study was to evaluate the possible therapeutic effect of venlafaxine in adults with ADHD.

Methods: In a double-blind setting, drug-naïve adults with a diagnosis of ADHD based on DSM-IV-TR criteria were randomly selected to receive either venlafaxine (up to 225 mg/day) or a placebo for 6 weeks. The Conners Adult ADHD Rating Scale self-report screening version was administered before and during the treatment at 2-week intervals to measure the therapeutic effects.

Results: The mean age (SD) of patients was 30.5 (8.1) years. Eleven out of 20 patients receiving venlafaxine and 13 out of 21 patients receiving the placebo were male. The two groups were not significantly different in terms of age, educational level, weight, or blood pressure. Significant decrease was observed in both subscales (inattentive, hyperactive/impulsive), total ADHD symptoms score, and ADHD index in both the venlafaxine and the placebo groups. Seventy-five percent of treatment group versus 20% of placebo group met treatment response criteria when defined as a 25% drop in total ADHD score ($p = 0.001$). No serious adverse effects were reported during the trial.

Conclusions: In this double-blind trial, the symptoms of adult ADHD decreased after a 6-week trial of either venlafaxine or a placebo with no significant difference. However, a significant treatment response defined as a 25% drop in ADHD index (measured by a self-report scale) was achieved by venlafaxine. The interpretation of these results is limited by the short duration of follow-up in this study.

Int J Neuropsychopharmacol. 2012 Feb;15:1-13.

LONG-TERM EFFICACY AND SAFETY OUTCOMES WITH OROS-MPH IN ADULTS WITH ADHD.

Buitelaar JK, Trott GtE, Hofecker M, et al.

Methylphenidate (MPH) is widely prescribed for adults with attention deficit hyperactivity disorder (ADHD), but data on long-term treatment and maintenance of effect are lacking. Osmotic release oral system-methylphenidate (OROS-MPH) was evaluated in a 52-wk open-label study in subjects who had previously completed a short-term placebo-controlled trial and short-term open-label extension. Efficacy was assessed using the investigator- and subject-rated Conners Adult ADHD Rating Scales (CAARS:O-SV and CAARS:S-S), and the Clinical Global Impression Severity (CGI-S), Sheehan Disability Scale (SDS) and Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). Subjects completing 52 wk of treatment were eligible for a 4-wk randomized, placebo-controlled withdrawal phase in which loss of treatment effect was assessed using CAARS:O-SV and CGI-S. In the open-label phase ($n = 156$), mean CAARS:O-SV score decreased from baseline by 1.9 ± 7.8 ($p < 0.01$), and small, statistically significant improvements from baseline were observed for CAARS:S-S, CGI-S and SDS. In the double-blind phase (OROS-MPH, $n = 23$; placebo, $n = 22$), CAARS:O-SV increased from double-blind baseline in the OROS-MPH and placebo arms (4.0 ± 7.6 vs. 6.5 ± 7.8 , not statistically significant). Long-term OROS-MPH treatment was well tolerated, and there was no evidence of withdrawal or rebound after discontinuation. In conclusion, the short-term benefits of OROS-MPH continue during long-term open-label treatment. Maintenance of efficacy in a placebo-controlled withdrawal design remains to be confirmed in larger patient populations.

Int J Neuropsychopharmacol. 2012 Feb;15:41-53.

COGNITIVE AND EMOTIONAL BEHAVIOURAL CHANGES ASSOCIATED WITH METHYLPHENIDATE TREATMENT: A REVIEW OF PRECLINICAL STUDIES.

Britton GB.

There is evidence from animal studies that repeated exposure to methylphenidate (MPH), a widely used psychostimulant for the treatment of attention deficit hyperactivity disorder (ADHD), produces behavioural, structural and neurochemical changes that persist long after drug administration has ended. However, the translational utility of much of this work is compromised by the use of drug doses and routes of administration that produce plasma and brain MPH levels that fall outside the clinical range, i.e. experimental parameters more relevant to drug abuse than ADHD. We used PubMed to identify pre-clinical studies that employed repeated MPH administration at low doses in young rodents and examined long-term effects on cognition, emotion, and brain structure and function. A review of this work suggests that repeated MPH treatment during early development can modify a number of cognitive, behavioural and brain processes, but these are reduced when low therapeutic doses are employed. Moreover, MPH sites of action extend beyond those implicated in ADHD. Studies that combined neurobiological and behavioural approaches provide important insights into the mechanisms underlying MPH-produced effects on cognitive and behavioural processes, which may be relevant to MPH therapeutic efficacy. There is an emerging consensus that pharmacological treatment of childhood psychiatric disorders produces persistent neuroadaptations, highlighting the need for studies that assess long-term effects of early developmental pharmacotherapy. In this regard, studies that mimic clinical therapy with rodents are useful experimental approaches for defining the behavioural and neural plasticity associated with stimulant therapy in paediatric populations.

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2012 Apr;40:425-35.

THE EFFECTS OF CHILDHOOD ADHD SYMPTOMS ON EARLY-ONSET SUBSTANCE USE: A SWEDISH TWIN STUDY.

Chang Z, Lichtenstein P, Larsson H.

Research has documented that children and adolescents with attention-deficit/hyperactivity disorder (ADHD) are at increased risk of substance use problems. Few studies, however, have focused on early-onset substance use. This study therefore investigated how the two symptom dimensions of ADHD (hyperactivity/impulsivity and inattention) are associated with early-onset substance use, the role of persistent ADHD for the association, and to what extent the association is influenced by genetic and environmental factors. Twins (1,480 pairs) in the Swedish Twin Study of Child and Adolescent Development were followed from childhood to adolescence. ADHD symptoms were measured at age 8-9 and age 13-14 via parent-report, whereas substance use was assessed at age 13-14 via self-report. Results revealed that hyperactive/impulsive symptoms predicted early-onset sometimes tobacco use (adjusted odds ratios, 1.12, for one symptom count), controlling for inattentive symptoms and conduct problem behaviors. There is no independent effect of inattentive symptoms on early-onset substance use. Children with persistent hyperactivity/impulsivity (defined as scoring above the 75th percentile at both time points) had a pronounced risk of both early-onset tobacco and alcohol use (adjusted odds ratios from 1.86 to 3.35, compared to the reference group). The associations between hyperactivity/impulsivity and early-onset substance use were primarily influenced by genetic factors. Our results indicated that hyperactivity/impulsivity, but not inattention, is an important early predictor for early-onset substance use, and a shared genetic susceptibility is suggested to explain this association.

Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2012 Jan;40:145-57.

REWARD AND PUNISHMENT SENSITIVITY IN CHILDREN WITH ADHD: VALIDATING THE SENSITIVITY TO PUNISHMENT AND SENSITIVITY TO REWARD QUESTIONNAIRE FOR CHILDREN (SPSRQ-C).

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

This study validates the Sensitivity to Punishment and Sensitivity to Reward Questionnaire for children (SPSRQ-C), using a Dutch sample of 1234 children between 6-13 years old. Factor analysis determined that a 4-factor and a 5-factor solution were best fitting, explaining 41% and 50% of the variance respectively. The 4-factor model was highly similar to the original SPSRQ factors found in adults (Punishment Sensitivity, Reward Responsivity, Impulsivity/Fun-Seeking, and Drive). The 5-factor model was similar to the 4-factor model, with the exception of a subdivision of the Punishment Sensitivity factor into a factor with social-fear items and a factor with anxiety items. To determine external validity, scores of three groups of children with attention deficit hyperactivity disorder (ADHD) were compared on the EFA models: ADHD-only (n = 34), ADHD and autism spectrum disorder (ADHD+ASD; n = 22), ADHD and oppositional defiant disorder (ADHD+ODD; n = 22). All ADHD groups scored higher than typical controls on Reward Responsivity and on the anxiety factor (n = 75). The ADHD-only and ADHD+ODD group scored higher than other groups on Impulsivity/Fun-Seeking and Drive, while the ADHD+ASD group scored higher on Punishment Sensitivity. The findings emphasize the value of the SPSRQ-C to quickly and reliably assess a child sensitivity to reinforcement, with the aim to provide individually-tailored behavioral interventions that utilize reward and reprimands.

Journal of Addictive Diseases. 2012 Jan;31:45-59.

ADDICTION IN DEVELOPMENTAL PERSPECTIVE: INFLUENCE OF CONDUCT DISORDER SEVERITY, SUBTYPE, AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER ON PROBLEM SEVERITY AND COMORBIDITY IN ADULTS WITH OPIOID DEPENDENCE.

Carpentier PJ, Knapen LJM, van Gogh MT, et al.

This retrospective cross-sectional study examines whether conduct disorder and attention deficit hyperactivity disorder are associated with problem severity and psychiatric comorbidity in 193 middle-aged, opioid-dependent patients. Conduct disorder history, attention deficit hyperactivity disorder, psychiatric comorbidity, and problem severity were assessed by structured interviews and validated instruments. A conduct disorder history was confirmed in 116 (60.1%) participants. Conduct disorder patients had significantly higher problem severity scores, more frequent comorbid substance use disorders, and more severe psychiatric comorbidity. Attention deficit hyperactivity disorder was found to increase the risk for psychiatric comorbidity. Conduct disorder persistence is a useful model for elucidating complex psychiatric comorbidity of opioid-dependent patients.

Journal of Attention Disorders. 2012 Feb;16:109-17.

SEX DIFFERENCES IN THE MANIFESTATION OF ADHD IN EMERGING ADULTS.

Fedele DA, Lefler EK, Hartung CM, et al.

Objective: Given the mixed literature in the area, the aim of the current study was to determine whether sex differences exist in inattention, hyperactivity, and impairment in college adults with ADHD.

Method: Individuals from three universities were recruited for the study. Participants with (n = 164) and without ADHD (n = 710) completed on-line measures of symptoms and impairment.

Results: College women with ADHD were shown to have higher rates of inattention, hyperactivity, and impairment than college women without ADHD and college men with ADHD. Analyses revealed that women in college who have ADHD experience higher levels of impairment in the following domains: home life, social life, education, money management, and daily life activities.

Conclusion: Overall, clear differences emerged between men and women with ADHD. Implications and future directions are discussed.

Journal of Attention Disorders. 2012 Jan;16:23-33.

READING PERFORMANCE AS A FUNCTION OF TREATMENT WITH LISDEXAMFETAMINE DIMESYLATE IN ELEMENTARY SCHOOL CHILDREN DIAGNOSED WITH ADHD.

Wigal SB, Maltas S, Crinella F, et al.

Background: Medication treatment studies of ADHD have typically not assessed effects on reading performance, although reading difficulties frequently co-occur in children with ADHD. The current study characterizes the effects of lisdexamfetamine dimesylate (LDX; Vyvanse[sup][sup], Shire US Inc.), at peak efficacy, on reading performance in children with ADHD.

Method: Children (ages 6-12; N = 26) with ADHD enrolled in a modified laboratory school study with an open-label, dose-optimization phase of LDX (30-70 mg/d). The Gray Oral Reading Test-4 (GORT-4) with measures of rate, accuracy, and comprehension was administered at baseline and 3-4 hr postdose, following 4 to 5 weeks of optimal dose titration.

Results: Treatment reduced ADHD symptoms. Reading rate was improved, especially among children with higher verbal fluid reasoning without additional symptoms of neurodevelopmental delay. No differences were observed for reading accuracy or comprehension.

Conclusion: Endophenotypical profiles may predict drug effects in specific skill areas, such as reading rate.

.....

Journal of Attention Disorders. 2012 Feb;16:118-27.

DOSE RESPONSE EFFECTS OF LISDEXAMFETAMINE DIMESYLATE TREATMENT IN ADULTS WITH ADHD: AN EXPLORATORY STUDY.

Faraone SV, Spencer TJ, Kollins SH, et al.

Objective: To explore dose response effects of lisdexamfetamine dimesylate (LDX) treatment for ADHD.

Method: This was a 4-week, randomized, double-blinded, placebo-controlled, parallel-group, forced-dose titration study in adult participants, aged 18 to 55 years, meeting Diagnostic and Statistical Manual of Mental Disorders (4th ed., text rev.) criteria for ADHD.

Results: Nearly all participants assigned to an LDX dose achieved their assigned dose with the exception of about 4% of participants assigned to the 50 mg or 14% assigned to the 70 mg doses. Higher doses of LDX led to greater improvements in ADHD-rating scale scores, independent of prior pharmacotherapy. This was evident for both inattentive and hyperactive impulsive symptoms. The authors found some evidence for an interaction between LDX dose and baseline severity of ADHD symptoms.

Conclusion: For LDX doses between 30 and 70 mg/d, the dose response efficacy effect for LDX is not affected by prior pharmacotherapy, but patients with a greater severity of illness may benefit more from higher doses, especially for hyperactive impulsive symptoms. The results do not provide information about doses above 70 mg/d, which is the maximum approved dose of LDX and the highest dose studied in ADHD clinical trials.

.....

Journal of Attention Disorders. 2012 Feb;16:101-08.

EXPLORING THE GENDER GAP IN REFERRALS FOR CHILDREN WITH ADHD AND OTHER DISRUPTIVE BEHAVIOR DISORDERS.

Coles EK, Slavec J, Bernstein M, et al.

Objective: The current study examined the impact of the gender of children with ADHD on teachers perceptions toward inattentive, hyperactive, or oppositional behaviors, and how these perceptions relate to teachers ratings of children impairment and referral recommendations.

Method: Teachers read eight vignettes depicting boys and girls with different subtypes of ADHD, as well as one depicting comorbidity (ADHD + ODD). Teachers then completed measures of impairment, and responded to questions about what services they would likely refer for the child and why.

Results: Teachers rated girls as being significantly more impaired and more in need of services than boys. Regardless of gender, teachers overwhelmingly reported preferring the use of behavior modification for the described child. Also, children who were described with symptoms of ADHD-predominately inattentive

subtype were rated as being the least impaired, while girls described as hyperactive and impulsive were rated by teachers as being the most impaired.

Conclusion: The current study adds to previous literature on gender bias in ADHD referrals by providing evidence for the differential referral of ADHD boys and girls to treatment based on presentation of symptoms.

Journal of Attention Disorders. 2012 Jan;16:13-22.

COEXISTING PSYCHIATRIC PROBLEMS AND STRESSFUL LIFE EVENTS IN ADULTS WITH SYMPTOMS OF ADHD A LARGE SWEDISH POPULATION-BASED STUDY OF TWINS.

Friedrichs B, Igl W, Larsson H, et al.

Objective: To explore the associations of subtypes of adult ADHD with other psychiatric problems, stressful life events, and sex differences.

Method: Odds ratios were calculated using information from 17,899 participants from a population-based survey of adult twins born in Sweden between 1959 and 1985.

Results: Symptoms of attention deficit hyperactivity disorder (ADHD) were associated with an increased risk for symptoms of (odds ratio [95% confidence interval]): generalized anxiety disorder (5.6 [4.3; 6.5]), major depression (2.8 [2.4; 3.2]), bipolar disorder (8.0 [5.1; 12.6]), obsessive-compulsive disorder (3.9 [3.1; 4.9]), and alcohol dependence (2.6 [2.2; 3.1]). Symptoms of ADHD were found to be associated with an increased risk for stressful life events (1.8 [1.3; 2.4]). No significant difference in comorbidity was observed between the two sexes.

Conclusion: Both women and men with ADHD are at increased risk for symptoms of other psychiatric disorders. They are also at increased risk for stressful life events.

Journal of Attention Disorders. 2012 Feb;16:87-100.

ADHD AND FEMALE SPECIFIC CONCERNS: A REVIEW OF THE LITERATURE AND CLINICAL IMPLICATIONS.

Nussbaum NL.

ADHD was once thought of as a predominantly male disorder. While this may be true for ADHD in childhood, extant research suggests that the number of women with ADHD may be nearly equal to that of men with the disorder (Faraone et al., 2000). There is accumulating research which clearly indicates subtle but important sex differences exist in the symptom profile, neuropathology and clinical course of ADHD. Compared to males with ADHD, females with ADHD are more prone to have difficulties with inattentive symptoms than hyperactive and impulsive symptoms, and females often receive a diagnosis of ADHD significantly later than do males (Gaub & Carlson, 1997; Gershon, 2002a, 2002b). Emerging evidence suggests differences exist in the neuropathology of ADHD, and there are hormonal factors which may play an important role in understanding ADHD in females. Although research demonstrates females with ADHD differ from males in important ways, little research exists that evaluates differences in treatment response. Given the subtle but important differences in presentation and developmental course of ADHD, it is essential that both clinical practice and research be informed by awareness of these differences in order to better identify and promote improved quality of care to girls and women with ADHD.

Journal of Attention Disorders. 2012 Feb;16:164-73.

DECISION MAKING IN ADULTS WITH ADHD.

Mantyla T, Still J, Gullberg S, et al.

Objectives: This study examined decision-making competence in ADHD by using multiple decision tasks with varying demands on analytic versus affective processes.

Methods: Adults with ADHD and healthy controls completed two tasks of analytic decision making, as measured by the Adult Decision-Making Competence (A-DMC) battery, and two affective decision tasks (the Balloon Analog Risk Task and the Iowa Gambling Task).

Results: Although a majority of the ADHD participants were tested under medication, they showed impairments in both types of task. However, logistic regression analysis showed that the applying-decision-rules task of the A-DMC battery was the only significant predictor of ADHD status.

Conclusions: These findings suggested that ADHD is associated with impaired decision making in tasks involving a significant degree of cognitive control. Although both deliberative and affective neurocognitive systems probably contributed to ADHD-related problems in decision making, the findings underlined the involvement of prefrontally mediated executive functions.

Journal of Attention Disorders. 2012 Jan;16:81-82.

REVIEW OF TAKING CHARGE OF ADULT ADHD (1ST ED).

Ritvo DZ.

Reviews the book, "Taking charge of adult ADHD (1st Ed.)" by Russell A. Barkley (see record 2010-18011-000). This is a book written for adults with attention deficit hyperactivity disorder (ADHD). The strength of the book lies in the attitude that Barkley has toward those who suffer from ADHD. Barkley's empathy for those with ADHD, as well as his appreciation for the difficulties people with ADHD might have seeking and accepting treatment, takes on a poignant personal dimension when he talks candidly about the devastation ADHD wreaked in his own family. Given the author's expertise, it is not surprising that the information in the book is, overall, reliable. However, I question whether it is presented in the most useful way, especially for people with ADHD. Given that the book was put together in conjunction with a writer and editor, I would have expected better writing and organization. The important question, however, is whether a better written and organized book with essentially the same content, but with fewer distractions would allow the information to be better used by adults with ADHD or for that matter by anyone. If that is the case, it is a shame, for it means that much of what the author has to offer, which is considerable, is lost to the reader.

Journal of Attention Disorders. 2012 Jan;16:3-12.

THE RELATIONSHIP BETWEEN ADHD SYMPTOMOLOGY AND DECISION MAKING .

Schepman S, Weyandt L, Schlect SD, et al.

Objective: To explore the relationship between the symptoms of ADHD, the extent to which college students seek to maximize their decisions, and the degree to which students feel regret for their decisions.

Method: Undergraduate students (N=275) completed four questionnaires measuring ADHD symptomology, internal restlessness, maximization tendencies, and regret. It was hypothesized that (a) participants who reported more behaviors associated with ADHD and internal restlessness would report more maximizing tendencies, (b) participants reporting greater ADHD symptoms and internal restlessness symptoms would be more likely to report feelings of regret, (c) men would report more symptoms of ADHD and internal restlessness than women, and (d) men would be more likely to report maximization tendencies than women.

Results: Findings supported the hypotheses and interaction were found.

Conclusions: Findings provided new information concerning relationships between ADHD symptomology, internal restlessness, maximization tendencies, and regret.

Journal of Attention Disorders. 2012 Jan;16:44-59.

A 12-MONTH PROSPECTIVE, OBSERVATIONAL STUDY OF TREATMENT REGIMEN AND QUALITY OF LIFE ASSOCIATED WITH ADHD IN CENTRAL AND EASTERN EUROPE AND EASTERN ASIA.

Goetz M, Yeh CB, Ondrejka I, et al.

Objectives: This prospective, observational, non-randomized study aimed to describe the relationship between treatment regimen prescribed and the quality of life (QoL) of ADHD patients in countries of Central and Eastern Europe (CEE) and Eastern Asia over 12 months.

Methods: 977 Male and female patients aged 6-17 years seeking treatment for symptoms of ADHD were assessed using the Child and Adolescent Symptom Inventory-4 Parent Checklists, and the Clinical Global

Impressions-ADHD-Severity scale. QoL was assessed using the Child Health and Illness Profile-Child Edition parent report form. Patients were grouped according to whether they were prescribed psycho- and/or pharmacotherapy (treatment) or not (no/ other treatment).

Results: No statistically significant differences were observed between cohorts (treatment vs. no/ other treatment) in terms of change in QoL, although there was improvement over 12 months, with a greater improvement experienced by patients in the treatment cohort in both study regions (CEE and Eastern Asia). Psychoeducation/counselling and methylphenidate were the predominant ADHD treatments prescribed.

Conclusions: Although both treatment and no/ other treatment cohorts showed improvements in mean QoL over 12 months, the difference was small and not statistically significant. A major limitation was the higher than anticipated number of patients switching treatments, predominantly from the no/ other treatment cohort.

.....
J Autism Dev Disord. 2012 Feb;42:323-24.

REVIEW OF 'THE ZUCKERMAN PARKER HANDBOOK OF DEVELOPMENTAL AND BEHAVIORAL PEDIATRICS FOR PRIMARY CARE'.

Aitken K.

Reviews the book, "The Zuckerman Parker Handbook of Developmental and Behavioral Pediatrics for Primary Care" edited by M. Augustyn, B. Zuckerman and E. B. Caronna (2011). This is the third edition of a well-established handbook in the 'Vade Mecum' mould of pocketbook texts avidly purchased by US junior doctors in training. It first appeared in 1995 and was last revised in 2005. It provides a compendium of brief but authoritative summaries of a wide range of topics that need to be assimilated by the generalist learning the essentials of primary care ambulatory pediatrics. The editors and the majority of the more than 120 contributing authors are from Boston University School of Medicine. The authors by and large provide a good basic grounding in the areas covered and are experts on their topics areas. In addition to the paper copy, the purchaser receives an access code that provides searchable on-line access to the text. This minor addition is welcome as it makes searching for specific information much faster. The scope of this work is impressive: there are twenty chapters covering broad, general topics; sixty-eight on specific child concerns; eighteen chapters on family issues; and three appendices giving brief details for specific screening. The section on specific concerns is wide ranging, dealing with many of the issues likely to be considered for tertiary referral to Developmental and Behavioral Pediatricians such as ADHD, ASD, Cerebral Palsy, Fetal alcohol syndrome, obesity, elective mutism and tic disorders and the effects of non-specific issues like media coverage of disasters, bullying, lying, stealing, sexuality, sleep problems and unpopularity. Most chapters adhere to a consistent structure first describing the issue; then arriving at a diagnosis; key clinical features; differential diagnosis; key points in the history; relevant features for physical examination; clinical tests and other evaluations; issues for management; medications; family support and prognosis, some, in addition giving 'clinical pearls and pitfalls'. With particular reference to the ASD aspects of the book, there are separate chapters devoted to Asperger syndrome, Autism Spectrum disorders; Complementary and Alternative Medicine (CAM) use in ASD; and Treatment and Medical Management of ASD. The appendices cover key presenting psychosocial symptoms, language milestones and temperament. The psychosocial and language appendices are brief but present standardized referenced assessment tools. The temperament scale, however, is appended without referencing or normative data and it is unclear to the reader how this would be used, scored or interpreted. I was somewhat surprised by the lack of a general chapter on genetic screening given its increasing relevance to the target clinical population for this text. The only recent direct competitor in terms of target market approach, going into more detail and dealing with a far smaller range of issues. The books are more complementary than competitive in their breadth and depth of coverage.

J Child Adolesc Psychopharmacol. 2012 Feb;22:65-71.

DOES COMORBID DEPRESSION PREDICT SUBSEQUENT ADVERSE LIFE EVENTS IN YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDERS?

Daviss WB, Diler R.

Objectives: Studies have primarily focused on adverse life events (ALEs) as potential causes rather than as outcomes of pediatric depression. The current study prospectively examines ALEs in a sample of youth with attention-deficit/hyperactivity disorders (ADHD) to determine whether having a major depressive disorder (MDD) at baseline (T1) predicts counts of child-dependent or child-independent ALEs at a second assessment (T2) 8 months later.

Methods: Subjects with ADHD 11-18 years old were drawn mostly from a tertiary mental health clinic and evaluated with semi-structured diagnostic interviews, and parent and teacher questionnaires of ADHD severity. Eighteen with and 61 without initial MDD at T1 were compared at T2 regarding counts of subsequent overall, child-dependent, and child-independent ALEs reported on life events questionnaires by the child or parent.

Results: The group initially with MDD had higher overall ALEs ($p = 0.01$) and child-dependent ALEs ($p = 0.001$) but not child-independent ALEs ($p = 0.12$) at T2 relative to the nondepressed group, although only 3 of 18 continued to meet full criteria for MDD. The group initially with MDD also had a higher baseline ADHD severity ($p = 0.04$) and proportion of oppositional or conduct disorders ($p = 0.004$). In multivariate analyses, the group initially having MDD had a higher adjusted mean at T2 of child-dependent ALEs ($p = 0.02$), but not of overall ALEs ($p = 0.06$), after controlling for other T1 variables, including ALEs of the same type, ADHD severity, externalizing disorders, and the interaction of externalizing disorders with MDD.

Conclusions: These findings suggest that child-dependent ALEs are potentially an important outcome after youth with ADHD have an episode of MDD. Youth with ADHD who develop comorbid MDD should be closely monitored and offered interventions to address the potential burden of child-dependent ALEs lingering after a depressive episode.

Journal of Child Psychology and Psychiatry. 2012 Mar;53:252-53.

TRANSLATING QUANTITATIVE GENETICS INTO MOLECULAR GENETICS: DECOUPLING READING DISORDER AND ADHD REFLECTIONS ON GREVEN ET AL. AND ROSENBERG ET AL. (2012).

Grigorenko EL.

Comments on the articles by Greven et al. (see record 2012-03239-003) & Rosenberg et al. (see record 2012-03239-004). The articles by Greven & colleagues and Rosenberg & colleagues presented in this issue are focused on a well established but still unexplained observation that specific reading disability (SRD) and attention deficit/hyperactivity disorder (ADHD) co-occur in the same individuals much more often than would be expected by chance, given the population rates of both of these developmental disorders. The two articles attempt to take our understanding of the complex relationships between SRD and ADHD forward. All in all, here we have an interesting duet of articles. Both are quantitative-genetic in nature and, although both elegant, present the reader with observations limited by the constraints of models of quantitative genetics.

Journal of Child Psychology and Psychiatry. 2012 Feb;53:141-42.

ADDRESSING THE CHALLENGES RESPONSE TO THE COMMENTARY OF JARROLD AND HALL (2012): REPLY.

Coghill D, Rhodes Sa.

Reply by the current author to the comments made by Christopher Jarrold & Debhora Hall (see record 2012-01555-005) on the original article (see record 2012-01555-004). As pointed out by Jarrold and Hall we adopted a theoretically driven approach to our analyses. In view of Jarrold and Hall scepticism of our conclusions, we are pleased to now have the opportunity to present the results of an alternative analysis that compares those with and without Attention Deficit Disorder with Hyperactivity (ADHD) and those with and without oppositional defiant disorder (ODD) using a 2 into 2 design. Jarrold and Hall make several further comments about our study that we feel obliged to address. We chose to use a theoretically driven approach to our analyses. An exploratory approach, which is essentially a theoretical, would have

required that we, as Jarrold and Hall suggest, first extract a factor structure from the data, which would then need to be tested against existing theoretical models. Jarrold and Hall were also concerned that the group differences may reflect differences in either intelligence or socio-economic status. Here it is important to recognize that, unlike disorders such as William and Down syndromes, ADHD is not generally characterized by significant levels of intellectual disability.

.....
Journal of Child Psychology and Psychiatry. 2012 Feb;53:138-40.

COMMENTARY: THEORETICAL AND METHODOLOGICAL CHALLENGES TO THE STUDY OF WORKING MEMORY IN DEVELOPMENTAL DISORDERS A COMMENT ON RHODES ET AL. (2012).

Jarrold C, Hall D.

Comments on an article by Sinead M. Rhodes et al. (see record 2012-01555-004). The approach taken by Rhodes et al. is much more theoretically motivated than one often sees in studies of this kind. It makes excellent sense to decompose working memory performance into its executive control and non-executive storage aspects, the latter of which appears to have distinct verbal and spatial components. We know from our own experience that it is all too easy to generate an inappropriate factor structure from a dataset, and, from that, questionable estimates of latent variables, and we would argue that aspects of Rhodes et al. confirmatory factor analysis may be open to question. Although the confirmatory factor analysis supports a model that includes separable domains for visual and verbal material, the model itself arguably does not give an entirely parsimonious account of the data because it also includes a general short-term memory latent variable. One might argue that it makes sense to dissociate domain-specific short-term memory content from the domain-general processes that support the ordering of that content and if so then there may be a theoretical rationale for this type of model. A further issue with the factor analysis employed by Rhodes et al. is the use of a single solution for four apparently distinct groups.

.....
Journal of Child Psychology and Psychiatry. 2012 Apr;53:371-80.

UNDERSTANDING DESISTING AND PERSISTING FORMS OF DELINQUENCY: THE UNIQUE CONTRIBUTIONS OF DISRUPTIVE BEHAVIOR DISORDERS AND INTERPERSONAL CALLOUSNESS.

Byrd AL, Loeber R, Pardini DA.

Background: While associations between conduct disorder (CD), oppositional defiant disorder (ODD), attention deficit hyperactivity disorder (ADHD), and interpersonal callousness (IC) symptoms and delinquency onset are well established, less is known about whether these characteristics differentiate desisting and persisting delinquency. The current study examined whether childhood and adolescent CD, ODD, ADHD, and IC symptoms uniquely distinguished boys who exhibited persisting versus desisting delinquency from adolescence into adulthood.

Methods: Participants were 503 boys (57% African American) repeatedly assessed from ages 7 to 25. Associations between childhood and adolescent CD, ODD, ADHD, and IC symptoms and desisting and persisting delinquency were examined independently and after controlling for their co-occurrence and multiple covariates.

Results: Conduct disorder and IC symptoms in childhood and adolescence were higher among boys whose delinquency persisted into adulthood relative to those boys whose delinquency desisted across time. After controlling for the overlap between symptoms of ADHD, ODD, CD and IC, only adolescent CD and IC symptoms emerged as unique predictors of the differentiation between persisters and desisters. Moreover, adolescent CD and IC symptoms continued to contribute unique variance even after childhood levels of these characteristics were accounted for.

Conclusions: Boys with elevated levels of CD and IC symptoms in childhood and adolescence are at risk for exhibiting a pattern of delinquency that persists from adolescence into adulthood. Intervention efforts designed to prevent chronic delinquency should target youth with co-occurring CD and IC symptoms in childhood and adolescence.

Journal of Child Psychology and Psychiatry. 2012 Jan;53:73-80.

CHILDHOOD ATTENTION DEFICIT HYPERACTIVITY DISORDER AS AN EXTREME OF A CONTINUOUS TRAIT: A QUANTITATIVE GENETIC STUDY OF 8,500 TWIN PAIRS.

Larsson H, Anckarsater H, Rostam M, et al.

Background: Although the clinical utility of categorically defined attention-deficit hyperactivity disorder (ADHD) is well established, there is also strong evidence supporting the notion of ADHD as an extreme of a continuous trait. Nevertheless, the question of whether the etiology is the same for different levels of DSM IV ADHD symptoms remains to be investigated. The aim of this study was to assess genetic links between the extreme and the subthreshold range of ADHD symptoms.

Method: Parents of all Swedish 9- and 12-year-old twins born between 1992 and 2000 were interviewed for DSM IV ADHD symptoms and associated conditions. Two validated cutoff values were used for screening and assigning research diagnoses. Response rate was 80%. Twin methods were applied to investigate the extent to which ADHD is etiologically distinct from subthreshold variations in ADHD symptoms.

Results: Extremes analyses indicated a strong genetic link between the extreme and the subthreshold variation, with almost identical group heritability estimates around .60 for the diagnostic (prevalence 1.78%) and screening (prevalence 9.75%) criteria of ADHD.

Conclusion: A strong genetic link between the extreme and the subthreshold variation of DSM IV based assessments of ADHD symptoms was found. The data suggest that ADHD is best viewed as the quantitative extreme of genetic and environmental factors operating dimensionally throughout the distribution of ADHD symptoms, indicating that the same etiologic factors are involved in the full range of symptoms of inattention, hyperactivity and impulsivity.

.....

Journal of Child Psychology and Psychiatry. 2012 Apr;53:390-400.

EXAMINATION OF NEUROLOGICAL SUBTLE SIGNS IN ADHD AS A CLINICAL TOOL FOR THE DIAGNOSIS AND THEIR RELATIONSHIP TO SPATIAL WORKING MEMORY.

Ferrin M, Vance A.

Background: Neurological subtle signs (NSS) are minor neurological abnormalities that have been shown to be increased in a number of neurodevelopmental conditions. For attention deficit/hyperactivity disorder (ADHD), it remains unclear whether NSS may aid the clinical diagnostic process.

Methods: This study explored the association of total and specific domains of NSS in 1,055 children and adolescents with ADHD compared to 130 age-matched typically developing participants; the relationship between NSS and Spatial Working Memory (SWM) as a cognitive process integrally involved in ADHD was also assessed. To determine the diagnostic and predictive efficiency of NSS, a receiver operating curve analysis was performed and the area under the curve (AUC) quantified. The best discriminant points for differentiating between ADHD and typically developing participants and the predictive power of NSS for SWM impairment in ADHD young people were also calculated.

Results: Area under the curves for total NSS, smoothness/accuracy, cerebellar signs and choreo-athetoid movements scores were considered good (.84, .79, .74 and .73 respectively), and the results remained after controlling for gender and IQ. A total score of 13 or over on the Scored Developmental Neurological Examination proved to be a good threshold point for differentiating between the ADHD and typically developing participants. For ADHD children, the AUC of total NSS to distinguish between those below 25th and above 75th percentile were .77 and .73 for Spatial Span and for Between Search Errors respectively (the two SWM-dependent measures examined).

Conclusions: This study provides evidence suggesting that NSS may aid the clinical evaluation of a child or adolescent with ADHD. In children and adolescents with ADHD, NSS are associated with difficulties in SWM, specifically the Spatial Span and Between Search Error components.

.....

Journal of Clinical Child and Adolescent Psychology. 2012 Mar;41:117-26.

ATTENTION MECHANISMS IN CHILDREN WITH ANXIETY DISORDERS AND IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: IMPLICATIONS FOR RESEARCH AND PRACTICE.

Weissman AS, Chu BC, Reddy LA, et al.

Inattention is among the most commonly referred problems for school-aged youth. Research suggests distinct mechanisms may contribute to attention problems in youth with anxiety disorders versus youth with attention deficit hyperactivity disorder (ADHD). This study compared children (8-17 years) with anxiety disorders (n = 24) and children (8-16 years) with ADHD (n = 23) on neurocognitive tests of both general and emotion-based attention processes. As hypothesized, children with ADHD demonstrated poorer selective and sustained attention, whereas youth with anxiety disorders demonstrated greater attentional bias toward threatening faces on a visual probe task. Findings suggest the neuropsychological differentiation of attention problems in anxious and ADHD children, despite potentially similar phenotypes.

Journal of College Student Psychotherapy. 2012 Jan;26:5-21.

MAKING THE CASE FOR A COMPREHENSIVE ADHD ASSESSMENT MODEL ON A COLLEGE CAMPUS.

Pazol RB, Griggins C.

Despite increased demands on university counseling center resources, some centers are offering comprehensive assessments for Attention Deficit Hyperactivity Disorder (ADHD). The rationale for one counseling center decision to provide comprehensive ADHD assessments is presented, including the clinical, legal, social, medical, financial, and philosophical factors influencing such a decision. The general characteristics of the students presenting for assessment and the specific ADHD assessment process are described. In addition, the benefits of and drawbacks to such a program, as well as its applicability to other university counseling centers, are discussed.

J Consult Clin Psychol. 2012 Apr;80:239-44.

TREATMENT OF COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ANXIETY IN CHILDREN: A MULTIPLE BASELINE DESIGN ANALYSIS.

Jarrett MA, Ollendick TH.

Objective: The present study evaluated a 10-week psychosocial treatment designed specifically for children with attention-deficit/hyperactivity disorder (ADHD) and a comorbid anxiety disorder.

Method: Using a nonconcurrent multiple baseline design, the authors treated 8 children ages 8-12 with ADHD, combined type, and at least 1 of 3 major anxiety disorders (separation anxiety disorder, generalized anxiety disorder, social phobia). The integrated treatment protocol involved parent management training for ADHD and family-based cognitive-behavioral therapy for anxiety. Pretreatment assessments included semistructured diagnostic interviews and other standardized measures to determine study eligibility. Children were randomized to 1 of 3 baseline control conditions (i.e., 2, 3, or 4 weeks) and subsequently treated in a university-based psychosocial treatment clinic. Weekly assessments of ADHD and anxiety disorder symptoms occurred throughout treatment and comprehensive assessments were obtained at pretreatment, 1-week post treatment, and 6-months post treatment.

Results: Single-case results supported greater success in the treatment phase relative to the baseline phase for both ADHD and anxiety symptoms, and ADHD and anxiety symptoms appeared to change concurrently. Pre-post group analyses revealed significant and clinically meaningful improvements in ADHD and anxiety symptoms at 1-week post treatment, but only anxiety symptoms moved into the subclinical range. At 6-months follow-up, treatment effects were maintained with new movement into the subclinical range for ADHD.

Conclusions: The present study provides initial data on an integrated treatment protocol for ADHD and anxiety. Further replication and evaluation are needed. Implications of the findings are discussed.

J Consult Clin Psychol. 2012 Apr;80:245-54.

CAN CHILDREN WITH ADHD BE MOTIVATED TO REDUCE BIAS IN SELF-REPORTS OF COMPETENCE?

Hoza B, Vaughn A, Waschbusch DA, et al.

Objective: Our purpose in the current study was to examine whether children with attention-deficit/hyperactivity disorder (ADHD) and comparison children, if adequately motivated, are able to purposefully match their teachers' ratings of competence in multiple domains and whether any reductions in self-perceptual bias normalize self-views in relation to comparison children's self-perceptions.

Method: Participants included children with ADHD (n = 178) and comparison children (n = 86), between 7 and 12 years of age. The majority of participants were Caucasian (81.4%) and male (77.3%). Primary measures included the Self-Perception Profile for Children (SPPC; Harter, 1985), which was administered during a baseline assessment. In a subsequent session, children completed the SPPC twice more following instructions to first attempt to match their teachers' ratings of competence and then following the offer of an incentive for matching their teachers' ratings. Repeated measures analyses of covariance were conducted with between- and within-subjects factors.

Results: Significant reductions in 2 of 3 domains (scholastic, behavioral conduct) were found for children with ADHD. No reductions were found across domains for comparison children or in the social domain for children with ADHD. Across conditions, the amount of bias exhibited by children with ADHD was never normalized in relation to comparison children's ratings.

Conclusions: Explicit instructions to match teacher ratings of competence and implementation of incentives were only partially effective in reducing the biased self-perceptions of children with ADHD. Results suggest that children with ADHD, on average, cannot view themselves in a completely unbiased fashion, rather than that they will not do so, although self-protection clearly plays a partial role.

.....

J Consult Clin Psychol. 2012 Feb;80:128-38.

IS ADHD DIAGNOSED IN ACCORD WITH DIAGNOSTIC CRITERIA? OVERDIAGNOSIS AND INFLUENCE OF CLIENT GENDER ON DIAGNOSIS.

Bruchmiller K, Margraf JA, Schneider S.

Objective: Unresolved questions exist concerning diagnosis of ADHD. First, some studies suggest a potential overdiagnosis. Second, compared with the male-female ratio in the general population (3:1), many more boys receive ADHD treatment compared with girls (6-9:1). We hypothesized that this occurs because therapists do not adhere to Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV) and International Classification of Diseases (10th rev.; ICD-10) criteria. Instead, we hypothesized that, in accordance with the representativeness heuristic, therapists might diagnose attention-deficit/hyperactivity disorder (ADHD) if a patient resembles their concept of a prototypical ADHD child, leading therapists to overlook certain exclusion criteria. This may result in overdiagnosis. Furthermore, as ADHD is more frequent in males, a boy might be seen as a more prototypical ADHD child and might therefore receive an ADHD diagnosis more readily than a girl would.

Method: We sent a case vignette to 1,000 child psychologists, psychiatrists, and social workers and asked them to give a diagnosis. Four versions of the vignette existed: Vignette 1 (ADHD) fulfilled all DSM-IV/ICD-10 criteria of ADHD. Vignettes 2-4 (non-ADHD) included several ADHD symptoms but stated other ADHD criteria were nonfulfilled. Therefore, an ADHD diagnosis could not be given. Furthermore, boy and girl versions of each vignette were created.

Results: In Vignettes 2-4 (non-ADHD), 16.7% of therapists diagnosed ADHD. In the boy version of these vignettes, therapists diagnosed ADHD around 2 times more than they did with the girl vignettes.

Conclusions: Therapists do not adhere strictly to diagnostic manuals. Our study suggests that overdiagnosis of ADHD occurs in clinical routine and that the patient's gender influences diagnosis considerably. Thorough diagnostic training might help therapists to avoid these biases.

.....

Journal of Developmental and Physical Disabilities. 2012 Feb;24:53-64.

OBSTETRIC COMPLICATIONS IN ADULTS WITH ADHD: A RETROSPECTIVE COHORT STUDY.

Adamou M, Russell A, Sanghera P.

Obstetric complications have been associated with a number of mental disorders. In this study, we investigate how obstetric complications relate with clinically significant determinants of adult attention deficit hyperactivity disorder (ADHD), such as gender, age of diagnosis, psychiatric co morbidity, severity of symptomatology and general functioning. Presence of obstetric complications as reported in the psychiatric history of 64 patients in transition from adolescence to adulthood referred to the Yorkshire service for adults with ADHD between June 2009 and October 2010 were recorded. The presence or not of these complications was examined as a factor determining a number of clinically significant variables, such as gender, age at first diagnosis, psychiatric comorbidity, severity of symptomatology (measured with Conners Adult ADHD Rating Scale (CAARS)) and general functioning (measured using the DSM-IV General Assessment of Functioning (GAF) index). Obstetric complications were not associated with any of the variables examined. Adults with ADHD in transition to adult services were highly symptomatic and disabled with a mean Conner score (n = 56) of 30.5 (SD = 12.8) and the most common frequency of the GAF score (n = 55) on the 60-51 range. Although it has been reported that environmental factors are associated with ADHD, the presence or absence of obstetric complications in an adult ADHD population was not associated with a number of proxy measures clinically associated with organic aetiology in mental health conditions. Future research on etiology and etiopathology should focus on prenatal and genetic factors instead.

J Neural Transm. 2012 Jan;119:95-106.

SET SHIFTING AND WORKING MEMORY IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Rohlf H, Jucksch V, Gawrilow C, et al.

Compared to the high number of studies that investigated executive functions (EF) in children with attention-deficit/hyperactivity disorder (ADHD), a little is known about the EF performance of adults with ADHD. This study compared 37 adults with ADHD (ADHD_{total}) and 32 control participants who were equivalent in age, intelligence quotient (IQ), sex, and years of education, in two domains of EF set shifting and working memory. Additionally, the ADHD_{total} group was subdivided into two subgroups: ADHD patients without comorbidity (ADHD[~], n = 19) and patients with at least one comorbid disorder (ADHD⁺, n = 18). Participants fulfilled two measures for set shifting (i.e., the trail making test, TMT and a computerized card sorting test, CKV) and one measure for working memory (i.e., digit span test, DS). Compared to the control group the ADHD_{total} group displayed deficits in set shifting and working memory. The differences between the groups were of medium-to-large effect size (TMT: d = 0.48; DS: d = 0.51; CKV: d = 0.74). The subgroup comparison of the ADHD⁺ group and the ADHD⁻ group revealed a poorer performance in general information processing speed for the ADHD⁺ group. With regard to set shifting and working memory, no significant differences could be found between the two subgroups. These results suggest that the deficits of the ADHD_{total} group are attributable to ADHD rather than to comorbidity. An influence of comorbidity, however, could not be completely ruled out as there was a trend of a poorer performance in the ADHD⁺ group on some of the outcome measures.

J Neurother. 2012 Jan;16:37-45.

NEUROFEEDBACK FOR ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: INVESTIGATION OF SLOW CORTICAL POTENTIAL NEUROFEEDBACK PRELIMINARY RESULTS.

Mayer K, Wyckoff SN, Schulz U, et al.

Attention deficit/hyperactivity disorder (ADHD) is characterized by symptoms of inattention, impulsivity, and hyperactivity. Compared to ADHD in children, only a few studies have investigated ADHD in an adult population, and even less have investigated new forms of treatment such as neurofeedback. Neurofeedback has been applied effectively in various areas, especially in the treatment of children with ADHD, and symptom improvements were associated with increased amplitude of the contingent negative

variation (CNV). This study investigated if any behavioral and electrophysiological changes reflected in the CNV can be observed after 15 sessions of SCP neurofeedback training. Furthermore, a comparison of CNV amplitude in adults with ADHD and a healthy control group was conducted. Continuous 22-channel EEG was acquired from 10 adults who met DSM IV criteria for ADHD and 8 matched healthy controls. EEG recordings were collected pre/mid-treatment and included resting EEG, P300, and CNV tasks as well as ADHD behavioral questionnaires. The adult ADHD group received 15 sessions of SCP training at Cz (referenced to A1, ground A2). The control group only underwent the EEG recording. After 15 sessions of SCP-training a significant improvement in self-ratings of ADHD symptoms was reported. In addition, a trend in increasing CNV mean amplitude was observed after training. A significant difference in baseline CNV between the adult ADHD group and the healthy control group was observed. These results give a promising outlook to the outcome after the completion of 30 sessions of SCP training. The differences in CNV amplitude between the ADHD group and healthy controls are in line with other studies about adult ADHD and CNV. This supports the idea of impaired self-regulation in adult ADHD. The behavioral improvements and increase in CNV after SCP training suggests that SCP training has a positive effect on adult ADHD symptoms and their origin.

J Neurother. 2012 Jan;16.

CLINICAL CORNER.

Hammond DC.

The purpose of the Clinical Corner is to provide space for clinically oriented material which may not, in many cases, have been evaluated yet by controlled research. Therefore, the personal opinions expressed in the column are exactly that, the opinions of the individual authors, often based on their clinical experience. The initial article in this Clinical Corner presents the first published report of the use of neurofeedback in the treatment of fetal alcohol spectrum disorder. This is a widespread condition that represents one of the etiologic factors associated with mental retardation, ADHD, and conduct disorder. Another article is an evaluation of cranial electrotherapy stimulation in military veterans with posttraumatic stress disorder. Each article holds out hope for technologies that may assist in the treatment of these challenging conditions.

J Psychiatr Res. 2012 Mar;46:415-16.

THE CHANGE OF THE CORTISOL LEVELS IN CHILDREN WITH ADHD TREATED BY METHYLPHENIDATE OR ATOMOXETINE': LETTER TO THE EDITOR.

Chen YH, Lin XX, Chen H, et al.

This article presents a prospective, double-blind, randomized case-control trial, which investigated 111 male children with ADHD aged between 6 and 14 years old, while 30 healthy male children were chosen as a control group. The diagnoses for ADHD were made according to DSM-IV criteria. All recruited children were also excluded above comorbidities such as childhood schizophrenia, mood disorder, autism, mental retardation, oppositional defiance disorder, conduct disorder, anxiety disorder and so on. The levels of cortisol were evaluated by the automatic particle enzyme immunoassay. The results showed that the base plasma cortisol levels of the ADHD group were significantly lower than those of the control group.

Journal of Psychiatry & Neuroscience. 2012 Jan;37:46-52.

PARENT-OF-ORIGIN EFFECTS OF FAS AND PDLIM1 IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Wang KS, Liu X, Zhang Q, et al.

Background: Previous studies have suggested that there may be a parent-of-origin effect for attention-deficit/hyperactivity disorder (ADHD) candidate genes. The objective of the present study was to investigate parent-of-origin effects using a genome-wide association analysis of the International Multicentre ADHD Genetics (IMAGE) study sample.

Methods: Family-based association analysis for ADHD using 846 ADHD probands and their parents was performed using the PLINK program, and parent-of-origin effects were studied using a Z score for the difference in paternal versus maternal odds ratios.

Results: We identified 44 single nucleotide polymorphisms (SNPs) showing parent-of-origin effects at a significance level of $p < 0.001$. The most significant SNP, rs7614907, is at position 3q13.33 in the CDGAP gene ($p = 0.000064$ for parent-of-origin effect). Furthermore, 2 genes (FAS and PDLIM1) showed moderate parent-of-origin effects ($p = 0.00086$ for rs9658691 and $p = 0.00077$ for rs11188249) and strong maternal transmission ($p = 0.000059$ for rs9658691 and $p = 0.000068$ for rs11188249). In addition, ZNF775 showed a moderate parent-of-origin effect ($p = 0.00036$ for rs7790549) and strong paternal transmission ($p = 0.000041$ for rs7790549).

Limitations: We only had 1 sample available for analysis.

Conclusion: These results suggest several genes or regions with moderate parent-of-origin effects, and these findings will serve as a resource for replication in other populations to elucidate the potential role of these genetic variants in ADHD.

J Psychopathol Behav Assess. 2012 Mar;34:1-10.

COMPARING FOUR METHODS OF INTEGRATING PARENT AND TEACHER SYMPTOM RATINGS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Shemmassian SK, Lee SS.

Although parents and teachers are valid informants in the assessment of childhood attention-deficit/hyperactivity disorder (ADHD), there is relatively little systematic research on how these ratings should be optimally combined. We compared four methods of ADHD assessment to determine how well they identified impaired children: (1) parent only, (2) teacher only, (3) parent or teacher (or rule™), and (4) parent and teacher (and rule™). We obtained parent and teacher ratings of ADHD from the Disruptive Behavior Disorder Rating Scale on 232 5- to 10-year-old children (69% male; 47% Caucasian) with ($n = 121$) and without ($n = 111$) ADHD. We used receiver operating characteristic curves (ROC) and seemingly unrelated regression analyses (SUR) to evaluate how accurately each method identified categorically- and dimensionally-defined measures of functional impairment. Parent ratings of ADHD optimally identified globally impaired children based on categorical and dimensional measures. However, teacher ratings of ADHD most accurately identified children who were negatively regarded by peers using categorical, but not dimensional, measures. No ADHD assessment method effectively identified children with academic difficulties. Although multiple informants are valuable in the assessment of ADHD, no single method was consistently superior in identifying impaired children across domains. We consider alternative assessment strategies in ADHD as well as other potential factors that may contribute to modest agreement among informants.

J Psychopharmacol. 2012 Mar;26:380-89.

NOREPINEPHRINE TRANSPORTER -3081(A/T) AND ALPHA-2A-ADRENERGIC RECEPTOR MspI POLYMORPHISMS ARE ASSOCIATED WITH CARDIOVASCULAR SIDE EFFECTS OF OROS-METHYLPHENIDATE TREATMENT.

Cho SC, Kim BN, Cummins TDR, et al.

The purpose of this study was to investigate a possible association between norepinephrine genes and cardiovascular side effects of the Osmotic Controlled-Release Oral Delivery System-methylphenidate (OROS-MPH) in Korean children with attention-deficit/hyperactivity disorder (ADHD). One hundred and one children with ADHD (8.7 ± 1.7 years) were recruited from child psychiatric centers at six university hospitals in South Korea. All participants were drug-naïve ADHD children treated with OROS-MPH for 12 weeks. During the treatment period the investigators titrated the OROS-MPH dosage on the basis of symptom severity and side effects. Resting heart rate (HR), diastolic blood pressure (DBP), and systolic blood pressure (SBP) were examined before and after treatment. The percentage change score (post-treatment pretreatment/pretreatment $\times 100$) of each parameter was calculated. Genotyping of SLC6A2 -3081(A/T) and G1287A, and alpha-2A-adrenergic receptor (ADRA2A) MspI and DraI polymorphisms was performed. Clinically significant changes were not found in cardiovascular monitoring during the course of

treatment. An increase of HR after OROS-MPH treatment was found to be statistically significant ($t = 3.54$, $p = 0.001$). Changes in SBP and DBP were not significant and no specific change was found in the ECGs. However, an additive regression analysis demonstrated a significant association between SLC6A2 - 3081(A/T) and percentage change in HR post-treatment ($p = 0.01$) after controlling for age, gender, dosage of MPH and response and baseline pulse rate. Children with ADHD having the T/T genotype of SLC6A2 showed a 12.5% increase in HR compared to baseline, whereas children with the A/T or A/A genotype showed a 3.5% and 2.5% increase after OROS-MPH treatment, respectively. There was also a significant association between the ADRA2A MspI genotype and percentage change of DBP post-treatment after controlling for age, gender, dosage of MPH and response and baseline DBP ($p = 0.009$). Children with ADHD having the C/C genotype of ADRA2A MspI showed an 18.5% increase in DBP compared to baseline, but children with the G/G or G/C genotype showed a 0.2% decrease after OROS-MPH treatment. The overall cardiovascular effects of OROS-MPH were modest. However, our findings show a positive association between norepinephrine-related gene polymorphisms and cardiovascular response induced by MPH in Korean children with ADHD. Consideration must be given to such children or adults with specific norepinephrine-related genotypes, especially if they show significant changes in HR or DBP after OROS-MPH administration.

Journal of Studies on Alcohol and Drugs. 2012 Mar;73:185-94.

TWIN STUDY OF THE RELATIONSHIP BETWEEN ADOLESCENT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ADULT ALCOHOL DEPENDENCE.

Edwards AC, Kendler KS.

Objective: Adolescent problem behaviors such as conduct disorder and attention-deficit/hyperactivity disorder (ADHD) are often associated with alcohol problems in adulthood, particularly alcohol dependence. This association is partly a result of shared genetic liability. However, it is unclear whether ADHD, or an ADHD subtype, shares genetic influences with alcohol dependence beyond those also shared by conduct disorder.

Method: We evaluated phenotypic associations between adolescent conduct disorder and ADHD phenotypes with adult alcohol dependence in a population-based sample of adult male twins ($N = 1,774$). We then assessed genetic and environmental relationships among phenotypes using structural equation modeling.

Results: Individually, conduct disorder and each ADHD factor were associated with adult alcohol dependence. Results from twin modeling indicate that a genetic factor common to conduct disorder and ADHD also loads strongly onto alcohol dependence. Even after controlling for genetic factors shared with conduct disorder and other ADHD factors, the hyperactivity component of ADHD shared significant residual genetic influences with alcohol dependence.

Conclusions: Most of the genetically mediated association between adolescent ADHD and adult alcohol dependence is shared with conduct disorder, reflecting a generalized risk to externalizing behaviors. The significant residual genetic covariance between the ADHD factor hyperactivity/impulsivity and alcohol dependence implies that impulsive behaviors less destructive/harmful than those manifested by conduct disorder can be indicative of genetic risk for adult alcohol dependence. However, the ADHD factors inattention and forgetfulness are not uniquely predictive of genetic/environmental risk for alcohol dependence.

Journal of the American Academy of Child & Adolescent Psychiatry. 2012 Feb;51:132-33.

CAUTIOUS REASSURANCE: CARDIOVASCULAR RISK IN THE CONTEXT OF STIMULANT USE.

Greenhill LL.

Comments on an article by Mark Olfson and colleagues (see record 2012-02207-010). In their article, Olfson and colleagues report on the association of cardiovascular events to stimulant treatment based on claims of privately insured youth 6 to 21 years old with ADHD. This study is unique in its large size, its focus on youth, and, importantly, its controlling for pre-existing cardiovascular risk factors. The conclusions drawn by authors and those of other epidemiologic studies are in keeping with some, but not all, other

studies. The work of authors and of two other large epidemiologic studies have established a risk of 0.3 to 3.1 serious cardiovascular events per 100,000 person-years no different from the risk in un medicated youth. Although the data support the conclusion that stimulants are safe for long-term use, for any given child, the clinician must be vigilant, assess children for cardiac risk, and monitor them closely during treatment.

Journal of the American Academy of Child & Adolescent Psychiatry. 2012 Jan;51:86-97.

META-ANALYSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER OR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS, RESTRICTION DIET, AND SYNTHETIC FOOD COLOR ADDITIVES.

Nigg JT, Lewis K, Edinger T, et al.

Objective: The role of diet and of food colors in attention-deficit/hyperactivity disorder (ADHD) or its symptoms warrants updated quantitative meta-analysis, in light of recent divergent policy in Europe and the United States.

Method: Studies were identified through a literature search using the PubMed, Cochrane Library, and PsycNET databases through February 2011. Twenty-four publications met inclusion criteria for synthetic food colors; 10 additional studies informed analysis of dietary restriction. A random-effects meta-analytic model generated summary effect sizes.

Results: Restriction diets reduced ADHD symptoms at an effect of $g = 0.29$ (95% CI, 0.07- 0.53). For food colors, parent reports yielded an effect size of $g = 0.18$ (95% CI, 0.08-0.24; $p = .0007$), which decreased to 0.12 (95% CI, 0.01- 0.23; $p < .05$) after adjustment for possible publication bias. The effect was reliable in studies restricted to food color additives ($g = 0.21$, 95% CI = 0.06-0.36) but did not survive correction for possible publication bias and was not reliable in studies confined to Food and Drug Administration-approved food colors. Teacher/observer reports yielded a nonsignificant effect of 0.07 (95% CI = \hat{a} 0.03 to 0.18; $p = .14$). However, high-quality studies confined to color additives yielded a reliable effect ($g = 0.22$, 95% CI = 0.10-0.41, $p = .030$) that survived correction. In psychometric tests of attention, the summary effect size was 0.27 (95% CI = 0.07-0.47; $p = .007$) and survived correction. An estimated 8% of children with ADHD may have symptoms related to synthetic food colors.

Conclusions: A restriction diet benefits some children with ADHD. Effects of food colors were notable were but susceptible to publication bias or were derived from small, nongeneralizable samples. Renewed investigation of diet and ADHD is warranted.

Journal of the American Academy of Child & Adolescent Psychiatry. 2012 Mar;51:325-26.

DRS. HAMMERNESS AND WILENS REPLY.

Hammerness PG, Wilens TE.

Reply by the current authors to the comments made by Yueh-Ming Tai and colleagues (see record 2012-05353-015) on the original article (see record 2011-22667-010). We are pleased to see the report by Tai and colleagues on the risk of cardiovascular events in individuals exposed to methylphenidate in Taiwan. These findings extend the current literature drawn from samples of primarily Caucasian children¹ by examining the risk of serious cardiovascular events in an ethnic Chinese population. Tai and colleagues used a nested matched case-control design to examine rates of cardiovascular events derived from a decade of national health insurance claims data in Taiwan. This study adds to a growing literature of large-scale investigations on the association of serious cardiovascular events and therapeutic ADHD pharmacotherapy. The small number of serious cardiac events in pharmacoepidemiologic studies is a fundamental limitation of the statistical power of the studies; however, based on current data, if present, the absolute magnitude of any increased cardiovascular risk would be low. Despite these reassuring findings, the field will benefit from continued research and surveillance on this important clinical and public health topic.

Journal of the American Academy of Child & Adolescent Psychiatry. 2012 Mar;51:324-25.

CARDIOVASCULAR EVENTS AND METHYLPHENIDATE USE IN TAIWAN.

Tai YM, Gau SS-F, Gau CS .

Comments on an article by P. G. Hammerness and colleagues (see record 2011-22667-010). We read with great interest the review article by Hammerness and colleagues. Their 10-year contemporary literature review of the cardiovascular risk of stimulant medications in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) provides valuable insights in this field. In response to the authors comments that the difficulty in such an investigation is due mainly to an extreme scarcity of cardiovascular events in youngsters taking ADHD medications and to the uncertainty about a generalization of findings based mainly on samples from Caucasian children, we would like to share similar findings from our study in an ethnic Chinese population. We compared the rates of cardiovascular events that occurred after the index day between the two groups for a period lasting at least 5 years. Consistent with Western studies, our analysis of clinical data based on national health insurance claims records had a similar limitation in that there were relatively few cardiovascular events in individuals with ADHD. Nevertheless, our results showed no increased risk for cardiovascular events with methylphenidate use, even after excluding subjects with a history of head injury. In summary, consistent with Western research, our findings did not support an association between cardiovascular events and the use of methylphenidate.

.....

Mind, Brain, and Education. 2012 Mar;6:27-40.

DISTINGUISHING AND IMPROVING MOUSE BEHAVIOR WITH EDUCATIONAL COMPUTER GAMES IN YOUNG CHILDREN WITH AUTISTIC SPECTRUM DISORDER OR ATTENTION DEFICIT/HYPERACTIVITY DISORDER: AN EXECUTIVE FUNCTION BASED INTERPRETATION.

Veenstra B, van Geert PLC, van der Meulen BF.

In this exploratory multiple case study, it is examined how a computer game focused on improving ineffective learning behavior can be used as a tool to assess, improve, and study real-time mouse behavior (MB) in different types of children: 18 children (3.8-6.3 years) with Autistic Spectrum Disorder (ASD), Attention Deficit/Hyperactivity Disorder (ADHD), or comorbid ASD and ADHD, and 5 effectively learning (EL) children (3.5-3.8 years). The children MB processes, for example "Errors" and "Reaction times," were interpreted in terms of executive functions (EFs). Trajectories of averaged MB were compared among the groups of ASD, ADHD, comorbid, and EL children. Clinical groups showed differences in their MB, which were similar to the expected differences based on EF tests. In addition, a case study of a typical ASD, ADHD, and EL child was included in order to demonstrate typical individual MB patterns across time. MB processes might therefore provide a window into the processes of EF (dys)functioning.

.....

NeuroImage. 2012 Mar;60:353-61.

ORBITOFRONTAL REWARD SENSITIVITY AND IMPULSIVITY IN ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Wilbertz G, van Elst LT, Delgado MR, et al.

Impulsivity symptoms of adult attention deficit hyperactivity disorder (ADHD) such as increased risk taking have been linked with impaired reward processing. Previous studies have focused on reward anticipation or on rewarded executive functioning tasks and have described a striatal hyporesponsiveness and orbitofrontal alterations in adult and adolescent ADHD. Passive reward delivery and its link to behavioral impulsivity are less well understood. To study this crucial aspect of reward processing we used functional magnetic resonance imaging (fMRI) combined with electrodermal assessment in male and female adult ADHD patients (N = 28) and matched healthy control participants (N = 28) during delivery of monetary and non-monetary rewards. Further, two behavioral tasks assessed risky decision making (game of dice task) and delay discounting. Results indicated that both groups activated ventral and dorsal striatum and the medial orbitofrontal cortex (mOFC) in response to high-incentive (i.e. monetary) rewards. A similar, albeit less strong activation pattern was found for low-incentive (i.e. non-monetary) rewards. Group differences emerged when comparing high and low incentive rewards directly: activation in the mOFC coded for the motivational change in reward delivery in healthy controls, but not ADHD patients. Additionally, this dysfunctional mOFC activity in patients correlated with risky decision making and delay discounting and

was paralleled by physiological arousal. Together, these results suggest that the mOFC codes reward value and type in healthy individuals whereas this function is deficient in ADHD. The brain-behavior correlations suggest that this deficit might be related to behavioral impulsivity. Reward value processing difficulties in ADHD should be considered when assessing reward anticipation and emotional learning in research and applied settings.

.....

Neuropsychiatr Enfance Adolesc. 2012 Jan;60:30-34.

LES PSYCHOSTIMULANTS DANS LE TROUBLE DEFICIT DE ATTENTION AVEC OU SANS HYPERACTIVITE (TDA/H) CHEZ L'ENFANT ET L'ADOLESCENT.

Renier JP.

Attention deficit hyperactivity disorder (ADHD) is frequent and impairing. Pharmacological treatments have demonstrated efficacy in decreasing symptoms of hyperactivity, inattention, and impulsivity. In France, methylphenidate (MPH) is the sole psychostimulant available in officines. Many forms of MPH exist, varying for their duration of action. Also, amphetamines may be delivered under particular circumstances and temporary legal authorisation for prescription. Tolerance to psychostimulants is rather good, the most frequent side effect being appetite loss and decreased weight. Once a year, psychostimulants should be interrupted for a few weeks, in order to assess whether ADHD is still impairing and justifies pharmacological treatment.

.....

Neuropsychology Review. 2012 Mar;22:54-68.

THE ROLE OF NEUROPSYCHOLOGICAL ASSESSMENT IN THE FUNCTIONAL OUTCOMES OF CHILDREN WITH ADHD.

Pritchard AE, Nigro CA, Jacobson LA, et al.

The value of evidence-based services is now recognized both within clinical communities and by the public at large. Increasingly, neuropsychologists must justify the necessity of often costly and time-consuming neuropsychological assessments in the diagnosis and treatment of common childhood disorders, such as Attention-deficit/ Hyperactivity Disorder (ADHD). Published medical guidelines and prominent researchers, however, have argued against the need for formal neuropsychological assessment of ADHD. The present review examines the literature on developmental outcomes in childhood ADHD, with emphasis on the utility of formal neuropsychological assessment among children diagnosed and treated in primary care settings. The review yields three central findings: 1) adherence to published diagnostic guidelines for ADHD is poor among pediatric and primary care physicians; 2) ADHD most often co-exists with other disorders, thus diagnoses made without formal psychometric assessment can be incomplete or incorrect, ultimately increasing treatment costs; and, 3) untreated children with ADHD, and those who have untreated comorbidities, are at greater risk for poor outcomes in social, academic, vocational, and practical settings. The available literature suggests that neuropsychological assessment provides information that can potentially reduce risks for poor outcomes and improve quality of life among children with ADHD. Controlled studies directly examining the impact of neuropsychological assessments in improving outcomes among children with ADHD are needed.

.....

Nicotine & Tobacco Research. 2012 Feb;14:229-33.

A PRELIMINARY ANALYSIS OF INTERACTIONS BETWEEN GENOTYPE, RETROSPECTIVE ADHD SYMPTOMS, AND INITIAL REACTIONS TO SMOKING IN A SAMPLE OF YOUNG ADULTS.

Bidwell LC, Garrett ME, McClernon FJ, et al.

Introduction: Initial reactions to cigarettes predict later regular smoking. Symptoms of attention deficit hyperactivity disorder (ADHD) have also been shown to increase smoking risk and may moderate the relationship between genotype and smoking. We conducted an exploratory study to assess whether ADHD symptoms interact with genetic variation to predict self-reported initial reactions to smoking.

Methods: Participants were a subsample of 1,900 unrelated individuals with genotype data drawn from the National Longitudinal Study of Adolescent Health (Add Health), a nationally representative sample of

adolescents followed from 1995 to 2002. Linear regression was used to examine relationships among self-reported ADHD symptoms, genotype, and self-reported initial reactions to cigarettes (index scores reflecting pleasant and unpleasant reactions).

Results: Polymorphisms in the DRD2 gene, SLC6A4 gene, and among males, the MAOA gene interacted with retrospective reports of ADHD symptoms in predicting pleasant initial reaction to cigarettes. Polymorphisms in the CYP2A6 gene and, among females, the MAOA gene interacted with retrospective reports of ADHD symptoms in predicting unpleasant initial reaction to cigarettes. No main effect for any of these polymorphisms was observed nor were any interactions with DRD4 and DAT genes.

Conclusions: These findings suggest that genotypes associated with monoamine neurotransmission interact with ADHD symptoms to influence initial reactions to cigarette smoking. Given that an initial pleasant reaction to cigarettes increases risk for lifetime smoking, these results add to a growing body of literature that suggests that ADHD symptoms increase risk for smoking and should be accounted for in genetic studies of smoking.

.....

Nord J Psychiatry. 2012 Feb;66:70-71.

PRESCRIPTION RATES OF ADHD MEDICATION IN THE SCANDINAVIAN COUNTRIES AND THEIR NATIONAL GUIDELINES.

Bilenberg N, Gillberg C, Houmann T, et al.

This article discusses prescription rates of ADHD medication in the Scandinavian countries and their national guidelines. In search of relevant causes for the variation, it seemed appropriate to turn to the guidelines for diagnosis and treatment of ADHD published in the three different Scandinavian countries. Although it is a fact that working groups behind these guidelines in each country consisted of specialists from different professions, and that guidelines were developed with a view to reaching different target populations, it is believed that it is important to point out that basic recommendations with respect to indication, dosage and follow-up of medication were divergent in the three guidelines. Even though the guidelines agree that clinical specialists of psychiatry and child-and adolescent psychiatry, pediatrics and neurology are authorized to initiate and prescribe medication, recommendations on laboratory tests before the prescription vary to some extent.

.....

Personality and Individual Differences. 2012 Feb;52:290-94.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN AN ADULT SAMPLE: ASSOCIATIONS WITH CLONINGER TEMPERAMENT AND CHARACTER DIMENSIONS.

Gomez R, Woodworth R, Waugh M, et al.

Relationships between C.R. Cloninger temperament and character dimensions and the Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms of inattention (IA) and hyperactivity/impulsivity (HI) were examined in 231 adults from the general population. Regression analyses that predicated overall ADHD, IA and HI by the seven temperament/character dimensions revealed: IA was predicted positively by Harm Avoidance and negatively by Self-Directedness; HI was predicted positively by Persistence; and overall ADHD was predicted negatively by Self-Directedness. These findings are also interpreted in terms of current theories of ADHD, and the related original and revised versions of Gray reinforcement sensitivity theory (RST) of personality.

.....

Personality and Individual Differences. 2012 Apr;52:696-701.

FALSE CONFESSIONS TO POLICE AND THEIR RELATIONSHIP WITH CONDUCT DISORDER, ADHD, AND LIFE ADVERSITY.

Gudjonsson GH, Sigurdsson JF, Sigfusdottir ID, et al.

Attention deficit hyperactivity (ADHD) symptoms and life adversity have been associated with the reporting of false confessions to crime, but it is not known if these predict false confessions beyond conduct disorder. The participants were 11,388 students in further education in Iceland, who completed a questionnaire anonymously in class. Current ADHD symptoms were measured by the Barkley Current Symptom Scale.

Conduct disorder was measured by the Oregon Adolescent Conduct Disorder Screen. Emotional lability was measured by items from the Symptom Check List-90. Negative life events and victimisation from group bullying were measured as indicators of life adversity. Out of 10,749 participants who provided information about interrogation and false confessions, 2104 (19.6%) reported having been interrogated at a police station as a suspect, and of those 261 (12.4%) reported having given a false confession to the police. Logistic regression showed that after controlling for gender, age and emotional lability both ADHD and negative life events predicted false confession above that of conduct disorder. The findings suggest that suspects resilience to resist pressure from police and peers is weakened by their condition rather than their false confession representing irresponsible and delinquent behaviour associated with conduct disorder.

Pharmacology, Biochemistry and Behavior. 2012 Apr;101:208-16.

SELECTIVE BILATERAL LESION TO CAUDATE NUCLEUS MODULATES THE ACUTE AND CHRONIC METHYLPHENIDATE EFFECTS.

Claussen CM, Chong SL, Dafny N.

The psychostimulant methylphenidate (MPD) is currently the most prescribed drug therapy for attention deficit hyperactivity disorder (ADHD) and is used by students as a cognitive enhancer. The caudate nucleus (CN) is a structure within the motive circuit where MPD exerts its effects, it is known to contain high levels of dopaminergic cells and directly influence motor activity. The objective of this study was to understand the role of CN in response to acute and chronic administration of MPD. Specific and non-specific bilateral ablations were created in the CN using electrolytic lesion and 6-Hydroxydopamine (6-OHDA). Four groups of rats were used: control (n = 4), sham (n = 4), CN electrolytic lesion group (n = 8) and CN 6-OHDA injected group (n = 8). On experimental day one (ED 1) all rats received a saline injection and baseline locomotive activity was recorded. On ED 2 and ED 3 CN sham, electrolytic lesion and/or 6-OHDA injected groups were made followed by four to five days recovery (ED 3-7), followed by six daily 2.5 mg/kg MPD injections (ED 9-14), three days of washout (ED 15-17) and an MPD re-challenge of drug proceeding the washout days (ED 18). Locomotor activity was obtained at ED 1, 8, 9, and 18 using an open field assay. The results show that the CN electrolytic lesion group responded to the acute and chronic MPD administration similar to the control and sham group, while the CN 6-OHDA injected group prevented the acute and the chronic effects of MPD administration. One possible interpretation why nonspecific electrolytic lesioning of the CN failed to prevent acute and chronic effects of MPD administration is due to destruction of both the direct and the indirect CN pathways which act as an inhibitory/excitatory balance, electrolytic/electrolytic. The selective dopaminergic lesioning prevented the effects of MPD administration suggesting that dopaminergic pathways in CN play a significant role in the effects of MPD.

Psychiatr Serv. 2012;63:122-29.

TREATMENT OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER: PATTERNS OF EVOLVING CARE DURING THE FIRST TREATMENT EPISODE.

Stein BD, Klein GR, Greenhouse JB, et al.

Objective: This study sought to better understand factors associated with different patterns of treatment among children starting treatment for attention-deficit hyperactivity disorder (ADHD).

Methods: Factors associated with service utilization and pharmacy claims data for 2,077 Medicaid-enrolled children aged six to 12 who started treatment for ADHD between October 2006 and December 2007 in a large mid-Atlantic state were investigated by using logistic regressions and Cox proportional hazard models.

Results: A total of 45% of children started ADHD treatment with a psychosocial intervention alone, 41% of children started treatment with medication alone, and 14% of children started treatment with a combination of both treatments. By the end of the treatment episode, 42% of children who initiated treatment with psychosocial interventions alone had added medication. Within six months of starting treatment, approximately 40% of children had discontinued treatment. Among those who continued receiving treatment, a majority received medication, either alone or with a psychosocial intervention. Treatment with a psychosocial intervention was significantly more likely to be initiated among nonwhite versus white

children and among younger versus older children. Younger versus older children and African-American versus Caucasian children were significantly more likely to drop out of treatment sooner.

Conclusions: During the first episode of treatment for ADHD, the interventions children received frequently changed, suggesting dissatisfaction with initial treatment. Further research is needed to better understand what underlies the patterns of evolving care so that all families seeking care for children with ADHD may receive preferred and effective treatment

Psychiatry Res. 2010;178:137-41.

INTERACTION OF RECALLED PARENTAL ADHD SYMPTOMS AND REARING BEHAVIOR WITH CURRENT ATTACHMENT AND EMOTIONAL DYSFUNCTION IN ADULT OFFSPRING WITH ADHD.

Edel MA, Juckel G, Brune M.

Research into attachment and emotion regulation has shown that children with ADHD are at risk of developing attachment disorders and emotion regulation disturbances, which in part may be due to the rearing style of their parents. No such data exists for adults with persistent ADHD. We hypothesized that current attachment style and emotion processing of adult patients with ADHD may be influenced by the presence of parental ADHD symptoms when the now adult patients were children, assuming that ADHD symptoms of parents have an impact on their parenting style. We examined recalled parental ADHD symptoms and rearing style as well as current attachment and emotion regulation abilities in a sample of 73 adults with ADHD using several self-rating instruments. Recalled prevalence of ADHD symptoms in the mother, and less so in the father, of adult patients with ADHD was significantly associated with partly adverse parental rearing styles, current attachment problems in romantic partnerships and emotion regulation disturbances compared with adult ADHD patients without possibly affected parent. ADHD symptoms in parents of children with ADHD may present a risk factor for attachment problems and poor emotion regulation when ADHD children are grown.

Psychol Assess. 2012 Mar;24:166-72.

EFFECTS OF DIURNAL VARIATION ON THE TEST OF VARIABLES OF ATTENTION PERFORMANCE IN YOUNG ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Hunt MG, Bienstock SW, Qiang JK.

The Test of Variables of Attention (TOVA) is a continuous performance test that assesses attention, impulsivity, and processing speed. Continuous performance tests are used in the assessment of attention-deficit/hyperactivity disorder (ADHD) in children and adults. TOVA norms are based on a morning administration, and any TOVA administered after 1:00 p.m. is flagged as potentially invalid. Whereas the testing time recommendations make sense for pediatric samples, it is unclear whether they are appropriate for young adults, who typically show significant phase delay in their diurnal rhythms. The current study explores the impact of time of day on TOVA performance in young adults with ADHD. Participants were randomly assigned to either morning or afternoon administration. We found no significant diurnal variation in TOVA performance. We also found no interaction between diurnal preference and time of day of administration. Night owls endorsed more inattention symptoms on a self-report measure than more intermediate individuals but actually made significantly fewer omission (inattention) errors on the TOVA. Self-reported symptoms of inattention showed moderate, significant correlations with various TOVA performance indices. Self-reported symptoms of hyperactivity and impulsivity, however, showed no relationship to TOVA performance. These results suggest that the TOVA can be administered to adults with ADHD outside of the hours recommended in the manual without significantly compromising the interpretative validity of test score interpretation. Thus, a TOVA report that is consistent with ADHD should not be dismissed simply because it was administered in the late afternoon.

Psychological Medicine: A Journal of Research in Psychiatry and the Allied Sciences. 2012 Jan;42:195-204.

FUNCTIONAL IMPROVEMENT AND CORRELATIONS WITH SYMPTOMATIC IMPROVEMENT IN ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER RECEIVING LONG-ACTING METHYLPHENIDATE.

Buitelaar JK, Casas M, Philipson A, et al.

Background: Data on the relationship between core symptoms and daily functioning in adults with attention deficit hyperactivity disorder (ADHD) are limited. Daily functioning was assessed as part of an open-label extension, and associations with symptom scores were evaluated.

Method: After a 5-week double-blind study with adults with ADHD receiving osmotic-controlled release oral delivery system (OROS) methylphenidate (MPH) 18, 36 or 72 mg/day, or placebo, participants were eligible for a 7-week open-label extension in which all patients received OROS MPH. Data for the Conners' Adult ADHD Rating Scale - Observer: Screening Version (CAARS-O:SV) (primary endpoint) have been presented previously. Secondary endpoints included the observer self-reported short version of the CAARS (CAARS-S:S) and the Clinical Global Impressions Severity Scale (CGI-S) Daily functioning and quality of life were assessed using the Sheehan Disability Scale (SDS) and the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) respectively. In post-hoc analyses, changes in CAARS-O:SV were evaluated in subgroups. Relationships between symptom and functional outcomes were evaluated in a multivariate regression analysis.

Results: A total of 370 patients entered the open-label extension Significant improvements from baseline in CAARS-O:SV were similar regardless of sex, ADHD subtype, prior treatment or psychiatric co-morbidity. Significant improvements from double-blind baseline were also seen for the CAARS-S:S, CGI-S, SDS and Q-LES-Q. Improvements in the CAARS-O:SV Hyperactivity/Impulsivity subscale were associated with improvements in SDS total and subscale scores, and in the Q-LES-Q score at open-label endpoint. Improvements in CAARS-O:SV Inattention subscale and CGI-S scores were not significantly associated with functional changes.

Conclusions: Improvements in ADHD symptoms relating to hyperactivity and impulsivity in adults receiving OROS MPH are associated with improvements in daily functioning and quality of life.

Psychological Medicine: A Journal of Research in Psychiatry and the Allied Sciences. 2012 Apr;42:875-87.

THE LIFETIME IMPACT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: RESULTS FROM THE NATIONAL EPIDEMIOLOGIC SURVEY ON ALCOHOL AND RELATED CONDITIONS (NESARC).

Bernardi S, Faraone SV, Cortese S, et al.

Background: The aim of the study was to present nationally representative data on the lifetime independent association between attention deficit hyperactivity disorder (ADHD) and psychiatric co-morbidity, correlates, quality of life and treatment seeking in the USA.

Method: Data were derived from a large national sample of the US population. Face-to-face surveys of more than 34 000 adults aged 18 years and older residing in households were conducted during the 2004-2005 period. Diagnoses of ADHD, Axis I and II disorders were based on the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV version.

Results: ADHD was associated independently of the effects of other psychiatric co-morbidity with increased risk of bipolar disorder, generalized anxiety disorder, post-traumatic stress disorder, specific phobia, and narcissistic, histrionic, borderline, antisocial and schizotypal personality disorders. A lifetime history of ADHD was also associated with increased risk of engaging in behaviors reflecting lack of planning and deficient inhibitory control, with high rates of adverse events, lower perceived health, social support and higher perceived stress. Fewer than half of individuals with ADHD had ever sought treatment, and about one-quarter had ever received medication. The average age of first treatment contact was 18.40 years.

Conclusions: ADHD is common and associated with a broad range of psychiatric disorders, impulsive behaviors, greater number of traumas, lower quality of life, perceived social support and social functioning, even after adjusting for additional co-morbidity. When treatment is sought, it is often in late adolescence or early adulthood, suggesting the need to improve diagnosis and treatment of ADHD.

Psychoneuroendocrinology. 2012 Feb;37:221-29.

STEROID SULFATASE-DEFICIENT MICE EXHIBIT ENDOPHENOTYPES RELEVANT TO ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Trent S, Dennehy A, Richardson H, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental condition characterised by inattention, impulsivity and hyperactivity; it is frequently co-morbid with anxiety and conduct disorders, sleep perturbation and abnormal consummatory behaviours. Recent studies have implicated the neurosteroid-modulating enzyme steroid sulfatase (STS) as a modulator of ADHD-related endophenotypes. The effects of steroid sulfatase deficiency on homecage activity, feeding/drinking behaviours, anxiety-related behaviours (assayed in light-dark box and open field paradigms), social dominance and serum steroid hormone levels were determined by comparing 40,XY and 39,X(Y*)O mice. Subsequently, mice administered the steroid sulfatase inhibitor COUMATE acutely were compared to vehicle-treated mice on behavioural tasks sensitive to enzyme deficiency to dissociate between its developmental and ongoing effects. 39,X(Y*)O mice exhibited heightened reactivity to a novel environment, hyperactivity in the active phase, and increased water (but not food) consumption relative to 40,XY mice during a 24h period; the former group also demonstrated evidence for heightened emotional reactivity. There was no difference in social dominance between the 40,XY and 39,X(Y*)O mice. COUMATE administration had no effect on homecage activity, water consumption or anxiety measures in the open field. 39,X(Y*)O mice exhibited significantly lower dehydroepiandrosterone (DHEA) serum levels than 40,XY mice, but equivalent corticosterone levels. Together with previous data, the present results suggest that steroid sulfatase may influence core and associated ADHD behavioural endophenotypes via both developmental and ongoing mechanisms, and that the 39,X(Y*)O model may represent a useful tool for elucidating the neurobiological basis of these endophenotypes.

Psychopharmacology. 2012 Feb;219:715-25.

EFFICACY AND SAFETY OF THE NOVEL ALFA (4) BETA (2) NEURONAL NICOTINIC RECEPTOR PARTIAL AGONIST ABT-089 IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED CROSSOVER STUDY.

Apostol G, Abi-Saab W, Kratochvil CJ, et al.

RATIONALE: $\alpha(4)\beta(2)$ Neuronal nicotinic receptors (NNRs) are implicated in the pathophysiology of attention-deficit/hyperactivity disorder (ADHD).

OBJECTIVES: This study examined the efficacy and safety of the $\alpha(4)\beta(2)$ NNR partial agonist ABT-089 versus placebo in adults with ADHD.

METHODS: In this multicenter, randomized, double-blind, placebo-controlled crossover study, subjects received placebo followed by ABT-089 (2 mg once daily [QD], 5 mg QD, 15 mg QD, 40 mg QD, or 40 mg twice daily [BID]), or vice versa, in a 2 x 2 crossover design. Each treatment period was 4 weeks, separated by a 2-week washout period. The primary efficacy endpoint was the Conners' Adult ADHD Rating Scale-Investigator Rated (CAARS:Inv) total score at the end of each treatment period. Secondary outcomes based on clinician- and self-rated efficacy scales were evaluated.

RESULTS: Of the 221 subjects enrolled, 171 met criteria for inclusion in the completers dataset for efficacy analyses. ABT-089 was superior to placebo on the CAARS:Inv total score at 40 mg QD and 40 mg BID (model-based least square mean difference from placebo: -4.33, P=0.02; -3.02, P=0.03, respectively). ABT-089 also demonstrated significant improvements on several secondary measures of efficacy. ABT-089 was generally safe and well tolerated. The most commonly reported adverse events ($\geq 5\%$) for total ABT-089-treated subjects at rates higher than placebo were headache, upper respiratory tract infection, irritability, insomnia, and nasopharyngitis.

CONCLUSIONS: In this phase 2 crossover study, the NNR partial agonist ABT-089, at doses of 40 mg QD and 40 mg BID, was efficacious and generally well tolerated in treatment of adults with ADHD.

Psychopharmacology. 2012 Jan;219:537-47.

EFFECTS OF SMOKING ABSTINENCE ON IMPULSIVE BEHAVIOR AMONG SMOKERS HIGH AND LOW IN ADHD-LIKE SYMPTOMS.

Ashare RL, Hawk LW, Jr.

Rationale: Impulsivity, a multifaceted construct that includes inhibitory control and heightened preference for immediate reward, is central to models of drug use and abuse. Within a self-medication framework, abstinence from smoking may lead to an increase in impulsive behavior and the likelihood of relapse, particularly among persons with disorders (e.g., attention-deficit/hyperactivity disorder, ADHD) and personality traits (e.g., impulsivity) linked to impulsive behavior.

Objectives: This study aimed to examine the effects of smoking abstinence on multiple measures of impulsivity among a non-clinical sample of adult smokers selected for high and low levels of ADHD symptoms.

Methods: In a within-subjects design, participants selected for high or low levels of self-reported ADHD symptoms (N = 56) completed sessions following overnight abstinence and when smoking as usual (order counterbalanced). Measures of impulsive behavior included response inhibition (i.e., stop signal task), interference control (i.e., attentional modification of prepulse inhibition (PPI) of startle), and impulsive choice (i.e., hypothetical delay discounting).

Results: As hypothesized, abstinence decreased response inhibition and PPI. Although ADHD symptoms moderated abstinence effects on impulsive choice and response inhibition, the pattern was opposite to our predictions: the low-ADHD group responded more impulsively when abstinent, whereas the high-ADHD group was relatively unaffected by abstinence.

Conclusions: These findings highlight the importance of utilizing multiple laboratory measures to examine a multifactorial construct such as impulsive behavior and raise questions about how best to assess symptoms of ADHD and impulsivity among non-abstinent smokers.

Res Autism Spectr Disord. 2012 Jan;6:500-07.

PARENTAL AGE AND ASSISTED REPRODUCTIVE TECHNOLOGY IN AUTISM SPECTRUM DISORDERS, ATTENTION DEFICIT HYPERACTIVITY DISORDER, AND TOURETTE SYNDROME IN A JAPANESE POPULATION.

Shimada T, Kitamoto A, Todokoro A, et al.

We investigated whether advanced parental age and assisted reproductive technology (ART) are risk factors in autism spectrum disorders (ASDs), attention deficit hyperactivity disorder (ADHD), and Tourette syndrome (TS). Clinical charts of Japanese outpatients with ASD (n =552), ADHD (n =87), and TS (n =123) were reviewed. Parental age of individuals with ASD, ADHD, or TS was compared with parental age in the general population (GP) of Tokyo after adjusting for year of birth. Paternal and maternal ages were significantly higher in persons with ASD and ADHD, but not those with TS. In final steps of stepwise logistic regression analysis, both maternal and paternal age were associated with ASD after controlling for the other parent's age, gender, and birth order. In cases where the presence or absence of ART could be ascertained (ASD n =467; ADHD n =64; TS n =83), the rate of ART in cases of persons with ASD (4.5%) was 1.8 times the frequency expected in the GP, while ART was not present in cases of persons with ADHD and TS. These preliminary results remain tentative pending replication with larger, community-based samples.

Res Dev Disabil. 2012 Mar;33:682-87.

WITH A LITTLE HELP FROM MY FRIENDS: PSYCHOLOGICAL, ENDOCRINE AND HEALTH COROLLARIES OF SOCIAL SUPPORT IN PARENTAL CAREGIVERS OF CHILDREN WITH AUTISM OR ADHD.

Lovell B, Moss M, Wetherell MA.

Elevated psychological distress and concomitant dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis has been implicated as one pathway that links the stress of caregiving with adverse health outcomes. This study assessed whether perceived social support might mitigate the psychological, endocrine and health consequences of caregiver stress in parents of children with autism and attention deficit hyperactivity disorder (ADHD). Parental caregivers completed measures of psychological distress,

perceived availability of social support and physical health complaints. To capture important parameters of the basal diurnal cortisol pattern, caregivers collected salivary cortisol at waking, 30 min post waking, 1200 h and 2200 h on two consecutive weekdays. Psychological distress and self reported physical health complaints were inversely related to scores on all support subscales: tangible, belonging, self esteem and appraisal. Results further revealed a significant, positive association between magnitude of the cortisol awakening response (CAR) and caregivers' self esteem. As a buffer between the stress of caregiving and adverse physical health outcomes, social support acts to reduce stress appraisals and mitigate disturbances of the HPA axis. Moving forward, intervention programmes might seek to increase caregivers' perceived availability of social resources.

.....

Schweiz Arch Neurol Psychiatr. 2011;162:29S.

TOPOGRAPHY OF SLEEP SLOW WAVE ACTIVITY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Ringli M, Souissi S, Kurth S, et al.

Introduction: Attention deficit hyperactivity disorder (ADHD) is the most common disorder in childhood (Olfson, 1992), whose genesis is still discussed. Supporting the idea that ADHD may be the result of a maturational delay (e.g. Gustafsson et al., 2010) it was shown that in children with ADHD gray matter maturation lagged behind that of typically developing children (Shaw et al., 2011). Recently, the topography of sleep slow wave activity (SWA), the major characteristics of non-rapid eye movement (NREM) sleep, was shown to mirror the actual state of cortical maturation and functioning during development (Kurth et al., 2010). We therefore investigated the sleep EEG of children with ADHD and age-matched healthy controls, asking, if a maturational delay would be reflected in the SWA topography.

Methods: All-night high density EEG (128 electrodes) was recorded in nine children with ADHD and nine age- and sexmatched healthy controls (ADHD: mean age 11.8 (plus or minus) 0.4 years; controls: 11.6 (plus or minus) 0.5). EEG recordings were sleep staged, subjected to semi-automatic artefact removal and processed using power spectral analysis. Mean SWA (1-4.5 Hz) was calculated for the first hour of NREM sleep. For statistical analysis mean SWA was calculated in a frontal and central cluster of 8-9 electrodes (fig. 1). (Figure presented)

Results: A comparison of the SWA topography of the first 60 minutes of NREM sleep revealed differences between the two groups: Compared to healthy controls children with ADHD showed more SWA over the central region (+12% (plus or minus) 4%, $p = 0.004$) and less SWA over the frontal cortex (-22% (plus or minus) 7%, $p = 0.02$) (fig. 1). No other area showed significant group differences.

Discussion: During cortical maturation maximal SWA shifts along the posterior-anterior-axis (Kurth et al., 2010). Thus, the major differences in SWA topography found in ADHD children depict a pattern typically seen in children of younger age. This pattern may well be due to a maturational delay. However, as major symptoms of ADHD include deficits in inhibitory control and motor hyperactivity the observed differences in topography could also reflect functional differences in the underlying areas.

.....

The Journal of Neuroscience. 2012 Jan;32:841-49.

METHYLPHENIDATE-ELICITED DOPAMINE INCREASES IN VENTRAL STRIATUM ARE ASSOCIATED WITH LONG-TERM SYMPTOM IMPROVEMENT IN ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Volkow ND, Wang GJ, Tomasi D, et al.

Stimulant medications, such as methylphenidate, which are effective treatments for attention deficit hyperactivity disorder (ADHD), enhance brain dopamine signaling. However, the relationship between regional brain dopamine enhancement and treatment response has not been evaluated. Here, we assessed whether the dopamine increases elicited by methylphenidate are associated with long-term clinical response. We used a prospective design to study 20 treatment-naïve adults with ADHD who were evaluated before treatment initiation and after 12 months of clinical treatment with a titrated regimen of oral methylphenidate. Methylphenidate-induced dopamine changes were evaluated with positron emission tomography and [^{11}C]raclopride ($D\alpha_2/D\alpha_1$ receptor radioligand sensitive to competition with endogenous dopamine). Clinical responses were assessed using the Conners' Adult ADHD Rating Scale and revealed a significant reduction in symptoms of inattention and hyperactivity with long-term methylphenidate treatment.

A challenge dose of 0.5 mg/kg intravenous methylphenidate significantly increased dopamine in striatum (assessed as decreases in $D\alpha_1/D\alpha_2$ receptor availability). In the ventral striatum, these dopamine increases were associated with the reductions in ratings of symptoms of inattention with clinical treatment. Statistical parametric mapping additionally showed dopamine increases in prefrontal and temporal cortices with intravenous methylphenidate that were also associated with decreases in symptoms of inattention. Our findings indicate that dopamine enhancement in ventral striatum (the brain region involved with reward and motivation) was associated with therapeutic response to methylphenidate, further corroborating the relevance of the dopamine reward/motivation circuitry in ADHD. It also provides preliminary evidence that methylphenidate-elicited dopamine increases in prefrontal and temporal cortices may also contribute to the clinical response.

.....

The Psychiatrist. 2012 Jan;36.

CRITICAL ANALYSIS OF THE CONCEPT OF ADULT ATTENTION-DEFICIT HYPERACTIVITY DISORDER': AUTHOR'S REPLY.
Moncrieff J, Timimi S.

Reply to the comments made by J. Moncrieff and S. Timimi (see record 2012-00110-012) on the current authors' original article (see record 2011-19964-004). In response to Tyrie & Knibbs, positive accounts of improvement and recovery from any disorder or difficulties are important and inspiring, but they cannot be taken as evidence for the efficacy of a particular treatment. The efficacy of treatments can only be established by randomized controlled trials, and these demonstrate that people taking stimulants for adult attention-deficit hyperactivity disorder do only slightly better than those taking a placebo in the short term and do no better in the long term. The effectiveness of a drug is then judged by balancing the gains against placebo, if there are any, with the adverse effects associated with the drug, as well as other considerations. Stimulants do have effects, of course. They are not inert. Low-dose stimulants modify behavior in animals and humans alike, improving attention and focus on mundane tasks. Animal studies also show that this effect is accompanied by a reduction in spontaneous exploratory behavior, interest in the environment and social interaction. Moreover, any initial effects may decline due to tolerance, which, although little investigated in the case of therapeutic stimulant use, is known to occur in response to most psychoactive substances.

.....

The Psychiatrist. 2012 Jan;36:36-37.

ADULT ATTENTION-DEFICIT HYPERACTIVITY DISORDER A VERY MUCH REAL DIAGNOSIS.
Tyrie CM, Knibbs P.

Comments on an article by J. Moncrieff and S. Timimi (see record 2011-19964-004). Moncrieff & Timimi have challenged whether adult attention-deficit hyperactivity disorder (ADHD) exists as a discrete condition. They suggest that it is merely the medicalization of ordinary human difficulties and that the diagnosis is being pushed by pharmaceutical companies who then make a tidy profit. They point out the discrepancies between childhood ADHD and adult ADHD and based on this state that adult ADHD is not the same condition. Presumably they subscribe to the view that childhood ADHD suddenly disappears on the child's 18th birthday. Drawing on evidence-based medicine, Moncrieff & Timimi report studies where there is no significant difference between stimulant drug and placebo in adult ADHD, yet individual experience has shown dramatic, positive and sustained benefit to the quality of life of individual patients and their ability to function. The suggestion that adult ADHD is the medicalization of various common difficulties is unreasonable. The persisting difficulties in ADHD are very much those of inattention and concentration rather than the overt hyperactivity seen in childhood ADHD and it is these very levels of inattention and concentration which have a huge impact on the ability of individuals with ADHD to function in the adult world. The fact that ADHD symptoms overlap with a number of other disorders does not negate the existence of the condition. There are symptoms overlapping in a number of psychiatric conditions but this does not lead us to be reductionist with our diagnoses. Indeed, to suggest that those with ADHD have personality disorders is doing them a great disservice. Adults who, after appropriate assessment, are diagnosed with adult ADHD and treated with stimulants have achieved stability in their lives and success in

their academic endeavors, employment and relationships which otherwise would never have been possible.

.....
The World Journal of Biological Psychiatry. 2012 Jan;13:48-59.

MULTISCALE ASSESSMENT OF TREATMENT EFFICACY IN ADULTS WITH ADHD: A RANDOMIZED PLACEBO-CONTROLLED, MULTI-CENTRE STUDY WITH EXTENDED-RELEASE METHYLPHENIDATE.

Retz W, Rösler M, Ose C, Scherag A, Alm B, Philipsen A, Fischer R, Ammer R; Study Group.

OBJECTIVES: This trial was performed to test the efficacy and safety of an extended-release formulation of methylphenidate (MPH ER).

METHODS: A total of 162 adults with ADHD according to DSM-IV were treated for 8 weeks with either two daily individually body weight-adjusted doses of MPH ER up to 1 mg/kg per day (N = 84) or placebo (N = 78). The primary efficacy outcome was the Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) 8 weeks after randomization. Secondary efficacy measures were the ADHD Diagnostic Checklist (ADHD-DC), the Conners Adult Attention Deficit Disorder Scale (CAARS-S:L), the Clinical Global Impression (CGI) and the Sheehan Disability Scale (SDS).

RESULTS: At week 8 a significantly higher decline of the total WRAADDS score was found in the MPH ER group as compared to the placebo group (P = 0.0003). The rates of responders were 50% in the MPH ER and 18% in the placebo group (P < 0.0001). Furthermore, similar effects were observed for the secondary efficacy variable: ADHD-DC score (P = 0.004), CAARS-S:L score (P = 0.008) and the SDS score (P = 0.017). 50% of the MPH ER group and 24.4% of the placebo group were improved "much" or "very much" according to the CGI rating (P = 0.0001). MPH ER treatment was well tolerated. At week 2 also the mean heart rate was significantly higher in the MPH ER group as compared to the placebo group (P = 0.01). No differences between the study groups were observed regarding mean blood pressure at any visit.

CONCLUSIONS: This clinical trial demonstrated statistically significant and clinical relevant effects of MPH ER in adults with ADHD for several self- and investigator-rated ADHD psychopathology and also functional efficacy measures.

.....
Trends in Cognitive Sciences. 2012 Jan;16:17-26.

LARGE-SCALE BRAIN SYSTEMS IN ADHD: BEYOND THE PREFRONTAL STRIATAL MODEL.

Castellanos FX, Proal E.

Attention-deficit/hyperactivity disorder (ADHD) has long been thought to reflect dysfunction of prefrontal striatal circuitry, with involvement of other circuits largely ignored. Recent advances in systems neuroscience-based approaches to brain dysfunction have facilitated the development of models of ADHD pathophysiology that encompass a number of different large-scale resting-state networks. Here we review progress in delineating large-scale neural systems and illustrate their relevance to ADHD. We relate frontoparietal, dorsal attentional, motor, visual and default networks to the ADHD functional and structural literature. Insights emerging from mapping intrinsic brain connectivity networks provide a potentially mechanistic framework for an understanding of aspects of ADHD such as neuropsychological and behavioral inconsistency, and the possible role of primary visual cortex in attentional dysfunction in the disorder.

.....
Z Kinder- Jugendpsychiatr Psychother. 2012;40:95-103.

DEFICIENT ADAPTIVE REGULATION OF EMOTION IN CHILDREN WITH ADHD .

Schmitt K, Gold A, Rauch WA.

Objectives: The current study investigates whether children with and without ADHD differ in their implementation of emotion-regulation strategies. In addition, it explores whether the regulation patterns of ADHD children are related to co-occurring behavioral and emotional problems.

Methods: A group of 21 children with ADHD and a group of 20 children without ADHD (ages 10-13) completed the Questionnaire on Emotion Regulation in Children and Adolescents (FEEL-KJ, Grob &

Smolenski, 2005). Furthermore, we employed the parent-rated Strengths and Difficulties Questionnaire (Woerner, Becker & Rothenberger, 2004) to assess the socioemotional problems of ADHD children.

Results: Self-reports revealed group differences in terms of adaptive emotion regulation, though no group differences were found in terms of maladaptive emotion regulation. Specifically, children with ADHD reported less frequently applying the strategies "Cognitive Problem Solving," "Problem-Oriented Acting," "Mood Enhancement," "Reevaluation," and "Distraction." Children with ADHD also reported seeking social support less frequently than the controls. Moreover, significant negative correlations were found between adaptive coping and co-occurring behavioral and emotional problems.

Conclusions: Children with and without ADHD specifically differ in their application of problem-oriented emotion-regulation strategies, especially those ADHD children suffer from co-occurring problems who particularly infrequently apply adaptive emotion regulation strategies.

.....

Reviews and Overviews

Mechanisms of Psychiatric Illness

Striatal Dopamine Transporter Alterations in ADHD: Pathophysiology or Adaptation to Psychostimulants? A Meta-Analysis

Paolo Fusar-Poli, Ph.D.

Katya Rubia, Ph.D.

Giorgio Rossi, M.D.

Giuseppe Sartori, Ph.D.

Umberto Balottin, M.D., Ph.D.

Background: Striatal dopamine transporter abnormalities are thought to underlie the pathophysiology and psychostimulant treatment of attention deficit hyperactivity disorder (ADHD). However, individual studies using single photon emission tomography (SPECT) or positron emission tomography (PET) have yielded inconsistent results, i.e., both high and low striatal dopamine transporter levels.

Method: Nine SPECT and PET studies investigating striatal dopamine transporter density in ADHD patients (N=169) and age-, gender-, and IQ-matched healthy comparison subjects (N=173) were included in a quantitative meta-analysis. Binding potentials in the striatum and demographic, clinical, and methodological variables were extracted from each publication or obtained directly from authors. Hedges' *g* was used as a measure of effect size in an analysis using Comprehensive Meta-Analysis software. Publication bias was assessed with funnel plots and Egger's intercept. Heterogeneity was ad-

ressed with the *Q* statistic and *I*² index.

Results: Striatal dopamine transporter density was 14% higher on average in the ADHD group than in the healthy comparison group. However, heterogeneity across studies was large and statistically significant. Meta-regression analyses showed that the percentage of subjects without exposure to psychostimulants was negatively correlated with dopamine transporter density; density was higher in patients with previous medication exposure and lower in medication-naïve patients. There was no moderating effect for age, comorbidity, gender, year of publication, or imaging technique. There was no publication bias, and sensitivity analysis confirmed robustness of the results.

Conclusions: Striatal dopamine transporter density in ADHD appears to depend on previous psychostimulant exposure, with lower density in drug-naïve subjects and higher density in previously medicated patients.

(*Am J Psychiatry* 2012; 169:264–272)

Attention deficit hyperactivity disorder (ADHD) is characterized by age-inappropriate symptoms of inattention, impulsiveness, and hyperactivity (1). It affects 3%–8% of school-age children, disrupting academic and social development, and persists into adulthood in 65% of those affected, amounting to 4% of the adult population (2, 3). Cognitively, children and adults with ADHD have deficits in late-developing cognitive functions, most prominently inhibition, attention, motivation, and timing functions that are known to be mediated by late-developing frontostriatal and cerebellar networks (4, 5).

The biological origins of ADHD are complicated by heterogeneous clinical symptoms, comorbidity (in approximately 65% of the cases) with other disorders (conduct, mood, and anxiety disorders and Tourette's syndrome), and exacerbation by adverse environments and psychosocial events (6). The last two decades of structural and functional imaging studies have shown that ADHD is associated with deficits in the structure, functioning, and

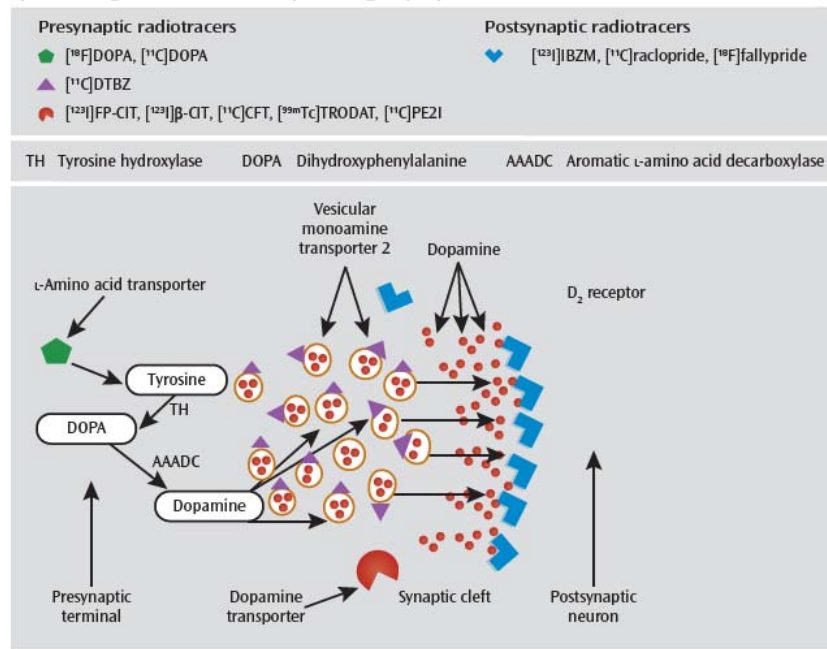
connectivity of frontostriatal, parietotemporal, and frontocerebellar networks (5, 7, 8). A recent meta-analysis of all structural voxel-based morphometry studies in ADHD, however, showed that the most consistent deficit is low gray matter volume in the basal ganglia (9).

Studies using positron emission tomography (PET) and single photon emission tomography (SPECT), conducted mostly in adults with the disorder, have focused predominantly on the neurotransmitter dopamine, given that it is known to have a central role in the regulation of psychomotor activity, motivation, and the frontostriatal-mediated inhibitory, timing, and attention functions that are compromised in the disorder (10). The focus on striatal dopamine has been reinforced by structural, functional, and neurochemical imaging findings of striatal deficits (5, 7–9). The striatum receives dense ascending projections from the mesencephalic dopamine neurons of the substantia nigra and ventral tegmental area (11). The interest in striatal dopamine was further heightened by the

This article is featured in this month's **AJP Audio**

FUSAR-POLI, RUBIA, ROSSI, ET AL.

FIGURE 1. Simplified Diagram of a Striatal Dopaminergic Synapse^a



^a On the presynaptic side, potential markers for imaging of the integrity of dopaminergic neurons are shown. A measure of dopamine-synthesizing capacity is provided by [¹⁸F]DOPA PET and [¹¹C]DOPA PET. In the case of [¹⁸F]DOPA PET, the radiotracer is taken up in the dopaminergic neuron via an L-amino acid transporter and is then decarboxylated to [¹⁸F]fluorodopamine by aromatic L-amino acid decarboxylase (AAADC) and temporarily stored in vesicles (vesicular monoamine transporter, type 2) within the nerve terminals. In humans, [¹¹C]dihydroxytetrahydrozoline ([¹¹C]DTBZ) is a commonly used marker for the vesicular monoamine transporter 2, which provides an index of monoamine presynaptic terminal density. Substituted (nor)phenyltropanes ([¹²³I]FP-CIT, [¹²³I]β-CIT, [¹¹C]PE2I, [¹¹C]CFT, and [^{99m}Tc]TRODAT) are frequently used PET and SPECT tracers for imaging of dopamine active transporters in humans. Striatal density of dopamine active transporters provides another measure of the density of dopaminergic presynaptic terminals or innervation into the striatum. Finally, commonly used radiotracers for D_{2/3} receptors are substituted benzamides ([¹²³I]BZM, [¹¹C]raclopride, and [¹⁸F]fallypride) and are used to address postsynaptic functioning. For convenience, only D₂ receptors are shown on the postsynaptic cell.

fact that the striatal dopamine transporter is the main target for one of the most effective treatments of ADHD, methylphenidate (12–15), which has been shown to block about 70% of striatal dopamine transporters (16), leading to enhanced striatal dopamine availability (12). Last, dopamine receptor and transporter genotypes have been associated with the disorder (for a meta-analysis, see reference 13).

The membrane-bound presynaptic dopamine active transporter plays a key role in regulating the dopamine content in the synaptic cleft by removing the dopamine molecules from the synaptic cleft and returning them to the presynaptic cell (16a). Dopamine transporters are localized in dopaminergic axons, with the highest levels in the striatum and olfactory tubercle and much lower levels in the amygdala, hypothalamus, hippocampus, thalamic nuclei, and neocortex (14). Because striatal dopamine transporters are located exclusively on dopamine-synthesizing neurons, the measurement of striatal dopamine transporter density is a specific marker of presynaptic dopaminergic neuron integrity (15). It is possible to simultaneously visu-

alize and quantify dopamine transporter binding by using radioligands and SPECT or PET (Figure 1).

The findings on dopamine transporter levels in the striatum of patients with ADHD relative to those of comparison subjects have been inconsistent. While several of the earlier studies showed higher dopamine transporter levels in ADHD patients (16), some showed no difference (17) and others indicated lower dopamine transporter levels in ADHD (10). Reasons for the discrepancies could be 1) differences in radiotracers or the methods used, 2) differences in patients' characteristics, including medication history, comorbid conditions, and age, and 3) differences in study group sizes. One of the most compelling confounds is psychostimulant medication, given the known acute effect of psychostimulants of modulating striatal dopamine transporters (12). A number of critical reviews have addressed dopamine transporter alterations in ADHD (6, 18–21); however, to our knowledge, no formal meta-analysis has ever tested the magnitude of these abnormalities while controlling for the aforementioned confounds, particularly medication effects.

STRIATAL DOPAMINE TRANSPORTERS IN ADHD

In this meta-analysis of PET and SPECT studies, we aimed to examine the meta-analytic evidence for a consistent alteration of striatal dopamine transporter density across studies. In addition, we aimed to assess the effect of medication history and a number of other moderator variables, including age, comorbid conditions, gender, and publication year.

Method

Selection Procedures

A systematic search strategy was used to identify relevant studies. First, we carried out a search of PubMed, Science Direct, and Scopus to identify putative studies of striatal dopamine transporters in ADHD subjects. We used the following search terms: "DAT," "dopamine transporter," "ADHD," "PET," and "SPECT." In a second step, the reference lists of the articles included in the review were manually checked for relevant studies not identified by computerized literature searching. Next, the corresponding authors were contacted by e-mail with a request for any details not included in the original manuscripts.

Studies were included if they met the following criteria: 1) were reported in an original article in a peer-reviewed journal, 2) had involved subjects affected with DSM- or ICD-defined ADHD, 3) had analyzed data for the two groups obtained with SPECT or PET techniques assessing striatal dopamine transporter density, 4) had calculated the mean and standard deviation for striatal dopamine transporter density in both groups, 5) included a healthy comparison group, and 6) did not involve a study group that overlapped with a previous group.

Recorded Variables

The recorded variables for each article included in the meta-analysis were type of radiotracer and imaging technique, gender, mean age of participants, IQ, year of publication, exposure to previous stimulant treatments, presence of comorbid conditions, smoking status, and statistical significance of the core findings. To achieve a high standard of reporting we adopted the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines (22) and the QUOROM statement on the quality of reporting of meta-analyses (23).

Quality Assessment

Although quality assessments can be reliably conducted in meta-analyses of experimental studies, their use in observational research is controversial, with no clear consensus on rating methods or their appropriate use in analysis (24). In the present meta-analysis, we used a simple objective rating system based on a meta-analysis by Paulson and Bazemore (25). We coded each study's quality on a scale of 0 to 10, assigning 2 points each for a description of the sampling method, the presence of clearly stated inclusion criteria, assessment of ethnic diversity, assessment of educational diversity, and a comprehensive description of the main outcome measure. Studies that included these features thus received a higher quality rating. Because evidence about the validity of quality ratings in observational research is lacking, we adopted the MOOSE (meta-analysis of observational studies in epidemiology) approach of broadly including studies and using sensitivity analysis to determine incremental effects of lower-quality studies (26).

Statistical Analysis

Data were analyzed by using Comprehensive Meta-Analysis software, version 2 (Biostat, Englewood, N.J.). The primary outcome was striatal dopamine transporter binding in the patients

and the comparison group. To measure effect size, we adopted Hedges' g , i.e., the difference between the means of the patient and comparison groups, divided by the standard deviation and weighted for group size in order to correct for bias from small groups (27). This metric is computed by using the square root of the mean square error from the analysis of variance testing for differences between the two groups (27), along with the 95% confidence interval (CI).

Subanalyses were conducted to assess the impact of categorical moderator variables. Meta-regression analyses were used to test the influence of continuous moderator variables: year of publication, age of participants, and gender (percentage of females). The slope of meta-regression, i.e., the β coefficient, either direct (+) or inverse (-), of the regression line indicates the strength of the relationship between moderator and outcome. To limit the risk of false positive (type I) errors arising from multiple comparisons, we adjusted $p < 0.05$ by dividing α by the number of meta-regressions, i.e., 7.

In general, random-effects models are more conservative than fixed-effect models and appear to better address heterogeneity among studies and study groups, allowing for greater flexibility in parsing effect size variability. Moreover, they are less influenced by extreme variations in group size (28). Because the studies in this meta-analysis were characterized by heterogeneity, random-effects models were used. Heterogeneity among study point estimates was assessed with the Q statistic, and the magnitude of heterogeneity was evaluated with the I^2 index (29). Studies with negative results are less likely to be published than studies with statistically significant results. The possibility of a publication bias in the present study was examined by visually inspecting funnel plots and applying the regression intercept of Egger et al. (30). In this way we assessed whether there was a tendency for selective publication of studies based on the nature and direction of their results. In addition, we used the fail-safe procedure (31) to generate the number of unpublished studies that would be needed to move estimates to a nonsignificant threshold. To assess the robustness of the results, we performed sensitivity analyses by sequentially removing each study and rerunning the analysis.

Results

Studies Found

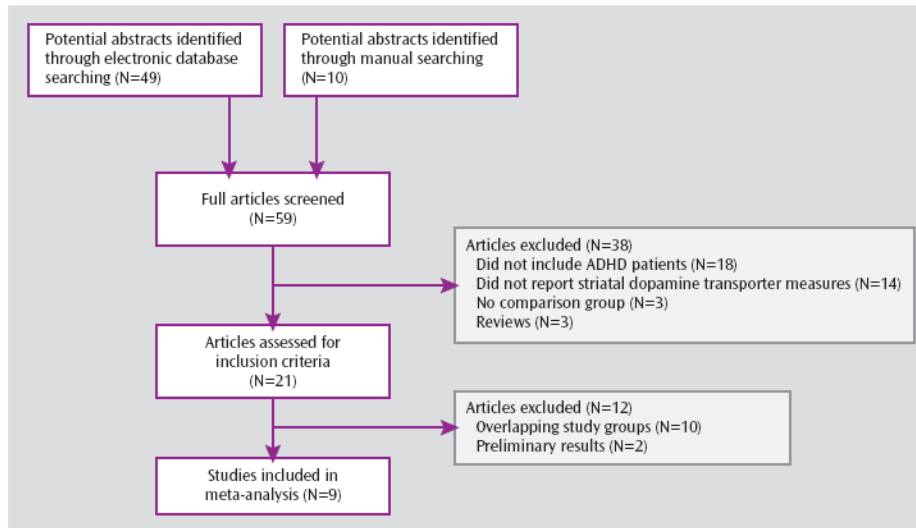
The combined search strategies yielded a total of 59 articles, of which 38 were excluded. Of the 21 that were considered eligible, nine PET or SPECT studies published between 1999 and 2009 met our inclusion criteria and were included in the present meta-analysis (Figure 2). The overall database contained 169 subjects with ADHD (mean age=29.9 years, SD=11.8; 43% females) and 173 healthy comparison subjects (mean age=29.1 years, SD=9.3; 38% females), all well matched with respect to age, IQ, and gender ($p > 0.05$ in all cases) (Table 1).

Dopamine Transporter Density in Striatum

Two out of the nine studies showed no significant difference in striatal dopamine transporter density between the ADHD and comparison groups (17, 33), while five studies showed higher dopamine transporter density in the ADHD group (16, 32, 34–36) and two studies showed lower dopamine transporter density in ADHD (10, 37). The pooled meta-analysis indicated consistent statistical evidence for greater dopamine transporter density in the

FUSAR-POLI, RUBIA, ROSSI, ET AL.

FIGURE 2. Strategy for Identifying Studies for a Meta-Analysis of Striatal Dopamine Transporter Density in ADHD



ADHD group than in the comparison group in the whole striatum (Figure 3), although the magnitude of the effect size was small. The ratio of striatal dopamine transporter density in the ADHD group to the density in the comparison group ranged from 0.80 to 1.70 (Table 1), with an average value of 1.14. No laterality effect was detected.

Effect of Moderators

The type of imaging technique (PET or SPECT) did not influence the meta-analytical results ($Q=2.74$, $p=0.61$). Meta-regression analyses revealed no significant effects on the findings for gender ($\beta=-0.41$, 95% CI=-0.53 to 1.35, $z=0.86$, $p=0.39$), year of publication ($\beta=-0.00$, 95% CI=-0.08 to 0.08, $z=-0.09$, $p=0.93$), or age of the patients ($\beta=0.02$, 95% CI=-0.01 to 0.04, $z=1.09$, $p=0.28$) or the healthy comparison subjects ($\beta=-0.01$, 95% CI=-0.05 to 0.03, $z=-0.68$, $p=0.50$). However, within the comparison group, when age was treated as a categorical variable and the studies were divided into those whose comparison group had a mean age above 40 years (39 subjects) and studies with comparison subjects having a mean age below 30 years (42 subjects), we detected a nearly significant difference in dopamine transporter density, with a lower density in the older group (Hedges' $g=-0.03$, $p=0.07$). The percentage of ADHD subjects without previous psychostimulant exposure had a significant negative effect on the Hedges' g value for striatal dopamine transporter levels, in that lower and negative effect sizes were detected in studies involving drug-naïve ADHD patients (Figure 4). Thus, lower dopamine transporter levels were associated with the absence of medication exposure, while higher dopamine transporter levels were associated with a history of medication. Post hoc analyses confirmed higher dopamine transporter levels

(Hedges' $g=1.56$) for the medication-history subgroup and lower dopamine transporter levels for the medication-naïve subgroup (Hedges' $g=-0.10$) relative to the comparison subjects. The modulating effect of stimulant exposure accounted for 48% of the overall variance ($Q=29.73$, $p<0.001$). Finally, all of the studies but one excluded individuals with comorbid psychiatric or neurological conditions from the ADHD and comparison groups.

Tests for Publication Bias and Heterogeneity and Sensitivity Analysis

Visual inspection of funnel plots revealed no evidence of publication bias. Quantitative evaluation of publication bias, as measured by the Egger intercept, indicated a non-significant effect ($p=0.14$). The fail-safe procedure estimated that 17 unpublished studies would be needed to bring the overall meta-analytic estimate to nonsignificance. According to the criteria set by Higgins and Thompson (38), the heterogeneity in the published studies was large and statistically significant ($Q=61.69$, $p<0.001$; $I^2=87.03$). As the overall interstudy variance in effect sizes was substantial, it encouraged consideration of possible explanatory factors. Removing studies with poor quality ratings influenced the meta-analytic estimate by only 4%.

Discussion

To our knowledge, this is the first comprehensive meta-analysis addressing striatal dopamine transporter density in ADHD. Meta-analytic evidence from approximately 170 ADHD patients showed on average 14% greater density of striatal dopamine terminals in the ADHD patients than in healthy comparison subjects. However, the effect size was

STRIATAL DOPAMINE TRANSPORTERS IN ADHD

TABLE 1. PET or SPECT Studies Included in a Meta-Analysis of Striatal Dopamine Transporter Density in ADHD Patients and Healthy Comparison Subjects

Study and Group	Radiotracer	Technique	N		Age (years)		ADHD Treatment Status	ADHD/Comparison Ratio of Dopamine Transporters
			Total	Female	Mean	SD		
Dougherty et al., 1999 (16)	^[123I] altropane	SPECT	6	4	41.33	4.46	Drug-free	1.70 ^a
ADHD Comparison			30	—	40.80	— ^b		
van Dyck et al., 2002 (17)	^[123I] β-CIT	SPECT	9	3	41	11	8 drug-naive, 1 drug-free	1.00
ADHD Comparison			9	3	41	11		
Cheon et al., 2004 (32)	^[123I] IPT	SPECT	9	2	9.67	2.12	Drug-naive	1.51 ^a
ADHD Comparison			6	—	10.33	2.88		
Jucaite et al., 2005 (33)	^[11C] PE2I	PET	12	0	13.8	1.2	9 drug-naive, 3 drug-free	1.08
ADHD Comparison			10	0	29.5	5.8		
la Fougere et al., 2006 (34)	^[99mTc] TRODAT-1	SPECT	22	11	39.1	10.2	Drug-free	1.16 ^a
ADHD Comparison			14	6	— ^c	—		
Larisch et al., 2006 (35)	^[123I] FP-CIT	SPECT	20	11	35	7	Drug-naive	1.06 ^a
ADHD Comparison			20	11	32	8		
Spencer et al., 2007 (36)	^[11C] altropane	PET	21	7	34.4	9.2	Drug-naive	1.15 ^a
ADHD Comparison			26	15	27.4	7.6		
Volkow et al., 2009 (10)	^[11C] cocaine	PET	53	26	32	8	Drug-naive	0.80 ^a
ADHD Comparison			44	14	31	6		
Hesse et al., 2009 (37)	^[123I] FP-CIT	SPECT	17 ^d	9	32	8	Drug-naive	0.81 ^a
ADHD Comparison			14	6	32	9		

^a Statistically significant.

^b Age range=21–60.

^c Age range=21–63.

^d With psychiatric or neurological comorbidity.

small and heterogeneity across studies was substantial, with a prominent effect of psychostimulant history on the findings, accounting for a substantial proportion of variance across studies. Thus, the meta-regression analysis showed that the percentage of patients without a medication history was negatively associated with dopamine transporter level, so that studies of patients receiving long-term medication showed higher dopamine transporter levels, while an absence of medication exposure was associated with lower dopamine transporter levels relative to the healthy comparison subjects. Conversely, age, gender, comorbid conditions, year of publication, and type of imaging technique had no effect on the meta-analytical estimates of striatal dopamine transporter density.

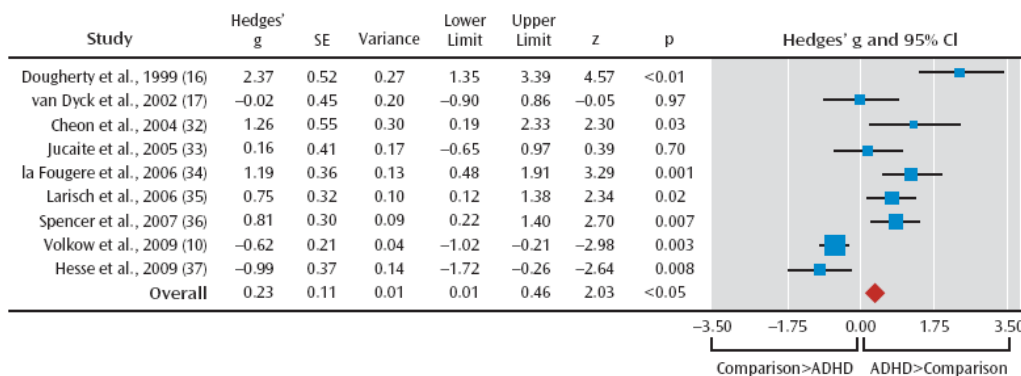
The negative correlation accounted for about half of the overall variance across studies. This suggests that the higher striatal dopamine transporter density in ADHD may be the consequence of previous treatment with stimulants and hence be the result of an adaptive response of the brain to the continuous dopamine transporter blockade with psychostimulants. This suggests that a high dopamine transporter level is not part of the key ADHD pathophysiology but is secondary to years of psychostimulant

treatment and reflects an adaptive brain response to the long-term blockade of dopamine transporters by psychostimulants. This notion of an adaptation to psychostimulants is in line with the finding that methylphenidate is effective in improving clinical symptoms of ADHD in the short term but that long-term effectiveness is limited; larger doses are often required to maintain clinical effectiveness, and clinical effectiveness appears to wane after years of medication (39). A caveat is that these findings are from cross-sectional analyses, with a selection bias, and we therefore cannot infer direct causality. The theory of an adaptive response of the brain to psychostimulant medication would have to be tested directly in longitudinal imaging studies using a randomized controlled design.

The meta-analytical finding of lower dopamine transporter levels in medication-naive patients is in line with the findings from the study by Volkow et al. (10), which was one of the largest weighted studies in our meta-analysis and one of the best-controlled studies, enrolling a large number of drug-naive ADHD subjects with no comorbid psychiatric or neurological conditions and adopting stringent inclusion criteria to control for past ADHD medication and/or drug abuse history. The finding of lower

FUSAR-POLI, RUBIA, ROSSI, ET AL.

FIGURE 3. Meta-Analysis of Striatal Dopamine Transporter Density in ADHD Patients and Healthy Comparison Subjects Employing Random-Effects Models



striatal dopamine transporter levels in medication-naïve patients is also consistent with the prominent theory that ADHD is a dysfunction of dopamine neurotransmission, with a consequent dysregulation of dopamine-modulated circuits. In particular, the striatum appears to play a prominent role in ADHD symptoms (12).

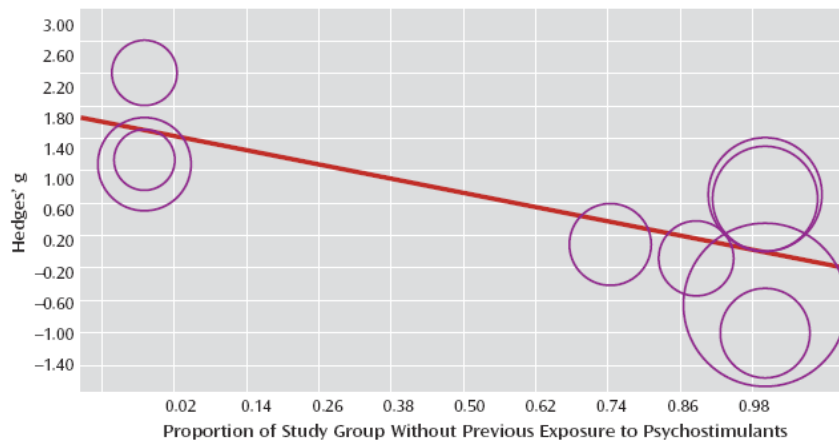
In normal development, a 6%–8% decline in striatal dopamine transporters has been observed per decade in PET and SPECT studies (40). We observed nonsignificantly lower striatal dopamine transporter levels in older relative to younger adults in the comparison group but no difference in the patients. This may hint at abnormalities in the normal age-associated striatal dopamine transporter development in ADHD patients, or it may be related to stimulant treatment.

Methylphenidate hydrochloride is one of the most efficacious treatments for ADHD, reducing symptoms in up to 70% of children (12). PET studies have shown that methylphenidate blocks dopamine transporters in the striatum in a dose-dependent fashion (41, 42), leading to an increase in extracellular striatal dopamine (43). The amount of extracellular dopamine (44) released by psychostimulants, however, is likely to depend on a combination of the blockade of dopamine transporters and the baseline rate of dopamine release, which is regulated by individual differences in dopamine cell firing and by environmental stimulation (12). Studies using [¹⁸F]DOPA or [¹¹C]DOPA PET (43, 45) confirmed low dopamine synthesis capacity in the striatum of ADHD patients. Studies using [¹¹C]raclopride PET to investigate postsynaptic receptor binding further showed that dopamine activity is depressed in ADHD, supporting the dopamine deficit theory of ADHD (46). Given that dopamine signals the saliency of stimuli and drives the motivation to perform goal-directed behaviors, the methylphenidate-induced amplification of the striatal dopaminergic signal would cause increased saliency perception, motivating the individual to engage and improving attention and performance (12).

Our meta-analysis finding that previous treatment with psychostimulants increased striatal dopamine transporter density in ADHD patients may seem counterintuitive, given the dopamine transporter blockade by methylphenidate. Enhanced striatal dopamine transporter density in patients receiving long-term treatment, however, could reflect a secondary adaptive brain response to the chronic striatal dopamine transporter blockade, i.e., adjustment to chronically elevated striatal dopamine availability through up-regulation of dopamine transporter levels. There is evidence in favor of this theory from a small prospective study, which showed that after 1 year of stimulant medication the striatal dopamine transporter levels of ADHD patients in fact increased (47). Furthermore, there is evidence indicating that cocaine—which is a stimulant drug that, like methylphenidate, blocks dopamine transporters—not only blocks the acute regulatory effect of the dopamine transporter on synaptic dopamine levels but also may exert the opposite effect: insertion of dopamine transporters from the endosomal recycling pool into the plasma membrane (48). In rhesus monkeys, chronic administration of cocaine up-regulates striatal dopamine transporter expression, which persists for more than 30 days after cocaine withdrawal (48). High dopamine transporter expression has also been shown in postmortem analyses of brain tissue from human cocaine addicts, and synaptosomes prepared from this tissue exhibit greater dopamine uptake than synaptosomes from age-matched cocaine-naïve individuals (48).

Methylphenidate-associated changes have also been observed in brain function and structure. Functional MRI studies in patients with ADHD have shown that single and long-term doses of methylphenidate up-regulate and normalize typically low frontostriatal brain activation (49–54). Because striatal dopamine transporters are located exclusively on dopamine-synthesizing neurons, their measurement is a specific marker of dopaminergic neuron integrity in the basal ganglia. The notion of adaptive brain changes

STRIATAL DOPAMINE TRANSPORTERS IN ADHD

FIGURE 4. Meta-Regression Showing Effect of Stimulant Exposure on Striatal Dopamine Transporter Density in ADHD^a

^a Circle size reflects the weight a study obtained in the meta-regression. Lower effect sizes were detected in studies involving drug-naïve ADHD patients ($\beta = -1.61$, 95% CI = -2.19 to -1.03 , $z = -5.45$, $p < 0.001$).

in response to long-term psychostimulant treatment is also in line with the results of several structural imaging studies showing that patients with ADHD receiving long-term medication have more normal structure and morphometry in the basal ganglia than medication-naïve patients (55, 56). These findings are further confirmed by a recent meta-analysis of whole-brain structural imaging studies, which showed that the lower basal ganglia gray matter volume in ADHD patients, relative to that in comparison subjects, is dependent on long-term medication (9). The percentage of patients receiving long-term medication was linearly associated with basal ganglia size, such that studies in which more than 70% of the patients were medicated did not show striatal abnormalities, while the greatest deficits were observed in studies of medication-naïve patients.

It is, however, also possible that lower dopamine transporter density and lower dopamine release in medication-naïve ADHD patients reflect prefrontal pathology, well demonstrated in neuroimaging results for ADHD (5), since frontostriatal glutamatergic circuits regulate striatal dopamine release.

The present study has several limitations. The meta-regression finding of an association between medication and dopamine transporter density is limited by the cross-sectional nature of the analysis, and causality of the regression findings needs to be established in longitudinal prospective studies using a randomized controlled design. It has been suggested that high heterogeneity across studies may be due to differing dopamine transporter sensitivity across the different radiotracers employed. For example, there is evidence that the specific-to-nonspecific ratio of labeled cocaine is relatively low and that this radioligand may occupy binding sites other than those occupied by FP-CIT, al-tropane, TRODAT-1, and IPT (57). Furthermore, dopamine transporter binding may be influenced by a complex net-

work of interactions with other receptors or neurotransmitters. For example, there is recent evidence that norepinephrine transporters contribute to the pathophysiology of ADHD, with norepinephrine transporter blockade in frontal regions underlying some of the therapeutic effects of methylphenidate (58). However, while methylphenidate enhances both norepinephrine and dopamine in prefrontal brain regions, where it blocks both the relatively densely distributed norepinephrine transporters and the less densely distributed dopamine transporters (58), in the basal ganglia methylphenidate has minimal effects on norepinephrine levels, since the norepinephrine transporter density is vanishingly low (6). Other studies have found that presynaptic D_2 autoreceptor activation, normally constraining dopamine action at synapses, regulates dopamine transporter activity that modulates synaptic dopamine homeostasis (59). The picture is further complicated by a potential interplay between dopamine transporter functioning and nicotinic neurotransmission at the presynaptic level (60). Finally, there is recent evidence suggesting that the ADHD diagnostic category comprises multiple entities with different underlying pathophysiologies and abnormalities of neurotransmitter profiles (61). In particular, children with the combined/hyperactive subtype of ADHD show a higher frequency of conduct disorder and good response to treatment, are exposed to more moderate stress during their mothers' pregnancies, and have a higher frequency of the L genotype for a polymorphic region of the serotonin transporter gene, as compared to children with the inattentive ADHD subtype (61). On the basis of animal studies showing dopamine transporter differences in the pathophysiology of the two subtypes, it is possible to speculate that treatment with methylphenidate might normalize abnormal dopamine transporter levels more effectively in the combined subtype (62).

The meta-analysis and meta-regression analysis show that striatal dopamine transporter levels in ADHD depend on chronic psychostimulant treatment, so that medication-naïve patients have low striatal dopamine transporter levels, whereas patients receiving long-term medication have high levels. Consequently, the previously reported high dopamine transporter density in ADHD patients may potentially represent up-regulation secondary to chronic administration of psychostimulants, rather than primary pathophysiology of ADHD. Future prospective studies using randomized controlled trials in large groups of drug-naïve individuals with ADHD will be needed to definitively clarify the long-term effect of psychostimulants on striatal dopaminergic neurotransmission.

Received June 20, 2011; revisions received Sept. 25 and Oct. 22, 2011; accepted Oct. 27, 2011 (doi: 10.1176/appi.ajp.2011.11060940). From the Department of Psychosis Studies and the Department of Child and Adolescent Psychiatry, Institute of Psychiatry, King's College London; the Child Neuropsychiatry Unit, IRCCS C. Mondino National Institute of Neurology Foundation, University of Pavia, Pavia, Italy; and the Department of Psychology, University of Padua, Padua, Italy. Address correspondence to Dr. Fusar-Poli (p.fusar@libero.it).

Dr. Rubia has received speakers' honoraria from Eli Lilly, Medice, Novartis, and Shire. Dr. Rossi served as principal investigator in Shire study SPD503-316 in 2011 and as an investigator in Eli Lilly study B4Z-IT- LICY in 2006. The other authors report no financial relationships with commercial interests.

References

- American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 4th ed (DSM-IV). Washington, DC, APA, 1994
- Polanczyk G, Moffitt TE, Arseneault L, Cannon M, Ambler A, Keefe RS, Houts R, Odgers CL, Caspi A: Etiological and clinical features of childhood psychotic symptoms: results from a birth cohort. *Arch Gen Psychiatry* 2010; 67:328–338
- Biederman J, Petty C, Faraone SV, Hirshfeld-Becker DR, Henin A, Rauf A, Scott M, Pollack M, Rosenbaum JF: Childhood antecedents to panic disorder in referred and nonreferred adults. *J Child Adolesc Psychopharmacol* 2005; 15:549–561
- Cubillo A, Rubia K: Structural and functional brain imaging in adult attention-deficit/hyperactivity disorder. *Expert Rev Neurother* 2010; 10:603–620
- Rubia K: "Cool" inferior frontostriatal dysfunction in attention-deficit/hyperactivity disorder versus "hot" ventromedial orbitofrontal-limbic dysfunction in conduct disorder: a review. *Biol Psychiatry* 2011; 69(12):e69–87
- Madras BK, Miller GM, Fischman AJ: The dopamine transporter and attention-deficit/hyperactivity disorder. *Biol Psychiatry* 2005; 57:1397–1409
- Konrad K, Eickhoff SB: Is the ADHD brain wired differently? a review on structural and functional connectivity in attention deficit hyperactivity disorder. *Hum Brain Mapp* 2010; 31:904–916
- Valera EM, Faraone SV, Murray KE, Seidman LJ: Meta-analysis of structural imaging findings in attention-deficit/hyperactivity disorder. *Biol Psychiatry* 2007; 61:1361–1369
- Nakao T, Radua J, Rubia K, Mataix-Cols D: Gray matter volume abnormalities in ADHD: voxel-based meta-analysis exploring the effects of age and stimulant medication. *Am J Psychiatry* 2011; 168:1154–1163
- Volkow ND, Wang GJ, Kollins SH, Wigal TL, Newcorn JH, Telang F, Fowler JS, Zhu W, Logan J, Ma Y, Pradhan K, Wong C, Swanson JM: Evaluating dopamine reward pathway in ADHD: clinical implications. *JAMA* 2009; 302:1084–1091
- Holt DJ, Graybiel AM, Saper CB: Neurochemical architecture of the human striatum. *J Comp Neurol* 1997; 384:1–25
- Volkow ND, Wang GJ, Fowler JS, Ding YS: Imaging the effects of methylphenidate on brain dopamine: new model on its therapeutic actions for attention-deficit/hyperactivity disorder. *Biol Psychiatry* 2005; 57:1410–1415
- Gizer IR, Ficks C, Waldman ID: Candidate gene studies of ADHD: a meta-analytic review. *Hum Genet* 2009; 126:51–90
- Piccini PP: Dopamine transporter: basic aspects and neuroimaging. *Mov Disord* 2003; 18(suppl 7):S3–S8
- Meisenzahl EM, Schmitt GJ, Scheuerecker J, Moller HJ: The role of dopamine for the pathophysiology of schizophrenia. *Int Rev Psychiatry* 2007; 19:337–345
- Dougherty DD, Bonab AA, Spencer TJ, Rauch SL, Madras BK, Fischman AJ: Dopamine transporter density in patients with attention deficit hyperactivity disorder. *Lancet* 1999; 354:2132–2133
- Fusar-Poli P, Meyer-Lindenberg A: Striatal presynaptic dopamine in schizophrenia, part I: meta-analysis of dopamine active transporter density. *Schizophr Bull* (in press)
- van Dyck CH, Quinlan DM, Cretella LM, Staley JK, Malison RT, Baldwin RM, Seibyl JP, Innis RB: Unaltered dopamine transporter availability in adult attention deficit hyperactivity disorder. *Am J Psychiatry* 2002; 159:309–312
- Zimmer L: Positron emission tomography neuroimaging for a better understanding of the biology of ADHD. *Neuropharmacology* 2009; 57:601–607
- Spencer TJ, Biederman J, Madras BK, Faraone SV, Dougherty DD, Bonab AA, Fischman AJ: In vivo neuroreceptor imaging in attention-deficit/hyperactivity disorder: a focus on the dopamine transporter. *Biol Psychiatry* 2005; 57:1293–1300
- Krause KH, Dresel SH, Krause J, la Fougere C, Ackenheil M: The dopamine transporter and neuroimaging in attention deficit hyperactivity disorder. *Neurosci Biobehav Rev* 2003; 27:605–613
- van der Kooij MA, Glennon JC: Animal models concerning the role of dopamine in attention-deficit hyperactivity disorder. *Neurosci Biobehav Rev* 2007; 31:597–618
- Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; 339:b2535
- Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF, QUOROM group: Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. *Br J Surg* 2000; 87:1448–1454
- Juni P, Witschi A, Bloch R, Egger M: The hazards of scoring the quality of clinical trials for meta-analysis. *JAMA* 1999; 282:1054–1060
- Paulson JF, Bazemore SD: Prenatal and postpartum depression in fathers and its association with maternal depression: a meta-analysis. *JAMA* 2010; 303:1961–1969
- Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB, Meta-Analysis of Observational Studies in Epidemiology (MOOSE) Group: Meta-analysis of observational studies in epidemiology: a proposal for reporting. *JAMA* 2000; 283:2008–2012
- Hedges L, Holkin I: *Statistical Methods for Meta-Analysis*. New York, Academic, 1985
- Cooper H, Hedges L, Valentine J (eds): *Handbook of Research Synthesis and Meta-Analysis*. New York, Russell Sage Foundation, 2009
- Lipsey M, Wilson D: *Practical Meta-Analysis*. Thousand Oaks, Calif, Sage Publications, 2000
- Egger M, Davey Smith G, Schneider M, Minder C: Bias in meta-analysis detected by a simple, graphical test. *BMJ* 1997; 315:629–634

STRIATAL DOPAMINE TRANSPORTERS IN ADHD

31. Orwin R: A fail-safe N for effect size in meta-analysis. *J Edu Stat* 1983; 8:157–159
32. Cheon KA, Ryu YH, Namkoong K, Kim CH, Kim JJ, Lee JD: Dopamine transporter density of the basal ganglia assessed with [¹²³I]IPT SPECT in drug-naive children with Tourette's disorder. *Psychiatry Res* 2004; 130:85–95
33. Jucaite A, Fernell E, Hallidin C, Forsberg H, Farde L: Reduced midbrain dopamine transporter binding in male adolescents with attention-deficit/hyperactivity disorder: association between striatal dopamine markers and motor hyperactivity. *Biol Psychiatry* 2005; 57:229–238
34. la Fougere C, Krause J, Krause KH, Josef Gildehaus F, Hacker M, Koch W, Hahn K, Tatsch K, Dresel S: Value of ^{99m}Tc-TRODAT-1. SPECT to predict clinical response to methylphenidate treatment in adults with attention deficit hyperactivity disorder. *Nucl Med Commun* 2006; 27:733–737
35. Larisch R, Sitte W, Antke C, Nikolaus S, Franz M, Tress W, Müller H-W: Striatal dopamine transporter density in drug naive patients with attention-deficit/hyperactivity disorder. *Nucl Med Commun* 2006; 27:267–270
36. Spencer TJ, Biederman J, Madras BK, Dougherty DD, Bonab AA, Livni E, Meltzer PC, Martin J, Rauch S, Fischman AJ: Further evidence of dopamine transporter dysregulation in ADHD: a controlled PET imaging study using altoprane. *Biol Psychiatry* 2007; 62:1059–1061
37. Hesse S, Ballaschke O, Barthel H, Sabri O: Dopamine transporter imaging in adult patients with attention-deficit/hyperactivity disorder. *Psychiatry Res* 2009; 171:120–128
38. Higgins J, Thompson S: Quantifying heterogeneity in a meta-analysis. *Stat Med* 2002; 21:1539–1558
39. Hazell P: The challenges to demonstrating long-term effects of psychostimulant treatment for attention-deficit/hyperactivity disorder. *Curr Opin Psychiatry* 2011; 24:286–290
40. Varrone A, Hallidin C: Molecular imaging of the dopamine transporter. *J Nucl Med* 2010; 51:1331–1334
41. Vles JS, Feron FJ, Hendriksen JG, Jolles J, van Kroonenburgh MJ, Weber WE: Methylphenidate down-regulates the dopamine receptor and transporter system in children with attention deficit hyperkinetic disorder (ADHD). *Neuropediatrics* 2003; 34:77–80
42. Krause J, la Fougere C, Krause KH, Ackenheil M, Dresel SH: Influence of striatal dopamine transporter availability on the response to methylphenidate in adult patients with ADHD. *Eur Arch Psychiatry Clin Neurosci* 2005; 255:428–431
43. Ludolph AG, Kassubek J, Schmeck K, Glaser C, Wunderlich A, Buck AK, Reske SN, Fegert JM, Mottaghy FM: Dopaminergic dysfunction in attention deficit hyperactivity disorder (ADHD), differences between pharmacologically treated and never treated young adults: a 3,4-dihydroxy-6-[¹⁸F]fluorophenyl-alanine PET study. *Neuroimage* 2008; 41:718–727
44. Volkow N, Wang GJ, Fowler J, Logan J, Gerasimov M, Maynard L, Ding Y, Gattley SJ, Gifford A, Franceschi D: Therapeutic doses of oral methylphenidate significantly increase extracellular dopamine in the human brain. *J Neurosci* 2001; 21(2):RC121
45. Forsberg H, Fernell E, Waters S, Waters N, Tedroff J: Altered pattern of brain dopamine synthesis in male adolescents with attention deficit hyperactivity disorder. *Behav Brain Funct* 2006; 2:40
46. Volkow ND, Wang GJ, Newcorn J, Telang F, Solanto MV, Fowler JS, Logan J, Ma Y, Schulz K, Pradhan K, Wong C, Swanson JM: Depressed dopamine activity in caudate and preliminary evidence of limbic involvement in adults with attention-deficit/hyperactivity disorder. *Arch Gen Psychiatry* 2007; 64:932–940
47. Wang G-J, Volkow N, Wigal T, Kollins S, Newcorn J, Telang F, Logan J, Wong C, Fowler JS, Swanson JM: Chronic treatment with methylphenidate increases dopamine transporter density in patients with attention deficit hyperactive disorder. *J Nucl Med* 2009; 50(suppl 2):1283
48. Schmitt KC, Reith ME: Regulation of the dopamine transporter: aspects relevant to psychostimulant drugs of abuse. *Ann NY Acad Sci* 2010; 1187:316–340
49. Rubia K, Halari R, Cubillo A, Mohammad AM, Brammer M, Taylor E: Methylphenidate normalises activation and functional connectivity deficits in attention and motivation networks in medication-naive children with ADHD during a rewarded continuous performance task. *Neuropharmacology* 2009; 57:640–652
50. Rubia K, Halari R, Cubillo A, Smith AB, Mohammad AM, Brammer M, Taylor E: Methylphenidate normalizes fronto-striatal underactivation during interference inhibition in medication-naive boys with attention-deficit hyperactivity disorder. *Neuropsychopharmacology* 2011; 36:1575–1586
51. Rubia K, Halari R, Mohammad AM, Taylor E, Brammer M: Methylphenidate normalizes frontocingulate underactivation during error processing in attention-deficit hyperactivity disorder. *Biol Psychiatry* 2011; 70:255–262
52. Rubia K, Halari R, Christakou A, Taylor E: Impulsiveness as a timing disturbance: neurocognitive abnormalities in attention-deficit hyperactivity disorder during temporal processes and normalization with methylphenidate. *Philos Trans R Soc Lond B Biol Sci* 2009; 364:1919–1931
53. Shafritz KM, Marchione KE, Gore JC, Shaywitz SE, Shaywitz BA: The effects of methylphenidate on neural systems of attention in attention deficit hyperactivity disorder. *Am J Psychiatry* 2004; 161:1990–1997
54. Bush G: Neuroimaging of attention deficit hyperactivity disorder: can new imaging findings be integrated in clinical practice? *Child Adolesc Psychiatr Clin N Am* 2008; 17:385–404
55. Sobel LJ, Bansal R, Maia TV, Sanchez J, Mazzone L, Durkin K, Liu J, Hao X, Ivanov I, Miller A, Greenhill LL, Peterson BS: Basal ganglia surface morphology and the effects of stimulant medications in youth with attention deficit hyperactivity disorder. *Am J Psychiatry* 2010; 167:977–986
56. Semrud-Clikeman M, Pliszka SR, Lancaster J, Liotti M: Volumetric MRI differences in treatment-naive vs chronically treated children with ADHD. *Neurology* 2006; 67:1023–1027
57. Krause J: SPECT and PET of the dopamine transporter in attention-deficit/hyperactivity disorder. *Expert Rev Neurother* 2008; 8:611–625
58. Hannestad J, Gallezot JD, Planeta-Wilson B, Lin SF, Williams WA, van Dyck CH, Malison RT, Carson RE, Ding YS: Clinically relevant doses of methylphenidate significantly occupy norepinephrine transporters in humans in vivo. *Biol Psychiatry* 2010; 68:854–860
59. Bowton E, Saunders C, Erreger K, Sakrikar D, Matthies HJ, Sen N, Jessen T, Colbran RJ, Caron MG, Javitch JA, Blakely RD, Galli A: Dysregulation of dopamine transporters via dopamine D2 autoreceptors triggers anomalous dopamine efflux associated with attention-deficit hyperactivity disorder. *J Neurosci* 2010; 30:6048–6057
60. Weiss S, Tzavara ET, Davis RJ, Nomikos GG, McIntosh JM, Giros B, Martres MP: Functional alterations of nicotinic neurotransmission in dopamine transporter knock-out mice. *Neuropharmacology* 2007; 52:1496–1508
61. Grizenko N, Paci M, Joobee R: Is the inattentive subtype of ADHD different from the combined/hyperactive subtype? *J Atten Disord* 2010; 13:649–657
62. Roessner V, Sagvolden T, Dasbanerjee T, Middleton FA, Faraone SV, Walaas SI, Becker A, Rothenberger A, Bock N: Methylphenidate normalizes elevated dopamine transporter densities in an animal model of the attention-deficit/hyperactivity disorder combined type, but not to the same extent in one of the attention-deficit/hyperactivity disorder inattentive type. *Neuroscience* 2010; 167:1183–1191

Per ricevere la newsletter iscriversi al seguente indirizzo:
<http://crc.marionegri.it/bonati/adhdnews/subscribe.html>

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3250 del 11/04/2011)
Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia"
"Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia".

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI
DIPARTIMENTO DI SALUTE PUBBLICA
Laboratorio per la Salute Materno Infantile
Via Giuseppe La Masa, 19 - 20156 Milano MI - Italia - www.marionegri.it
tel +39 02 39014.511 - fax +39 02 3550924 - mother_child@marionegri.it