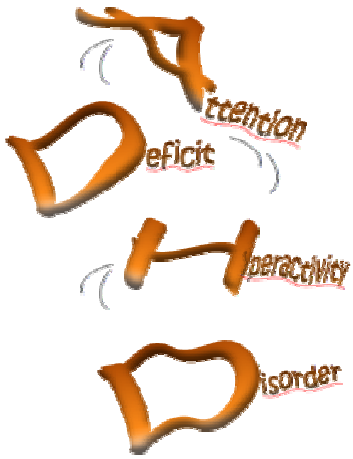
NEWSLETTER



INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD AGOSTO 2013

Acta Paediatr. 2013 Aug.

DISRUPTIVE BEHAVIOUR DISORDER WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER IS A RISK OF PSYCHIATRIC HOSPITALIZATION.

Nordstrom T, Hurtig T, Moilanen I, et al.

AIM: To evaluate the psychiatric hospitalization among adolescents diagnosed with disruptive behaviour disorders (DBD) and/or attention deficit hyperactivity disorder (ADHD).

METHODS: The sample (N = 457) was drawn from the Northern Finland Birth Cohort 1986. Four groups were formed, based on the K-SADS-PL diagnostic interview procedure: adolescents with DBD (n = 44), ADHD (n = 91), comorbid DBD and ADHD (n = 72) and without either DBD or ADHD (n = 250). Information from the Finnish Hospital Discharge Register (FHDR) was used to evaluate the psychiatric hospitalization among the study subjects.

RESULTS: When compared with no diagnosis group, the adolescents with behavioural disorders had an increased risk (adjusted odds ratios: DBD = 4.4, ADHD = 2.2, comorbid DBD & ADHD = 5.6) of having also psychiatric disorder in the FHDR. The onset age of the psychiatric disorders in the FHDR (medians: DBD = 14.9, ADHD = 7.5 and DBD & ADHD = 15.3 years) and the combined length of hospitalization (medians: 25, 50 and 26 days, respectively) differed among adolescents with behavioural disorders compared with those with no diagnosis (median age 12.1 years and length of hospitalization 4 days).

CONCLUSION: Adolescents diagnosed with DBD (with and without ADHD) are at high risk of undergoing psychiatric hospitalization during their life.

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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.

Acta Paediatr Int J Paediatr. 2013.
THE IMPORTANCE OF SCREENING FOR ADHD IN CHILDREN AND ADOLESCENTS WITH OBESITY.
Fernell E, Wentz E, Gillberg C.

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Acta Paediatr Int J Paediatr. 2013.
MILD INTELLECTUAL DISABILITY AND ADHD; A COMPARATIVE STUDY OF SCHOOL AGE CHILDREN'S ADAPTIVE ABILITIES.
Lindblad I, Svensson L, Landgren M, et al.
Aim: To compare adaptive functioning in children with mild intellectual disability (MID) with that of children with attention-deficit/hyperactivity disorder (ADHD).
Methods: Thirty-three children with MID were contrasted with 27 children with ADHD with regard to adaptive functioning as measured by the Adaptive Behaviour Assessment System (ABAS-II). The group with MID was population-based, and the group with ADHD was considered representative of a clinically referred group with that diagnosis. The two groups were subdivided into those (less-than or equal to)11 years and those (greater-than or equal to)12 years.
Results: The group with ADHD had lower adaptive functioning, but differences were not significant at total group levels. In children 12 years or older, the group with ADHD had significantly lower adaptive functioning.
Conclusion: Older children with ADHD had poorer adaptive functioning than those with MID, a finding which should be of interest to school and other authorities mapping out education and intervention plans for children with special needs.

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Addict Behav. 2013 Nov;38:2683-89.
NICOTINIC RECEPTOR GENE VARIANTS INTERACT WITH ATTENTION DEFICIENT HYPERACTIVE DISORDER SYMPTOMS TO PREDICT SMOKING TRAJECTORIES FROM EARLY ADOLESCENCE TO ADULTHOOD.
Lee CT, Fuemmeler BF, McClernon FJ, et al.
OBJECTIVE: To examine the association of single nucleotide polymorphisms (SNPs) of the CHRNB3 (rs13280604) and CHRNA6 (rs892413) nicotinic acetylcholine receptor (nAChR) genes and symptoms of attention deficit hyperactivity disorder (ADHD) in predicting smoking patterns from early adolescence to adulthood.
METHOD: A longitudinal cohort of 1137 unrelated youths from the National Longitudinal Study of Adolescent Health provided responses to four surveys from Waves I to IV, and a genetic sample in Wave III. Growth mixture modeling was used to identify smoking patterns and to assess the effects of the two SNPs and ADHD symptoms on cigarette use over time.
RESULTS: There were significant main effects of ADHD symptoms and CHRNA6 variants in predicting the number of cigarettes smoked and the pattern of use over time, respectively. There were no main effects of the CHRNB3 variants. However, a significant CHRNB3 variantx ADHD symptom interaction was observed, such that individuals with elevated ADHD symptoms and a particular CHRNB3 variant were at increased risk of cigarette use over time.
CONCLUSIONS: These findings demonstrate that a SNP in a nicotinic receptor gene may interact with ADHD symptoms to link with increased cigarette use across adolescence and young adulthood. Unique associations between specific variants and patterns of ADHD symptoms were identified which may be useful for targeting prevention efforts to individuals at greatest risk for cigarette smoking.

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Addiction. 2013 Aug;108:1503-11.

SUBSTANCE USE DISORDERS IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A 4-YEAR FOLLOW-UP STUDY.

Groenman AP, Oosterlaan J, Rommelse N, et al.

Aim: To examine the relationship between a childhood diagnosis of attention deficit hyperactivity disorder (ADHD) with or without oppositional defiant disorder (ODD)/conduct disorder (CD) and the development of later alcohol/drug use disorder [psychoactive substance use disorder (PSUD)] and nicotine dependence in a large European sample of ADHD probands, their siblings and healthy control subjects.

Participants, design and setting: Subjects (n = 1017) were participants in the Belgian, Dutch and German part of the International Multicenter ADHD Genetics (IMAGE) study. IMAGE families were identified through ADHD probands aged 5–17 years attending out-patient clinics, and control subjects from the same geographic areas. After a follow-up period (mean: 4.4 years) this subsample was re-assessed at a mean age of 16.4 years.

Measurements: PSUD and nicotine dependence were assessed using the Diagnostic Interview Schedule for Children, Alcohol Use Disorders Identification Test, Drug Abuse Screening Test and Fagerström test for Nicotine Dependence.

Findings: The ADHD sample was at higher risk of developing PSUD [hazard ratio (HR) = 1.77, 95% confidence interval (CI) = 1.05–3.00] and nicotine dependence (HR = 8.61, 95% CI = 2.44–30.34) than healthy controls. The rates of these disorders were highest for ADHD youth who also had CD, but could not be accounted for by this comorbidity.We did not find an increased risk of developing PSUD (HR = 1.18, 95% CI = 0.62–2.27) or nicotine dependence (HR = 1.89, 95% CI = 0.46–7.77) among unaffected siblings of ADHD youth.

Conclusions: A childhood diagnosis of attention deficit hyperactivity disorder is a risk factor for psychoactive substance use disorder and nicotine dependence in adolescence and comorbid conduct disorder, but not oppositional defiant disorder, further increases the risk of developing psychoactive substance use disorder and nicotine dependence.

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Am Fam Physician. 2013 Aug;88:266-68.

ADHD INTERVENTIONS IN CHILDREN YOUNGER THAN SIX YEARS.

Salisbury-Afshar E.

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Am J Med Genet Part A. 2013;161:1923-28.

INSERTIONAL TRANSLOCATION LEADING TO A 4Q13 DUPLICATION INCLUDING THE EPHA5 GENE IN TWO SIBLINGS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Matoso E, Melo JB, Ferreira SI, et al.

An insertional translocation (IT) can result in pure segmental aneusomy for the inserted genomic segment allowing to define a more accurate clinical phenotype. Here, we report on two siblings sharing an unbalanced IT inherited from the mother with a history of learning difficulty. An 8-year-old girl with developmental delay, speech disability, and attention-deficit hyperactivity disorder (ADHD), showed by GTG banding analysis a subtle interstitial alteration in 21q21. Oligonucleotide array comparative genomic hybridization (array-CGH) analysis showed a 4q13.1-q13.3 duplication spanning 8.6Mb. Fluorescence in situ hybridization (FISH) with bacterial artificial chromosome (BAC) clones confirmed the rearrangement, a der(21)ins(21;4)(q21;q13.1q13.3). The duplication described involves 50 RefSeq genes including the EPHA5 gene that encodes for the EphA5 receptor involved in embryonic development of the brain and also in synaptic remodeling and plasticity thought to underlie learning and memory. The same rearrangement was observed in a younger brother with behavioral problems and also exhibiting ADHD. ADHD is among the most heritable of neuropsychiatric disorders. There are few reports of patients with duplications involving the proximal region of 4q and a mild phenotype. To the best of our knowledge this is the first report of a duplication restricted to band 4q13. This abnormality could be easily missed in children who

have nonspecific cognitive impairment. The presence of this behavioral disorder in the two siblings reinforces the hypothesis that the region involved could include genes involved in ADHD.

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Am J Orthopsychiatry. 2013;83:165-75.

INDIVIDUAL DIFFERENCES IN ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS AND ASSOCIATED EXECUTIVE DYSFUNCTION AND TRAITS: SEX, ETHNICITY, AND FAMILY INCOME .

Martel MM.

The goal of the present investigation was to investigate sex, ethnic, and socioeconomic status (SES) influences on attention deficit hyperactivity disorder (ADHD) symptoms and risk markers, including executive dysfunction and temperament traits. Participants were 109 children who were 3 to 6 years old (64% male; 36% ethnic minority) and their primary caregivers and teachers who completed a multistage, multi-informant screening, and diagnostic procedure. Parents completed a diagnostic interview and diagnostic and temperament questionnaires, teachers completed questionnaires, and children completed cognitive control tasks. Because of targeted overrecruitment of clinical cases, 56% of children in the sample were diagnosed with ADHD. Results suggested minimal sex differences, but prominent ethnic differences, in ADHD symptoms and temperament and executive function risk markers. Further, low family income was associated with increased ADHD symptoms and more temperament and executive function risk markers, and low family income explained many ethnic differences in ADHD symptoms and these risk markers. There were prominent interactions among child sex, ethnicity, and family income. Thus, study results suggest that children with multiple individual difference demographic risk factors (e.g., such as being male and ethnic minority) are at highly increased risk of ADHD symptoms and associated risk markers in the temperament and executive function domains.

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Ann Allergy Asthma Immunol. 2013;111:102-06.

ASSOCIATION OF CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH ATOPIC DISEASES AND SKIN INFECTIONS? A MATCHED CASE-CONTROL STUDY USING THE GENERAL PRACTICE RESEARCH DATABASE.

Hak E, De Vries TW, Hoekstra PJ, et al.

Background Data to support the hypothesis of a relationship between attention-deficit/hyperactivity disorder (ADHD) and allergies are conflicting.

Objective To assess whether children with ADHD are more likely to have a history of atopic disorders, skin infections, and medical prescriptions than children without ADHD.

Methods We conducted a nested case-control study among boys using the UK General Practice Research Database (GPRD). Cases were defined as children with first-time diagnosis of ADHD who were treated with methylphenidate. Four controls who had neither ADHD nor ADHD drug prescriptions in their medical records were matched to each case on age and general practice.

Results We identified 884 boys with a first-time diagnosis of drug-treated ADHD and 3,536 controls. The independent odds ratios adjusted for age and presence of low birth weight or preterm delivery were 1.4 (95% confidence interval [CI], 1.2-1.7; P <.001) for a medical history of asthma, 1.5 (95% CI, 1.3-1.9; P <.001) for impetigo, and 1.5 (95% CI, 1.3-1.7; P <.001) for any antihistamine drug prescriptions. Other exposures that were more common in cases than controls, though not independently, were cow's milk intolerance and any prescription from the drug categories antiasthmatics, respiratory corticosteroids, topical steroids, antibacterials, or antifungals.

Conclusion Despite possible limitations inherent to observational studies, this study lends support to the emerging evidence that childhood ADHD is associated with atopic diseases and impetigo. Further interdisciplinary research is needed to understand the underlying mechanisms and to evaluate targeted preventive, diagnostic, and therapeutic interventions.

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Arch Clin Neuropsychol. 2013 Aug.

SLEEP, ATTENTION, AND EXECUTIVE FUNCTIONING IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Moreau V, Rouleau N, Morin CM.

The objective of this study was to investigate potential relationships between two measures of sleep impairments (i.e., sleep duration and sleep efficiency [SE]) and attention and executive functioning in children with attention-deficit/hyperactivity disorder (ADHD). Parents of 43 children (mean age = 10 +/- 1.8 years) with ADHD completed sleep and behavioral questionnaires. Children also wore a wrist actigraph for seven nights and were subsequently assessed with the Conners' continuous performance test (CPT)-2. A significant relationship was found between lower SE and increased variability in reaction time on the CPT. Shorter sleep duration was associated with a range of executive functioning problems as reported by the parents. The relationships between sleep duration and the executive functioning measures held even after controlling for age, gender, and use of medication, but not the relationships with SE. These results suggest that sleep quantity is an important correlate of executive functioning in children with ADHD.

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Arch Iran Med. 2013 Sep;16:513-17.

PSYCHIATRIC COMORBIDITIES IN ADHD CHILDREN: AN IRANIAN STUDY AMONG PRIMARY SCHOOL STUDENTS.

Amiri S, Shafiee-Kandjani AR, Fakhari A, et al.

BACKGROUND: This study was performed to determine the lifetime prevalence of psychiatric disorders concomitant with attention deficit/hyperactivity disorder (ADHD) among primary school students.

METHODS: One thousand six hundred fifty-eight primary school students (781 females and 877 males) were selected in a cluster random manner in 2010. The first screening was performed by the Conner's teacher rating scale revised and Teacher ADHD rating scale-IV and then the students, in whom the ADHD was diagnosed by a child and adolescent psychiatrist according to DSM-IV-TR, were evaluated by K-SADS-PL semi-structured interview to detect the psychiatric comorbidities.

RESULTS: The prevalence of psychiatric comorbidities in ADHD subjects was 62.5%. Oppositional defiant disorder (29.4%), specific phobia (21.9%), and enuresis (17.5%) were the most common comorbidities. The most common comorbidities in ADHD-IA (inattentive type) (n = 29) were specific phobia (34.5%), oppositional defiant disorder (20.7%), chronic motor tic disorder (17.2%), and enuresis (17.2%). The most common comorbidities in ADHD-HI (hyperactive/impulsive type) (n = 15) were chronic motor tic disorder (33.3%), oppositional defiant disorder (26.7%), and specific phobia (26.7%). The most common comorbidities in ADHD-C (combined type) (n = 116) were oppositional defiant (31.9%), enuresis (19%), and specific phobia (18.1%). The frequency of chronic vocal tic disorder was higher in ADHD-HI compared with ADHD-C (P = 0.01).

CONCLUSION: The results of this study indicated that the frequency of other psychiatric comorbidities in primary school students with ADHD is high that may affect disease course and treatment. Hence, evaluation for other comorbidities in ADHD patients should be considered.

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Arch Clin Neuropsychol. 2013 Aug;28:476-84.

INDIVIDUAL AND COMBINED EFFECTS OF LD AND ADHD ON COMPUTERIZED NEUROCOGNITIVE CONCUSSION TEST PERFORMANCE: EVIDENCE FOR SEPARATE NORMS.

Elbin RJ, Kontos AP, Kegel N, et al.

Decreased neurocognitive performance in individuals with self-reported attention deficit hyperactivity disorder (ADHD) and learning disability (LD) is well documented in the neuropsychological research literature. Previous studies employing paper-and-pencil neurocognitive assessments report lower performance in individuals with ADHD and LD. The purpose of the current study was to examine the influence of a self-reported diagnosis of LD, ADHD, and combined LD/ADHD on baseline computerized neurocognitive testing (CNT) used for the concussion assessment. Results revealed athletes with a self-reported diagnosis of LD, ADHD, and/or combined LD/ADHD demonstrated lower performance on baseline

CNT and reported larger numbers of symptoms than did control athletes without these diagnoses. These findings provide evidence for the development of separate normative data for athletes with LD, ADHD, and LD/ADHD diagnoses on CNT batteries commonly used for concussion management.

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Biol Psychiatry. 2013;73:56S.

NEUROMODULATION OF RESPONSE INHIBITION IN AD/HD.

Stevens MC, Von Pechmann DF, Bessette K, et al.

Background: AD/HD has been linked to abnormal brain activity during and preceding goal-directed errors in lateral and midline prefrontal cortex regions. Although impairment of cognitive systems has become a familiar aspect of AD/ HD neurocognitive theories, few studies have examined whether such deficits can be modulated through intervention. In this preliminary study, we examined whether Combined-subtype AD/HD adolescents could voluntarily modulate their brain activity when committing an error on a response inhibition task.

Methods: Six ADHD male subjects (age=16) preformed a Go/No-Go FMRI task under differing instructions to either nullincrease brain response to each mistakenull or to perform normally. SPM8 was used to preprocess data, model subject-level activation, and compare study conditions to either INCREASE or MAINTAIN their brain response to errors.

Results:AD/HD adolescents up-modulated activation to errors in dorsal anterior cingulate, bilateral dlPFC (BA 9/46), and bilateral putamen, along with changes in reaction time to post-error trials indicating the presence of greater cognitive control. Instructional effects were not limited to No-Go errors, as greater activation also was seen in all these areas except left dlPFCin response to correctly rejected No-Go stimuli.

Conclusions: Compared to our previous similar studies of non-AD/HD participants, AD/HD adolescents recruit additional prefrontal regions known to be deficient in AD/HD. In addition tofurther supporting the notion that attenuated error awareness neural activity may underlie clinical symptoms AD/ HD, these AD/HD teens appear to possess the capacity to voluntarily alter brain response to errors, possibly representing the basis for formal interventions targeting error feedback neural mechanisms.

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Biol Psychiatry. 2013;73:56S-7S.

DUAL-HYPOTHESIS MODEL OF THE DEVELOPMENT OF SELF-CONTROL: OPPORTUNITIES FOR INTERVENTION.

Schweitzer JB.

Background: Concerns with impulsivity are frequently associated with ADHD and typical development during adolescence and young adulthood. We discuss how the dual-system model (cognitive control and reward function) of brain development during adolescence may provide complementary opportunities to alter the trajectory of self-control.

Methods: In order to identify the factors that regulate self-control and are potential targets for intervention, we assessed self-control in adolescents and young adults (Mean age = 17.9 years) with and without ADHD using a delay discounting paradigm. We assessed for the effects of development, gender and context manipulation on choice within delay discounting paradigms. The context of the reward was altered by modifying the presentation of the values of the rewards by offering delay discounting trials with decimal values (e.g., $1.12 now versus $10.15 later) versus trials with rounded values (e.g., $1.00 now versus $10.00 later).

Results: Development increases self-control (p=.05). Persons with ADHD are more impulsive on delay discounting measures than controls (p=0.03), as are males versus females (p=.05). Adding decimals to the numbers in the delay discounting trials increases self-control in ADHD and control groups (p< .01) via either the reward or cognitive control systems. We also present examples from our laboratory showing how cognitive training procedures could improve selfcontrol in children with ADHD.

Conclusions: While there are unmodifiable factors that affect self-control (age, sex) a dual-system model and our laboratory findings (including Green et al., 2012) suggest development may provide opportunities to alter impulsivity by directly targeting reward and cognitive mechanisms.

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Biol Psychiatry. 2013;73:57S.

DO YOUTH WITH ADHD HAVE SIMILAR OR DIFFERENT FACE-PROCESSING DEFICITS WHEN COMPARED TO YOUTH WITH PBD?

Lowes AS, Jacobs RH, Pavuluri MN.

Background: Frequent comorbidity and overlap in symptomology between attention deficit hyperactivity disorder (ADHD) and pediatric bipolar disorder (PBD) have yielded challenging yet worthwhile investigations into phenotypic distinction. Characterizing emotional profiles within both populations is necessary, as research suggests both groups have difficulty processing emotional stimuli.
Methods: Penn Emotion Regulation (ER40) Task performance and clinical data were collected for 45 youth with ADHD, 48 youth with PBD, and 48 healthy controls (HCs) ages 9-17 (M=12.67, SD=1.96) matched on age, sex, and IQ. ANOVAs were used to test group differences in accuracy on affect recognition for faces displaying 'happy', 'sad', 'angry', 'fearful', or 'no emotion' as well as group differences on interference (positive interference = accuracy on happy - accuracy on neutral; negative interference = accuracy on combined fearful/angry/ sad - neutral).
Results: We found that the ADHD group did not significantly differ from the PBD group in accurately identifying emotional faces. Specifically, an interaction of valence and group was detected (F(8, 552) = 2.16, p<=.03), wherein youth with ADHD correctly identified fewer sad faces than the HC group and youth with PBD correctly identified significantly fewer fearful and neutral faces than the HC group. Positive interference was found to correlate with YMRS mania score (r-.76, p<.01).
Conclusions: The ADHD phenotype may contain a more notable deficit in faceprocessing or emotional recognition than is currently understood, and mania may be associated with greater positive interference.

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Biol Psychiatry. 2013;73:103S.

IS OCULOMOTRICITY A GOOD MARKER OF MPH EFFICIENCY IN ADHD?

Seassau M, Weiss T, Carcangiu R, et al.

Background: Attention-Deficit/hyperactivity disorder (ADHD) is characterized by behavioral symptoms of inattention and may include hyperactivity and impulsivity. The impulsivity and inattention suggest deficits in the voluntary control of behavior. Eye movements depend on structures implicated in attention and in motor control, both criteria areas of dysfunction in ADHD. In the present study, objective was to evaluate the effect of methylphenidate (MPH) using oculomotricity in ADHD children.
Methods: Subjects were aged 7-12 years, with ADHD on and off MPH (N=9), and control subjects (N=9). Saccade latencies, precision, accuracy and percentage of anticipatory errors were determined in automatic attentional tasks (visuallyguided- saccades) and voluntary attentional tasks (overlap, antisaccades and fixations tasks).
Results: Significant differences existed between ADHD on MPH and ADHD off MPH, in latencies (p<0.02), precision (p<0.04), accuracy (p<0.05) and percentage of anticipatory errors (p<0.05). Compared to controls, ADHD on MPH had normalized performances in automatic task, while they still impaired in voluntary attentional tasks.
Conclusions: MPH modified motor planning and response inhibition in ADHD children. Benefits depend of the type of tasks, automatic and voluntary attention. These results suggest that eye movements could be a good marker of MPH efficiency in ADHD.

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Biol Psychiatry. 2013;73:279S-80S.

NEUROCORRELATES OF MARIJUANA USE IN ADOLESCENTS WITH AND WITHOUT ADHD.

Ehrler MR, Lopez-Larson M, Locatelli AE, et al.

Background: Research suggests adolescents are more vulnerable than adults to neurocognitive abnormalities associated with marijuana (MJ) use; however, the impact of preexisting risk factors, such as ADHD, is unclear. This study examines differences in self-reported impulsivity in the dorsolateral prefrontal cortex (DLPFC) among MJ-using adolescents with and without comorbid ADHD.

Methods: Forty-five adolescents with chronic MJ use (MJ aged 17.9 (plus or minus) 1.2) and 12 adolescents with MJ use and ADHD (MJ+ADHD aged 17.3 (plus or minus) 1.6) had a 3T MRI. Subjects completed a diagnostic interview and Barratt Impulsivity Scale. Morphometric analyses were performed in Freesurfer and DLPFC volumes were extracted and corrected for total brain volume. Group differences in DLPFC were examined via Univariate analyses, and correlations with BIS scores and MJ use indices were performed.

Results: MJ+ADHD reported higher total impulsivity (p=.003) and higher impulsivity on subscales of non-planning (p=.01) and attention (p=.05). MJ+ADHD trended toward being younger at age of first use compared to MJ only (p=0.07). There were no significant differences in DLPFC volumes between groups; however MJ+ADHD demonstrated a positive correlation between right DLPFC and age at first use (r=.579, p=.048) and left hemisphere DLPFC and age at regular use (r=.646, p=.023), while MJ only users did not.

Conclusions: Adolescents with MJ+ADHD had increased levels of impulsivity compared to MJ users. Although MJ users with and without ADHD did not differ in volumes or MJ use variables, MJ+ADHD and MJ users evidenced differential associations between DLPFC and age of onset of initial and regular use.

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Biol Psychiatry. 2013;73:58S.

EFFECTS OF INTENSIVE WORKING MEMORY TREATMENT ON BRAIN ACTIVITY IN ADOLESCENT COMBINED-SUBTYPE ADHD.

Gaynor A, Whitman J, Bessette K, et al.

Background: Past studies have shown that working memory is a common deficit in ADHD. Although several randomized clinical trials have shown that an innovative cognitive training program improves working memory and lowers ADHD symptoms, it is not yet known how such treatments alter brain function in ADHD. Based on previous work in healthy adults, we predicted that intensive working memory treatment would increase ADHD brain activation.

Methods: Eighteen adolescents (mean age 15.2; 67% male) diagnosed with Combined-subtype ADHD underwent FMRI scanning during a nonverbal Sternberg working task, before and after five weeks of Cogmed treatment - a computer-based at-home working memory training program. A finite impulse response (FIR) SPM8 model was used to examine whether brain function differed between encoding, maintenance, and retrieval phases of each trial. Activity within prefrontal and parietal regions-of-interest (ROIs) was compared between pre-treatment and post-treatment scans.

Results: FIR time courses revealed increased levels of brain activity in right dorsolateral prefrontal cortex and bilateral posterior parietal cortex at posttreatment FMRI assessment. There was also a significant improvement in working memory performance, as indexed by Cogmed exercise performance estimates ($p < .0001$).

Conclusions: This is the first study to show which ADHD brain regions are targeted by intensive working memory training, showing that 5 weeks of neardaily working memory practice alters brain function in regions known to underlie working memory ability. The results set the stage for additional examination of pre-treatment response predictors, whether brain changes are sustained, and possible relationships between brain changes and clinical improvement.

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Biol Psychiatry. 2013;73:86S-7S.

PARENTAL SUBSTANCE USE, BIOLOGICAL CORRELATES OF RISK AND EFFECTS OF STIMULANTS IN ADHD.

Ivanov I.

Background: Evidence from studies of substance using adults and adolescents suggest two competing models for addiction vulnerability manifested by either hypo- or hyper-sensitivity of the motivational brain system. However, this system's activation patterns and response to abusable drugs in drug-naive youths are unknown.

Methods: We recruited 20 drug-naive children with Attention Deficit/ Hyperactivity Disorder (ADHD), 10 of whom also had positive family history of substance abuse, as well as 9 controls. All subjects performed a hybrid functional magnetic resonance (FMRI) task that indexes activation in the brain motivational and behavioral control systems during reward conditions, assessed with appropriate linear contrasts. Additionally we scanned 16 healthy adult volunteers who performed the same FMRI task in placebo and methylphenidate (MPH) conditions.

Results: Our neuroimaging results showed that the combination of two clinical risk factors for substance abuse (i.e. childhood ADHD and parental substance abuse) was associated with increased activity in the motivational system, particularly the insula, when compared to children with ADHD alone and controls. Similar to other reports in children with ADHD, MPH consistently decreased the activity in wide distributed networks associated with motivation and behavioral control. Interaction analyses showed that MPH decreased activation in the motivational system independent of task difficulty, possibly through improved signal-to-noise information processing.

Conclusions: Together these results provide preliminary evidence of a hyperactive motivation system in children with combined clinical risk factors for later substance abuse and that MPH may influence task performance through increased motivation to obtain both nulleasynull and nulldifficultnull rewards.

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Biol Psychiatry. 2013;73:128S.

MAKING SENSE OF ADHD PHARMACOGENETICS: DAT1, ANCESTRAL MARKERS, DOSE, AND STUDY METHODOLOGY.

Stein MA.

Background: A variable number of tandem repeats (VNTR) in the dopamine transporter gene (DAT1) has been the most frequently studied candidate gene because of the mechanism of action of stimulant medications. Findings have been inconsistent, as studies differ in their methods and subject characteristics. The use of ancestral informative markers (AIMs) can provide quantifiable estimates of genetic ancestry that are useful in populations with significant admixture, such as in the United States.

Methods: 56 ADHD youth (mean age 11.7 + 2.2) participated in a 10 week, double blind, two period crossover dose response study with weekly switches. Each period consisted of 3 dose levels (10, 20, 25-30 mg, placebo) of ER d-MPH and MAS with the placebo period randomized. Subjects were genotyped for DAT1 and a panel of 105 ancestral informative markers were used to estimate individual genetic ancestry (percent European Caucasian, West African, and Native American) to assess potential population stratification.

Results: Children and adolescents absent the 10 repeat (i.e., 9/9 genotype) displayed a different dose response pattern for Total ADHD (p = .01) and Hyperactive-Impulsive (p = .006) ADHD RS scores compared to children with either the 10/10 and 10/9 genotype groups, regardless of stimulant formulation.

Conclusions: In this dose response study, children absent the 10 allele were less sensitive to both the beneficial and adverse effects of stimulants, including Somatic Complaints (e.g. decreased appetite, insomnia) and Emotionality (e.g. sadness, irritability) at low to moderate dose levels.

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Biol Psychiatry. 2013;73:98S-9S.

ADHD IN CHILDREN, BALANCING DEFICITS AND PRIMITIVE REFLEXES.

Konicarova J, Bob P.

Background: Particularly important functional disturbances developed early in life are balance deficits linked to dysfunctions of higher levels of coordination related to neurophysiological and mental functions that typically occur in ADHD. Several studies also suggest that disturbed coordination functions in ADHD are also linked to persisting primitive reflexes that usually diminish in early stages of development. According to current knowledge there is no evidence to which extent balance deficits are related to persistence of the primitive reflexes and whether this relationship may play a role in Attention Deficit and Hyperactivity Disorder (ADHD).

Methods: We measured balance deficits according to PANNES (Standing Eyes Closed-SEC; Walking FWD and Back-WF,WB with eyes open; Tandem walking fwd with eyes closed-TWF), Asymmetric Tonic Neck Reflex (ATNR) and Symmetric Tonic Neck Reflex (STNR) in 55 children in the school age (8-11 years) using standard neurological procedures and their relationship to ADHD symptoms (Conner's Parent Questionnaire- CPQ).

Results: Balancing deficits have significant Spearman correlation with ATNR and STNR scores and ADHD symptoms measured by total score of the CPQ and its subscales, main Results: SEC&ATNR, 0.53; SEC&CPQ 0.58; WF&ATNR 0.39; WF&STNR 0.32; WF&CPQ 0.54; TWF&ATNR 0.46; TWF&STNR 0.48; TWF&CPQ 0.66.

Conclusions: ADHD symptoms may present a compensatory process related to interference of more primitive neural mechanisms with higher levels of brain functions related to coordination and balancing mechanisms due to insufficiently developed cognitive and motor integration.

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Biol Psychiatry. 2013;73:47S.

COGNITIVE AND EMOTION PREDICTORS OF RESPONSE TO ATOMOXETINE IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER, WITH AND WITHOUT COMORBID ANXIETY.

Tsang TW, Kohn MR, Clarke SD, et al.

Background: ADHD is defined by cognitive impairments and is commonly comorbid with anxiety. Anxiety in ADHD has been associated with emotion impairments, therefore behavioral measures of cognition and emotion are viable candidates to test as markers of treatment outcome. We coupled a standardized behavioral battery with a clinical trial design to assess predictors of response to Atomoxetine in ADHD with and without anxiety.

Methods: 134 participants with ADHD (81% males, aged 11.0(plus or minus)2.6 years) were randomized to a 6-week Atomoxetine or placebo phase in a cross-over design. Behavioral testing was undertaken using the touchscreen IntegNeuroTM battery pre- and post-treatment/placebo phases. Clinical response was defined by (greater-than or equal to)25% improvement on the ADHD Rating Scale IV total score. Logistic regression models were used to test if behavioral performance at baseline (pre-treatment) predicts subsequent response.

Results: 31.3% had a comorbid anxiety disorder (GAD: 11.2%, SAD: 4.5%, OCD: 3.7%), diagnosed using the ADISC. Response rates were not significantly different in those with and without anxiety (29.6% vs. 36.4% respectively; p=0.813). In the total sample, response was predicted by Go-NoGo test omission errors, reflecting inattention, and less interference on the Stroop test (R2=0.679, p<0.0001; sensitivity=62.5%, specificity=86.0%). In ADHD only, better response was differentiated by better inhibition (fewer Go-NoGo errors, p<0.0001); while in ADHD+anxiety better motor coordination (p=0.043) but poorer accuracy in identifying sad facial expressions (p=0.044) were associated with better response.

Conclusions: A combination of cognitive and emotional behavioral measures may provide objective markers to assist clinical decisions about non-stimulants, especially when anxiety is comorbid with ADHD.

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Biol Psychiatry. 2013;73:87S.

MAPPING THE DEVELOPMENT OF THE STRIATUM IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Wharton A, Chakravarty M, Aitken W, et al.

Background: Striatal anomalies are linked with childhood ADHD. To date, neuroanatomic studies have been exclusively cross-sectional, and most have examined changes in gross volume. Herein, we define childhood striatal development using both a novel method to define striatal surfaces with exquisite spatial resolution and longitudinal data.

Methods: 270 children with ADHD (Mean 9.8 years, SD 3.2, range 4-18) and 270 matched typically developing controls had at least one magnetic resonance neuroanatomic scan at 1.5Telsa; 220 individuals (41%) had repeated imaging. Definition of striatal surfaces used a novel a multi-atlas based approach which matched each individual's striatum to multiple manually labeled templates.

Results: At baseline, striatal volumes and total surface area were significantly decreased in ADHD (striatal volumes: typical 18099mm3, SD 1841; ADHD 17315mm3, SD 1897; t(867)=6.1, p<0.0001; surface area: typical 7788mm2, SD 532; ADHD 7617mm2, SD 544; t(867)=3.7, p=0.0003). Considering developmental trajectories, a reduced surface area of the head of caudate and dorsal putamen persisted throughout childhood. Contrastingly, in the ventral striatum , typically developing individuals showed expansion of the ventral striatal surface (0.82mm2/year, SE 0.24) whereas in ADHD a significant surface contraction was found (-1.11mm2/year, SE 0.34; trajectory difference t=5.9, p<0.0001). This surface contraction did not correlate with time on psychostimulants.

Conclusions: ADHD is characterized by a fixed decrease in dorsal striatal surfaces, but a dynamic contraction with age in the ventral striatum. Such alterations may be the neural substrate for abnormal reward processing and perhaps could contribute to the increased risk for substance misuse associated with ADHD.

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Biol Psychiatry. 2013;73:56S.

MOTOR CONTROL DYSFUNCTION AND ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Watson B, Malek M, Wharton A, et al.

Background: Gross and fine motor control problems are common in those with ADHD. It has even been argued that the combination of motor dysfunction with ADHD defines a subtype of the disorder (Gillberg, 2003). We tested the competing hypotheses that (1) ADHD and motor dysfunction represents a discrete disorder, with a subset of children affected by ADHD having impaired motor function and the remainder having typical performance OR (2) ADHD is associated with motor dysfunction in general, with an overall shift toward impairment.

Methods:

Subjects: 113 children with DSM-IV defined ADHD (Mean age 6.9 years) and 50 typically developing controls (Mean age 6.4 years)

Assessment: The Movement Assessment Battery for Children (Movement-ABC) gives an age and sex standardized score describing overall movement capabilities. Intelligence was assessed using age-appropriate Weschler tests of general intelligence.

Results: Children with ADHD (M=8.46, SD=2.997) had significantly lower overall standard Movement-ABC scores than typically developing controls (M=10.6, SD=2.640), t(155)=-4.335, p<0.0001). This effect held when IQ was controlled for. The distribution of Movement-ABC scores resembled that of the controls (normal distribution) but shifted toward impairment. There was no evidence of a discrete group characterized by motor impairment and ADHD.

Conclusions: The shifted distribution of Movement-ABC in children with ADHD when compared to their healthy controls suggests that motor problems in ADHD lie on a continuous spectrum rather than constituting a discrete disorder. This informs our understanding of deficits associated with ADHD and provides direction for studies delineating the neuroanatomic basis for the movement anomalies seen in ADHD.

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Biol Psychiatry. 2013;73:88S.

DEVELOPMENTAL CHANGES IN NEURAL MECHANISMS UNDERLYING SPATIAL WORKING MEMORY DEFICITS IN ADHD.

Loo SK, Lenartowicz A, Galvan A, et al.

Background: The goal of the current study is to compare developmental changes in brain activation during spatial working memory (SWM) among children with attention-deficit/hyperactivity disorder (ADHD) and age-matched controls.

Methods: The sample consisted of 81 participants (41 children with ADHD, 40 typically developing (TD) children), aged 7-14 years old. Functional magnetic resonance imaging (FMRI) and electroencephalography (EEG) data were collected using a Sternberg SWM task with low (1 & 3 dots) and high (5 & 7 dots) memory loads. Data for each modality (FMRI, EEG) were integrated using joint independent component analysis (ICA; Calhoun et al., 2009) to describe changes in shared features of brain activity that underlie SWM task performance. The joint ICA produces component scores that were tested for diagnostic and age differences by load using ANOVA.

Results: Children with ADHD exhibited poorer SWM accuracy ($p<.05$) compared to controls. In parieto-occipital regions during SWM encoding, the ADHD group had reduced activation across age compared to controls ($p<.05$, corrected), suggesting maturational delay in visual processing of stimuli. In frontal regions during SWM maintenance, the ADHD group displayed increased activation relative to controls, particularly among older subjects ($p<.05$, corrected), suggesting aberrant development of executive control.

Conclusions: Neural mechanisms underlying SWM deficits represent both maturational delay and developmental deviation in ADHD.

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Bipolar Disord. 2013 Aug.

FAMILIAL TRANSMISSION OF PARENTAL MOOD DISORDERS: UNIPOLAR AND BIPOLAR DISORDERS IN OFFSPRING.

Oquendo MA, Ellis SP, Chesin MS, et al.

OBJECTIVES: Offspring of depressed parents are at increased risk for psychiatric disorders. Although bipolar disorder (BD) and major depressive disorder (MDD) are both found in the same families, it is not clear whether transmission to offspring of BD or MDD tends to occur from parents with the same mood disorder subtype. Our primary hypothesis was that the offspring of parents with BD would be at increased risk for BD and other comorbid disorders common to BD, such as anxiety and substance use, relative to the offspring of parents with MDD. The offspring of parents with BD versus those with MDD were also hypothesized to be at greater risk for externalizing disorders (i.e., conduct disorder, attention-deficit hyperactivity disorder, or antisocial personality disorder).

METHODS: Parents (n = 320) with mood disorders and their offspring (n = 679) were studied. Adult offspring were administered the Structured Clinical Interview for DSM-IV Axis I Disorders to establish the presence of psychopathology. Offspring aged 10-18 years were assessed using the School Aged Schedule for Affective Disorders and Schizophrenia, Present and Lifetime version, and parents of children under the age of ten completed the Child Behavioral Checklist. Data were examined using Cox proportional hazard regression.

RESULTS: There was no difference in hazard of mood disorders in the offspring of parents with BD as compared to the offspring of parents with MDD. However, a number of other parent and offspring characteristics increased the risk of mood, anxiety, externalizing, and substance use disorders in the offspring, including self-reported childhood abuse in the parent or offspring, offspring impulsive aggression, and the age at onset of parental mood disorder.

CONCLUSIONS: Mood disorders are highly familial, a finding that appears independent of whether the parent's condition is unipolar or bipolar, suggesting considerable overlap in the heritability of MDD and BD. Although parental characteristics had a limited influence on the risk of offspring psychopathology, reported childhood adversity, be it in the parent or child, is a harbinger of negative outcomes. These risk factors extend previous findings, and are consistent with diathesis-stress conceptualizations.

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BMC Psychiatry. 2013 Aug;13:215.

ASSOCIATION BETWEEN FAMILY ENVIRONMENT AND ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN -- MOTHERS' AND TEACHERS' VIEWS.

Pires TD, da Silva CM, de Assis SG.

BACKGROUND: To ascertain whether factors of the family environment and gestational period are associated with the appearance of ADHD in children, as reported by various different informants (mothers and teachers).

METHODS: This paper presents results from the dataset of a longitudinal study to evaluate behavioral problems among schoolchildren in Sao Goncalo, Rio de Janeiro State, in 2005 and 2006. The cross-section considered for this paper comprises records of exposure factors and ADHD. In all, 370 schoolchildren of the public school system were assessed by 3-stage cluster sampling. The Child Behavior Checklist (CBCL) and the Teacher Report Form (TRF) were used to measure outcomes. The exposure factors examined were: profile of child and mother, variables relating to the family environment, and perinatal considerations. The questions were answered by mothers and teachers. A hierarchical logistic regression model was used.

RESULTS: Precariously functioning families, lack of social support for mothers, adverse life events and discord during pregnancy were the factors associated with mother-reported ADHD. When ADHD was reported by teachers, the variables selected were: Intelligence quotient (IQ) and sex, with children with low IQ scores and boys more likely to display the disorder.

CONCLUSIONS: Assessment of ADHD by teachers or mothers reveals specific characteristics that reflect how each of these informants understands the children. This highlights the importance of using informants from different environments in diagnosing the disorder.

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Br J Psychiatry. 2013 Aug.

PRE-SCHOOL HYPERACTIVITY/ATTENTION PROBLEMS AND EDUCATIONAL OUTCOMES IN ADOLESCENCE: PROSPECTIVE LONGITUDINAL STUDY.

Washbrook E, Propper C, Sayal K.

BACKGROUND: High levels of attentional and hyperactivity problems in school-aged children, even if subthreshold for attention-deficit hyperactivity disorder (ADHD), are associated with academic under-achievement. Few large-scale, community-based studies have investigated the relationship between pre-school and adolescence. AIMS: To investigate whether pre-school hyperactivity/inattention and conduct problems are independently associated with academic outcomes at age 16.

METHOD: Data from the prospective, population-based Avon Longitudinal Study of Parents and Children (ALSPAC) were used. After adjusting for a broad range of confounder variables, the associations between parent-rated hyperactivity/inattention and conduct problems measured at age 3 and academic outcomes at age 16 (national General Certificate of Secondary Education (GCSE) examination results) were investigated (n = 11 640).

RESULTS: Both early hyperactivity/inattention and conduct problems had negative effects on academic outcomes. In adjusted analyses, abnormal hyperactivity/inattention scores were associated with reductions of ten GCSE points in boys. Borderline and abnormal conduct problem scores were associated with reductions of 9-10 and 12-15 points respectively.

CONCLUSIONS: Pre-school hyperactivity/inattention and conduct problems carry risk of worse academic outcomes at 16.

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Brain Cogn. 2013;83:10-20.

EMOTIONAL DISTRACTION IN BOYS WITH ADHD: NEURAL AND BEHAVIORAL CORRELATES.

Lopez-Martin S, Albert J, Fernandez-Jaen A, et al.

Although, in everyday life, patients with attention deficit hyperactivity disorder (ADHD) are frequently distracted by goal-irrelevant affective stimuli, little is known about the neural and behavioral substrates

underlying this emotional distractibility. Because some of the most important brain responses associated with the sudden onset of an emotional distracter are characterized by their early latency onset and short duration, we addressed this issue by using a temporally agile neural signal capable of detecting and distinguishing them. Specifically, scalp event-related potentials (ERPs) were recorded while 20 boys with ADHD combined type and 20 healthy comparison subjects performed a digit categorization task during the presentation of three types of irrelevant, distracting stimuli: arousing negative (A-), neutral (N) and arousing positive (A+). Behavioral data showed that emotional distracters (both A- and A+) were associated with longer reaction times than neutral ones in the ADHD group, whereas no differences were found in the control group. ERP data revealed that, compared with control subjects, boys with ADHD showed larger anterior N2 amplitudes for emotional than for neutral distracters. Furthermore, regression analyses between ERP data and subjects' emotional ratings of distracting stimuli showed that only in the ADHD group, emotional arousal (ranging from calming to arousing) was associated with anterior N2: its amplitude increased as the arousal content of the visual distracter increased. These results suggest that boys with ADHD are more vulnerable to the distracting effects of irrelevant emotional stimuli than control subjects. The present study provides first data on the neural substrates underlying emotional distractibility in ADHD.

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Breastfeeding Med. 2013;8:363-67.

BREASTFEEDING MAY PROTECT FROM DEVELOPING ATTENTION-DEFICIT/HYPERACTIVITY DISORDER .

Mimouni-Bloch A, Kachevanskaya A, Mimouni FB, et al.

Introduction: Breastfeeding has a positive influence on physical and mental development. Attention-deficit/hyperactivity disorder (ADHD) is a common neurobehavioral disorder with major social, familial, and academic influences. The present study aimed to evaluate whether ADHD is associated with a shorter duration of breastfeeding.

Subjects and Methods: In this retrospective matched study, children 6-12 years old diagnosed at Schneider's Children Medical Center (Petach Tikva, Israel) with ADHD between 2008 and 2009 were compared with two control groups. The first one consisted of healthy (no ADHD) siblings of ADHD children; the second control group consisted of children without ADHD who consulted at the otolaryngology clinic. A constructed questionnaire about demographic, medical, and perinatal findings, feeding history during the first year of life, and a validated adult ADHD screening questionnaire were given to both parents of every child in each group.

Results: In children later diagnosed as having ADHD, 43% were breastfed at 3 months of age compared with 69% in the siblings group and 73% in the control non-related group (p=0.002). By 6 months of age 29% of ADHD children were breastfed compared with 50% in the siblings group and 57% in the control non-related group (p=0.011). A stepwise logistic regression that included the variables found to be significant in univariate analysis demonstrated a significant association between ADHD and lack of breastfeeding at 3 months of age, maternal age at birth, male gender, and parental divorce.

Conclusions: Children with ADHD were less likely to breastfeed at 3 months and 6 months of age than children in the two control groups. We speculate that breastfeeding may have a protective effect from developing ADHD later in childhood.

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Br J Psychiatry. 2013;203:103-06.

RISK OF BIPOLAR DISORDER AND SCHIZOPHRENIA IN RELATIVES OF PEOPLE WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Larsson H, Ryden E, Boman M, et al.

Background: Attention-deficit hyperactivity disorder (ADHD) is associated with bipolar disorder and schizophrenia, and it has been suggested that combined bipolar disorder and ADHD is aetiologically distinct from the pure disorders.

Aims: To clarify whether ADHD shares genetic and environmental factors with bipolar disorder and schizophrenia.

Method: By linking longitudinal Swedish national registers, we identified 61 187 persons with ADHD (the proband group) and their first- and second-degree relatives, and matched them with a control group of people without ADHD and their corresponding relatives. Conditional logistic regression was used to determine the risks of bipolar disorder and schizophrenia in the relatives of the two groups.
Results: First-degree relatives of the ADHD proband group were at increased risk of both bipolar disorder (odds ratio (OR) = 1.84-2.54 for parents, offspring and full siblings) and schizophrenia (OR = 1.71-2.22 for parents, offspring and full siblings). The risks of bipolar disorder and schizophrenia among second-degree relatives were substantially lower than among full siblings.
Conclusions: These findings suggest that the co-occurrence of ADHD and bipolar disorder as well as ADHD and schizophrenia is due to shared genetic factors, rather than representing completely aetiologically distinct subsyndromes.

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Br J Psychiatry. 2013;203:112-19.

STIMULANT TREATMENT FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND RISK OF DEVELOPING SUBSTANCE USE DISORDER.

Groenman AP, Oosterlaan J, Rommelse NNJ, et al.

Background: Attention-deficit hyperactivity disorder (ADHD) is linked to increased risk for substance use disorders and nicotine dependence. Aims: To examine the effects of stimulant treatment on subsequent risk for substance use disorder and nicotine dependence in a prospective longitudinal ADHD case-control study.
Method: At baseline we assessed ADHD, conduct disorder and oppositional defiant disorder. Substance use disorders, nicotine dependence and stimulant treatment were assessed retrospectively after a mean follow-up of 4.4 years, at a mean age of 16.4 years.
Results: Stimulant treatment of ADHD was linked to a reduced risk for substance use disorders compared with no stimulant treatment, even after controlling for conduct disorder and oppositional defiant disorder (hazard ratio (HR) = 1.91, 95% CI 1.10-3.36), but not to nicotine dependence (HR = 1.12, 95% CI 0.45-2.96). Within the stimulant-treated group, a protective effect of age at first stimulant use on substance use disorder development was found, which diminished with age, and seemed to reverse around the age of 18.
Conclusions: Stimulant treatment appears to lower the risk of developing substance use disorders and does not have an impact on the development of nicotine dependence in adolescents with ADHD.

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Br J Psychiatry. 2013;203:107-11.

SHARED POLYGENIC CONTRIBUTION BETWEEN CHILDHOOD ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND ADULT SCHIZOPHRENIA.

Hamshere ML, Stergiakouli E, Langley K, et al.

Background: There is recent evidence of some degree of shared genetic susceptibility between adult schizophrenia and childhood attention-deficit hyperactivity disorder (ADHD) for rare chromosomal variants.
Aims: To determine whether there is overlap between common alleles conferring risk of schizophrenia in adults with those that do so for ADHD in children.
Method: We used recently published Psychiatric Genome-wide Association Study (GWAS) Consortium (PGC) adult schizophrenia data to define alleles over-represented in people with schizophrenia and tested whether those alleles were more common in 727 children with ADHD than in 2067 controls.
Results: Schizophrenia risk alleles discriminated ADHD cases from controls (P = 1.04null10-4, R 2 = 0.45%); stronger discrimination was given by alleles that were risk alleles for both adult schizophrenia and adult bipolar disorder (also derived from a PGC data-set) (P = 9.98null10-6, R2 = 0.59%).

Conclusions: This increasing evidence for a small, but significant, shared genetic susceptibility between adult schizophrenia and childhood ADHD highlights the importance of research work across traditional diagnostic boundaries.

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Child Adolesc Psychiatry Ment Health. 2013;7:1-10.

PREVALENCE AND DIAGNOSTIC STABILITY OF ADHD AND ODD IN TURKISH CHILDREN: A 4-YEAR LONGITUDINAL STUDY.

Ercan ES, Kandulu R, Uslu E, et al.

Background: This study was designed to assess the prevalence of Attention-Deficit/Hyperactivity Disorder (ADHD) and Oppositional Defiant Disorder (ODD) in a representative sample of second grade students from a country in a region where no previous rates are available (Turkey). The second aim is to evaluate the differences in ADHD and ODD prevalence rates among four different waves with one-year gap in reassessments.

Method: Sixteen schools were randomly selected and stratified according to socioeconomic classes. The DSM-IV Disruptive Behavior Disorders Rating Scale (T-DSM-IV-S) was delivered to parents and teachers for screening in around 1500 children. Screen positive cases and matched controls were extensively assessed using the K-SADS-PL and a scale to assess impairment criterion. The sample was reassessed in the second, third and fourth waves with the same methodology.

Results: The prevalence rates of ADHD in the four waves were respectively 13.38%, 12.53%, 12.22% and 12.91%. The ODD prevalence was found to be 3.77% in the first wave, 0.96% in the second, 5.41% in the third and 5.35% in the fourth wave. Mean ODD prevalence was found to be 3.87%.

Conclusions: The prevalence rates of ADHD in the four waves were remarkably higher than the worldwide pooled childhood prevalence. ADHD diagnosis was quite stable in reassessments after one, two and three years. A mean ODD prevalence consistent with the worldwide-pooled prevalence was found; but diagnostic stability was much lower compared to ADHD.

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Child Neuropsychol. 2013 Aug.

RECALL INITIATION STRATEGIES MUST BE CONTROLLED IN TRAINING STUDIES THAT USE IMMEDIATE FREE RECALL TASKS TO MEASURE THE COMPONENTS OF WORKING MEMORY CAPACITY ACROSS TIME.

Gibson BS, Gondoli DM, Johnson AC, et al.

There has been great interest in using working memory (WM) training regimens as an alternative treatment for ADHD, but it has recently been concluded that existing training regimens may not be optimally designed because they target the primary memory component but not the secondary component of WM capacity. This conclusion requires the ability to accurately measure changes in primary and secondary memory abilities over time. The immediate free recall task has been used in previous studies to measure these changes; however, one concern with these tasks is that the recall order required on training exercises may influence the recall strategy used during free recall, which may in turn influence the relative number of items recalled from primary and secondary memory. To address this issue, previous training studies have explicitly controlled recall strategy before and after training. However, the necessity of controlling for recall strategies has not been explicitly tested. The present study investigated the effects of forward-serial-order training on free recall performance under conditions in which recall strategy was not controlled using a sample of adolescents with ADHD. Unlike when recall order was controlled, the main findings showed selective improvement of the secondary memory component (as opposed to the primary memory component) when recall order was uncontrolled. This finding advances our understanding of WM training by highlighting the importance of controlling for recall strategies when free recall tasks are used to measure changes in the primary and secondary components of WM across time.

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Child Psychiatry Hum Dev. 2013 Aug.

PSYCHOPATHOLOGY AND ACADEMIC PERFORMANCE, SOCIAL WELL-BEING, AND SOCIAL PREFERENCE AT SCHOOL: THE TRAILS STUDY.

Sijtsema JJ, Verboom CE, Penninx BW, et al.

Psychopathology during adolescence has been associated with poor academic performance, low social well-being, and low social preference by peers at school. However, previous research has not accounted for comorbid psychopathology, informant-specific associations between psychopathology and functioning, and gender and age differences. This study addresses these limitations by examining adolescents' psychopathology and functioning at school, reported by child, parent, teacher, and peers during primary and secondary school in a large Dutch longitudinal cohort study (N = 2230). Teacher reports of psychopathology, especially regarding attention problems and withdrawn/depressed problems, followed by parent reports regarding hyperactivity, were most strongly associated with academic performance. The same held for social preference which was associated with teacher and parent ratings of withdrawn/depressed problems and hyperactivity. In contrast, social well-being was best predicted by child reports (at primary school) of affective problems. In girls, the association between ADHD problems and poor academic performance was stronger than in boys and conduct problems were more often associated with poor school functioning in general. These findings can help identify adolescents at risk for poor functioning and design interventions that effectively reduce or prevent poor school functioning.

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Child Care Health Dev. 2013 Jul;39:614-15.

PRACTITIONER REVIEW: CURRENT BEST PRACTICE IN THE MANAGEMENT OF ADVERSE EVENTS DURING TREATMENT WITH ADHD MEDICATIONS IN CHILDREN AND ADOLESCENTS.

Reading R.

Medication is an important element of therapeutic strategies for ADHD. While medications for ADHD are generally well-tolerated, there are common, although less severe, as well as rare but severe adverse events AEs during treatment with ADHD drugs. The aim of this review is to provide evidence- and expert-based guidance concerning the management of (AEs) with medications for ADHD. The review covers monitoring and management strategies of loss of appetite and growth delay, cardiovascular risks, sleep disturbance, tics, substance misuse/abuse, seizures, suicidal thoughts/behaviors and psychotic symptoms.

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Clin Gov. 2013;18:210-19.

TRANSITIONAL CARE TO ADULT ADHD SERVICES IN A NORTH WEST ENGLAND DISTRICT.

Ogundele MO.

Purpose - ADHD is the commonest neurodevelopmental disorder of children and adolescents. ADHD is no longer conceptualized as a predominantly childhood disorder but is a chronic disorder that persists into adolescence and adulthood. The paper aims to analyse the transitional care of adolescents diagnosed with ADHD in childhood into adult specialist ADHD services in a local district. The paper also seeks to review current practice and to design a multi-disciplinary transitional care pathway to adult services for adolescents with complex health needs based on best practice and available clinical guidelines.

Design/methodology/approach - Adolescents diagnosed with ADHD from childhood who were eligible for transition to adult ADHD services and who reached the age of 16 years over a period of two years consecutively (July 2009 to June 2011) were studied by a retrospective analysis of their clinical records. The current transitional care pathway was reviewed and revised.

Findings - Out of 504 patients on the specialist ADHD database, 104 adolescents were eligible for transition to adult services. A total of 19 patients (18 per cent) were referred to CAMHS. A total of 68 adolescents (65 per cent) were discharged from the paediatric services following voluntary discontinuation of medications and non-attendance at follow-up clinics. Only 16 patients (15 per cent) were successfully referred to the specialist adult ADHD services (three of them already discharged). A multi-disciplinary transitional care pathway to adult services for young people with complex health needs and learning

difficulties and information for the carers and young people have been designed and adopted in the local city borough, agreed by all the stakeholders.
Practical implications - A total of 73 per cent of eligible patients were either discharged or lost to follow-up. There must be some flexibility in the referral pathway to the adult ADHD services to allow some of the adolescents who were previously lost to follow-up to be re-referred by other primary or secondary care healthcare professionals if the need arises in the future.
Originality/value - The paper shows that there is a high rate of discontinuation of medications, loss to follow-up and a remarkably low rate of successful transition to locally commissioned adult ADHD services among adolescents diagnosed with ADHD in childhood.

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Clin Neuropharmacol. 2013;36:117-21.
EXTENDED-RELEASE DEXMETHYLPHENIDATE 30 MG/D VERSUS 20 MG/D: DURATION OF ATTENTION, BEHAVIOR, AND PERFORMANCE BENEFITS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Silva RR, Brams M, McCague K, et al.
OBJECTIVE: This study aimed to compare the effects of dexmethylphenidate (D-MPH) extended-release (ER) 30 mg and D-MPH-ER 20 mg on attention, behavior, and performance in children with attention-deficit/hyperactivity disorder.
METHODS: In a randomized, double-blind, 3-period-by-3-treatment, crossover study, children aged 6 to 12 years with attention-deficit/hyperactivity disorder stabilized on methylphenidate (40-60 mg/d) or D-MPH (20-30 mg/d) received D-MPH-ER 20 mg/d, 30 mg/d, and placebo for 7 days each (final dose of each treatment period administered in a laboratory classroom). Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) Combined (Attention and Deportment) rating scale and Permanent Product Measure of Performance (PERMP) math test assessments were conducted at baseline and 3, 6, 9, 10, 11, and 12 hours postdose.
RESULTS: A total of 165 children (94 boys; mean age, 9.6 years) were randomized (162 included in intent-to-treat analyses). Significant improvements were noted for D-MPH-ER 30 mg over D-MPH-ER 20 mg at various late time points on the SKAMP scales (Combined scores at 9, 10, 11, and 12 hours postdose; Attention scores at 10, 11, and 12 hours postdose; deportment scores at 9 and 12 hours postdose). The PERMP math test-attempted and -correct scores (change from predose) were significantly higher with D-MPH-ER 30 mg than with D-MPH-ER 20 mg at 10, 11, and 12 hours postdose. Both D-MPH-ER doses were superior to placebo at all time points.
CONCLUSIONS: D-MPH-ER 30 mg was superior to D-MPH-ER 20 mg at later time points in the day, suggesting that higher doses of D-MPH-ER may be more effective later in the day.

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Clin Neuropsychiatry. 2013;10:63-71.
SEMANTIC AND PHONOLOGIC VERBAL FLUENCY TESTS FOR ADOLESCENTS WITH ADHD.
Abreu N, Argollo N, Oliveira F, et al.
Objective: One-minute Semantic Verbal Fluency (SVF) test for the category "animals" and one-minute Phonemic Verbal Fluency (PVF) test for words starting with the letters "F", "A" and "S" (usually called FAS tests), besides DSM-IV criteria, have been used for assessment of Attention Deficit/Hyperactivity Disorder (ADHD). Even though, no criterion validity has been developed for SVF and FAS tests. This study evaluated criterion validity (discriminant), an important step on neuropsychological test validation for SVF and FAS tests, by comparing performance of healthy adolescents (Control Group) and adolescents with ADHD (ADHD Group) in these tests.
Method: Forty-four 12.8 year-old adolescents with ADHD and 6.1 years of formal education, and forty-three 12.11 year-old healthy adolescents and 6.4 years of formal education, were exposed to SVF and FAS tests, to the Weschler Intelligence Scale for Children (WISC-III) and to a test for visual attention (TAVIS-III). For the SVF, letters F, A, S, and sum of F, A and S (FAS), a Receiver Operating Curve (ROC) analysis was used to evaluate discriminant validity in healthy and ADHD groups.

Results: Performance of the subjects with ADHD in the FAS test, particularly for letters starting with "F", was significantly poorer as compared to that seen in the Controls (P < 0.05). Whilst the area under ROC curve for both groups was smaller for the SVF test (ROC area = 0.65, P < 0.015), it did differ significantly and was greater for FAS scores particularly for letters starting with "F" (ROC = 0.84, P < 0.001), "A" (ROC = 0.72, P < 0.001), "S" (ROC= 0.70, P = 0.001), and the FAS (ROC = 0.81, P < 0.001).
Conclusions: These results indicate that one-minute FAS test using the "F" letter is suitable for discriminating healthy and ADHD Brazilian adolescents's verbal fluency.

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Clin Psychol Rev. 2013;33:795-811.

REACTION TIME VARIABILITY IN ADHD: A META-ANALYTIC REVIEW OF 319 STUDIES.

Kofler MJ, Rapport MD, Sarver DE, et al.

Individuals with ADHD are characterized as ubiquitously slower and more variable than their unaffected peers, and increased reaction time (RT) variability is considered by many to reflect an etiologically important characteristic of ADHD. The present review critically evaluates these claims through meta-analysis of 319 studies of RT variability in children, adolescents, and adults with ADHD relative to typically developing (TD) groups, clinical control groups, and themselves (subtype comparisons, treatment and motivation effects). Random effects models corrected for measurement unreliability and publication bias revealed that children/adolescents (Hedges' g=. 0.76) and adults (g=. 0.46) with ADHD demonstrated greater RT variability relative to TD groups. This increased variability was attenuated by psychostimulant treatment (g=. -. 0.74), but unaffected by non-stimulant medical and psychosocial interventions. Individuals with ADHD did not evince slower processing speed (mean RT) after accounting for RT variability, whereas large magnitude RT variability deficits remained after accounting for mean RT. Adolescents and adults with ADHD were indistinguishable from clinical control groups, and children with ADHD were only minimally more variable than clinical control children (g=. 0.25). Collectively, results of the meta-analysis indicate that RT variability reflects a stable feature of ADHD and other clinical disorders that is robust to systematic differences across studies.

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CNS Drugs. 2013 Aug.

COMPARATIVE EFFICACY OF GUANFACINE EXTENDED RELEASE VERSUS ATOMOXETINE FOR THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS: APPLYING MATCHING-ADJUSTED INDIRECT COMPARISON METHODOLOGY.

Sikirica V, Findling RL, Signorovitch J, et al.

BACKGROUND: No head-to-head clinical trials have been published comparing guanfacine extended release (GXR) and atomoxetine (ATX): two nonstimulants approved for the treatment of attention-deficit/hyperactivity disorder (ADHD). However, other study designs or methods could be used to indirectly compare these two medications. Matching-adjusted indirect comparison (MAIC) is a recent methodology that utilizes individual patient data (IPD) from clinical trials for one treatment and published aggregate data from another treatment to estimate the relative efficacy of both, providing rapid, reliable comparative efficacy results.
OBJECTIVE: The aim of this study was to compare the efficacy of GXR and ATX for the treatment of ADHD using MAIC.
STUDY DESIGN: A systematic literature search was conducted to identify ATX and GXR trials published through December 2012. Studies were selected for MAIC analyses on the basis of having comparable trial characteristics and study designs. Summary data from selected ATX trials and IPD from selected GXR trials were used. MAIC methodology ensured comparable populations: target doses for the 'base case' comparison were selected on the basis of maximum effective dosage ranges from the US FDA-approved product labels (GXR 0.09-0.12 mg/kg/day, ATX 1.2 mg/kg/day for children and adolescents weighing </=70 kg). Individuals from GXR trials were selected if they matched inclusion/exclusion criteria from selected ATX trials; selected GXR IPD were then re-weighted to match the published ATX trial mean baseline

characteristics and placebo outcomes. Sensitivity analyses were conducted, examining different dosage ranges and repeating the analysis in a larger number of trials, allowing for larger and more heterogeneous trial populations.
MAIN OUTCOME MEASURE: The primary outcome measure was change in ADHD Rating Scale IV (ADHD-RS-IV) total score.
RESULTS: Using MAIC in the base case comparison, significantly greater reductions in mean (standard error; SE) ADHD-RS-IV total scores from baseline to end of study were observed in patients treated with GXR relative to ATX [-7.0 (2.2); p < 0.01]. Significantly greater reductions for GXR over ATX were also demonstrated for hyperactivity/impulsivity [-3.8 (1.2); p < 0.01] and inattention [-3.2 (1.3); p < 0.05] subscales of the ADHD-RS-IV. Similar results were observed in MAIC sensitivity analyses evaluating other dosage ranges and using more heterogeneous trial populations (e.g., larger randomized sample, broader subject weight range, additional trials). Mean (SE) decreases in ADHD-RS-IV total scores were greater for GXR relative to ATX when including IPD for those administered GXR at lower than target dosage (0.075-0.090 mg/kg/day) compared with ATX at target dosage (1.2 mg/kg/day), with a relative improvement of -6.0 (2.7) (p < 0.05). Reductions in ADHD-RS-IV total scores were also greater for GXR in another MAIC examining GXR at target dosage (0.09-0.12 mg/kg/day) and a broader range of ATX dosages (including three additional trials evaluating ATX >/=1.2 mg/kg/day); relative improvement for GXR versus ATX administered at target dosage or higher was -7.6 (1.4) (p < 0.01).
CONCLUSION: After adjusting for difference in baseline trial characteristics using MAIC, GXR appears to be more efficacious than ATX for the treatment of ADHD. Results were consistent in a variety of dosage range comparisons and within increasingly heterogeneous trial populations.

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CNS Drugs. 2013 Aug.
EFFICACY AND SAFETY OF LISDEXAMFETAMINE DIMESYLATE AND ATOMOXETINE IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A HEAD-TO-HEAD, RANDOMIZED, DOUBLE-BLIND, PHASE IIIB STUDY.
Dittmann RW, Cardo E, Nagy P, et al.
OBJECTIVES: The aim of this study was to compare the efficacy and safety of the prodrug psychostimulant lisdexamfetamine dimesylate (LDX) and the non-stimulant noradrenergic compound atomoxetine (ATX) in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) who had previously responded inadequately to methylphenidate (MPH).
METHODS: This 9-week, head-to-head, randomized, double-blind, active-controlled study (SPD489-317; ClinicalTrials.gov NCT01106430) enrolled patients (aged 6-17 years) with at least moderately symptomatic ADHD and an inadequate response to previous MPH therapy. Patients were randomized (1:1) to an optimized daily dose of LDX (30, 50 or 70 mg) or ATX (patients <70 kg, 0.5-1.2 mg/kg with total daily dose not to exceed 1.4 mg/kg; patients >/=70 kg, 40, 80 or 100 mg). The primary efficacy outcome was time (days) to first clinical response. Clinical response was defined as a Clinical Global Impressions-Improvement (CGI-I) score of 1 (very much improved) or 2 (much improved). Secondary efficacy outcomes included the proportion of responders at each study visit and the change from baseline in ADHD Rating Scale (ADHD-RS-IV) and CGI-Severity scores. Tolerability and safety were assessed by monitoring treatment-emergent adverse events (TEAEs), height and weight, vital signs and electrocardiogram parameters. Endpoint was defined as the last post-baseline, on-treatment visit with a valid assessment.
RESULTS: Of 267 patients randomized (LDX, n = 133; ATX, n = 134), 200 (74.9 %) completed the study. The median time to first clinical response [95 % confidence interval (CI)] was significantly shorter for patients receiving LDX [12.0 days (8.0-16.0)] than for those receiving ATX [21.0 days (15.0-23.0)] (p = 0.001). By week 9, 81.7 % (95 % CI 75.0-88.5) of patients receiving LDX had responded to treatment compared with 63.6 % (95 % CI 55.4-71.8) of those receiving ATX (p = 0.001). Also by week 9, the difference between LDX and ATX in least-squares mean change from baseline (95 % CI) was significant in favour of LDX for the ADHD-RS-IV total score [-6.5 (-9.3 to -3.6); p < 0.001; effect size 0.56], inattentiveness subscale score [-3.4 (-4.9 to -1.8); p < 0.001; effect size 0.53] and the hyperactivity/impulsivity subscale score [-3.2 (-4.6 to -1.7); p < 0.001; effect size 0.53]. TEAEs were reported by 71.9 and 70.9 % of patients receiving LDX and ATX, respectively. At endpoint, both treatments

were associated with mean (standard deviation) increases in systolic blood pressure [LDX, +0.7 mmHg (9.08); ATX, +0.6 mmHg (7.96)], diastolic blood pressure [LDX, +0.1 mmHg (8.33); ATX, +1.3 mmHg (8.24)] and pulse rate [LDX, +3.6 bpm (10.49); ATX, +3.7 bpm (10.75)], and decreases in weight [LDX, -1.30 kg (1.806); ATX, -0.15 kg (1.434)].
CONCLUSIONS: LDX was associated with a faster and more robust treatment response than ATX in children and adolescents with at least moderately symptomatic ADHD who had previously responded inadequately to MPH. Both treatments displayed safety profiles consistent with findings from previous clinical trials.

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Cogn Behav Pract. 2013.
A PARENT-TEEN COLLABORATIVE TREATMENT MODEL FOR ACADEMICALLY IMPAIRED HIGH SCHOOL STUDENTS WITH ADHD.
Sibley MH, Altszuler AR, Ross JM, et al.
The current study pilots a low-intensity behavioral intervention for parents and high school students with ADHD that promotes parent-teen collaboration at home and in session (Supporting Teens' Academic Needs Daily-Group; STAND-G). Twenty-three high school students with ADHD and their parents were randomly assigned to receive an 8-week behavioral treatment beginning in October, January, or March. Weekly data were collected from students' online grade books for 37 weeks of the school year to monitor changes in academic functioning through baseline, posttreatment, and follow-up phases. Students who had not yet received the treatment served as a control group for students who completed treatment. Qualitative and quantitative ratings of satisfaction, improvement, and parent implementation of home-based behavioral strategies were collected. Results indicated parent and teen satisfaction with STAND-G, parent compliance with intervention strategies, and a range of parent-rated therapeutic benefits (i.e., organization and time-management skills, academic conscientiousness, parent-teen communication, adolescent autonomy). Findings for the objective grade book data were mixed, with Group 2 (January), but not Group 1 (October), displaying identifiable acute improvements relative to control students. However, both groups evaluated at follow-up displayed meaningful improvements in the percentage of work turned in up to 2 months out of treatment. With these results in mind, we discuss the importance of tailoring interventions to the lives of high school students with ADHD and the future of treatment development and delivery for this often underserved population.

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Curr Neuropharmacol. 2013 Mar;11:186-96.
EFFECTS OF LOW DOSES OF POLYUNSATURATED FATTY ACIDS ON THE ATTENTION DEFICIT/HYPERACTIVITY DISORDER OF CHILDREN: A SYSTEMATIC REVIEW.
Grassmann V, Santos-Galduroz RF, Galduroz JC.
Since attention deficit/hyperactivity disorder (ADHD) presents high prevalence among children, science has been researching alternative forms of treatment that do not involve medication.
OBJECTIVE: To evaluate the effects of polyunsaturated fatty acids (PUFAs) on attention deficit/hyperactivity disorder.
METHODS: We reviewed the articles published between 1980 and 2012 indexed in the databases PubMed, APA psychNET, Scopus and Web of Knowledge.
RESULTS: Initially 231 articles were selected, out of which 12 met the inclusion criteria. The articles selected reported a modest cognitive and behavioral improvement of the patients after treatment with low doses of PUFAs. Those results might be associated with the evaluation methodology, the doses of PUFAs administered or the duration of treatment.

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Curr Drug Saf. 2013;8:169-74.

A SYSTEMATIC REVIEW OF THE EFFICACY AND SAFETY OF DESIPRAMINE FOR TREATING ADHD.

Ghanizadeh A.

This review article systematically and critically summarizes the current evidence regarding desipramine for treating children and adolescents with attention deficit hyperactivity disorder (ADHD).PRISMA guideline was used for gathering the data. The databases of PubMed/Medline and Google scholar were electronically searched. This review included controlled clinical trials investigating the efficacy of desipramine for treating children and adolescents with ADHD. The primary outcome measure was clinical improvement measured by valid and reliable objective instruments in order to assess the severity of ADHD clinical symptoms. Adverse effects were evaluated as well. Out of 267 titles under the study, thirty three articles mentioned desipramine for treating ADHD. Two trials met the inclusion criteria. Desipramine decreases ADHD clinical symptoms. However, there are many concerns about its safety and efficacy. In view of serious concerns about its safety and lack of enough well-controlled trials providing strong evidence about the efficacy of desipraimine, it should be prescribed for treating children with ADHD with a high precaution, and further well-controlled trials should be performed.

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Curr Psychiatry Rep. 2013;15.

KNOWLEDGE AND ATTITUDES ABOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND ITS TREATMENT: THE VIEWS OF CHILDREN, ADOLESCENTS, PARENTS, TEACHERS AND HEALTHCARE PROFESSIONALS.

Moldavsky M, Sayal K.

Attention-deficit/hyperactivity disorder (ADHD) is a common neuro-developmental disorder that causes controversy; this may have a negative effect on the ability of families, teachers and healthcare professionals to achieve shared understanding and goals. This article reviews recent research of the knowledge and attitudes of children, adolescents, parents, teachers, healthcare professionals and the public about ADHD. Findings suggest that misconceptions about ADHD persist, and children with ADHD and their parents report stigmatizing experiences. Educational interventions to improve the knowledge of teachers about ADHD appeared to be effective in the short term. Parents and professionals working together in the diagnosis and treatment of children with ADHD may have different views about their roles in the shared decision-making process. Studies have reported both similarities and differences in parents' and professionals' views about the effectiveness of treatments for ADHD, but all stakeholders supported the principles of information-sharing and working in partnership.

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Curr Psychiatry Rep. 2013;15:1-9.

GLOBALIZATION AND COGNITIVE ENHANCEMENT: EMERGING SOCIAL AND ETHICAL CHALLENGES FOR ADHD CLINICIANS.

Singh I, Filipe AM, Bard I, et al.

Globalization of ADHD and the rise of cognitive enhancement have raised fresh concerns about the validity of ADHD diagnosis and the ethics of stimulant drug treatment. We review the literature on these two emerging phenomena, with a focus on the corresponding social, scientific and ethical debates over the universality of ADHD and the use of stimulant drug treatments in a global population of children and adolescents. Drawing on this literature, we reflect on the importance of ethically informed, ecologically sensitive clinical practices in relation to ADHD diagnosis and treatment.

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Curr Psychiatry Rep. 2013;15.

CARDIOVASCULAR SAFETY OF STIMULANTS IN CHILDREN: FINDINGS FROM RECENT POPULATION-BASED COHORT STUDIES.

Winterstein AG.

The past decade has seen a heated debate over the cardiac safety of central nervous system stimulants in the treatment of ADHD. This review discusses five controlled population-based studies that investigated this risk in children in the United States. All studies utilized administrative claims data of private or public insurance to compare risk of stimulant use to non-use. Two studies with smaller sample size lacked the ability to investigate serious events but report a slightly increased risk of emergency department visits attributed to cardiac symptoms such as tachycardia or palpitation. Three studies that enrolled more than one million patients found no association between stimulants and composite endpoints of sudden cardiac death, myocardial infarction, stroke and ventricular arrhythmia. The studies concur that background rates of serious cardiovascular events in children are extremely small. No study exceeded an average follow-up of two years, prohibiting inferences about long-term effects of stimulants.

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Dent Traumatol. 2013 Sep.

KNOWLEDGE AND ATTITUDE OF SAUDI TEACHERS OF STUDENTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER TOWARDS TRAUMATIC DENTAL INJURIES.

Pani SC, Hillis H, Chaballout T, et al.

BACKGROUND AND AIM: Attention-deficit hyperactivity disorder (ADHD) is one of the most common childhood mental disorders that manifest with difficulties in staying focused and hyperactivity. Such children have been reported to have a higher incidence of traumatic dental injuries. The aim of this article was to study the knowledge and attitude of Saudi teachers of children with ADHD towards the management of traumatic dental injuries and compare them to their counterparts in mainstream schools. MATERIAL AND **METHODS**: A four-part structured Arabic questionnaire was administered to 281 teachers of children with ADHD and 384 teachers in mainstream schools. The questionnaire recorded the demographic data, type of children taught, experience of the teacher in dealing with traumatic dental injuries, the teachers' perceived importance of managing traumatic dental injuries and their knowledge of emergency management of these injuries. The difference in knowledge and attitude between teachers of mainstream schools and schools for children with ADHD was assessed.

RESULTS AND CONCLUSIONS: The results of the study indicate that teachers of children with ADHD have a greater experience of witnessing traumatic dental injuries and place significantly more importance towards the management of these injuries than their counterparts in mainstream schools. The influence of demographic variables on knowledge seen in teachers from mainstream schools is absent in those teaching children with ADHD.

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Early Child Res Q. 2013 Oct;28:668-82.

PREDICTORS OF DISCREPANCIES BETWEEN INFORMANTS' RATINGS OF PRESCHOOL-AGED CHILDREN'S BEHAVIOR: AN EXAMINATION OF ETHNICITY, CHILD CHARACTERISTICS, AND FAMILY FUNCTIONING.

Harvey EA, Fischer C, Weieneth JL, et al.

The present study examined predictors of discrepancies between mothers', fathers', and teachers' ratings of 3-year-old children's hyperactivity, attention problems, and aggression. Participants were families of 196 3-year-old children who took part in child and family assessments. Ethnicity was one of the most consistent predictors of discrepancies. African American mothers and fathers were more likely to rate their children's hyperactivity, attention problems, and aggression lower than teachers. In contrast, Latina mothers were more likely to rate their children as more hyperactive and inattentive than teachers. ADHD/ODD diagnoses, parental depression, number of children, and children's pre-academic skills were also predictive of

discrepancies for some measures for some informants. These findings provide insight into factors that may contribute to informant discrepancies in ratings of preschool children.

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Eat Behav. 2013 Aug;14:390-93.

EXPLORING THE CO-MORBIDITY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH EATING DISORDERS AND DISORDERED EATING BEHAVIORS IN A NATIONALLY REPRESENTATIVE COMMUNITY-BASED SAMPLE.

Bleck J, Debate RD.

Emerging evidence signifies the co-occurrence of attention-deficit/hyperactivity disorder (ADHD) with clinical and sub-threshold disordered eating behaviors. However, many existing studies have assessed this co-occurrence among inpatient or intensive outpatient populations. The purpose of this study was to examine the co-occurrence of ADHD with clinical eating disorders and disordered eating behaviors in a nationally representative sample via a secondary data analysis of data from the National Longitudinal Study of Adolescent Health (n=4,862; 2,243 males; 2,619 females). Results reveal that females have higher rates of co-occurrence of ADHD and diagnosed eating disorders than males (1.05% vs. 0.20%, p<.01). When controlling for age and race, ADHD predicted diagnosed eating disorders in females (incidence rate ratio (IRR): 2.06; 95% CI: 1.09-3.88; p<.05), but did not predict diagnosed eating disorders in males. With regard to disordered eating behaviors, when controlling for age, gender, and race, ADHD significantly predicted disordered eating behaviors (OR: 1.82; 95% CI: 1.21-2.74). When stratifying by type of disordered eating behavior, ADHD predicted binging and/or purging behavior (OR: 2.86; 95% CI: 1.78-4.61), but not restrictive behaviors. Implications of study findings pertain to both secondary/targeted prevention efforts in addition to tertiary prevention via patient-specific treatment plans.

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Epilepsia. 2013;54:331.

THE COMORBIDITY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH EPILEPSY.

Kim WS, Sim GY, Son JW.

Purpose: Attention Deficit Hyperactivity Disorder (ADHD) is known to be more common in children with epilepsy than in the general population. Thirty one to forty percent of ADHDis accompanied with epilepsy. Few studies regarding this matter have been reported in Korea. This study was aimed to evaluate the comorbidity of ADHD in children with epilepsy.

Method: This is a two center based, retrospective and controlled study. Thirty four ADHD children with epilepsy from Chungbuk National University hospital and 38 ADHD children without epilepsy from Cheonju St. Mary's hospital were recruited from January 2005 to June 2010.

Results: In ADHD children with epilepsy, twelve (35.2%) had partial seizures 11 (32.2%) did generalized seizures and 11 (32.2%) were unclassified. EEG abnormalities were found inthe frontal lobe (15 cases), in the central lobe (7 cases), in the temporal lobe (6 cases), and in the occipital lobe (3 cases). In ADHD children with epilepsy, the combined type was major (76.4%) and in ADHD children without epilepsy, the inattentive type was major (50.5%; p = 0.004). Learning disability was more common in ADHD with epilepsy than in ADHD without epilepsy (p = 0.01).

Conclusion: This study showed that ADHD children with epilepsy are more likely to have combined type (76.4%) and learning disability as compared with ADHD without epilepsy.

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Epilepsia. 2013;54:348.

USE OF THEMOXO TEST TO EVALUATE THE CORE COMPONENTS OF ADHD IN EPILEPTIC PATIENTS.

Cohen R, Halevi A, Shuper A.

Purpose: To apply the MOXO, a continuous performance test for the measurement of the four core components of ADHD [Berger I, Goldzweig G. Isr Med Assoc J 2010;12(9):531-535.], in children with epilepsy.

Method: All epileptic children aged 6-18 years attending the Neurology Clinic of Schneider Children's Medical Center of Israel in 2012-2013 were evaluated with the DSM-IV and completed the MOXO test. Background data were collected from the patient files and revision of the electroencephalograms. Scores for the ADHD components (hyperactivity, inattention, timing, impulsivity) were compared to norms using analysis of variance (ANOVA), controlling for age and sex.
Results: The sample included 49 children (26 boys 23 girls) with epilepsy: 32 benign epilepsy of childhood with central spikes (BECCTS), 9 generalized epilepsy 6 complex partial epilepsy, and 2 juvenile myoclonic epilepsy. Twenty-six children (53%) had a DSM-IV diagnosis of ADHD 11 with attention deficit only. Eighteen children with BECCTS (56%) had ADHD 7 (38%) with attention deficit only. On statistical analysis, the effect of group was significant for all ADHD components by the MOXO test ($p < 0.001$). The BECCTS group had significantly less hyperactivity than the other epilepsy groups ($p = 0.01$) and a higher proportion of patients free of ADHD symptoms (48.3% vs. 29.4%).
Conclusion: Epileptic children have a high incidence of ADHD according to the MOXO test. The manifestations are no worse in children with BECCTS than children with other epilepsy types. The main disturbances associated with BECCTS are timing and attention rather than hyperactivity or impulsivity.

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Eur Child Adolesc Psychiatry. 2013 Sep.

SEARCHING FOR THE BEST APPROACH TO ASSESS TEACHERS' PERCEPTION OF INATTENTION AND HYPERACTIVITY PROBLEMS AT SCHOOL.

Kieling RR, Kieling C, Aguiar AP, et al.

Although major guidelines in the field and current diagnostic criteria clearly demand an assessment of children's attention deficit/hyperactivity disorder (ADHD) symptoms at school, few studies address the fundamental question of which is the best approach for clinicians to get this information from teachers. Three screening strategies for ADHD were applied to teachers of 247 third grade students. They were asked (1) an overt question about potential cases of ADHD in their classroom; (2) to complete a broad-band questionnaire assessing common child mental health problems; (3) to rate ADHD-specific symptoms in a narrow-band questionnaire. Based on the overt question, teachers identified one in five students (21.1 %) as having ADHD; 28 cases (11.3 %) were identified using standard cut-offs for the narrow-band, and 13 (5.3 %) using a standard threshold for the sub-scale of hyperactivity from the broad-band questionnaire. Agreement among strategies was low ($k = 0.28$). A subsample of students, clinically assessed to confirm screenings, showed modest agreement with final diagnosis. The narrow-band questionnaire had the best diagnostic performance. Multivariate analysis indicated that the presence of a comorbid externalizing disorder was the only variable associated with teachers' ascertainment of ADHD caseness or non-caseness. Choice of screening strategy significantly affects how teachers report on ADHD symptoms at school. The halo effect of externalizing behaviors impacts the correct identification of true cases of ADHD in the school setting. Clinicians can rely on narrow-band instruments like the SNAP-IV to get information on ADHD symptoms at school from teachers.

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Eur Neuropsychopharmacol. 2013 Aug.

PHARMACOLOGICAL TREATMENT AND DEMOGRAPHIC CHARACTERISTICS OF PEDIATRIC PATIENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER, SWEDEN.

Bahmanyar S, Sundstrom A, Kaijser M, et al.

The aim of this study was to describe the pediatric population with ADHD and their pharmacological treatment. Using the Swedish National Patient Register and the Prescribed Drug Register we identified individuals below 19 years of age who were diagnosed or medically treated for ADHD for the first time 2006-2007. The unique patient identifiers were used to link information from the two registers to describe demographic characteristics, hospital care and drug treatments. Logistic regression model estimated the association between age, sex, frequency of hospitalization, diagnosis or treatment for other mental disorders and risk of gap in the treatment. Totally the study included 7931 patients of whom 74% were

males. The mean age at first diagnosis was 12 years. Some 84% were medically treated for ADHD and approximately 90% received methylphenidate as the first substance. Combination therapy was rare and the most common combination was methylphenidate and atomoxetine. More than 55% of the patients, which could be followed up for two years after start of treatment, had at least one treatment gap of six months. Older age at diagnosis, lower number of hospitalizations and comorbidity with other mental disorders increased risks of gaps in medication. Approximately one fifth of the patients recorded in the National Patient Register as diagnosed with ADHD did not receive pharmacological treatment. Medication adherence seems to be low, when measured as gaps in treatment.

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Evid Based Ment Health. 2013 Aug.

METHYLPHENIDATE REDUCES ADHD SYMPTOMS IN CHILDREN WITH SEVERE ADHD AND INTELLECTUAL DISABILITY.

Lipkin PH.

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Gene 2013 Oct 10;528(2):320-7

THE RELATIONSHIP BETWEEN THE PRESENCE OF ADHD AND CERTAIN CANDIDATE GENE POLYMORPHISMS IN A TURKISH SAMPLE.

Pazvantoglu O, Gunes S, Karabekiroglu K, et al.

Due to the high heritability of attention-deficit hyperactivity disorder (ADHD), parents of children with ADHD appear to represent a good sample group for investigating the genetics of the disorder. The aim of this study was to investigate the association between ADHD and six polymorphisms in five candidate genes [5-HT2A (rs6311), NET1 (rs2242447), COMT (rs4818), NTF3 (rs6332), SNAP-25 (rs3746544) and (rs1051312)]. We included 228 parents of children diagnosed with ADHD and 109 healthy parents as the control group. The polymorphisms were genotyped using polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) assays and analyzed using the chi-square test and the multinomial logit model. SNAP-25 (rs3746544) polymorphism was associated with loading for ADHD, while 5-HT2A (rs6311) and NET1 (rs2242447) polymorphisms were associated with ADHD. On the other hand, there was no significant association between the SNAP-25 (rs1051312), NTF3 (rs6332), or COMT (rs4818) gene polymorphisms and ADHD. In addition, we found that even if variation in the SNAP-25 gene alone does not affect the phenotype, it may nevertheless lead to the emergence of a clinical ADHD picture in the presence of other genetic factors. Our findings suggest that a combination of NET1 (rs2242447) and SNAP-25 (rs3746544) is a risk factor for ADHD. Problems associated with the noradrenergic and serotonergic systems and SNAP-25 may play a role, both alone and in interaction with one another, in the pathophysiological mechanisms of ADHD.

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HEC Forum. 2013 Aug.

ADDERALL FOR ALL: A DEFENSE OF PEDIATRIC NEUROENHANCEMENT.

Flanigan J.

I argue that young patients should be able to access neuroenhancing drugs without a diagnosis of ADHD. The current framework of consent for pediatric patients can be adapted to accommodate neuroenhancement. After a brief overview of pediatric neuroenhancement, I develop three arguments in favor of greater acceptance of neuroenhancement for young patients. First, ADHD is not relevantly different from other disadvantages that could be treated with stimulant medication. Second, establishing a legitimate framework for pediatric neuroenhancement would mitigate the bad effects of diversion and improve research on neuroenhancement and ADHD. Third, some pediatric patients have rights to access neuroenhancements. I then consider several objections to pediatric neuroenhancement. I address concerns about addiction, advertising, authentic development, the parent-child relationship and equal

opportunity and conclude that these concerns may inform a framework for prescribing neuroenhancement but they do not justify limits on prescribing.

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Hum Brain Mapp. 2013.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITHOUT COMORBIDITY IS ASSOCIATED WITH DISTINCT ATYPICAL PATTERNS OF CEREBRAL MICROSTRUCTURAL DEVELOPMENT.

Adisetiyo V, Tabesh A, Di Martino A, et al.

Differential core symptoms and treatment responses are associated with the pure versus comorbid forms of attention-deficit/hyperactivity disorder (ADHD). However, comorbidity has largely been unaccounted for in neuroimaging studies of ADHD. We used diffusional kurtosis imaging to investigate gray matter (GM) and white matter (WM) microstructure of children and adolescents with ADHD (n=22) compared to typically developing controls (TDC, n=27) and examined whether differing developmental patterns are related to comorbidity. The ADHD group (ADHD-mixed) consisted of subgroups with and without comorbidity (ADHD-comorbid, n = 11; ADHD-pure, n=11, respectively). Age-related changes and group differences in cerebral microstructure of the ADHD-mixed group and each ADHD subgroup were compared to TDC. Whole-brain voxel-based analyses with mean kurtosis (MK) and mean diffusivity (MD) metrics were conducted to probe GM and WM. Tract-based spatial statistics analyses of WM were performed with MK, MD, fractional anisotropy, and directional (axial, radial) kurtosis and diffusivity metrics. ADHD-pure patients lacked significant age-related changes in GM and WM microstructure that were observed globally in TDC and had significantly greater WM microstructural complexity than TDC in bilateral frontal and parietal lobes, insula, corpus callosum, and right external and internal capsules. Including ADHD patients with diverse comorbidities in analyses masked these findings. A distinct atypical age-related trajectory and aberrant regional differences in brain microstructure were detected in ADHD without comorbidity. Our results suggest that different phenotypic manifestations of ADHD, defined by the presence or absence of comorbidity, differ in cerebral microstructural markers.

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Intern J Hypertens. 2013;2013.

AMBULATORY BLOOD PRESSURE MONITORING IN A COHORT OF CHILDREN REFERRED WITH SUSPECTED HYPERTENSION: CHARACTERISTICS OF CHILDREN WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Grisaru S, Yue MW, Mah JC, et al.

Childhood hypertension's increasing prevalence has generally been linked to the obesity epidemic. We observed that a significant proportion of children referred to our pediatric center with documented office hypertension are nonobese and have a history of attention deficit hyperactivity disorder (ADHD). To define the extent of this anecdotal observation, we performed a retrospective analysis of ambulatory blood pressure monitoring (ABPM) tests which in our center are routinely performed in newly referred children suspected of hypertension. Twenty-one percent (48 of 227 new referrals) had a history of ADHD, and 81% of them were treated with psychostimulant medications at the time of their ABPM test. Children in this group had a significantly lower average BMI z-score compared with the rest of the children (0.18 versus 0.75) and were significantly more likely to have abnormally elevated wake systolic loads on ABPM (38% versus 4%). The overall proportion of children with any abnormality on ABPM was comparable in both groups (46% versus 40%). Conclusion. A significant proportion of children suspected of hypertension have ADHD which may be related to higher wake systolic BP values. The prevalence of hypertension among children with ADHD will have to be determined in prospective studies.

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Int J Disabil Hum Dev. 2013;12:283-87.

SEVERITY OF SYMPTOMATOLOGY AND SUBTYPES IN ADHD CHILDREN WITH COMORBID OPPOSITIONAL DEFIANT AND CONDUCT DISORDERS.

Di Trani M, Di Roma F, Scatena MC, et al.

Background: The relationship between attention-deficit/ hyperactivity disorder (ADHD), oppositional defiant and conduct disorders (ODD/CD) requires further studies.
Methods: The aim was to examine the relationship among ADHD severity [assessed by ADHD Rating Scale-Parent Version (PV)], ADHD subtypes, and the comorbidity with ODD/CD in 217 Italian ADHD children.
Results: A total of 35.02 % of the participants displayed ADHD with ODD, 14.29 % ADHD with CD, and 50.69 % no ODD/CD comorbid diagnosis. The Hyperactivity Score of the ADHD Rating Scale-PV was a significant predictor of ODD; age and the Hyperactivity Score were significant predictors of CD. The combined subtype was significantly higher in CD children.
Conclusions: Data, which confirm the only recent article on the topic, help to clarify the relationship between ADHD and externalizing disorders.

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Int J Disabil Hum Dev. 2013;12:289-95.

COMPARISON BETWEEN NEUROLOGICAL EXAMINATION AND COMPUTERIZED TEST OF ATTENTION FOR SUSPECTED ADHD: IMPLICATIONS FOR ASSESSMENT OF A COMMON CHILDHOOD DISABILITY.

Diamond G, Badir M, Sevilla P, et al.

Aim: The aim of this study was to determine the role of the Test of Variables of Attention (TOVA), a computer-based continuous performance test (CPT), in assessing suspected attention-deficit/hyperactivity disorder (ADHD), a pervasive cause of disability in children and adolescents.
Methods: One hundred and fifty children and adolescents referred to a community-hospital-based neurology clinic for suspected ADHD underwent a comprehensive clinical evaluation by a pediatric neurologist in addition to the TOVA test. Retrospective chart data were analyzed separately for children aged 6 - 12 years (n = 101) and adolescents (13 - 18 years) (n = 49). Parents and teachers completed Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR, 2000) questionnaires for children 6 - 12 years old.
Results: The correlation between the neurologist ' s impression of the presence of attention deficit and the TOVA scores was good in the younger group (r = 0.28, p = 0.001) and weaker in the older group (r = 0.29, p = 0.05). On nonparametric analysis, the neurological evaluation did not distinguish between low and high TOVA scorers in the older group. The neurologist ' s impression correlated more closely with the DSM-IV parents ratings (r = 0.29, p = 0.01) than the teachers ' (r = 0.08, p = 0.05).
Conclusions: The TOVA correlated well with clinical assessment of ADHD and has added value in the evaluation of ADHD in adolescents, for whom standardized rating scales are lacking. In younger children, an experienced clinician can usually reach an accurate diagnosis based on accepted clinical criteria, including parent and teacher reports.

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J Abnorm Child Psychol. 2013 Aug.

THE EFFECTS OF INSTRUCTIONS ON MOTHERS' RATINGS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN REFERRED CHILDREN.

Johnston C, Weiss MD, Murray C, et al.

Tested whether instructions for how to rate child attention-deficit/hyperactivity disorder (ADHD) symptoms would improve the agreement between mothers' ratings of symptoms in their children and ratings provided by teachers and objective observers. Sixty-eight mothers of 5 to 12 year old children (53 boys and 15 girls) referred for ADHD assessment were randomly assigned to receive or not receive the instructions. Mothers and teachers rated the children on the SNAP-IV Rating Scale and objective observers rated the children's behavior during structured tasks. Relations between mother and teacher, and mother and observer ratings

were generally stronger for mothers in the Instruction group compared to mothers in the No Instruction group, in some cases significantly stronger. The instructional materials also improved mothers' knowledge of how to rate ADHD symptoms and reduced some associations between mothers' ratings and family socioeconomic status. These instructions have the potential to improve clinical assessments of child ADHD symptoms.

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J Abnorm Child Psychol. 2013 Aug.

PREDICTION OF PRESCHOOL AGGRESSION FROM DRD4 RISK, PARENTAL ADHD SYMPTOMS, AND HOME CHAOS.

Farbiash T, Berger A, Atzaba-Poria N, et al.

This study investigated the influence of a child's DRD4 risk, parental levels of ADHD symptoms, and the interactive influence of these factors on the development of preschool aggression. Additionally, the study investigated the role of home chaos as a mediator between parental ADHD symptoms and child aggression. The sample consisted of 84 4.5-year-old children and their parents. Children were genotyped for the DRD4 polymorphism. ADHD symptoms were self-reported by parents when the child was 2 to 6 months old. Parental reports of home chaos and the child's aggression were collected 4 years later. Child's DRD4 risk and parental ADHD symptoms significantly contributed to the prediction of preschool aggression. However, contrary to our hypotheses, no interactions were found between the child's DRD4 risk and the levels of parental ADHD symptoms. Home chaos played a mediating role in the relation between paternal ADHD symptoms and the child's aggression. The relation between maternal ADHD symptoms and the child's aggression was not significantly mediated through the level of home chaos. The current study emphasizes the importance of longitudinally investigating the contribution of parental ADHD symptoms to child aggression, while also exploring the differential contribution of maternal/paternal inattention and hyperactivity-impulsivity symptoms. Moreover, home chaos was found to be a significant environmental mechanism through which paternal ADHD symptoms affect children's aggression in the preschool years.

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J Am Acad Child Adolesc Psychiatry. 2013 Sep;52:900-10.

PROTECTION FROM GENETIC DIATHESIS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: POSSIBLE COMPLEMENTARY ROLES OF EXERCISE.

Rommel AS, Halperin JM, Mill J, et al.

OBJECTIVE: The degree of functional impairment and adverse developmental outcomes in individuals with attention-deficit/hyperactivity disorder (ADHD) likely reflect interplay between genes and environment. To establish whether physical exercise might reduce the level of ADHD symptoms or ADHD-related impairments, we conducted a comprehensive review of the effect of exercise in children with ADHD. Findings on the impact of exercise in animals and typically developing human beings, and an overview of putative mechanisms involved, are also presented to provide the context in which to understand this review.

METHOD: The electronic databases PubMed, OVID, and Web of Knowledge were searched for all studies investigating the effect of exercise in children and adolescents with ADHD, as well as animal models of ADHD behaviors (available in January 2013). Of 2,150 initially identified records, 16 were included.

RESULTS: Animal studies indicate that exercise, especially early in development, may be beneficial for ADHD symptom reduction. The limited research investigating the effect of exercise in children and adolescents with ADHD suggests that exercise may improve executive functioning and behavioral symptoms associated with ADHD. Although animal research suggests that brain-derived neurotrophic factor (BDNF) and catecholamines (CAs) play a role in mediating these effects, the association between BDNF and ADHD remains unclear in human beings.

CONCLUSIONS: The potential protective qualities of exercise with regard to reducing symptoms and impairments commonly associated with ADHD may hold promise for the future. Further research is needed

to firmly establish whether there are clinically significant effects of exercise on the severity of ADHD symptoms, impairments, and associated developmental outcomes.

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J Am Acad Child Adolesc Psychiatry. 2013 Sep;52:894-96.
GYM FOR THE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BRAIN? STILL A LONG RUN AHEAD...
Cortese S.

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J Am Acad Child Adolesc Psychiatry. 2013 Sep;52:921-30.
RANDOMIZED, DOUBLE-BLIND TRIAL OF GUANFACINE EXTENDED RELEASE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: MORNING OR EVENING ADMINISTRATION.
Newcorn JH, Stein MA, Childress AC, et al.
OBJECTIVE: To examine the efficacy and tolerability of guanfacine extended release (GXR) administered in the morning or evening in children with attention-deficit/hyperactivity disorder (ADHD).
METHOD: In this multicenter, double-blind, placebo-controlled, dose-optimization study, children 6 to 12 years of age with ADHD were randomized to receive GXR (1-4 mg/d) in the morning and placebo in the evening (GXR am), placebo in the morning and GXR in the evening (GXR pm), or twice-daily placebo. The primary efficacy measure was the ADHD Rating Scale-IV (ADHD-RS-IV).
RESULTS: A total of 333 child participants received study drug in the following cohorts: GXR am (n = 107), GXR pm (n = 114), or placebo (n = 112). Mean (standard deviation) changes from baseline to week 8 (visit 10 or last observation carried forward) in ADHD-RS-IV total scores were significant for both GXR treatment groups combined (GXR all-active: -20.0 [12.97]) and separately (GXR am: -19.8 [12.95]; GXR pm: -20.1 [13.04]) compared with placebo (-11.0 [12.93]; p < .001 for all). Most spontaneously-elicited treatment-emergent adverse events were mild or moderate in severity; the most common was somnolence (GXR all-active: 44.3%; GXR am: 46.7%; GXR pm: 42.1%; placebo: 12.5%).
CONCLUSIONS: GXR administered either in the morning or evening was associated with significant and clinically meaningful improvements in ADHD symptoms. The levels of response and tolerability observed with GXR were similar regardless of time of dosing (morning versus evening), indicating that once-daily GXR monotherapy is effective whether administered in the morning or evening.
Clinical trial registration information-Tolerability and Efficacy of AM and PM Once Daily Dosing With Extended-release Guanfacine Hydrochloride in Children 6-12 With Attention-Deficit/Hyperactivity Disorder (ADHD) (The ADHD Tempo Study); http://clinicaltrials.gov/; NCT00997984.

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J Atten Disord. 2013 Aug.
PREVALENCE AND SMOKING BEHAVIOR CHARACTERISTICS OF NONSELECTED SMOKERS WITH CHILDHOOD AND/OR ADULT SELF-REPORTED ADHD SYMPTOMS IN A SMOKING-CESSATION PROGRAM: A CROSS-SECTIONAL STUDY.
Fond G, Guillaume S, Jaussent I, et al.
Background: ADHD involves impairing core symptoms of inattention and hyperactivity/impulsivity in children (childhood ADHD = CH) that may persist in adulthood (adult ADHD = AD). Conflicting findings have been found regarding AD prevalences among adult smokers, and it is unclear whether AD is associated with a more severe smoking behavior in adulthood.
Objective: The aim of this article is (a) to determine CH and AD prevalences in a nonselected sample of adult smokers, (b) to describe the characteristics of smokers with ADHD symptoms versus those without, and (c) to determine whether CH and/or AD symptoms are risk factors for more severe smoking in adulthood.
Method: Three hundred and seventy-three participants aged 18 years and over were prospectively recruited in a smoking-cessation unit. Participants were classified as "no ADHD symptoms," "CH

symptoms," or "AD symptoms" according to their baseline score on the Wender Utah Rating Scale (WURS) alone (for CH symptoms) and WURS combined to the Adult Self Report Scale (ASRS) for AD symptoms. Other clinical variables were reported at first consultation.
Results: (a) CH symptoms were reported in 15.3% (57/373) of the total sample, 42.1% (24/57) of whom also had persistent ADHD symptoms in adulthood (prevalence of AD was 24/373 = 6.4%). (b) In comparison with participants without ADHD symptoms, smokers with ADHD symptoms consume significantly more tobacco, but ADHD symptoms were no longer significantly associated with the daily number of smoked cigarettes after adjustment for sociodemographic variables. No significant association was found between the two groups and age at the first cigarette, age at onset daily smoking, and nicotine dependence. (c) Participants were categorized into three groups: Group 1 without ADHD symptoms lifetime (NH; n = 316), Group 2 with childhood history of ADHD symptoms (CH; n = 33), and Group 3 with Adult ADHD symptoms (AD; n = 24). The association with tobacco consumption (>20 cigarettes/day) was significant for CH only (p = .02). After adjustment for gender, age, professional status, and educational level, this association was not longer significant.
Conclusion: Childhood and adult ADHD symptoms are both highly prevalent among nonselected smokers but our study failed to show more severe smoking characteristics among these participants after adjustment with sociodemographic variables.

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J Atten Disord. 2013 Aug.
DEVELOPMENT OF A VERY BRIEF MEASURE OF ADHD: THE CHAOS SCALE.
Levy JD, Kronenberger WG, Dunn DW.
Objective: We sought to develop a brief, easy to use behavior checklist to address common limitations in the use of ADHD rating scales in busy clinical settings.
Method: Items for the CHAOS (Conduct-Hyperactive-Attention Problem-Oppositional Symptom) scale were developed based on the ratings of Diagnostic and Statistical Manual of Mental Disorders (4th ed.; DSM-IV) criteria provided by experienced clinicians. The scale was administered to mothers of 205 clinically referred children for the purpose of subscale creation based on principal components analysis (PCA). Reliability and validity were analyzed using a separate sample of 139 children referred for psychological testing.
Results: PCA resulted in four subscales (Attention Problems, Hyperactivity-Impulsivity, Oppositional Behavior, and Conduct Problems), which demonstrated moderate to high test-retest and interrater reliability. Subscale scores correlated significantly with subscales from a DSM-referenced behavior checklist, along with tests of executive functioning.
Conclusion: These data suggest that the CHAOS scale is a brief, psychometrically sound tool for evaluation and monitoring of ADHD symptoms.

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J Atten Disord. 2013 Aug.
COMPARATIVE EFFECTS OF EMOTION MANAGEMENT TRAINING AND SOCIAL SKILLS TRAINING IN KOREAN CHILDREN WITH ADHD.
Choi ES, Lee WK.
Objective: ADHD is associated with social and emotional impairment that goes beyond the core symptoms of hyperactivity, impulsivity, and attention deficits. This study evaluates the comparative efficacy of emotional management training (EMT) with social skills training (SST) and no treatment in children with ADHD.
Method: A randomized, controlled treatment outcome study was conducted with 32 boys and 40 girls (aged 10-12 years). The Child Behavior Checklist, Emotion Expression Scale for Children, Child Depression Inventory, and State-Trait Anxiety Inventory for children were completed before and after the intervention.

Results: The EMT group exhibited a significant improvement in emotion recognition and expressive reluctance. Therefore, focusing on emotion identification and expression in social cognitive processes (i.e., EMT), instead of merely focusing on social skills (SST), enhances treatment efficacy.
Conclusion: These results support the hypothesis that focusing on the identification and expression of emotional information processes, instead of merely focusing on social skills (SST) enhances treatment efficacy.

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J Atten Disord. 2013 Aug.
PARENTS' PERSPECTIVES ABOUT FACTORS INFLUENCING ADHERENCE TO PHARMACOTHERAPY FOR ADHD.
Ahmed R, Borst J, Wei YC, et al.
Objective: The aim of the present study was to explore factors influencing parents' decisions to adhere and persist with ADHD pharmacotherapy in children.
Method: Focus groups (n = 3) were conducted with 16 parents recruited from metropolitan Sydney. Group discussions explored factors impacting on treatment initiation, continuation, and cessation. Focus groups were audio-recorded, transcribed verbatim, and thematically content analyzed.
Results: Parents commenced and continued pharmacotherapy due to its positive impact on their child's behavior. Improvements in the child's academic performance and social interactions encouraged persistence with therapy. Parents elected to cease therapy after their children experienced side effects including appetite suppression, weight loss, and sleep disturbances. Concerns about long-term effects of ADHD medication use including potential for addiction and growth stunting, in addition to the stigma surrounding ADHD also contributed to parents ceasing treatment.
Conclusion: The findings highlight a need for the provision of accurate information about ADHD and its treatments to parents to empower their treatment decisions and promote adherence.

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J Atten Disord. 2013 Jul.
MOVEMENT SCALING IN CHILDREN WITH ADHD-COMBINED TYPE.
Langmaid RA, Papadopoulous N, Johnson BP, et al.
Objective: The aim of the study was to investigate motor performance in children with ADHD using a size-scaling handwriting task.
Method: In all, 14 male children with ADHD and 14 typically developing (TD) children (age 7-15) wrote 10-mm and 40-mm cursive letter "l."
Results: Children with ADHD were unable to maintain their writing accurately at 40 mm, falling short by several millimeters; this was not evident in the TD children. Children with ADHD also had slightly faster and more fluent writing than TD children.
Conclusion: It was concluded that children with ADHD have difficulties scaling handwriting movement in the larger 40-mm condition that may reflect poor planning and modulation of movement, despite having faster and more fluent movements.

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J Atten Disord. 2013 Aug.
LANGUAGE DELAY IN 3-YEAR-OLD CHILDREN WITH ADHD SYMPTOMS.
Rohrer-Baumgartner N, Zeiner P, Eadie P, et al.
Objective: Little is known about cognition in preschoolers with ADHD and language delay (LD). The objective was to investigate cognitive functions in preschoolers with ADHD symptoms and LD compared with children with ADHD symptoms only and to estimate the frequency of children with ADHD symptoms, co-occurring language delay, and delays on cognitive measures.

Method: Participants were recruited from the Norwegian Mother and Child Cohort Study. The teacher report of expressive language and the cognitive tests from 119 3-year-old children with parent reported ADHD symptoms and LD were compared with those of 258 children with ADHD symptoms only.
Results: The ADHD + LD group performed significantly worse than the ADHD group on most language-related measures. There were no differences between the groups on most nonverbal measures. Single measures had a limited potential of differentiating between the groups.
Conclusion: ADHD symptoms and co-occurring LD in preschoolers were characterized by cognitive deficits associated with both disorders, not with global neurodevelopmental delay.

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J Child Adolesc Psychopharmacol. 2013 Aug;23:379-85.
CAREGIVERS' DISTRESS: YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND COMORBID DISORDERS ASSESSED VIA TELEMENTAL HEALTH.
Rockhill C, Violette H, Stoep AV, et al.
Abstract Objective: This article evaluates the additive effects of children's comorbid conditions with attention-deficit/hyperactivity disorder (ADHD) in relation to caregivers' distress, in a clinical trial conducted through telemental health (TMH).
Methods: The Children's ADHD Telemental Health Treatment Study (CATTS) is examining the effectiveness of treatment delivered via TMH for children with ADHD who are living in underserved communities. The CATTS trial recruited 223 children (mu=9.53+/-2.06 years) and their caregivers. Diagnoses of ADHD and comorbid oppositional defiant disorder (ODD) and anxiety disorders (ADs) were established with the Child Behavior Checklist and the Computerized Diagnostic Interview Schedule for Children. We took advantage of rich baseline data from the CATTS trial to investigate associations between caregivers' distress and children's comorbid mental health conditions. Caregivers' distress was assessed with the Patient Health Questionnaire-9, Parenting Stress Index, and Caregiver Strain Questionnaire. ANOVAs were used to compare children with ADHD alone with children having one comorbid condition (ODD or ADs) and children having two comorbid conditions (ODD and ADs).
Results: Three quarters (75.3%) of participants met criteria for ODD and/or AD comorbid with ADHD: 24.7% had neither comorbidity; 47.5% had ODD or AD; and 27.8% had both ODD and AD comorbidities. The parents of children with multiple comorbid conditions experienced the highest levels of depression, stress, and burden of care.
Conclusions: The CATTS sample that was recruited from underserved communities provided evidence of additive effects of child psychiatric comorbidities with caregivers' distress, echoing earlier findings from the Multi-modal Treatment of ADHD (MTA) study that was conducted with a metropolitan sample of youth. Results indicate that caregivers' distress should be addressed in developing treatment models for children with ADHD.
Clinical Trials Registry: http://clinicaltrials.gov/show/NCT00830700.

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J Child Adolesc Psychopharmacol. 2013 Aug;23:410-14.
Baseline severity of parent-perceived inattentiveness is predictive of the difference between subjective and objective methylphenidate responses in children with attention-deficit/hyperactivity disorder.
Park S, Kim BN, Cho SC, et al.
Abstract Objective: The purpose of this study was to find potential variables associated with the difference between subjective and object treatment responses in children with attention-deficit/hyperactivity disorder (ADHD) treated with OROS-methylphenidate (MPH).
Methods: We conducted a post-hoc analysis of data from a multicenter, open-label, 12 week trial of OROS-MPH in Korean children with ADHD. The subjective outcome measurement was the parent version of the ADHD Rating Scale-IV (ARS-P), and the objective outcome measurement was the Continuous Performance Test (CPT). We compared the children's demographic and disease-related variables among

four groups, classified according to whether they showed subjective or objective improvement after MPH treatment.
Results: Higher baseline inattentive scores on the ARS-P were associated with a significantly higher probability of subjective treatment response among objective nonresponders (p=0.033). Lower baseline inattentive scores on the ARS-P were associated with a significantly higher probability of subjective nonresponse among objective responders (p=0.045). Lower baseline omission errors (p=0.006) and response time variability scores (p=0.011) on the CPT were associated with a significantly higher probability of both objective and subjective responses, compared with both types of nonresponse to treatment.
Conclusions: The baseline severity of parent-perceived inattentive symptoms was predictive of differences in subjective and objective treatment responses, and the baseline severity of neuropsychological deficit (inattention and inconsistency of attention) was predictive of responses, using both subjective and objective measurements.

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J Child Adolesc Psychopharmacol. 2013 Aug;23:386-93.
TREATMENT OUTCOMES WITH LISDEXAMFETAMINE DIMESYLATE IN CHILDREN WHO HAVE ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH EMOTIONAL CONTROL IMPAIRMENTS.
Katic A, Dirks B, Babcock T, et al.
Abstract Objective: The purpose of this study was to assess lisdexamfetamine dimesylate (LDX) treatment effects based on baseline emotional control dysfunction in children with attention-deficit/hyperactivity disorder (ADHD) categorized with or without impairments of executive function (EF) emotional control.
Methods: Post-hoc analyses of a 7 week, open-label LDX study in children with ADHD (American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, 4th ed., Text Revision [DSM-IV-TR] defined) and impairments in EF control of emotional response. At baseline, participants were dichotomized by Behavior Rating Inventory of EF (BRIEF) emotional control domain T-scores of >/=65 (with impairment) or <65 (without impairment). ADHD Rating Scale-IV (ADHD-RS-IV), BRIEF Global Executive Composite and emotional control domain, Expression and Emotion Scale for Children (EESC) scores, Pearson correlations for BRIEF versus ADHD-RS-IV and EESC, and Clinical Global Impressions scores were assessed at baseline and end of study (week 7)/early termination (EOS/ET) by baseline category of BRIEF emotional control impairment. Safety assessments included treatment-emergent adverse events (TEAEs).
Results: At baseline and EOS/ET, respectively, 53.0% and 20.7% met criteria for emotional control impairment. Participants with and without emotional control impairments had similar ADHD-RS-IV change scores. Mean (SD) change from baseline for those with and without emotional control impairments were -20.8 (12.89) and -14.6 (11.25) for BRIEF global scores and -16.0 (13.19) and -5.0 (9.48) for BRIEF emotional control domain scores. Participants with emotional control impairments had greater mean EESC total score changes. BRIEF emotional control domain and all ADHD-RS-IV scores indicated moderate correlations between change scores (all p<0.0001). Overall, 84.9% of participants had TEAEs (mostly mild-to-moderate in severity); 3.8% discontinued because of TEAEs.
Conclusions: The proportion of children with behavioral impairments in EF control of emotional response decreased during LDX treatment. ADHD symptoms improved in both groups. The moderate correlations between EF behaviors and ADHD symptoms suggest there may be utility in evaluating behavioral domains beyond core ADHD symptoms.

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J Child Adolesc Psychopharmacol. 2013 Aug;23:401-09.

THE IMPACT OF LONG-ACTING MEDICATIONS ON ATTENTION-DEFICIT/HYPERACTIVITY DISORDER TREATMENT DISPARITIES.

Saloner B, Fullerton C, McGuire T.

Abstract Objective: Long-acting stimulants have increased medication adherence for many children diagnosed with attention deficit/hyperactivity disorder (ADHD), but it is unknown whether the increase has been similar across racial/ethnic groups. Our objective was to determine whether differences in medication utilization and adherence among white, black, and Hispanic ADHD-diagnosed children and adolescents narrowed following the introduction of long-acting stimulants in the 1990s.

Methods: We conducted a retrospective analysis of Florida Medicaid claims data from fiscal years 1996-2005. At each of three cross sections, we identified children and adolescents 3-17 years of age with at least two claims with an ADHD diagnosis. We used linear regression to model disparities over the study period in utilization of any ADHD medications (utilization of long-acting medication specifically) and medication adherence, and identified patient level, treatment setting, and geographic contributors to disparities.

Results: Although ADHD medication utilization was lower for ADHD-diagnosed minorities than whites in all years, minorities were as likely as whites to switch to long-acting medications. The increase in prescribed days following long-acting medication diffusion was comparable for white and black medication users (40 and 43 days, respectively), but lower for Hispanics (27 days). Geography and provider setting helped to explain disparities in medication utilization overall, but disparities in adherence were not explained by any of the covariates.

Conclusions: Despite equivalent switching to long-acting medications in the study period, minorities continued to utilize all ADHD medications less than did whites, and for shorter periods. Provider setting helps explain the ADHD medication utilization gap. High-volume, minority-serving providers are potential targets for future interventions related to improved communication about medication and follow-up after medication initiation.

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J Child Adolesc Psychopharmacol. 2013 Aug;23:423-25.

DOPAMINE RECEPTORS AND THE PHARMACOGENETICS OF SIDE-EFFECTS OF STIMULANT TREATMENT FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Levy F, Wimalaweera S, Moul C, et al.

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J Child Adolesc Psychopharmacol. 2013 Aug;23:419-22.

OBSESSIVE-COMPULSIVE DISORDER AND COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A COMPLEX DIAGNOSTIC DISENTANGLEMENT AND TREATMENT.

Pedraza PJ, Coffey DB.

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J Child Adolesc Psychopharmacol. 2013 Aug;23:415-18.

COMBINATION USE OF ATOMOXETINE HYDROCHLORIDE AND OLANZAPINE IN THE TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH COMORBID DISRUPTIVE BEHAVIOR DISORDER IN CHILDREN AND ADOLESCENTS 10-18 YEARS OF AGE.

Holzer B, Lopes V, Lehman R.

Abstract Objective: The aim of this study was to assess the use of atomoxetine and olanzapine in combination to treat attention-deficit/hyperactivity disorder (ADHD) and comorbid disruptive behaviors in children and adolescents 10-18 years of age.

Methods: Eleven subjects ages 10-18 received open-label atomoxetine and olanzapine for a 10 week treatment period. Patients were assessed at baseline, 2 weeks, 4 weeks, 6 weeks, and 10 weeks

(posttreatment). ADHD improvement was measured through the ADHD Rating Scale (ADHD-RS) (Investigator and Parent ratings). Aggression was measured through the Modified Overt Aggression Scale (MOAS).
Results: The combined use of atomoxetine and olanzapine resulted in statistically significant improvement in ADHD symptoms and overt aggression from baseline to posttreatment. As evidenced by a 33% reduction in symptoms on the ADHD-RS-I and the MOAS, 73% of patients were considered responders to ADHD treatment, whereas 55% responded to treatment for aggression. Both medications were generally well tolerated. Olanzapine treatment was associated with significant weight gain. Patients gained, on average, 3.9 kg. throughout the treatment period.
Conclusions: These data provide initial evidence that combination use of atomoxetine and olanzapine for the treatment of ADHD and comorbid disruptive behaviors was effective in reducing ADHD symptoms and aggressive behavior in a 10 week treatment period.

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J Child Adolesc Psychopharmacol. 2013 Aug;23:372-78.
FEASIBILITY OF CONDUCTING A RANDOMIZED CONTROLLED TRIAL OF TELEMENTAL HEALTH WITH CHILDREN DIAGNOSED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN UNDERSERVED COMMUNITIES.
Myers K, Stoep AV, Lobdell C.
Abstract Objective: Telemental health (TMH), the use of videoteleconferencing to provide care that is usually delivered in person, is increasingly used to rectify disparities in access to care. Few studies, however, have been conducted to demonstrate the effectiveness of TMH as a service delivery model. The Children's Attention-Deficit/Hyperactivity Disorder (ADHD) Telemental Health Treatment Study (CATTS) is a randomized clinical trial (RCT) of TMH conducted in multiple underserved communities. This article reports on the feasibility of conducting an effectiveness trial of TMH with children.
Methods: The CATTS trial used videoteleconferencing to provide guideline-based care and secure web sites to coordinate key aspects of trial implementation, such as participant recruitment and retention, intervention fidelity, and completion of assessments.
Results: The CATTS trial engaged seven communities and 150 primary care providers as partners in the study, and enrolled 223 children 5.5-12.9 years old. The intervention group completed an average of 5.3 of 6.0 planned sessions and 96% of controls completed a TMH consultation. Both groups completed an average of 4.8 of the 5.0 assessments. Clinicians demonstrated high fidelity to their treatment protocols. Minor technical difficulties did not interfere with providing care.
Conclusions: The CATTS trial demonstrated the feasibility of conducting an RCT of TMH with children living in multiple underserved communities. Telecommunications technologies can facilitate the coordination of research activities across sites and clinicians. Future trials should work closely with study partners to ensure referral of a representative study sample. Further trials are needed to help establish the effectiveness of TMH as a service delivery model.
Trial Registration: http://clinicaltrials.gov/show/NCT00830700.

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J Clin Child Adolesc Psychol. 2013 Aug.
NEGATIVE SOCIAL PREFERENCE IN RELATION TO INTERNALIZING SYMPTOMS AMONG CHILDREN WITH ADHD PREDOMINANTLY INATTENTIVE TYPE: GIRLS FARE WORSE THAN BOYS.
Becker SP, McBurnett K, Hinshaw SP, et al.
Despite distinct peer difficulties, less is known about the peer functioning of children with attention-deficit/hyperactivity disorder (ADHD) predominantly inattentive type (ADHD-I) in comparison to the peer functioning of children with ADHD combined type. Our purpose was to examine whether child sex moderated the relations between negative social preference and internalizing/externalizing problems in children with ADHD-I. Participants included 188 children diagnosed with ADHD-I (110 boys; ages 7-11; 54% Caucasian). Teacher ratings of the proportion of classmates who "like/accept" and "dislike/reject" the participating child were used to calculate negative social preference scores. Children, parents, and

teachers provided ratings of anxious and depressive symptoms, and parents and teachers provided ratings of externalizing problems. Boys and girls did not differ on teachers' negative social preference scores. As hypothesized, however, the relation between negative social preference and internalizing symptoms was moderated by sex such that negative social preference was consistently and more strongly associated with internalizing symptoms among girls than in boys. In terms of externalizing problems, negative social preference was associated with teacher (but not parent) ratings, yet no moderation by child sex was found. Negative social preference is associated with teacher-report of externalizing problems for both boys and girls with ADHD-I, whereas negative social preference is consistently associated with girls' internalizing symptoms across child, parent, and teacher ratings. Implications for future research and interventions are discussed.

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J Clin Psychopharmacol. 2013 Aug.

LONG-TERM QUALITY-OF-LIFE AND FUNCTIONING COMPARISON OF ATOMOXETINE VERSUS OTHER STANDARD TREATMENT IN PEDIATRIC ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Fuentes J, Danckaerts M, Cardo E, et al.

Psychopharmacological agents were shown to be important for improving the quality of life (QoL) of patients with attention-deficit/hyperactivity disorder (ADHD). A short-term, 10-week study found atomoxetine (ATX) to be effective in improving QoL of ADHD patients. We compared, for the first time, long-term treatment outcomes of ATX and other early standard therapy (OEST, any pharmacological ADHD treatment except ATX) in QoL and functional impairment in pharmacologically naive children/adolescents in a randomized, controlled, open-label study at 6 and 12 months. Patients received ATX (0.5-1.8 mg/kg per day) or OEST (mainly methylphenidate). Quality of life and functioning were assessed by the Child Health and Illness Profile-Child Edition, Parent Rating Form and the Weiss Functional Impairment Rating Scale-Parent Report. Three hundred ninety-eight patients (79.4% male; mean age, 9.3 years) received study treatment. The Child Health and Illness Profile-Child Edition, Parent Rating Form achievement domain t scores significantly improved from baseline to 6 months from means of 28.0 to 37.1 for ATX and from 28.3 to 40.7 for OEST. Mean t scores at 12 months were 40.0 for ATX and 41.0 for OEST. The Weiss Functional Impairment Rating Scale-Parent Report total score improved from baseline to 6 months in both groups (ATX: mean 1.02 to 0.63; OEST: 0.96 to 0.59). Both treatments were safe with no statistically significant difference in the overall rate of adverse events. Overall, the improvements in QoL and functional impairment observed over time for ATX and OEST were meaningful and stable over the study period of 12 months. Between-group differences were small but sometimes statistically significant, providing the first-time long-term comparative symptomatic and QoL analysis between ATX and OEST.

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J Med Econ. 2013 Aug.

COMPARISON OF THERAPY AUGMENTATION AND DEVIATION RATES FROM THE RECOMMENDED ONCE-DAILY DOSING REGIMEN BETWEEN LDX AND COMMONLY PRESCRIBED LONG-ACTING STIMULANTS FOR THE TREATMENT OF ADHD IN YOUTH AND ADULTS.

Setyawan J, Hodgkins P, Guerin A, et al.

Abstract Objective: To compare therapy augmentation and deviation rates from the recommended once-daily dosing regimen in Attention Deficit Hyperactivity Disorder (ADHD) patients initiated on lisdexamfetamine (LDX) vs other once-daily Food and Drug Administration (FDA) approved stimulants.

Methods: ADHD patients initiated on a long-acting ADHD stimulant medication (index medication) in/after 2007 were selected from a large US administrative claims database. Patients were required to be persistent for >/=90 days and continuously enrolled in their healthcare plan for >/=12 months following treatment initiation date. Based on age and previous treatment status, patients were classified into treatment-naive children and adolescents (6-17 years old), previously treated children and adolescents, treatment-naive adults (>/=18 years old), and previously treated adults. Furthermore, patients were classified into four mutually exclusive treatment groups, based on index medication: lisdexamfetamine

(LDX), osmotic release methylphenidate hydrochloride long-acting (OROS MPH), other methylphenidate/dexmethylphenidate long-acting (MPH LA), and amphetamine/dextroamphetamine long-acting (AMPH LA). The average daily consumption was measured as the quantity of index medication supplied in the 12-month study period divided by the total number of days of supply. Therapy augmentation was defined as the use of another ADHD medication concomitantly with the index medication for >/=28 consecutive days. Therapy augmentation and deviation rates from the recommended once-daily dosing regimen were compared between treatment groups using multivariate logistic regression models.
Results: Compared to the other treatment groups, LDX patients were less likely to augment with another ADHD medication (range odds ratios [OR]; 1.28-3.30) and to deviate from the recommended once-daily dosing regimen (range OR; 1.73-4.55), except for previously treated adult patients, where therapy augmentation differences were not statistically significant when compared to OROS MPH and MPH LA patients.
Limitation: This study did not control for ADHD severity.
Conclusion: Overall, compared to LDX-treated patients, patients initiated on other ADHD medications were equally or more likely to have a therapy augmentation and more likely to deviate from the recommended once-daily dosing regimen.

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J Neurosurg Pediatr. 2013 Aug;12:97-102.

THE IMPACT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER ON RECOVERY FROM MILD TRAUMATIC BRAIN INJURY.

Bonfield CM, Lam S, Lin Y, et al.

Object Attention deficit hyperactivity disorder (ADHD) and traumatic brain injury (TBI) are significant independent public health concerns in the pediatric population. This study explores the impact of a premorbid diagnosis of ADHD on outcome following mild TBI.
Methods The charts of all patients with a diagnosis of mild closed head injury (CHI) and ADHD who were admitted to Children's Hospital of Pittsburgh between January 2003 and December 2010 were retrospectively reviewed after institutional review board approval was granted. Patient demographics, initial Glasgow Coma Scale (GCS) score, hospital course, and King's Outcome Scale for Childhood Head Injury (KOSCHI) score were recorded. The results were compared with a sample of age-matched controls admitted with a diagnosis of CHI without ADHD.
Results Forty-eight patients with mild CHI and ADHD, and 45 patients with mild CHI without ADHD were included in the statistical analysis. Mild TBI due to CHI was defined as an initial GCS score of 13-15. The ADHD group had a mean age of 12.2 years (range 6-17 years), and the control group had a mean age of 11.14 years (range 5-16 years). For patients with mild TBI who had ADHD, 25% were moderately disabled (KOSCHI Score 4b), and 56% had completely recovered (KOSCHI Score 5b) at follow-up. For patients with mild TBI without ADHD, 2% were moderately disabled and 84% had completely recovered at follow-up ($p < 0.01$). Patients with ADHD were statistically significantly more disabled after mild TBI than were control patients without ADHD, even when controlling for age, sex, initial GCS score, hospital length of stay, length of follow-up, mechanism of injury, and presence of other (extracranial) injury.
Conclusions Patients who sustain mild TBIs in the setting of a premorbid diagnosis of ADHD are more likely to be moderately disabled by the injury than are patients without ADHD.

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J Pers Assess. 2013 Aug.

DETECTING FEIGNED ADHD IN LATER ADOLESCENCE: AN EXAMINATION OF THREE PAI-A NEGATIVE DISTORTION INDICATORS.

Rios J, Morey LC.

The validity of various indicators of response distortion on the Personality Assessment Inventory-Adolescent (PAI-A; Morey, 2007a) and its potential usefulness to detect malingering were evaluated by having 17- and 18-year-old students complete the PAI-A attempting to simulate Attention-

Deficit/Hyperactivity Disorder (ADHD) under coached or noncoached conditions. Scores for these respondents on the Negative Impression and Positive Impression scales, the Malingering Index, and the Rogers Discriminant Function (RDF) were compared to those of 17- and 18-year-old patients receiving clinical diagnoses of ADHD. Simulating respondents also completed the Conners Adult ADHD Rating Scale (CAARS) to determine if they could successfully simulate self-reported symptoms of ADHD. A total of 45% of simulating participants obtained CAARS scores reflecting clinically significant symptoms of ADHD. All indicators demonstrated the ability to distinguish between actual patients and feigned responses of successful simulators, with the RDF demonstrating the greatest accuracy in distinguishing these groups.

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JAMA Pediatr. 2013 Aug.

IMPACT OF DISTRACTION ON THE DRIVING PERFORMANCE OF ADOLESCENTS WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Narad M, Garner AA, Brassell AA, et al.

IMPORTANCE This study extends the literature regarding attention-deficit/hyperactivity disorder (ADHD)-related driving impairments to a newly licensed, adolescent population.

OBJECTIVE To investigate the combined risks of adolescence, ADHD, and distracted driving (cell phone conversation and text messaging) on driving performance.

DESIGN, SETTING, AND PARTICIPANTS Adolescents aged 16 to 17 years with (n = 28) and without (n = 33) ADHD engaged in a simulated drive under 3 conditions (no distraction, cell phone conversation, and texting). During each condition, one unexpected event (eg, another car suddenly merging into driver's lane) was introduced.

INTERVENTIONS Cell phone conversation, texting, and no distraction while driving.

MAIN OUTCOMES AND MEASURES Self-report of driving history, average speed, standard deviation of speed, standard deviation of lateral position, and braking reaction time during driving simulation.

RESULTS Adolescents with ADHD reported fewer months of driving experience and a higher proportion of driving violations than control subjects. After controlling for months of driving history, adolescents with ADHD demonstrated more variability in speed and lane position than control subjects. There were no group differences for braking reaction time. Furthermore, texting negatively impacted the driving performance of all participants as evidenced by increased variability in speed and lane position.

CONCLUSIONS To our knowledge, this study is one of the first to investigate distracted driving in adolescents with ADHD and adds to a growing body of literature documenting that individuals with ADHD are at increased risk for negative driving outcomes. Furthermore, texting significantly impairs the driving performance of all adolescents and increases existing driving-related impairment in adolescents with ADHD, highlighting the need for education and enforcement of regulations against texting for this age group.

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J Abnorm Child Psychol. 2013 Aug;41:901-17.

WHAT PART OF WORKING MEMORY IS NOT WORKING IN ADHD? SHORT-TERM MEMORY, THE CENTRAL EXECUTIVE AND EFFECTS OF REINFORCEMENT.

Dovis S, van der Oord S, Wiers RW, et al.

Deficits in Working Memory (WM) are related to symptoms of Attention-Deficit/Hyperactivity Disorder (ADHD). In children with ADHD visuospatial WM is most impaired. WM is composed of Short-Term Memory (STM) and a Central Executive (CE). Therefore, deficits in either or both STM and the CE may account for WM impairments in children with ADHD. WM-component studies investigating this find deficits in both STM and the CE. However, recent studies show that not only cognitive deficits, but also motivational deficits give rise to the aberrant WM performance of children with ADHD. To date, the influence of these motivational deficits on the components of WM has not been investigated. This study examined the effects of a standard (feedback-only) and a high level of reinforcement (feedback + 10 euros) on the visuospatial WM-, visuospatial STM-, and the CE performance of 86 children with ADHD and 62

typically-developing controls. With standard reinforcement the STM, CE, and WM performance of children with ADHD was worse than that of controls. High reinforcement improved STM and WM performance more in children with ADHD than in controls, but was unable to normalize their performance. High reinforcement did not appear to improve the CE-related performance of children with ADHD and controls. Motivational deficits have a detrimental effect on both the visuospatial WM performance and the STM performance of children with ADHD. Aside from motivational deficits, both the visuospatial STM and the CE of children with ADHD are impaired, and give rise to their deficits in visuospatial WM.

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J Abnorm Child Psychol. 2013 Aug;41:891-900.

EXAMINATION OF SPATIAL WORKING MEMORY PERFORMANCE IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER, COMBINED TYPE (ADHD-CT) AND ANXIETY.

Vance A, Ferrin M, Winther J, et al.

Spatial working memory (SWM) is known to be impaired in children with ADHD-CT, whether anxiety is present or not. Yet, it remains unclear whether anxiety disorders add to the SWM impairments evident in ADHD-CT and whether these findings extend into adolescents with ADHD-CT and anxiety. Further, it is not yet known whether children and adolescents with carefully defined anxiety disorders alone, demonstrate SWM deficits. This study explored the association of SWM and its strategy and spatial span components in carefully defined children and adolescents (age 6–16 years) with ADHD-CT alone (N = 163; 14 % female), ADHD-CT and anxiety (N = 243; 23% female), anxiety disorders alone (N = 69; 25 % female) compared to age- and gender-matched healthy control participants (N = 116; 19 % female). The relationship between SWM and its strategy and span components and core ADHD-CT symptoms and anxiety symptoms were also examined. There was no evidence of an additive effect of ADHD and anxiety on SWM, strategy and spatial span deficits. But, anxiety disorders alone were associated with impaired SWM and span performance compared to healthy control participants. In contrast, strategy did not differ between children and adolescents with anxiety disorders alone and healthy control participants, suggesting that with anxiety span is the most affected component. Further, these findings were age-independent. This study concurs with and extends current influential models about the cognitive effects of anxiety on performance in the setting of ADHD-CT. Clinical implications and future research directions are discussed.

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J Abnorm Child Psychol. 2013 Aug;41:919-27.

STRESS-INDUCED DRINKING IN PARENTS OF BOYS WITH ATTENTION-DEFICIT-HYPERACTIVITY DISORDER: HETEROGENEOUS GROUPS IN AN EXPERIMENTAL STUDY OF ADULT-CHILD INTERACTIONS.

Kashdan TB, Adams LM, Kleiman EM, et al.

Research on whether parents of children with externalizing disorders are at elevated risk for alcohol problems is equivocal. To reduce this ambiguity, we examined how individual differences in stress reactivity might moderate the drinking behavior of such parents. Parents (119 mothers, 44 fathers) of ADHD sons interacted with different child confederates during each of two counter-balanced sessions. In one, the confederate portrayed a friendly, cooperative, “normal” boy; in the other, the confederate portrayed a “deviant” boy who exhibited behavior characteristic of externalizing disorders. Following each interaction, parents were given an opportunity for ad lib consumption of alcohol while anticipating a second interaction. Latent class analysis identified three subgroups of parents using distress scores and alcohol consumption: minimal stress reactivity; reacts to child deviance with increased distress, but not increased drinking; marked stress-induced drinking. Decisions about the nature and proper treatment of parents raising children with ADHD may be compromised by failure to attend to individual differences in stress reactivity and inclinations to use drinking to cope.

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J Clin Neurophysiol. 2013;30:357-61.

ELECTROENCEPHALOGRAM IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: SPIKE AND WAVE PAROXYSMS, FOCI, AND SEIZURES.

Altunel A, Altunel EO, Sever A.

Summary: Attention deficit hyperactivity disorder is a syndrome of unknown etiology that affects 3% to 7% of the population. Although no objective test exists to support the diagnosis, EEG discharges related to the neuropsychiatric abnormalities have a high incidence in attention deficit hyperactivity disorder. The aim of this study was to elucidate the quantitative and qualitative characteristics of EEG abnormality in attention deficit hyperactivity disorder. Nonrapid eye movement sleep EEGs were evaluated in 134 patients with attention deficit hyperactivity disorder in terms of age, EEG timing, spike and wave index, foci, and seizures. All patients had spike and wave paroxysms that changed with age at and time to first EEG. Only half of the patients had seizures and 46 patients had neither seizures nor foci. Thirty-eight patients had the EEG findings of benign focal epilepsy of childhood. Our data support the view that spike and wave activity evolves in time and that EEG discharges are related to neuropsychiatric symptoms even when a diagnosable seizure disorder is absent.

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J Clin Psychiatry. 2013 Jun;74:628-29.

BIPOLAR DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER COMORBIDITY IN CHILDREN AND ADOLESCENTS: EVIDENCE-BASED APPROACH TO DIAGNOSIS AND TREATMENT.

Miller S, Chang KD, Ketter TA.

This article provides an overview of evidence based approach to diagnosis and treatment of Bipolar disorder and attention deficit hyperactivity disorder (ADHD) comorbidity in children and adolescents. The relationship between bipolar disorder and ADHD has received considerable attention in psychiatric research. Elevated rates of bipolar disorder-ADHD comorbidity among youth and coaggregation within families raise questions as to whether co-occurring bipolar disorder and ADHD represent a more severe subtype of bipolar disorder, related disorders with a shared genetic predisposition, or separate though frequently comorbid disorders. In contrast to the typical demographic and clinical profile of bipolar disorder, ADHD has onset during childhood, is more prevalent in males and is characterized by prominent difficulties with sustaining attention and organizing and completing tasks, possibly in combination with hyperactive and impulsive behavior. Beyond the inherent diagnostic challenges of co-occurring ADHD and bipolar disorder, pharmacologic management of youth with both disorders can prove complicated given that stimulants, which are first-line treatments for ADHD, have been associated with earlier age at bipolar disorder onset and stimulant-induced mania and psychosis.

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J Contemp Psychother. 2013;1-10.

SHOOTING THE MESSENGER: THE CASE OF ADHD.

Watson GL, Arcona AP, Antonuccio DO, et al.

Medicating ADHD is a controversial subject that was acutely inflamed in 1995 when high rates of ADHD diagnosis and treatment were documented in southeastern Virginia. Psychologists in southeastern Virginia formed a regional school health coalition to implement and evaluate interventions to address the problem. Other professionals with strong ties to the pharmaceutical industry launched ad hominem attacks on the coalition's research and work. These attacks contributed to the work being terminated in 2005. In the ensuing years, ADHD drug treatment continued to escalate. Today, the national rate of ADHD diagnosis exceeds all reasonable estimates of the disorder's true prevalence, with 14 % of American children being diagnosed before reaching young adulthood. Notable key opinion leaders continue to claim that there is no cause for concern, but with a message shift from "the prevalence is not too high" to "high prevalence is not too concerning." This paper provides an object lesson about how innovative research can be derailed to the detriment of sound medical and mental health care of children when industry interests are threatened. Tenure may be the only option for protecting innovative research from specious attacks. The authors offer

a summary of the data on ADHD drug treatments, suggest judicious use of such treatments, and add their voices to others who are once again sounding a cautionary alarm.

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J Exp Clin Med. 2013;30:189-91.

SECONDARY ATTENTION DEFICIT/HYPERACTIVITY DISORDER DUE TO RIGHT BASAL GANGLIA INJURY: A CASE REPORT.

Ceylan MF, Akca OF.

Attention deficit/hyperactivity disorder (ADHD) is a frequent and commonly studied neuropsychiatric disorder in children and adolescents. The symptoms of ADHD include inattention and/or hyperactivity and impulsivity. Diagnosis of ADHD requires a persistent pattern of symptoms beginning before the age of 7 except for secondary ADHD. Secondary ADHD may occur as a consequence of childhood traumatic brain injury. A patient with secondary ADHD as a result of right basal ganglia injury is presented in this case report.

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J Forensic Psychiatry Psychol. 2013.

ADHD SYMPTOM FREQUENCY AND ADHD SYMPTOM COUNT CLUSTERING IN AFRICAN-AMERICAN ADOLESCENTS WITH JUVENILE COURT CONTACT.

Andretta JR, Woodland MH, Ramirez AM, et al.

The 1432 participants were mainly male (74.8%), aged 10-18 (M = 15.82, SD = 1.59) African-American juveniles arrested in a moderately sized Mid-Atlantic city in the USA. Using Conners Comprehensive Behavior Rating Scales-Self Report scores, two parallel cluster analyses were developed, one based on Attention Deficit/Hyperactivity Disorder (ADHD) symptom frequency and another based on ADHD symptom count. ADHD profiles were good predictors of functioning in both cluster solutions, as evidenced by differences in other indices of mental health (e.g. symptoms of depression) and academic problems across and between clusters. Further inquiry showed that ADHD symptom frequency clustering had a larger effect on functioning than symptom count clustering. Results also corroborated with the hypothesis that ADHD is best conceptualized as a single disorder that differs in symptom elevation. Higher rates of severe ADHD symptoms were identified in females than males, but no differences were found across age or socioeconomic groups.

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J Intellect Disabil Res. 2013.

THE PSYCHOPHYSIOLOGICAL AND HEALTH COROLLARIES OF CHILD PROBLEM BEHAVIOURS IN CAREGIVERS OF CHILDREN WITH AUTISM AND ADHD.

Lovell B, Moss M, Wetherell MA.

Background: The positive relationship between problem behaviours of children with additional complex needs and psychological distress in their caregivers has been widely evidenced. Fewer studies, however, have assessed the relationship between care recipients' problem behaviours and key physiological processes, relevant for the physical health status of their care providers. This study examined the psychological, endocrine and health corollaries of child problem behaviours in caregivers of children with autism and attention deficit hyperactivity disorder.

Methods: Caregivers (n=18) completed self-report measures of psychological distress, child problem behaviours and incidences of commonly occurring ailments. To capture important parameters of the basal diurnal cortisol pattern, caregivers collected saliva samples at waking, 30min post waking, 1200h and 2200h on two consecutive weekdays.

Results: Data revealed a positive relationship between caregivers' perceived levels of stress and problems with child conduct behaviours. In addition, caregivers who reported more problems with child emotional and hyperactivity behaviours displayed atypical cortisol patterns characterised by flatter diurnal cortisol slopes

and reduced cortisol awakening response magnitude. Subjective reports of commonly occurring ailments were also greater in caregivers experiencing more problems with child emotional behaviours.
Conclusions: These findings have implications for interventions that aim to improve the psychophysiological well-being of the caregiver by targeting problem behaviours of the care recipient.

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J Neursurg Pediatr. 2013;12:103-09.

BASELINE NEUROCOGNITIVE SCORES IN ATHLETES WITH ATTENTION DEFICIT-SPECTRUM DISORDERS AND/OR LEARNING DISABILITY: CLINICAL ARTICLE.

Zuckerman SL, Lee YM, Odom MJ, et al.

Object. Up to 16% of children in the US between the ages of 3 and 17 years have either attention deficit-spectrum disorder or a learning disability (LD). Sports-related concussions among youth athletes represent a significant public health concern, and neurocognitive testing is a method to evaluate the severity of cognitive impairment and recovery after a sports-related concussion. The goal of this study was to assess baseline neurocognitive differences between athletes with attention deficit hyperactivity disorder (ADHD) and/or LD versus those with neither disorder and to establish normative data for these special populations.
Methods. Between August 2007 and March 2012, 6636 young athletes underwent baseline neurocognitive testing performed using the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT) battery. Of these participants, 90 had self-reported LD only, 262 had self-reported ADHD only, and 55 reported both. Those with ADHD and/or LD were matched with 407 participants with no history of ADHD or LD by age, sex, and number of prior concussions. The mean scores and SDs were calculated for each group to obtain normative values. A pairwise comparison between each diagnostic group was done to assess whether LD and/or ADHD diagnostic status predicted participants' baseline neurocognitive scores.
Results. Participants with ADHD had significantly lower verbal memory, visual memory, and visual motor processing speed scores, along with significantly higher reaction time, impulse control, and symptom scores compared with those without LD or ADHD. Participants with LD had similar results, with significantly lower verbal memory, visual memory, and visual motor processing speed scores, higher reaction time and symptom score, but did not differ in their impulse control score compared with those without LD or ADHD. Participants with both LD and ADHD had a significantly lower visual motor speed score and a significantly higher reaction time and symptom score than those without LD or ADHD, but did not differ with regard to the other composite scores.
Conclusions. Athletes with ADHD and/or LD have lower baseline ImPACT neurocognitive scores compared with athletes without ADHD and LD. Preliminary normative neurocognitive data for these special populations are provided.

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J Pediatr Biochem. 2013;3:61-67.

ATTENTION DEFICIT HYPERACTIVITY DISORDER AND SLEEP DISORDERED BREATHING IN CHILDREN .

Sedky K, Nazir R, Carvalho KS, et al.

Children and adolescents suffering from attention deficit hyperactivity disorder (ADHD) and/or sleep disordered breathing (SDB) may present with similar symptoms, including inattention, irritability, and hyperactivity. SDB is under-diagnosed in young people and is not often recognized in patients with ADHD; we hypothesize that treating sleep disordered breathing in ADHD patients may diminish symptoms and reduce ADHD-focused pharmacotherapy. A Medline search was performed using the criteria for ADHD and SDB. English language publications through January, 2012 were surveyed. Correlation between these two disorders is confounded due to methodological errors in research. The investigations lack consistency due to studies with small sample size, a dearth of diagnostic polysomnography (PSG) to detect SDB, varying definitions for the apnea/hypopnea index, and lack of uniform evaluations to diagnose ADHD. Despite methodological inconsistencies, the data suggests that treating SDB may have a productive impact on treatment outcomes in children with mild ADHD. Patients with ADHD symptomatology should receive SDB screening. In those with comorbid SDB and ADHD, an adenotonsillectomy (AT) may improve the

prognosis. Treatment of SDB coexisting with ADHD aims to decrease clinical symptoms, reduce pharmacotherapy, and promote better health.

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J Psychopathol Behav Assess. 2013;35:283-92.

A MEASUREMENT FRAMEWORK TO DETERMINE THE CONSTRUCT VALIDITY OF ADHD/ODD RATING SCALES: ADDITIONAL EVALUATIONS OF THE CHILD AND ADOLESCENT DISRUPTIVE BEHAVIOR INVENTORY.

Khadka G, Burns GL.

A multiple group confirmatory factor analysis was used to test the invariance of an attention-deficit/hyperactivity disorder-inattention, attention-deficit/hyperactivity disorder-hyperactivity/impulsivity, oppositional defiant disorder toward adults, academic and social competence five-factor model across of independent groups of Thai adolescents with the Child and Adolescent Disruptive Behavior Inventory (CADBI). Mothers and fathers' ratings on 872 adolescents were compared to mothers and fathers' ratings on a different group of 983 adolescents. The design allowed four invariance analyses (i.e., mothers' ratings of the first group compared to mothers' ratings of the second group; fathers' ratings of first group compared to fathers' ratings of the second group; mothers' ratings of first group compared to fathers' ratings of the second group; and fathers' ratings of first group compared to mothers' ratings of second group). Support was found for the invariance of like-symptom loadings and symptom intercepts as well as like-factor variances, covariances, and factor means across the four invariance analyses. The findings further expand the construct validity of the CADBI. The paper also introduces a multiple indicators by multiple traits by multiple methods by multiple sources by multiple occasions by multiple groups' measurement matrix to guide the evaluation of the construct validity of ADHD/ODD rating scales.

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Journal of the American Academy of Child & Adolescent Psychiatry. 2013 Aug;52:784-96.

ASSESSMENT AND MANAGEMENT OF SLEEP PROBLEMS IN YOUTHS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Cortese S, Brown TE, Corkum P, et al.

Objective: To provide evidence- or consensus-based recommendations concerning the assessment and management of sleep problems in youths with attention-deficit/hyperactivity disorder (ADHD).

Method: PubMed, Ovid, EMBASE, and Web of Knowledge were searched through October 31, 2012. When no evidence was available, consensus of the authors was achieved. The evidence-level of the recommendations on the management of sleep disturbances was based on the Scottish Intercollegiate Guidelines Network (SIGN) system.

Results: A total of 139 original articles on sleep and childhood ADHD were retrieved, including 22 on treatment of sleep disturbances. This review focuses on behaviorally based insomnia, circadian rhythm disorder, sleep-disordered breathing, restless legs syndrome/periodic limb movement disorder, and sleep disturbances due to comorbid psychiatric disorders or ADHD medications. Healthy sleep practices are recommended as the foundation of management strategies. Behavioral interventions should be considered as first-line treatment of insomnia, although further evidence from randomized controlled trials (RCTs) is needed to prove their efficacy in ADHD. Among pharmacological treatments, RCTs support the use of melatonin to reduce sleep-onset delay, whereas there is more limited evidence for other medications.

Conclusion: Growing empirical evidence is informing assessment/management strategies of sleep problems in youths with ADHD. However, further RCTs are warranted to support current recommendations.

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J Formos Med Assoc. 2013;112:396-405.

ADHD-RELATED SYMPTOMS, EMOTIONAL/BEHAVIORAL PROBLEMS, AND PHYSICAL CONDITIONS IN TAIWANESE CHILDREN WITH EPILEPSY.

Tsai FJ, Liu ST, Lee CM, et al.

Background/Purpose: Little is known about whether Asian children with epilepsy have more attention-deficit hyperactivity disorder (ADHD)-related symptoms, emotional/behavioral problems, and physical conditions compared with those described in Western studies. The authors investigated the rates of ADHD-related symptoms, emotional/behavioral problems, and physical conditions among pediatric patients with epilepsy.

Methods: We recruited 61 patients with epilepsy, aged 6-16 years, and 122 age-, sex-, and parental education-matched school controls. Data on demographics, parental reports on the Child Behavior Checklist (CBCL) and Swanson, Nolan, and Pelham, version IV scale (SNAP-IV), and medical records were collected.

Results: The average full-scale intelligence quotient of the case group was 95.8. There were 11 (18.0%), 7 (11.5%), 26 (42.6%), and 26 (42.6%) of children with epilepsy ever clinically diagnosed with developmental delay, overt ADHD symptoms, allergies reported by physicians, and behavior problems measured by the CBCL, respectively. Those children with epilepsy had more severe ADHD-related symptoms and a wider range of emotional/behavioral problems than controls (Cohen's d 0.36-0.80). The rate of potential cases of ADHD among children with epilepsy was 24.6%. A history of developmental delay predicted ADHD- related symptoms and internalizing and externalizing problems. Among children with epilepsy, a longer duration of treatment with antiepileptic drugs predicted externalizing problems, and an earlier onset of epilepsy predicted inattention and hyperactivity/impulsivity.

Conclusion: Our findings imply that clinicians should assess physical and emotional/behavioral problems among children with epilepsy in order to provide interventions to offset possible adverse psychiatric outcomes.

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Nat Med J China. 2013;93:1881-85.

ALTERED PATTERNS OF FUNCTIONAL CONNECTIVITY OF POSTERIOR CINGULATE CORTEX ON RESTING-STATE MAGNETIC RESONANCE IMAGING IN CHILDREN WITH ATTENTION-DEFICIT OR HYPERACTIVITY DISORDER.

Yang S, Dong X, Wang SH, et al.

Objective: To explore the pathophysiological changes in the functional connectivity of posterior cingulate cortex (PCC) with other brain regions in children with attention-deficit or hyperactivity disorder (ADHD) on resting-state functional magnetic resonance imaging (fMRI) and explore the neural mechanisms of ADHD at the point of relationships between brain regions.

Methods: Thirty children with ADHD from the Third Affiliated Hospital of Soochow University from June 2008 to April 2010 and another 30 age-and-gender-matched controls from a normal primary school over the same period underwent resting-state fMRI scans. And blood oxygenation level dependent (BOLD) signal was acquired to calculate the functional connectivity of PCC with other brain regions controls. Singnificant differences of connectivity between groups were analyzed with REST software.

Results: The pattern of functional connectivity of PCC for the ADHD group was similar to that of the control group. Significant positive functional connectivity with PCC was observed in the default mode of network (DMN) while negative functional connectivity was present in dorlateral prefrontal cortex, anterior cingulate, parietal cotex and basal ganglia (all $P < 0.05$, corrected). Compared to the controls, the ADHD group exhibited decreased positive connectivity with PCC in bilateral medial prefrontal cortex (0.07(plus or minus)0.20 vs 0.33(plus or minus)0.23, t=-5.47), right posterior cingulate gyrus (0.25(plus or minus)0.28 vs 0.48(plus or minus)0.30, t=-3.44), right inferior temporal gyrus (-0.05(plus or minus)0.19 vs 0.22(plus or minus)0.22, t=-4.61) and cerebellar posterior lobe (-0.04(plus or minus)0.21 vs 0.17(plus or minus)0.16, t=-3.99), while decreased negative functional connectivity with PCC was observed in left insula (-0.10(plus or minus)0.26 vs -0.30(plus or minus)0.19, t=3.71), right inferior parietal lobule (0.02(plus or minus)0.18 vs -0.23(plus or minus)0.17, t=5.20), left postcentral gyrus (0.08(plus or minus)0.26 vs -0.17(plus or minus)0.25, t=4.06), left superior temporal gyrus (-0.04(plus or minus)0.25 vs -0.27(plus or minus)0.17,

t=4.27), right superior temporal gyrus (-0.08(plus or minus)0.25 vs -0.31(plus or minus)0.21, t=3.80) and left fusiform gyrus (-0.01(plus or minus)0.25 vs -0.18(plus or minus)0.17, t=3.57) (all P < 0.05, corrected).
Conclusions: The connectivity of DMN between brain regions is abnormal in ADHD group. And the strengthen of negative relationship between DMN and task activated network becomes reduced. It is surmised that the decreased internal synchronization of default network and disrupted balance between DMN and prefrontal-parietal attentional networks may be important neural mechanisms of ADHD.

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Neurology. 2013;80.
MOTOR CORTEX PHYSIOLOGY AND STOP SIGNAL REACTION TIMES AS PREDICTORS AND CORRELATES OF ATOMOXETINE RESPONSES IN CHILDREN WITH ADHD.
Chen T, Wu S, Dixon S, et al.
OBJECTIVE: To identify quantitative neurobehavioral and neurophysiological measures which predict responses to atomoxetine, a selective norepinephrine reuptake inhibitor, in children with Attention Deficit Hyperactivity Disorder (ADHD).
BACKGROUND: ADHD symptoms of inattention and/or hyperactivity/impulsivity likely involve inefficient neurophysiological function in frontal cortex. Mechanisms of clinical improvement on atomoxetine are unclear.
DESIGN/METHODS: Assessments of motor cortex physiology using Transcranial Magnetic Stimulation (TMS) and Response Inhibition using the Stop Signal Reaction Time (SSRT) task were performed pre- and post- treatment, blinded to symptom ratings and clinical responses. Treatment combined a single-dose, double-blind, placebo-controlled design, with pre- and post-dose physiology, and a 4-week open-label design, with baseline versus one month measures. In this interim analysis, we report data on 83 children. Clinical responses (yes, partial, no) were categorized based on pre-specified criteria. Group univariate comparisons were performed using one-way ANOVA using SAS v9.3 (Cary, NC) with p < .05 considered significant.
RESULTS: 74 children (51 males; 47 Caucasian, 18 African American, 5 Asian, 4 Mixed; Mean Age 9.2 years) completed both visits, of whom 40 were responders (69% mean improvement in ADHD rating scale scores), 22 non-responders (15% improvement), and 12 partial responders (45% improvement). Stop Signal Reaction Time was greater at baseline in nonresponders (mean 530.1ms; SD 187.3 ms) than in responders and partial responders (combined mean 372.1ms; SD 146.8 ms) ($F_{2,68} = 6.5$; $p = .003$). TMS-evoked motor cortex physiology at baseline did not strongly predict clinical responses. However, one-month changes in paired pulse TMS short interval cortical inhibition ($p = .01$) and intracortical facilitation ($p = .09$) were greater in clinical responders.
CONCLUSIONS: Atomoxetine nonresponders had worse baseline stop signal reaction times. Changes in paired pulse TMS-evoked motor cortex inhibition may elucidate atomoxetine response pathways but do not appear to predict them.

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Neurology. 2013;80.
PRESCRIPTION STIMULANTS IN INDIVIDUALS WITH AND WITHOUT ADHD-DO THEY IMPROVE COGNITION?
Lakhan S.
OBJECTIVE: Prescription stimulant abuse of drugs like methylphenidate (MPH), dextroamphetamine (d), and dextroamphetamine-amphetamine (d-AMP) has dramatically increased over recent years as a form of nullcognitive enhancementnull. In this inquiry, we discuss the cognitive effects of prescription stimulant use in individuals with and without ADHD.
BACKGROUND: The nonmedical use of prescription stimulants represents the second common most form of illicit drug use in college, second to marijuana. Stimulants, commonly called nullsmart pillsnull, are commonly abused by students for enhancing school or work performance.
DESIGN/METHODS: This inquiry was initiated with a PubMed search of the US National Library of Medicine.

RESULTS: ADHD-diagnosed college students did not differ in IQ from those without ADHD. In reviewing 17 studies, stimulants produced little improvement in the academic performance of hyperkinetic ADHD children. The drugs appeared to reduce disruptive behavior rather than improve academic performance. Stimulants do improve the ability to focus and pay attention. Both AMP and MPH do not improve (and may even impair) short-term acquisition of information. In addition, AMP and MPH do not improve, and may impair nullcognitive flexibilitynull. In non-ADHD individuals using stimulants, with single exposures of verbal material, there were no benefits seen immediately following learning, but late recall and recognition were enhanced. Of 6 studies, only 1 yielded significant memory enhancement on short delays. In contrast, retention was reliably enhanced by d-AMP when subjects were tested after longer delays.
CONCLUSIONS: Stimulants do not increase IQ. AMP and MPH might improve long-term retention of information in ADHD, if taken when memory is being nullconsolidated.null When ADHD patients are given rote-learning tasks their performance is improved by stimulants. However, studies only found a correlation with rote memory tasks, not complex memory. The rumored effects of nullsmart drugsnull may be a false promise, as research suggests that stimulants are more effective at correcting deficits than nullenhancing performance.null.

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Neuropediatrics. 2013;44.

VIDEO-ASSISTED BEHAVIOR OBSERVATION AS A TOOL FOR METHYLPHENIDATE DOSE FINDING IN ADHD: LONGER TERM OUTCOME.

Kuhle HJ, Lefering R.

Introduction: A standardized procedure of video-assisted observation of the variability of the smile allows the determination of an optimal regulation state in ADHD-children and adolescents treated with methylphenidate (MPH). Regulation worsens with changes of 2.5 mg MPH (1). A continuous performance test which includes head movements, reaction time, and accuracy (Qb-Test) follows the same curvilinear course when single dose of MPH is slowly augmented and passes the turning point which we denominate nulloptimal.null Use of this MPH dose improves highly significant all DSM-IV characteristics of ADHD.
Objectives: To test if improvements last for a long time and retesting shows similar results.
Methods: A sample of 12 ADHD patients (6 to 12-year-olds, 2 girls and 10 boys) was retested after 10 months. After 8 months Du Paul's ADHD rating scale was filled out by parents.
Results: Of the total samples 9 (8 boys and 1 girl) could be reexamined. In 8 of 9 patients, the optimal dose was the same. In one boy, video-assisted observation suggested a 2.5 mg lower dose. Qb-Test parameters showed again the same shape of the dose-dependent curve as video observation, both in the first and the repeated assessment. Student t-test for paired samples shows significant differences from nullwithout medicationnull to nulloptimalnull dose. Improvement in ADHD rating scale is highly significant and remains stable for 8 more months.
Conclusions: Although limited by the small sample size, results indicate that involuntary behavior features coincide with reaction time measures and help find a good MPH dose which keeps stable for a long time. The procedure offers stable improvements in behavior ratings and has proved to be a useful tool in our daily practice.

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Neuropsychiatr Dis Treat. 2013;9:977-83.

UPDATE ON OPTIMAL USE OF LISDEXAMFETAMINE IN THE TREATMENT OF ADHD.

Madaan V, Kolli V, Bestha DP, et al.

Lisdexamfetamine (LDX) has been a recent addition to the treatment armamentarium for Attention Deficit Hyperactivity Disorder (ADHD). It is unique among stimulants as it is a prodrug, and has been found to be safe and well-tolerated medication in children older than 6 years, adolescents and adults. It has a smooth onset of action, exerts its action up to 13 hours and may have less rebound symptoms. LDX has proven to be effective in the treatment of ADHD in placebo controlled trials, and improved performance in simulated academic and work environments have been noticed. Both stimulant-naive and stimulant-exposed patients

with ADHD appear to benefit from LDX. It has also shown some promise in improving emotional expression and executive function of patients with ADHD. Adverse effects such as decrease in sleep, loss of appetite and others have been reported with LDX use, just as with other stimulant formulations. Since most such studies exclude subjects with preexisting cardiac morbidity, prescribing precautions should be taken with LDX in such subjects, as with any other stimulant. Study subjects on LDX have been reported to have low scores on drug likability scales, even with intravenous use; as a result, LDX may have somewhat less potential for abuse and diversion. There is a need for future studies comparing other long acting stimulants with LDX in ADHD; in fact clinical trials comparing LDX with OROS (osmotic controlled-release oral delivery system) methylphenidate are currently underway. Furthermore, the utility of this medication in other psychiatric disorders and beyond ADHD is being investigated.

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Neuropsychology. 2013;27:201-09.

BEHAVIORAL CORRELATES OF REACTION TIME VARIABILITY IN CHILDREN WITH AND WITHOUT ADHD.

Antonini TN, Narad ME, Langberg JM, et al.

Reaction time (RT) variability is often purported to indicate behavioral attention. This study seeks to examine whether RT variability in children with Attention Deficit Hyperactivity Disorder (ADHD) is associated with observed behavioral indicators of attention. Method: One-hundred 47 participants with and without ADHD completed five computerized neuropsychological tasks and an analog math task. Linear mixed models were utilized to examine the relationship between observations of behavioral inattention during the analog task and measures of RT variability from the neuropsychological tasks. Results: Significant associations were observed between RT variability and mean duration of on-task behavior on the analog math task. Secondary analyses indicated that on-task behavior during the math task was also related to accuracy on the neuropsychological tasks. Conclusions: RT variability, especially the portion of RT variability characterized by long RTs, appears to measure a cognitive phenomenon that relates to successful on-task academic behavior across children with and without ADHD. The relationship between RT variability and on-task behavior is present across multiple neuropsychological tasks and does not appear to be moderated by age, sex, or the presence of anxiety or depression.

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Neuropsychology. 2013;27:107-20.

NEUROPSYCHOLOGICAL PERFORMANCE AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER SUBTYPES AND SYMPTOM DIMENSIONS.

Nikolas MA, Nigg JT.

Objective: Characterization of clinical heterogeneity in attention-deficit hyperactivity disorder (ADHD) remains controversial. Neuropsychological and cognitive studies provide one type of validation data, but too often have considered only a narrow range of functional domains.

Method: The current study examined ADHD subtype and presentation differences across a broad range of neurocognitive domains in a large clinically characterized, community-recruited sample of 498 youth (213 control, 107 ADHDprimarily inattentive [ADHD-PI], 137 ADHD-combined [ADHD-C]), ages 6-17 years. Domains assessed included inhibition, working memory, arousal, processing speed, response variability, and temporal information processing.

Results: Youth with ADHD-C performed worse than youth with ADHD-PI in all domains, consistent with a severity model. Performance among a subgroup with a "restrictive inattentive" presentation indicated potential deficits in processing speed relative to other ADHD-PI youth, but no other effects. When all measures were included in the same model, cognitive control (executive functions, working memory, and memory span), arousal, and response variability each provided uniquely incremental statistical prediction of specific symptom dimensions and of subtype/ presentation, but temporal information processing and processing speed did not.

Conclusion: Results suggest the potential to consolidate multiple neurocognitive theories of ADHD, and that such consolidation will apply across putative clinical subtypes or presentations.

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Neurosci Biobehav Rev. 2013;37:1692-701.

AGE-RELATED CHANGE OF NEUROCHEMICAL ABNORMALITY IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A META-ANALYSIS.

Aoki Y, Inokuchi R, Suwa H, et al.

Prevalence and symptoms of attention-deficit hyperactivity disorder (ADHD) change with advancing age. However, neurochemical background of such age-related change is yet to be elucidated. We therefore conducted a meta-analysis of 16 proton magnetic resonance spectroscopy studies comprising 270 individuals with ADHD and 235 controls. Standardized mean differences were calculated and used as an effect size. Sensitivity analyses and meta-regression to explore the effect of age on neurochemical abnormality were performed. A random effects model identified a significantly higher-than-normal N-acetylaspartate (NAA) in the medial prefrontal cortex (mPFC), but no significant differences of other metabolites in that area. No significant difference in metabolite levels was demonstrated in any other region. Sensitivity analysis of children with ADHD revealed significantly higher-than-normal NAA, whereas no significant difference was found in adults with ADHD. Meta-regression revealed significant correlation between advanced age and normal levels of NAA in the mPFC, suggesting that age-dependent abnormality of NAA level in the mPFC is a potential neural basis of age-related change of symptoms of ADHD.

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Neurosciences. 2013;18:278-80.

ABNORMAL SPINDLE-LIKE MICROCEPHALY GENE DETECTION IN AN AUTOSOMAL RECESSIVE MICROCEPHALIC SAUDI PATIENT WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND MENTAL RETARDATION.

Mahmoud AA, Siddiqui IA.

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Pediatr Emerg Care. 2013 Aug;29:929-31.

AN OVERDOSE OF EXTENDED-RELEASE GUANFACINE.

Fein DM, Hafeez ZF, Cavagnaro C.

Extended-release guanfacine is a centrally acting alpha2-adrenergic agonist that was recently approved for treatment of attention-deficit/hyperactivity disorder. The following is a case discussion of a 12-year-old boy with attention-deficit/hyperactivity disorder and Tourette syndrome, who presented 18 hours after ingestion of 3 times his usual dose of extended-release guanfacine. On presentation, he was lethargic, bradycardic, and hypertensive with an otherwise nonfocal neurological examination. He remained hypertensive until administration of an intravenous antihypertensive agent (nicardipine) 24 hours after ingestion. After cessation of the calcium-channel blocker, he continued to have intermittent episodes of symptomatic hypotension for the next 2(1/2) days. This extremely protracted course of hypertension followed by prolonged symptomatic hypotension is rare with ingestions of centrally acting alpha2-adrenergic agonists. As this drug is increasingly prescribed for treatment of a disease with increasing prevalence, it is imperative that emergency physicians become familiar with the varying presentations of its toxicity.

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Pediatr Nephrol. 2013;28:1682.

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN UNDERGOING PERITONEAL DIALYSIS.

Chaijan PY, Vazirian S, Seyed Zade SA, et al.

Objective: Attention deficit/ Hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood. This disorder is more prevalent in some chronic diseases. ADHD may has high prevalence in children with end stage renal disease (ESRD) undergoing peritoneal dialysis, due to negative body image. The aim of this study was evaluation of ADHD in children undergoing peritoneal dialysis at least for 6 months.

Methods: 30 peritoneal dialysis children (between 5 to 16 year) and 30 healthy children were enrolled in this case control study. ADHD was diagnosed by Conners Rating Scale and DSM IV criteria and was confirmed by psychologist consult. Data were analyzed by chi-square tests and SPSS statistics 15.

Results: 9 children (30%) of 30 children in peritoneal dialysis group (case group) and 1 child (3%) of 30 children in healthy group (control group) were affected to attention deficit (P value = 0.006). 8 children (26%) of 30 children in case group and no child in control group were affected to hyperactivity disorder.

Conclusion: ADHD is more prevalent in ESRD patient undergoing peritoneal dialysis. Therefore screening methods for ADHD is necessary in these patients.

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Pediatr Nephrol. 2013;28:1393.

USEFULNESS OF THE APPLICATION OF QUESTIONNAIRES TO DETECT ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AND OTHER PSYCHIATRIC DISORDERS IN CHILDREN WITH FUNCTIONAL VOIDING DISORDERS.

Gautreaux S.

Objective: Although the relationship between functional voiding disorders (FVD) and the presence of a psychological problem remains controversial, the greater frequency of ADHD among children with this condition is well known. The purpose of this study was to determine the diagnostic performance of the application of questionnaires to detect ADHD and other psychiatric disorders in children with functional voiding disorders in general pediatrics consultations

Methods: The study was conducted on 32 children between 6 and 13 years of age (20 males) diagnosed with FVD (patient group) and 32 children of the same age (21 males) who had no urinary symptoms (control group). The parents of these children responded to the questions in two standardized questionnaires: the Strengths and Difficulties Questionnaire (SDQ) to screen for mental health disorders and the Questionnaire for the detection of ADHD of the DSM-IV psychiatric disorders of American Academy of Psychiatry manual. The variables obtained from the questionnaire responses were compared between the two groups of children using the Student's t-test for unpaired samples when variables were quantitative and the chi-square test if the variables were qualitative. It was considered significant when $p<0.05$

Results: No significant differences were found between the two groups in the SDQ questionnaire in any of its sections (emotional symptoms, conduct problems, hyperactivity, peer problems and prosocial behavior) or global assessment test, in which only 2 patients of each group had an abnormal result. The questionnaire for the detection of ADHD, presented an altered overall result of 17.18% and 14.06% patients in the control group (p=ns). There were also no differences between the two groups on the results of this test concerning the inattention or hyperactivity-impulsivity sections.

Conclusion: The results of the application of questionnaires to detect ADHD and other psychiatric disorders in children with FVD are similar to those of the general population. The routine application of this type of questionnaires to all the patients in pediatrics consultations does not seem necessary.

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Pediatr Nephrol. 2013;28:1393.

CHARACTERIZATION OF VOIDING DYSFUNCTION IN CHIDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER.

Kim JY, Lee KH, Lee JW.

Objective: Attention deficit hyperacitivity disorder (ADHD) has been associated with impairment of frontal inhibitory function and catecholaminergic system. ADHD is diagnosed in 3~5 % of children. Children with ADHD seem to suffer from various forms of urinary problems such as nocturnal enuresis, dysfunctional voiding and diurnal incontinence. However, no data exist to confirm in Korean ADHD children. We investigate the clinical findings of voiding dysfunction in ADHD children.

Methods: Between October 2009 and March 2011, a total of 63 children (33 children with ADHD and the other 30 children with upper respiratory infection as control group) were enrolled in Gangnam Sacred Heart hospital, Hallymuniversity. ADHD children were diagnosed under diagnostic and statistical manual of mental disorders (DSM)-IV criteria. A comprehensive survey of voiding and defecating were administered.

Results: The patient group included 28 boys and 5 girls, and the control group 15 boys and 15 girls. Mean age were 9.09+/-2.8 year in ADHD group and 8.58+/-3.1 in control group. Children with ADHD had statistically significant higher incidence of enuresis (P=0.017), urgency (P=0.017), urge incontinence (P=0.033) and constipation (P=0.007). There was no significant differences in straining, intermitteny, holding maneuvers (P>0.05).

Conclusion: Children with ADHD in Korea have significantly higher rates of enuresis, urgency, urge incontinence and constipation than those without ADHD.

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Pediatrics. 2013 Sep;132:e612-e622.

AUTISTIC TRAITS IN CHILDREN WITH AND WITHOUT ADHD.

Kotte A, Joshi G, Fried R, et al.

OBJECTIVE: To assess the implications of autistic traits (ATs) in youth with attention-deficit/hyperactivity disorder (ADHD) without a diagnosis of autism.

METHODS: Participants were youth with (n = 242) and without (n = 227) ADHD and controls without ADHD in whom a diagnosis of autism was exclusionary. Assessment included measures of psychiatric, psychosocial, educational, and cognitive functioning. ATs were operationalized by using the withdrawn + social + thought problems T scores from the Child Behavior Checklist.

RESULTS: A positive AT profile was significantly overrepresented among ADHD children versus controls (18% vs 0.87%; P < .001). ADHD children with the AT profile were significantly more impaired than control subjects in psychopathology, interpersonal, school, family, and cognitive domains.

CONCLUSIONS: A substantial minority of ADHD children manifests ATs, and those exhibiting ATs have greater severity of illness and dysfunction.

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Pediatrics. 2013 Sep.

PARENTAL PREFERENCES AND GOALS REGARDING ADHD TREATMENT.

Fiks AG, Mayne S, DeBartolo E, et al.

OBJECTIVES: To describe the association between parents' attention-deficit/hyperactivity disorder (ADHD) treatment preferences and goals and treatment initiation.

METHODS: Parents/guardians of children aged 6 to 12 years diagnosed with ADHD in the past 18 months and not currently receiving combined treatment (both medication and behavior therapy [BT]) were recruited from 8 primary care sites and an ADHD treatment center. Parents completed the ADHD Preference and Goal Instrument, a validated measure, and reported treatment receipt at 6 months. Logistic regression was used to analyze the association of baseline preferences and goals with treatment initiation. Using linear regression, we compared the change in preferences and goals over 6 months for children who initiated treatment versus others.

RESULTS: The study included 148 parents/guardians. Baseline medication and BT preference were associated with treatment initiation (odds ratio [OR]: 2.6 [95% confidence interval (CI):1.2-5.5] and 2.2

[95% CI: 1.0-5.1], respectively). The goal of academic achievement was associated with medication initiation (OR: 2.1 [95% CI: 1.3-3.4]) and the goal of behavioral compliance with initiation of BT (OR: 1.6 [95% CI: 1.1-2.4]). At 6 months, parents whose children initiated medication or BT compared with others had decreased academic and behavioral goals, suggesting their goals were attained. However, only those initiating BT had diminished interpersonal relationship goals.
CONCLUSIONS: Parental treatment preferences were associated with treatment initiation, and those with distinct goals selected different treatments. Results support the formal measurement of preferences and goals in practice as prioritized in recent national guidelines for ADHD management.

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Pediatrics. 2013;132:260-66.
VIDEO GAME USE IN BOYS WITH AUTISM SPECTRUM DISORDER, ADHD, OR TYPICAL DEVELOPMENT.
Mazurek MO, Engelhardt CR.
OBJECTIVES: The study objectives were to examine video game use in boys with autism spectrum disorder (ASD) compared with those with ADHD or typical development (TD) and to examine how specific symptoms and game features relate to problematic video game use across groups.
METHODS: Participants included parents of boys (aged 8-18) with ASD (n = 56), ADHD (n = 44), or TD (n = 41). Questionnaires assessed daily hours of video game use, in-room video game access, video game genres, problematic video game use, ASD symptoms, and ADHD symptoms.
RESULTS: Boys with ASD spent more time than did boys with TD playing video games (2.1 vs 1.2 h/d). Both the ASD and ADHD groups had greater in-room video game access and greater problematic video game use than the TD group. Multivariate models showed that inattentive symptoms predicted problematic game use for both the ASD and ADHD groups; and preferences for role-playing games predicted problematic game use in the ASD group only.
CONCLUSIONS: Boys with ASD spend much more time playing video games than do boys with TD, and boys with ASD and ADHD are at greater risk for problematic video game use than are boys with TD. Inattentive symptoms, in particular, were strongly associated with problematic video game use for both groups, and role-playing game preferences may be an additional risk factor for problematic video game use among children with ASD. These findings suggest a need for longitudinal research to better understand predictors and outcomes of video game use in children with ASD and ADHD.

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Pediatrics. 2013 Sep;132:e623-e629.
USE OF A COMPUTERIZED DECISION AID FOR ADHD DIAGNOSIS: A RANDOMIZED CONTROLLED TRIAL.
Carroll AE, Bauer NS, Dugan TM, et al.
OBJECTIVE: To determine if implementing attention-deficit/hyperactivity disorder (ADHD) diagnosis and treatment guidelines in a clinical decision support system would result in better care, including higher rates of adherence to clinical care guidelines.
METHODS: We conducted a cluster randomized controlled trial in which we compared diagnosis and management of ADHD in 6- to 12-year-olds after implementation of a computer decision support system in 4 practices.
RESULTS: Eighty-four charts were reviewed. In the control group, the use of structured diagnostic assessments dropped from 50% in the baseline period to 38% in the intervention period. In the intervention group, however, it rose from 60% to 81%. This difference was statistically significant, even after controlling for age, gender, and race (odds ratio of structured diagnostic assessment in intervention group versus control group = 8.0, 95% confidence interval 1.6-40.6). Significant differences were also seen in the number of ADHD core symptoms noted at the time of diagnosis. Our study was not powered to detect changes in care and management, but the percent of patients who had documented medication adjustments, mental health referrals, and visits to mental health specialists were higher in the intervention group than the control.

CONCLUSIONS: The introduction of a clinical decision support module resulted in higher quality of care with respect to ADHD diagnosis including a prospect for higher quality of ADHD management in children. Future work will examine how to further develop the ADHD module and add support for other chronic conditions.

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Pediatrics. 2013 Sep;132:e630-e636.

ADHD AND LEARNING DISABILITIES IN FORMER LATE PRETERM INFANTS: A POPULATION-BASED BIRTH COHORT.

Harris MN, Voigt RG, Barbaresi WJ, et al.

BACKGROUND AND OBJECTIVE: Previous studies suggest that former late preterm infants are at increased risk for learning and behavioral problems compared with term infants. These studies have primarily used referred clinical samples of children followed only until early school age. Our objective was to determine the cumulative incidence of attention deficit/hyperactivity disorder (ADHD) and learning disabilities (LD) in former late preterm versus term infants in a population-based birth cohort.

METHODS: Subjects included all children born 1976 to 1982 in Rochester, MN who remained in the community after 5 years. This study focused on the comparison of subjects in 2 subgroups, late preterm (34 to <37 weeks) and term (37 to <42 weeks). School and medical records were available to identify individuals who met research criteria for ADHD and LD in reading, written language, and math. The Kaplan-Meier method was used to estimate the cumulative incidence of each condition by 19 years of age. Cox models were fit to evaluate the association between gestational age group and condition, after adjusting for maternal education and perinatal complications.

RESULTS: We found no statistically significant differences in the cumulative incidence of ADHD or LD between the late preterm (N = 256) versus term (N = 4419) groups: ADHD (cumulative incidence by age 19 years, 7.7% vs 7.2%; P = .84); reading LD (14.2% vs 13.1%; P = .57); written language LD (13.5% vs 15.7%; P = .36), and math LD (16.1% vs 15.5%; P = .89).

CONCLUSIONS: These data from a population-based birth cohort indicate that former late preterm infants have similar rates of LD and ADHD as term infants.

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Perfusion. 2013 Aug.

ATTENTION DEFICIT/HYPERACTIVITY DISORDER AFTER NEONATAL SURGERY: REVIEW OF THE PATHOPHYSIOLOGY AND RISK FACTORS.

Sistino J.

There are many factors that influence the long-term neurological outcomes in children following cardiac surgery. Because there is also complex interaction between these many factors, it is difficult to assess which are primary and modifiable and which can be used to make improvements in outcomes. As survival after complex neonatal heart surgery has increased, the number of children with long-term neurological deficits is becoming more evident and this affects quality of life for children and their families.One area of long-term assessment is the incidence of attention deficit/hyperactivity disorder (ADHD). The incidence rate for ADHD following pediatric cardiac surgery is significantly higher than the normal rate for children of the same age. Because this is a measureable long-term outcome, it can be used to evaluate methods for cerebral protection during surgery as well as the timing of surgical procedures to maximize cerebral oxygen levels.This paper will review the pathophysiological basis for ADHD in this population, based on the similarities between neonatal cardiac surgical patients and pre-term infants. Both populations have an increased risk for ADHD and the etiology and pathological changes in pre-term infants have been widely investigated over the past 25 years. The rate of ADHD in this population is a window into the effects of these pathological changes on long-term outcomes.Reducing the incidence of ADHD in the future in this population should be a primary goal in developing and assessing new cerebral protective strategies during cardiac surgery.

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Postgrad Med. 2013 Jul;125:78-86.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN A CHRONIC CARE PARADIGM.

Culpepper L, Fried R.

The prevalence and disease burden of adult attention-deficit/hyperactivity disorder (ADHD) suggests that primary care physicians (PCPs) have an opportunity to improve the functioning and quality of life of a significant number of adult patients. The American Academy of Pediatrics provides evidence-based clinical practice guidelines that recognize ADHD as a chronic condition, and a large proportion of children with ADHD continue to meet diagnostic criteria as adults. Therefore, the management of ADHD should incorporate principles common to the management of other chronic conditions, including proactive planning for continuity of treatment across the life span and integrated, multidisciplinary health care teams for optimal disease management. This article describes a clinical approach whereby adult ADHD is treated within a chronic care paradigm that prominently features the involvement of the PCP. If PCPs envision ADHD as a chronic illness, similar to asthma or diabetes, they may be less likely to refer individuals to be managed by specialists, and more likely to see their role in coordinating and monitoring adult ADHD care, knowing when and how to bring other resources into play, and when and how to educate patients.

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Postgrad Med. 2013 Jul;125:131-40.

CHALLENGES IN THE TRANSITION OF CARE FOR ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Robb A, Findling RL.

Attention-deficit/hyperactivity disorder (ADHD) is often considered a childhood disorder. However, in those diagnosed with ADHD as children, inattention, impulsivity, and hyperactivity can persist into adulthood, causing significant functional impairment and emotional distress, even if the condition no longer meets diagnostic criteria. This review examines the developmental and psychosocial factors to consider in adolescents with ADHD and the strategies that facilitate the transition from pediatric to adult care. Our findings are based on PubMed database searches conducted on November 29, 2011, that identified articles pertaining to ADHD and continuity or transition in medical care for adolescents published in English within the 5-year period preceding this date. Adolescents with ADHD face specific burdens associated with transitioning into adulthood that can impede the achievement of academic and occupational goals. The main finding of the literature review was that ADHD treatment rates decline sharply from childhood through young adulthood, despite the fact that functional impairment often persists. Moreover, although psychosocial therapy can play an important role in resolving functional difficulties and encouraging patient adherence to pharmacotherapy, the existing literature focuses mainly on pharmacotherapy as first-line treatment for ADHD. Therefore, careful, advanced planning to ensure continuity of medical and psychiatric care is essential. This planning involves the pediatric service that has been providing care, the adult service that will assume the responsibility of providing care, the young person with ADHD, and the family. Although recommendations for planning initiatives have been developed by a variety of professional organizations, they do not seem to be routinely implemented for the transition of ADHD care. Such careful advanced transition planning can ensure continuity of treatment, encourage treatment adherence, and help young individuals adjust to new life circumstances and avoid negative educational, social, and vocational results. Guidelines designed to facilitate this transition of care may be helpful.

Postgrad Med. 2013 Jul;125:47-52.

ARE MOTIVATION DEFICITS UNDERESTIMATED IN PATIENTS WITH ADHD? A REVIEW OF THE LITERATURE.

Modesto-Lowe V, Chaplin M, Soovajian V, et al.

Aims: Attention-deficit/hyperactivity disorder (ADHD) is characterized by impaired inhibition, inattention, and altered sensitivity to rewards. Behavioral studies support the presence of motivational disturbances as a distinct component of ADHD. Functional magnetic resonance imaging is a technology now used to research the brain circuitry underlying motivation. These studies indicate that individuals with ADHD exhibit hyporesponsitivity of the dopamine neurons in the ventral and dorsal striata in response to rewarding stimuli. Our article reviews the research examining interactions between external motivation and the responses of individuals with ADHD, from both neurobiologic and clinical perspectives.

Methods: A PubMed search of studies written in English between 2000 and 2012 with keywords ADHD and motivation was conducted.
Results: Motivational processes are examined using behavioral and neurobiologic paradigms. Behavioral studies show altered processing of reinforcement and incentives in children with ADHD. These children respond more impulsively to rewards and choose small, immediate rewards over larger, delayed incentives. Interestingly, a high intensity of reinforcement is effective in improving task performance in children with ADHD. Pharmacotherapy may also improve task persistence in these children.
Conclusion: Previous studies suggest that a clinical approach using interventions to improve motivational processes in patients with ADHD may improve outcomes as children with ADHD transition into adolescence and adulthood.

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Prog Neuropsychopharmacol Biol Psychiatry. 2013 Aug.
CHANGES IN PLASMA BDNF LEVELS INDUCED BY METHYLPHENIDATE IN CHILDREN WITH ADHD.
Amiri A, Parizi GT, Kousha M, et al.
OBJECTIVES: It has been suggested that BDNF may play a role in the pathogenesis of ADHD. Our aim is to determine whether methylphenidate can induce changes in plasma BDNF levels of children with ADHD.
METHODS: We assessed levels of plasma BDNF in 28 ADHD patients (age range=3.5-10years) before and after 6weeks treatment with effective dosages of methylphenidate. Then we evaluated the correlation of levels of plasma BDNF with clinical variables, especially ADHD Conner's parents rating scale.
RESULTS: According to the paired sample T-test, the mean plasma BDNF level in the baseline was 193.06pg/ml, whereas 271.06pg/ml in the end point, thus showing significantly higher mean plasma BDNF levels in the post-treatment situation than in the pretreatment (t=-3.393, df=27, p=0.002). Pearson's correlation test revealed that there was also significant negative correlation between levels of BDNF in the plasma of ADHD patients before treatment and improvement in hyperactivity symptoms with treatment (Pearson's correlation=-0.395, p=0.037).
CONCLUSION: The mean plasma BDNF levels increased after 6weeks of treatment with methylphenidate. Also, we found an improvement in hyperactivity symptoms with decreasing baseline plasma BDNF levels. We recommend that more studies should be conducted in order to assess the possible roles of plasma BDNF levels in treatment response prediction and prognosis.

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Psychiatr Serv. 2013 Aug.
GEOGRAPHIC VARIATION AND DISPARITY IN STIMULANT TREATMENT OF ADULTS AND CHILDREN IN THE UNITED STATES IN 2008.
McDonald DC, Jalbert SK.
OBJECTIVE This study estimated the prevalence of stimulant treatment among both adults and children at national, state, and county levels during 2008 and explored explanations for wide variations in treatment prevalence.
METHODS Records of 24.1 million stimulant prescriptions dispensed to insured and uninsured patients were obtained from approximately 76% of U.S. retail pharmacies. Data were weighted to estimate treatment prevalence on March 15, 2008, for all U.S. states and counties. Regression models were used to estimate the associations among the counties' treatment rates and the characteristics of the counties and their resident populations.
RESULTS An estimated 2.5% of children </=17 years of age (3.5% of males and 1.5% of females) and .6% of persons >17 years of age were being treated with stimulants in March 2008. Treatment prevalence among states varied widely, and variation among counties was even wider. Two-thirds of the variation among counties in treatment prevalence was associated with supply of physicians, socioeconomic composition of the population, and, among children, funding for special education. Rates of children and adults in treatment were highly correlated.

CONCLUSIONS Wide variations in treatment prevalence signal disparities between established clinical practice guidelines and actual practice, especially for primary care, where most patients prescribed stimulants are managed. Better education and training for physicians may improve identification and treatment, thereby reducing disparities in care for attention-deficit hyperactivity disorder and other disabling conditions.

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Psychiatr Psychol Klin. 2012;12:149-56.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN-THE ROLE OF PSYCHOEDUCATION IN LONGITUDINAL STUDY.

Kdziela-Olech H.

Attention-deficit/hyperactivity disorder (ADHD) is a neurobehavioral disorder characterized by excessive restlessness, inattention, distraction and impulsivity. Currently, there are two terms for his disorder: attention-deficit/hyperactivity disorder-ADHD (DSM-IV) and hyperkinetic disorder-HKD (ICD-10). ADHD in childhood can persist into adolescent and adulthood with long-term negative outcomes. The aim of treatment for ADHD is to decrease symptoms, enhance functionality, and improve well-being for the child and his or her close contacts and to prevent other psychopathology. Psychoeducation is a paradigm, which includes information about the illness and its treatment. Educating parents to apply consistent behaviour modification techniques at home can help improve to children with ADHD. This study was aimed at assessment remote consequences of psychoeducation in ten years observation of children with ADHD. The treatment was conducted during periodical visit (at 4-weeks intervals) with application of psychoeducation for parents and elements of behavioural therapy. The effects of the psychoeducation were evaluated after 12 months and ten years of its duration. The results were statistically analysed. Research finds that psychoeducational interventions are effective in preventing relapse and improving social functioning. The relevance of psychoeducation has long been recognized as an important part of effective treatment for ADHD. The parental psychopathology entail restrictions of effective therapy.

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Psychol Med. 2013 Aug;1-14.

NEURAL SUBSTRATES OF BEHAVIORAL VARIABILITY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: BASED ON EX-GAUSSIAN REACTION TIME DISTRIBUTION AND DIFFUSION SPECTRUM IMAGING TRACTOGRAPHY.

Lin HY, Gau SS, Huang-Gu SL, et al.

BACKGROUND: Increased intra-individual variability (IIV) in reaction time (RT) across various tasks is one ubiquitous neuropsychological finding in attention deficit hyperactivity disorder (ADHD). However, neurobiological underpinnings of IIV in individuals with ADHD have not yet been fully delineated. The ex-Gaussian distribution has been proved to capture IIV in RT. The authors explored the three parameters [mu (mu), sigma (sigma), tau (tau)] of an ex-Gaussian RT distribution derived from the Conners' continuous performance test (CCPT) and their correlations with the microstructural integrity of the frontostriatal-caudate tracts and the cingulum bundles. Method We assessed 28 youths with ADHD (8-17 years; 25 males) and 28 age-, sex-, IQ- and handedness-matched typically developing (TD) youths using the CCPT, Wechsler Intelligence Scale for Children, 3rd edition and magnetic resonance imaging (MRI). Microstructural integrity, indexed by generalized fractional anisotropy (GFA), was measured by diffusion spectrum imaging tractrography on a 3-T MRI system.

RESULTS: Youths with ADHD had larger sigma (s.d. of Gaussian distribution) and tau (mean of exponential distribution) and reduced GFA in four bilateral frontostriatal tracts. With increased inter-stimulus intervals of CCPT, the magnitude of greater tau in ADHD than TD increased. In ADHD youths, the cingulum bundles and frontostriatal integrity were associated with three ex-Gaussian parameters and with mu (mean of Gaussian distribution) and tau, respectively; while only frontostriatal GFA was associated with mu and tau in TD youths.

CONCLUSIONS: Our findings suggest the crucial role of the integrity of the cingulum bundles in accounting for IIV in ADHD. Involvement of different brain systems in mediating IIV may relate to a distinctive pathophysiological processing and/or adaptive compensatory mechanism.

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Psychol Assess. 2013;25:545-55.

TREATMENT OF COMORBID ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND ANXIETY IN CHILDREN: PROCESSES OF CHANGE.

Jarrett MA.

Approximately 30%-40% of children with attention-deficit/hyperactivity disorder (ADHD) meet criteria for a comorbid anxiety disorder in clinical samples (Tannock, 2009), but little is known about treatment response for this subgroup. The current study evaluated processes of change in a psychosocial treatment designed for children with ADHD and anxiety (Jarrett & Ollendick, 2012). Processes included the slope of symptom change during treatment, the temporal relations between ADHD and anxiety symptoms during treatment, and changes in neurocognitive functioning, parent-child relationships, and family functioning. Treatment involved a combination of parent management training for ADHD and family based cognitive-behavioral therapy for anxiety. Sessions lasted approximately 90 min, and the treatment consisted of 10 weekly sessions. Eight children ages 8-12 with ADHD, combined type (ADHD-C), and at least 1 of 3 anxiety disorders (separation anxiety disorder, generalized anxiety disorder, social phobia) were selected for the study. The study utilized a single-case design with weekly measures of ADHD and anxiety symptoms along with pretreatment, midtreatment, and 1-week posttreatment assessments. Slopes of symptom change and temporal relationships among symptom domains were examined using simulation modeling analysis (Borckardt et al., 2008), while other analyses involved standard comparisons across time points. Results generally supported declining slopes for ADHD and anxiety and greater concurrent change between anxiety and hyperactivity/ impulsivity than anxiety and inattention. Few changes were found for neurocognitive functioning, but some changes were found for parent-child relationships and family functioning. Future studies are needed to better understand the treatment of ADHD and comorbid anxiety.

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Recenti Prog Med. 2013 Jun;104(6):254-61.

ADHD REGISTER: POST-MARKETING EVALUATION OF THE BENEFIT-RISK PROFILE OF DRUGS AND PROMOTION OF THE APPROPRIATENESS.

Panei P, Arcieri R.

INTRODUCTION:

The Register was aimed at assessing the benefit-risk profile of the treatment of attention deficit hyperactivity disorder (ADHD) with atomoxetine and methylphenidate.

METHODS:

Post-marketing observational study, phase IV. Prescription medication to children and adolescents with ADHD aged between 6 and 18 years in the centres of reference for ADHD accredited by the Italian regions.

RESULTS:

In the period from September 2007 to October 2011, 1098 children and adolescents were treated with methylphenidate and 951 with atomoxetine. 411 (21.5%) patients are released from the register: 274 treated with atomoxetine and 167 with methylphenidate, with a greater risk of discontinuation for atomoxetine: RR 1.4 (1.3-1.6) p<0.001. The length of treatment at the time of removal from the register is 4.1 months for atomoxetine and 2 months for methylphenidate. Patients treated with atomoxetine are more likely to experience an adverse event compared to those treated with methylphenidate (RR 2.8; 1.9-4.2). The total number of serious adverse events observed was 110: 82 (75%) patients treated with atomoxetine and 28 (25%) individuals treated with methylphenidate. For 98 patients with serious adverse events, the adverse event led to the interruption of treatment with exit from the registry. The chance of a serious adverse event among those treated with atomoxetine compared to those with methylphenidate is RR 2.8 (1.8-4.2). There have been 14 cardiovascular events, all grown positively. 69 were found with a ECG

alterations, with an increased risk for methylphenidate (RR 2.4; 1.4-4.2). The incidence of suicidal ideation was 4.5/1000 patients treated with atomoxetine. Hepatic alterations occurred with an incidence of 1/1000 subjects treated with methylphenidate and 4/1000 of those who received atomoxetine.

DISCUSSION:

The survey was carried out on a population which represents appropriately the paediatric population. The observed prevalence of ADHD corresponds to the expectation based on data from previous epidemiological investigations in Italy but considerably lower than what is reported in the international scientific literature. The rate of exposure to pharmacological treatments is similar to that of other European countries.

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Res Dev Disabil. 2013 Aug;34:3545-52.

IMPACT OF ADHD SYMPTOMS ON AUTISM SPECTRUM DISORDER SYMPTOM SEVERITY.

Sprenger L, Buhler E, Poustka L, et al.

Despite the official exclusion criteria for autism spectrum disorder (ASD) and attention deficit/hyperactivity disorder (ADHD) in the DSM-IV and ICD-10, patients with ASD often show ADHD symptoms. We aimed to examine the potential influence of ADHD symptoms on autistic psychopathology in a large sample of patients with ASD. We tested the hypothesis that patients with ASD and an additional ADHD (ASD+) would show a higher severity of autistic symptoms than those with ASD only (ASD-). We measured autistic symptoms using the autism diagnostic observation schedule (ADOS-G), the autism diagnostic interview (ADI-R), and the social responsiveness scale (SRS). To measure overall psychopathology and ADHD symptoms, we used the child behavior checklist (CBCL) and the ADHD rating scale (FBB-ADHS), respectively. Group differences between the ASD+ and the ASD- group (group division was conducted according to the results of the FBB-ADHS) were calculated using a univariate analysis of variance (ANOVA). The ASD+ group showed a greater severity of autistic symptoms than the ASD- group, measured by the SRS and the ADI-R. Especially in the social interaction subscale (ADI-R), a significantly higher symptom severity was found in the ASD+ group. No significant group differences were found regarding autistic symptoms measured by the ADOS-G. Patients with ASD and an additional ADHD expressed a stronger severity of autistic symptoms than patients with ASD only. According to our results, the possibility of a co-diagnosis of ADS and ADHD, as is being planned in the DSM-5, is in line with earlier studies, is highly reasonable, will simplify research, and have therapeutic implications.

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Res Dev Disabil. 2013;34:3477-86.

OBJECTIVE MEASUREMENT OF WEEKLY PHYSICAL ACTIVITY AND SENSORY MODULATION PROBLEMS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Lin CY, Yang AL, Su CT.

This study aimed to objectively compare the daily physical activity (PA), as indicated by moderate-to-vigorous physical activity (MVPA) during a week and metabolic equivalents (METs) per minute, between children with attention deficit hyperactivity disorder (ADHD) and typically developing children. Moreover, sensory modulation problems were examined using behavioral and physiological measures. Twenty boys with ADHD (mean age 8.64. (plus or minus). 2.57 years), and 20 matched typically developing boys (mean age 9.10. (plus or minus). 1.79 years) participated in our study. Each child wore a PA monitor for 14. h a day, seven days a week. All participants' parents were asked to fill out daily activity logs for their children. The problems of sensory modulation were detected using sensory profile (SP) questionnaires and Sensory Challenge Protocol that measured electrodermal response (EDR) to repeated sensory stimulation. Compared with the controls, the children with ADHD had a generally higher level of PA (1.48. (plus or minus). 0.10 vs. 1.60. (plus or minus). 0.12. METs/min; p=. 001), and tended to spend more time in MVPA on weekdays (35.71%) and the weekend (57.14%). However, when analyzing hourly recorded PA, the group differences were obvious only for certain hours. Our data suggested that children with ADHD were more hyperactive in structure-free than structured settings. The ADHD group showed their sensory

modulation problems on the SP but not on the EDR. We found some correlations between sensory modulation problems and hyperactivity in children with ADHD.

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Res Dev Disabil. 2013;34:3104-11.

PROACTIVE AND REACTIVE CONTROL OF MOVEMENT ARE DIFFERENTLY AFFECTED IN ATTENTION DEFICIT HYPERACTIVITY DISORDER CHILDREN.

Pani P, Menghini D, Napolitano C, et al.

Attention-Deficit/Hyperactivity Disorder children are impaired in the ability to interrupt an ongoing action in relation to a sudden change in the environment (reactive control, measured by stop signal reaction time, SSRT). Less investigated is the ability to control the response when it is known in advance that it will be required to stop (proactive control, measured by change in Reaction time, RT). The study is aimed at exploring both the reactive and the proactive inhibitory control in a group of ADHD children compared to a group of age-matched controls. ADHD children (N=28) and Controls (N=28) performed 4 tasks: 2 tasks required to respond to the appearance of the go-signals (go task and nostop task) and 2 tasks to respond to the go signals in a context in which sometimes a restrain or suppression of the response was required (go-nogo task and stop task). ADHD children showed a longer SSRT compared to controls. Both groups showed an increment in RT by comparing the go-nogo to the go task and an increment in RT and SD by comparing the stop to the nostop task. ADHD children showed higher intra-individual variability (SD) compared to controls only in the stop and nostop task. ADHD children showed impaired reactive control but preserved proactive control, and the physical appearance of the go signal affected their reaction times intra-individual variability. A comparison between the reactive and proactive controls helps in defining neuropsychological profiles of ADHD children and can inspires therapeutic behavioral-cognitive strategies for response control.

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S Afr J Psychiatry. 2013;19:136-40.

ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS.

Flisher AJ, Hawkridge S.

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Swiss Med Wkly. 2013;143:w13838.

A RANDOMISED CONTROLLED TRIAL OF COMBINED EEG FEEDBACK AND METHYLPHENIDATE THERAPY FOR THE TREATMENT OF ADHD.

Li L, Yang L, Zhuo CJ, et al.

PURPOSE: To evaluate the efficacy of combined methylphenidate and EEG feedback treatment for children with ADHD.

METHODS: Forty patients with ADHD were randomly assigned to the combination group (methylphenidate therapy and EEG feedback training) or control group (methylphenidate therapy and non-feedback attention training) in a 1:1 ratio using the double-blind method. These patients, who met the DSM-IV diagnostic criteria and were aged between 7 and 16 years, had obtained optimal therapeutic effects by titrating the methylphenidate dose prior to the trial. The patients were assessed using multiple parameters at baseline, after 20 treatment sessions, after 40 treatment sessions, and in 6-month follow-up studies.

RESULTS: Compared to the control group, patients in the combination group had reduced ADHD symptoms and improved in related behavioural and brain functions.

CONCLUSION: The combination of EEG feedback and methylphenidate treatment is more effective than methylphenidate alone. The combined therapy is especially suitable for children and adolescents with ADHD who insufficiently respond to single drug treatment or experience drug side effects.

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Ther Adv Psychopharmacol. 2013;3:65-71.

A 12-WEEK NURSING SUPPORT PROGRAMME FOR CARERS OF CHILDREN AND ADOLESCENTS IN THE UK WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER PRESCRIBED ATOMOXETINE.

Savill N, Pelton J, Lenox-Smith A, et al.

Introduction: Patient support programmes are assuming greater importance in the UK in many therapeutic areas, mostly with the aim of improving adherence to medication and many being provided by the pharmaceutical industry. Atomoxetine is a noradrenaline reuptake inhibitor for the treatment of attention deficit hyperactivity disorder that has recently demonstrated incremental efficacy for at least 12 weeks. Issues of adherence may be predicted over this initial period particularly if adverse events are reported. The Strattera Support Service was initiated in 2006 (funded by Eli Lilly) to provide advice, initially through telephone contact, by trained nurses during the first 12 weeks of atomoxetine therapy and is offered to carers of patients diagnosed with ADHD after atomoxetine has been prescribed. The aim of this pilot service evaluation is to assess discontinuation rates and compare them with historical control data.
Methods: Data from patients in the service who initiated atomoxetine between 1 January 2009 and 31 March 2010 were analysed to provide a pilot service evaluation. Continuation rates of patients in the service who were taking atomoxetine at week 12 were assessed and compared with historical control data.
Results: Between 1 January 2009 and 31 March 2010, 346 patients (300 male patients) enrolled in the programme and commenced treatment with atomoxetine. The mean age of patients was 10.5 years. At 12 weeks, 33 (9.5%) patients had discontinued treatment; continuation rates were similar regardless of age and sex. Discontinuation rates of 39% are reported from historical control data.
Conclusions: Preliminary data from a 12-week atomoxetine patient support programme are supportive that discontinuation rates may be lower than historically expected. Further service evaluations of this programme may be required.

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Turk J Pediatr. 2013;55:190-97.

IDENTITY STATUS AND ATTACHMENT IN ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Cuhadaroglu-Cetin F, Akdemir D, Tuzun Z, et al.

Identity and attachment are two concepts of different theories that might be related and that are developmentally very important in adolescence. The aim of this study was to explore the sense of identity, attachment styles and their relation in a group of adolescents with attention deficit hyperactivity disorder (ADHD). Thirty-four adolescents who were diagnosed with ADHD in childhood were reevaluated at the age of 13-16 years. The comparison group consisted of age-and gender-matched adolescents without a psychiatric disorder. The Sense of Identity Assessment Form (SIAF) and the Relationship Scales Questionnaire (RSQ) were used to examine the sense of identity and attachment styles of adolescents, respectively. Compared to adolescents without a psychiatric disorder, adolescents with ADHD, independent of the presence of a comorbid psychiatric disorder, had a similar identity formation process; however, adolescents with ADHD and a comorbid psychiatric disorder experienced more preoccupied attachment styles. Comorbid psychiatric disorders seem to be related to the insecure attachment patterns in adolescents with ADHD.

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Proactive and reactive control of movement are differently affected in Attention Deficit Hyperactivity Disorder children

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ABSTRACT

Attention-Deficit/Hyperactivity Disorder children are impaired in the ability to interrupt an ongoing action in relation to a sudden change in the environment (reactive control, measured by stop signal reaction time, SSRT). Less investigated is the ability to control the response when it is known in advance that it will be required to stop (proactive control, measured by change in Reaction time, RT). The study is aimed at exploring both the reactive and the proactive inhibitory control in a group of ADHD children compared to a group of age-matched controls. ADHD children ($N = 28$) and Controls ($N = 28$) performed 4 tasks: 2 tasks required to respond to the appearance of the go-signals (go task and nostop task) and 2 tasks to respond to the go signals in a context in which sometimes a restrain or suppression of the response was required (go–nogo task and stop task). ADHD children showed a longer SSRT compared to controls. Both groups showed an increment in RT by comparing the go–nogo to the go task and an increment in RT and SD by comparing the stop to the nostop task. ADHD children showed higher intra-individual variability (SD) compared to controls only in the stop and nostop task. ADHD children showed impaired reactive control but preserved proactive control, and the physical appearance of the go signal affected their reaction times intra-individual variability. A comparison between the reactive and proactive controls helps in defining neuropsychological profiles of ADHD children and can inspires therapeutic behavioral-cognitive strategies for response control.

1. Introduction

Attention-Deficit/Hyperactivity Disorder (ADHD) is one of the most common developmental neuropsychiatric disorders. Children with ADHD typically show hyperactivity, impulsivity and inattention (American Psychiatric Association, 2000). These symptoms have been associated with impairments in a range of cognitive functions. Among these functions, the motor response inhibition has been considered the core deficit in both children and adults with ADHD (Crosbie & Schachar, 2001; Nigg, 2005; Rubia et al., 2001; Willcutt et al., 2010; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005). In trying to establish the role of movement inhibition in ADHD, a number of studies have been focused on the control of movement, which is the ability to interrupt an ongoing action in relation to a sudden change in the environment. Typically, these studies have been

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conducted by using two different paradigms: the stop signal task and the go–nogo task. In the stop signal task, subjects are required to inhibit a movement when a stop signal is presented after some time delay from the go signal. The measure that accounts for the ability to control the movement is the stop signal reaction time (SSRT, Logan & Cowan, 1984; Verbruggen & Logan, 2009a), that is the time it takes to suppress the response. In contrast, in the go–nogo task, subjects are required to withhold the response when the no-go signal is presented instead of the go signal. The measure used in this case is the probability to respond to the nogo signal. While the stop signal task requires suppressing a response, in the go–nogo task inhibition requires deciding to go or not to go *prior to response emission* (Aron, 2011).

ADHD individuals are typically found impaired in the stop signal task, showing longer SSRT (Lipszyc & Schachar, 2010; Lijffijt, Kenemans, Verbaten, & van Engeland, 2005; Oosterlaan, Logan, & Sergeant, 1998), while in the go–nogo task contrasting results have been obtained (see e.g. Rhodes, Coghill, & Matthews, 2005). The longer SSRT observed does not imply a pure inhibition deficit, as others cognitive process implicated in the detection of the stop signal, like attention, can affect the performance (Lijffijt et al., 2005; Salinas & Stanford, 2013). The inconsistencies between results on movement inhibition in ADHD measured by the stop task and the go–nogo task may be due to the difference between stimulus-response mapping in the stop signal task and the go–nogo task. In the stop task the mapping between the stimulus (go signal) and response typically involves a two choice task (e.g. press right button for X and left button for Y). Conversely, in the go–nogo task, subjects are typically asked to emit a single response (button press) to the go signal. The difference between the two tasks in the stimulus-response mapping could then affect the inhibitory performance. Consistently with this hypothesis, Huizenga, van Bers, Plat, van den Wildenber, and van der Molen (2009) found that children or adolescents with ADHD showed a pronounced inhibitory dysfunction for spatially non-compatible stimulus-response mapping (Huizenga et al., 2009).

In both the stop and the go–nogo task the subjects are required to promptly react to a signal instructing to refrain from moving (the stop signal in the stop task and the nogo signal in the go–nogo task). The two measures of the movement inhibition, that is the SSRT for the stop task and the probability to respond to the nogo signal (PRN) for the go–nogo task, can be considered part of a more general type of control that has been called *reactive* because is triggered by an external stimulus (Aron, 2011; Stuphorn & Emeric, 2012). This type of control can be detected in real life situations when, for example, just after the traffic light turns green an ambulance appears asking to stop (stop task), or when it is necessary to decide whether to go or not just looking at the gesture of the municipal police (go–nogo task).

Another type of control is performed in anticipation of known situations. For example, slowing down the driving speed close to a pedestrian crossing. In the motor control studies, this type of control has been called *proactive* control and it emerges as a more global and anticipatory approach to a situation for which it is known that a response should be inhibited (Aron, 2011; Stuphorn & Emeric, 2012; Verbruggen & Logan, 2009b).

In the stop task and the go–nogo task the proactive control can be studied by modifying the structure of the tasks introducing blocks of only go trials (single-task blocks) asking to the subject to respond always, and by comparing the performance in these blocks to the performance in blocks of go trials intermingled with stop or nogo trials (mixed-task blocks), in which the subject has to inhibit the response in some trials. A similar experimental design has been also adopted in task switching effect studies (e.g. Braver, Reynolds, & Donaldson, 2003). Longer go trial reaction times (RT) were reliably observed in the mixed-task blocks compared to single-task blocks (Logan, 1981; Mirabella, Pani, & Ferraina, 2008; Verbruggen & Logan, 2009b). When stop signals are expected, slowing down the go trial RT increases the probability to suppress the response. It is hypothesized that the proactive control operates through a sustained activation able to increase the accuracy of the response depending on the expected events (Bogacz, Wagenmakers, Forstmann, & Nieuwenhuis, 2010; Verbruggen & Logan, 2009b).

While reactive control has been extensively investigated in ADHD studies (Lijffijt et al., 2005; Lipszyc & Schachar, 2010) little attention has been given to the proactive control.

With the present study we explore both the reactive inhibitory control and the proactive inhibitory control in a group of ADHD children compared to a group of age-matched controls. Reactive inhibitory control was tested by a SSRT and PRN and proactive control was measured throughout RT changes when passing from a go only task to a task in which the stopping or not going is required.

Consistently with the previous cited studies, we expect to observe in ADHD group a deficit in the reactive inhibitory control as showed by longer SSRT and higher PRN. Concerning proactive inhibitory control, to our knowledge this is the first study with ADHD participants and, thus, we have no specific prediction based on literature. Nevertheless, since the proactive inhibitory control operates adjusting behavior to new contexts, we expect it to be impaired in ADHD population and to observe a failure in slowing down RT when expected.

2. Methods

2.1. Participants

Twenty-eight children with ADHD (2 females) were recruited for the study from the Child Neuropsychiatric Unit of the Children Hospital Bambino Gesù in Rome and 28 controls (8 females) were recruited from the local primary and secondary schools.

All participants with ADHD underwent a child psychiatric examination conducted by experienced developmental psychiatrists and neuropsychologists. ADHD diagnosis was based on developmental history, extensive clinical examination

and a semi-structured interview conduct to parent and child separately, KSADS P-IV-R (Kaufmann, Birmaher, Brent, & Rao, 1997).

For both groups exclusion criteria were general IQ below 85 (Leiter-R; Roid & Miller, 1997), evidence of neurological disorders, pervasive developmental disorders or depressive disorders as assessed by clinical evaluation, Schedule for Affective Disorders and Schizophrenia for School-Age Children-Present Lifetime version (KSADS P-IV-R; Kaufman et al., 1997), Conners Teacher Rating Scales-long version (CTRS-R:L; Conners, 2000), Conners Parent Rating Scales-long version (CPRS-R:L; Conners, 2000), Child Behavior Checklist (CBCL; Achenback & Rescorla, 2001), Children's Depression Inventory (CDI; Kovacs, 1992). None of the ADHD children was under stimulant medication. The ADHD group was composed by 14 children that met the criteria for the combined subtype, 10 for the primarily inattentive subtype and 4 for the hyperactive subtype.

The subtypes did not significantly differ on any on the experimental measure tested (minimum $p = 0.28$; Kruskal–Wallis test) and were then merged all together for comparison with the control group.

The two groups were matched for (mean ± se) chronological-age (ADHD: 8.61 ± 0.3; Controls: 8.21 ± 0.28), mental-age (ADHD: 8.09 ± 0.34; Controls: 8.46 ± 0.36) and IQ (ADHD: 99.44 ± 1.95; Controls: 103.89.21 ± 2.09). All subjects were naïve. All participants and their parents gave their written informed consent after receiving a comprehensive description of the study. The study was performed in accordance with the Declaration of Helsinki (2008) and was approved by the local ethical committee of the Children Hospital Bambino Gesù.

2.2. Stimuli and tasks

Task administration and participants' performance was controlled by a PC running E-Prime. All participants were engaged in two simple RT tasks (go and nostop task) in addition to the two inhibitory tasks (go–nogo and stop task). The simple RT tasks were composed by a single type of trial that required a quick button press on the appearance of the stimulus. In the go task, one out of three intermingled equi-probable colored circled stimuli (blue, green, yellow) was presented. In the nostop task the stimulus was a white arrow in a blue circle ("forced way"). In both go trials and nostop trials, a response was considered correct if participants pressed the button between 100 ms and 1500 ms after the stimulus appearance. The two inhibitory tasks were a go–nogo task and a stop task. In the go–nogo task, intermingled with the go trials were nogo trials, in which a red circle appeared asking the participants to refrain from pressing the button. In the stop task, the nostop trials were intermingled with stop trials, where a stop signal (a red signal indicating to stop the planned movement) appeared after the presentation of a nostop signal with a variable delay (Stop Signal Delay, SSD). The SSD varied from one stop trial to the next according to a staircase procedure: if the participants succeeded in withholding the response, the SSD increased by 64 ms; if they failed, the SSD decreased by 64 ms. In both the stop trials and the nogo trials, a response was considered correct if the participants were able to refrain from pressing the button.

We set accuracy criteria of 85% correct responses in go and nostop trials. All participants met this criterion. All trials started with a presentation of a cross in the center of the screen for 1000 ms (warning period). The different tasks were presented in a blocked manner. The tasks with inhibition signals were always administered after the corresponding version of the simple task (i.e. go–nogo after go task and stop task after nostop task), but the order of presentation of the tasks was randomized across participants. All participants were familiarized with the tasks, before the experimental session started: they performed about 10 trials of the go and nostop task, and about 25 trials of the go–nogo and the stop task. All participants had then a clear idea of the task demand before the collection of the data started.

2.3. Data analysis

An ANOVA was conducted on RTs with Groups (ADHD and Controls) as between factors and Go-signal Appearance (in go and nostop trials) and Inhibition Demand (*no inhibition* demand in go and nostop tasks and *yes inhibition* demand in go–nogo and stop tasks) as within factors. A similar analysis was also performed on within subject Standard Deviations (SDs), and on omissions.

The inhibitory ability was evaluated by estimating the probability to respond to a nogo signal (PRN) in the go–nogo task and the Stop Signal Reaction Time (SSRT) in the stop task.

3. Results

3.1. Task accuracy and omissions

All participants met the criteria of accuracy (see methods). Overall the only type of error that we detected was the omission. ADHD and Controls omission errors (mean ± SEM) were respectively 1.78 ± 1.03 and 2.3 ± 0.95 in the go task, 2.4 ± 0.98 and 1.3 ± 0.6 in the nostop task; 5.5 ± 1.29 and 4.1 ± 0.8 in the go–nogo and 7.7 ± 1.87 and 3.3 ± 0.7in the stop task.

No differences between groups were observed in the number of omissions. A significant effect of Inhibition Demand, $F(1,54) = 23.6$, $p < 0.0001$, partial eta squared = 0.3, was found. The number of omissions was higher for go–nogo and stop tasks than for go and nostop task (5.1 ± 1.1 and 1.9 ± 0.7, respectively). No interaction between Group and Inhibition Demand was observed ($F(1,54) = 2.6$, $p = 0.111$).

3.2. Reaction time

No differences between groups were observed in RT. The absence of differences between groups was also confirmed by the absence of interaction between Inhibition Demand and Group ($F(1,54) = 0.2$, $p = 0.658$). However, a significant effect of Inhibition Demand, $F(1,54) = 221.76$, $p < 0.0001$, partial eta square = 0.804, Go-signal Appearance, $F(1,54) = 64.46$, $p < 0.00001$, partial eta square = 0.544, and interaction between Inhibition Demand and Go-signal Appearance were found, $F(1,54) = 6.63$, $p = 0.013$, partial eta square = 0.109. Bonferroni post hoc analysis showed an increment in RT from the go to the go–nogo task ($p < 0.001$, Fig. 1, Panel A) and from the nostop to the stop task ($p < 0.001$, Fig. 1, Panel B). The comparison between the go and the nostop task revealed a significant difference, with RT in the go task faster than in the nostop task ($p < 0.001$).

3.3. Intraindivual variability (within subject Standard Deviation)

Main effect of Group $F(1,54) = 4.064$, $p = 0.0488$, partial eta square = 0.07, Inhibition Demand $F(1,54) = 133.12$, $p < 0.00001$, partial eta square = 0.711, Go-signal $F(1,54) = 107.58$, $p < 0.00001$, partial eta square = 0.667, and interaction between Group and Go-signal Appearance $F(1,54) = 5.033$, $p = 0.029$, partial eta square = 0.085, and Inhibition Demand and Go-signal Appearance $F(1,54) = 55.418$, $p < 0.00001$, partial eta square 0.506, were found. No interaction between Group and Inhibition Demand was observed ($F(1,54) = 0.4$, $p = 0.538$).

Bonferroni post hoc analysis showed a significant difference between ADHD and Control groups for the nostop and the stop task (Fig. 2, comparing Panel B). However, no difference between groups was observed in the go and go–nogo task (Fig. 2, Panel A).

The significant interaction between Inhibition Demand and Go-signal Appearance depended on the increased response variability in term of SD from the nostop to the stop task ($p < 0.001$, Fig. 2, Panel B); conversely, the response variability from the go to the go–nogo task was not significant ($p = 0.273$, Fig. 2, Panel A).

3.4. Reactive inhibitory ability

A difference between groups in inhibitory measures (i.e. PRN and SSRT) was found only in the stop task due to ADHD showing longer SSRT than Control group $F(1,54) = 7.29$, $p = 0.01$, partial eta squared = 0.119; ADHD: 296.97 ± 117.81;

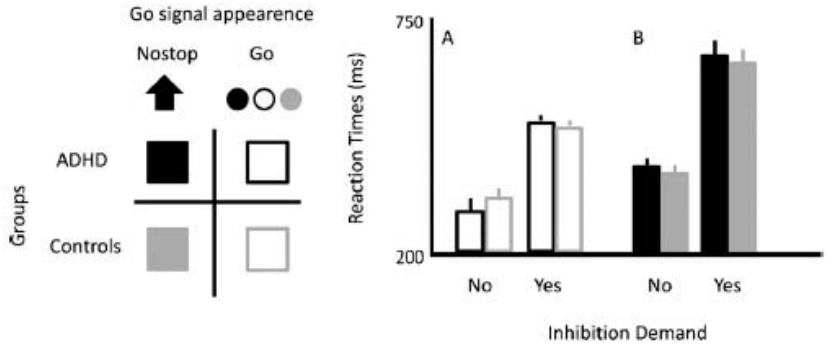

Fig. 1. RT of ADHD and Controls (mean ± SE) in the go and go–nogo task (Panel A) and in the nostop and stop task (Panel B).

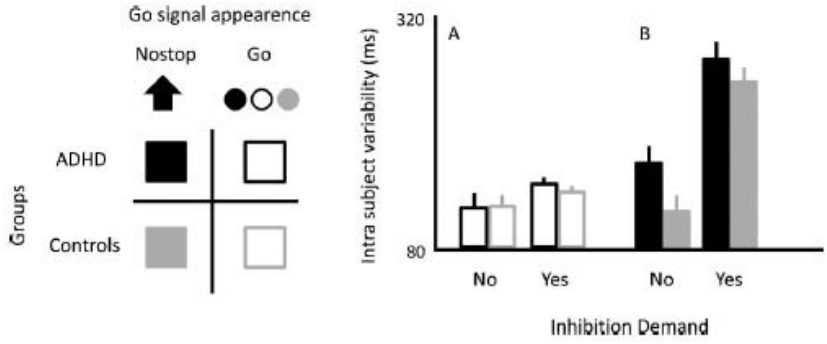

Fig. 2. Intra subject variability (within subject SD) of ADHD and Controls (mean ± SE) in the go and go–nogo task (Panel A) and in the nostop and stop task (Panel B).

Controls: 225.42 ± 75.90. PRN in the go–nogo task did not differ between groups $F(1,54) = 0.79$, $p = 0.38$, partial eta squared = 0.014; ADHD: 0.26 ± 0.19; Controls: 0.22 ± 0.14.

4. Discussion

This study investigated different aspects of the cognitive inhibitory control in ADHD. Specifically we were interested in investigating their reactive control of a prepotent response in the go–nogo and stop tasks and their proactive inhibitory control (changes in RT and SD depending on the inhibition demand) by comparing their performance to those of control children.

We found that the two groups did not differ in the probability to suppress the motor responses in the go–nogo task but the ADHD group had longer SSRT as consistently observed in the literature on reactive control (e.g. Lipszyc & Schachar, 2010; Oosterlaan et al., 1998).

Importantly, the two groups showed also similar strategies in proactive inhibitory control and these strategies depend on the context. Indeed, in both groups an increment in RT comparing the go–nogo to the go task was found, and an increment in RT and SD comparing the stop to the nostop task was observed. Both ADHD and controls showed higher number of omissions in tasks with inhibition demand (go–nogo and stop tasks) compared to tasks with no inhibition demand (go and nostop tasks). However, ADHD group showed higher intra-individual variability (SD) compared to controls only in the stop and nostop task. Finally, no differences were observed between the two groups in terms of RT in each task and in several other measures related to the performance in the go–nogo and stop tasks (see Table S1, Supplementary data).

In recent years, studies have investigated the reactive and proactive stopping, both in humans (Aron, 2011; Chikazoe, 2010) and non-human primates (Hanes, Patterson, & Schall, 1998; Mirabella, Pani, & Ferraina, 2011; Scangos & Stuphorn, 2010). Particularly, hemodyamic (fMRI, Aron, Behrens, Smith, Frank, & Poldrack, 2007; Aron & Poldrack, 2006), lesion (Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003; Picton et al., 2007; Rieger, Gauggel, & Burmeister, 2003), transcranial magnetic stimulation (Neubert, Mars, Buch, Olivier, & Rushworth 2010; Verbruggen, Aron, Stevens, & Chambers, 2010) and electrocorticography (Mattia et al., 2012; Swann et al., 2009, 2012) studies in humans and neurophysiological and stimulation studies in monkeys (Chen, Scangos, & Stuphorn, 2010; Hanes et al., 1998; Mirabella et al., 2011; Paré & Hanes, 2003; Sasaki, Gemba, & Tsujimoto, 1989; Scangos & Stuphorn, 2010) have unraveled a network of brain regions involved in the reactive control. The same regions seem to be involved also in the proactive control, although further studies are necessary to clarify the specific neurophysiological mechanisms (Aron, 2011; Chen et al., 2010). In fact a single brain area can be composed by different neural populations, each of them operating in different ways depending on the task at hand (e.g. Hanes et al., 1998). It is generally accepted that in the tasks we used a frontal–basal network acts both to inhibit a movement in response to the stop signal and to contextually adapt the performance to the potential presence of the stop signal. Different observations support specific roles of the right inferior frontal cortex (rIFC) and of the dorsomedial frontal cortex (preSMA and SMA) (Aron & Poldrack, 2006; Scangos & Stuphorn, 2010) in acting on the basal ganglia (purportedly subtalamic nucleus and striatum, Aron et al., 2007; Mink, 1996; Nambu, Tokudo, & Takada, 2002; Vink et al., 2005) to suppress the motor activity generated in the premotor and primary motor cortex (Mattia et al., 2012; Mirabella et al., 2011; Swann et al., 2009). The rIFC could accomplish its role through different processes: by detecting changes in the environment (more dorsal region), and by updating the action plan through the suppression of the movement (more ventral region). The fast detection of changes in the environment, i.e. unexpected shifts of attention can affect the duration of the stop process (Shulman et al., 2009; Salinas & Stanford, 2013). The role of dorsomedial frontal cortex (specifically pre-SMA) can be further related to other different aspects involved in the task as the conflict resolution (Nachev, Wydell, O'neill, Husain, & Kennard, 2007), the set-preparation for inhibition (Chikazoe et al., 2009) and the response threshold regulation (Stuphorn & Emeric, 2012). These processes are possibly more involved in promoting the behavioral adjustment necessary to optimize the performance in the different contexts, specifically in context in which inhibition demand is required or not. In the last years, resting state fMRI indicated rIFC be part of the ventral attentional network that supports the attentional reorienting to salient and behavioral relevant stimuli (Andrews-Hanna, Reidler, Sepulcre, Poulin, & Buckner, 2010; Fox, Corbetta, Snyder, Vincent, & Raichle, 2006; Raichle, MacLeod, Snyder, Powers, & Gusnard, 2001). Neuroimaging studies in ADHD populations have shown that these regions previously described were differently activated from controls when engaged in inhibitory tasks (Casey et al., 2007; Epstein et al., 2007; Rubia, Smith, Brammer, Toone, & Taylor, 2005; Rubia et al., 2008). In particular, the hypoactivation of the rIFC in ADHD is one of the most consistent observations between studies. A recent metanalysis (Cortese et al., 2012) showed that hypoactivation in ADHD children compared to controls are prevalent in the ventral attentional and frontoparietal networks, both possibly at work during movement suppression. Children with ADHD also showed different activations in motor and premotor regions compared to controls (Mostofsky et al., 2006; Suskauer et al., 2008).

Concerning the increment of RT found in both groups in tasks with inhibition demand, this effect could be read as a consequence of a change in the dynamic of the neural activity necessary to produce a movement. Indeed, when the probability to stop a movement increases, the pre-SMA and SMA could dispose a higher response threshold (at neural level) to produce a movement (Aron, 2011) or delay the onset of neural activity that generates the movement (Pouget et al., 2011). This means that population of neurons responsible for the generation of movement will have to fire "more" or will start to fire later when more control is necessary. In both cases, longer RTs will be observed. The proactive inhibition was also characterized by an increase in intra-individual variability (SD) only in the stop task in both groups. When the context

increases the level of conflict (between the tendencies to move and to stop) the neural mechanisms involved in responding and in inhibiting can be more variable within individuals (Vaurio, Simmonds, & Mostofsky, 2009).

In line with this hypothesis in a recent study it has been observed that the response time variability is related to the number of stop trials experienced in the recent trial history: the higher the number of stop trials the higher the response variability (Marcos et al., 2013). Neural signal predicting this relationship have been recorded in premotor cortex, and simulations experiments showed that these signal are the expression of a system able to monitors the trial history and updates the response times according to it. Anatomically this system could involve the dorsomedial frontal structures, like Pre-SMA. Therefore, the increased response variability in ADHD could be related to the different activation of structures implicated in the monitoring of the behavior (Mostofsky et al., 2006; Suskauer et al., 2008).

Conversely, a strong difference between ADHD and control groups was observed for the reactive control. The elongation of the SSRT in ADHD can be a sign of a deficiency in the prompt detection and/or in the change of motor plan through the suppression of the response, involving the rIFC. The same structure can be possibly involved also in promoting the proactive control but without the need to rapidly detect or adapt the motor plan.

Another critical result of our study is the higher intra-individual variability (SD) in ADHD group in the nostop and the stop task compared to controls. However, in the go–nogo and the go tasks groups did not differ in terms of SD.

In literature high intra-individual variability is consistently documented in ADHD compared to controls across different tasks (Di Martino et al., 2008; Geurts et al., 2008; Kuntsi & Klein, 2012; Scheres, Oosterlaan, & Sergeant, 2001). This phenomenon has been related to abnormal default network suppression (Castellanos et al., 2005; Fassbender et al., 2009). However, while this explanation accounts mostly for an increase of reaction time variability at low frequencies (Di Martino et al., 2008; Castellanos et al., 2005), the increase of response variability seems to be not specific to low frequencies only (Fair, Bathula, Nikolas, & Nigg, 2012; Karalunas, Huang-Pollock, & Nigg, 2012; Vaurio et al., 2009). In our study, an important difference across the tasks is the go signal appearance: in the go–nogo and in the go task the go signal changes (blue, green, yellow, red circle) while in the stop and nostop stop task the go signal is always the same (a white arrow in a blue circle). The presentation of always changing stimuli in go–nogo and in go task may increase the alertness during these tasks, promoting the default network suppression. The fluctuations of responses in ADHD are then reduced when the stimuli features change.

The observation that ADHD children showed impaired reactive inhibition but preserved proactive inhibition compared to controls can be useful to better define neuropsychological profiles in ADHD children. At the same time the observation of a dissociation between the two process can help in promoting new behavioral-cognitive therapeutic strategies and allow for more effective strategies for response control.

5. Conclusions

Reactive and proactive control of movement can be differentially affected in ADHD: ADHD children showed impaired reactive inhibition but preserved proactive inhibition compared to controls. The proactive control can be estimated by RT increase or by both RT and SD increase and it is strongly context dependent.

The physical appearance of the stimuli specifically affects ADHD responses: stimuli associated with change were faster response and had reduced intra-individual variability.

Differentiate reactive and proactive control is needed to better define neuropsychological profiles in ADHD children. This will help to define new behavioral-cognitive therapeutic strategies and have allowed for more accurate determination of strategies for response control.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ridd.2013.06.032.

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Il registro dell'ADHD: valutazione post-marketing del profilo beneficio-rischio dei farmaci e promozione dell'appropriatezza

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Riassunto. Introduzione. Obiettivo del Registro è stato quello di stimare il profilo beneficio/rischio del trattamento dell'iperattività con deficit di attenzione (ADHD) con atomoxetina e metilfenidato. **Metodi.** Studio osservazionale post-marketing, di fase IV. Prescrizione del farmaco a bambini e adolescenti affetti da ADHD di età compresa tra i 6 e i 18 anni nei centri di riferimento per l'ADHD accreditati dalle regioni italiane. **Risultati.** Da settembre 2007 a ottobre 2011, 1098 bambini e adolescenti sono stati trattati con metilfenidato e 951 con atomoxetina. 411 (21,5%) pazienti sono usciti dal registro: 274 trattati con atomoxetina e 167 con metilfenidato con un RR=1,4 (1,3-1,6) p<0,001 a svantaggio dell'atomoxetina. La durata del trattamento al momento dell'uscita dal registro, calcolata come tempo medio di ciascun gruppo di trattamento, è di 4,1 mesi per l'atomoxetina e 2 mesi per il metilfenidato. I pazienti trattati con atomoxetina hanno una maggiore probabilità di manifestare un evento avverso rispetto a quelli trattati con metilfenidato (RR=2,8; IC 95% 1,9-4,2). Il numero totale di eventi avversi gravi osservati è stato 110: 82 (75%) in pazienti trattati con atomoxetina e 28 (25%) in individui trattati con metilfenidato. Di questi, 98 hanno determinato l'interruzione del trattamento farmacologico con uscita dal registro. La probabilità di avere un evento avverso grave è maggiore tra i trattati con atomoxetina rispetto a quelli con metilfenidato (RR=2,8; IC 95% 1,8-4,2). Si sono verificati 14 eventi cardiovascolari, tutti risoltisi positivamente. Sono state riscontrate 69 alterazioni ECG con un RR=2,4 (IC 95% 1,4-4,2) che il metilfenidato provochi l'alterazione rispetto all'atomoxetina. È stata riscontrata un'incidenza di ideazione suicidaria di 4,5‰ casi, solo in pazienti trattati con atomoxetina. Le alterazioni epatiche si manifestano con una incidenza dell'1‰ in soggetti trattati con metilfenidato e 4‰ in quelli che ricevono atomoxetina. **Discussione.** Lo studio è stato condotto su una popolazione che rappresenta in maniera adeguata la popolazione pediatrica italiana. La prevalenza osservata di ADHD corrisponde a quella attesa in base ai dati di precedenti indagini epidemiologiche italiane, ma sensibilmente inferiore a quanto riportato nella letteratura scientifica internazionale. Il tasso di esposizione al trattamento farmacologico è simile a quello di altri paesi europei.

Parole chiave. ADHD, registro, sicurezza, trattamento multimodale.

ADHD Register: post-marketing evaluation of the benefit-risk profile of drugs and promotion of the appropriateness.

Summary. Introduction. The Register was aimed at assessing the benefit/risk profile of the treatment of attention deficit hyperactivity disorder (ADHD) with atomoxetine and methylphenidate. **Methods.** Post-marketing observational study, phase IV. Prescription medication to children and adolescents with ADHD aged between 6 and 18 years in the centres of reference for ADHD accredited by the Italian regions. **Results.** In the period from September 2007 to October 2011, 1098 children and adolescents were treated with methylphenidate and 951 with atomoxetine. 411 (21.5%) patients are released from the register: 274 treated with atomoxetine and 167 with methylphenidate, with a greater risk of discontinuation for atomoxetine: RR 1.4 (1.3-1.6) p<0.001. The length of treatment at the time of removal from the register is 4.1 months for atomoxetine and 2 months for methylphenidate. Patients treated with atomoxetine are more likely to experience an adverse event compared to those treated with methylphenidate (RR 2.8; 1.9-4.2). The total number of serious adverse events observed was 110: 82 (75%) patients treated with atomoxetine and 28 (25%) individuals treated with methylphenidate. For 98 patients with serious adverse events, the adverse event led to the interruption of treatment with exit from the registry. The chance of a serious adverse event among those treated with atomoxetine compared to those with methylphenidate is RR 2.8 (1.8-4.2). There have been 14 cardiovascular events, all grown positively. 69 were found with a ECG alterations, with an increased risk for methylphenidate (RR 2.4; 1.4-4.2). The incidence of suicidal ideation was 4.5/1000 patients treated with atomoxetine. Hepatic alterations occurred with an incidence of 1/1000 subjects treated with methylphenidate and 4/1000 of those who received atomoxetine. **Discussion.** The survey was carried out on a population which represents appropriately the paediatric population. The observed prevalence of ADHD corresponds to the expectation based on data from previous epidemiological investigations in Italy but considerably lower than what is reported in the international scientific literature. The rate of exposure to pharmacological treatments is similar to that of other European countries.

Key words. ADHD, multimodal treatment, register, safety.

Introduzione

La Consensus Conference italiana sulla sindrome da iperattività con deficit di attenzione (Attention Deficit Hyperactivity Disorder - ADHD), svoltasi a Cagliari nel marzo 2003, aveva richiamato l'attenzione sulla necessità di poter disporre di tutti gli strumenti diagnostici e terapeutici esistenti, di comprovato beneficio, per l'assistenza dei soggetti affetti dalla sindrome da deficit di attenzione e iperattività. I valori di prevalenza dell'ADHD desunti dalla letteratura internazionale oscillano dal 2% della Francia[1] all'8% negli USA[2]. Gli studi condotti in Italia dall'inizio degli anni Novanta, diffe-

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renti per setting, dimensioni e metodologia, mostrano prevalenze oscillanti tra lo 0,4% e il 3,6%. Si tratta perciò di una patologia che in Italia, assumendo il valore più basso, riguarderebbe oltre 30.000 bambini e adolescenti. Questo numero comprende i quadri clinici di ogni livello di gravità. I soggetti affetti da ADHD possono essere sottoposti a terapie: a) psico-sociali; b) farmacologiche (metilfenidato, atomoxetina); c) combinate (psico-comportamentali + farmacologiche). In questo contesto, la Commissione Unica del Farmaco (CUF) ha riclassificato, nell'ottobre 2003, il metilfenidato spostandolo dalla tabella I (Sostanze stupefacenti e psicotrope) alla tabella IV (Sostanze suscettibili di impiego per la produzione di sostanze stupefacenti o psicotrope) del D.P.R. n. 309/1990 e ne ha approvato l'uso per il trattamento dell'ADHD mediante predisposizione di piani terapeutici individuali.

I farmaci registrati in Italia per la terapia farmacologica dell'ADHD sono il metilfenidato, somministrato (in base al peso corporeo), mediamente a 0,3-0,6 mg/kg/dose in due-tre dosi-die, e l'atomoxetina, mediamente a 1,2 mg/kg/dose in singola dose giornaliera (raramente in due dosi dimezzate).

Le revisioni sistematiche[3-5] dei numerosi studi clinici condotti sugli psicostimolanti hanno dimostrato l'efficacia di questa categoria terapeutica nel migliorare il quadro clinico, riducendo il numero e la gravità dei sintomi. Anche le terapie non farmacologiche si sono dimostrate efficaci[6-10]. Tuttavia, i migliori risultati terapeutici si raggiungono combinando i due tipi di intervento[11,12]. Alcune osservazioni preliminari mostrano che l'omeopatia e la medicina complementare e alternativa (CAM) possono dare un contributo in termini di efficacia[13,14]. Dubbi permangono sul profilo di sicurezza dei farmaci per l'ADHD, in primo luogo per il metilfenidato, considerato un farmaco con elevato rischio di eventi cardiovascolari[4,15-17]. L'autorizzazione all'immissione in commercio del metilfenidato e dell'atomoxetina in Italia, dispensabili da parte del Servizio Sanitario Nazionale (SSN), ha reso necessario il monitoraggio dell'uso di queste sostanze nella popolazione pediatrica affetta da ADHD, trattata con questi farmaci da soli o in associazione con terapie non farmacologiche, al fine di garantirne la sicurezza d'uso. Il metilfenidato appartiene al gruppo delle amfetamine e ciò spiega le remore all'uso nei minori. L'atomoxetina, invece, è una molecola appartenente al raggruppamento degli SNRI, inibitori selettivi della ricaptazione della noradrenalina. Sono stati autorizzati per il trattamento dell'ADHD[18] nella fascia d'età 6-18 anni nell'aprile 2007 e il 21 giugno dello stesso anno è stato attivato il registro italiano dell'ADHD, progettato dal CINECA e gestito dall'Istituto Superiore di Sanità su mandato dell'Agenzia Italiana del Farmaco (AIFA). Gli obiettivi del registro sono, nell'ordine: a) valutare la sicurezza dei farmaci; b) garantire una diagnosi accurata; c) garantire una terapia adeguata al quadro clinico della sindrome[19]. Questo strumento, inoltre, doveva rappresentare una garanzia nei confronti di quella parte di opinione pubblica contraria all'uso degli psicofarmaci nella popolazione in età evolutiva.

Metodi

Tutti i bambini con sospetto ADHD di un territorio vengono inviati ad un centro di riferimento che è il solo autorizzato a prescrivere i farmaci. Nel registro sono inclusi solo i bambini ai quali viene prescritta la terapia farmacologica con metilfenidato o atomoxetina. La diagnosi si basa sui criteri del DSM-IV[20,21] o, in Emilia-Romagna, sui criteri dell'ICD 10. I bambini, prima di assumere la dose-test di metilfenidato o di iniziare la titolazione dell'atomoxetina, vengono sottoposti a un ECG basale. È previsto un follow-up ogni sei mesi con ECG, visita clinica, somministrazione dei test utilizzati per porre la diagnosi e di test di valutazione della gravità del quadro clinico (ADHD rating scale, Clinical Global Impression-Severity - CGI-S), che rappresentano le misure di esito principali di efficacia insieme al grado di integrazione scolastica, sociale e familiare del paziente. I principali indicatori di rischio[15] sono rappresentati dall'allungamento patologico del tratto QT dell'ECG, da segni di insufficienza epatica grave, dall'ideazione suicidaria, da convulsioni, dal rallentamento della velocità di crescita staturale e dalla perdita di almeno 5 punti dell'indice di massa corporea (BMI) in un semestre in soggetti con BMI basale normale (punteggio 18-25). L'intervento prevede l'integrazione di diverse figure professionali e strutture: pediatri di libera scelta (PLS), neuropsichiatri dell'infanzia e adolescenza (NPIA), insegnanti e psicologi. Le strutture coinvolte sono: la scuola, i servizi territoriali di neuropsichiatria infantile, i centri di riferimento per l'ADHD, le strutture specialistiche di secondo livello accreditate a predisporre piani terapeutici multimodali[18-22] (trattamento psico-sociale e farmacologico) (figura 1). Il trattamento multimodale vede l'intervento sul nucleo familiare come priorità[6-8]; il parent e il child training rappresentano i trattamenti più numerosi (tabella 1) dopo il counseling, che è un intervento diffuso ma poco specifico. Tutti i pazienti iscritti nel registro vengono seguiti nel tempo[23] per raccogliere le informazioni sugli eventi avversi[15] e sull'efficacia del trattamento multimodale.

I centri di riferimento sono stati accreditati dalle Autorità sanitarie regionali in base ai criteri forniti dall'Istituto Superiore di Sanità con la finalità di garantire una presa in carico globale del soggetto affetto da ADHD; operano sulla base del protocollo scientifico e delle procedure operative standard[24], redatti da un comitato scientifico.

Il centro di riferimento è responsabile della diagnosi che si basa sui criteri definiti dal protocollo italiano dell'ADHD, che riprende il Manuale di Diagnostica e Statistica dei Disordini Mentali-IV revisione (DSM-IV)[20,21] ed è anche responsabile della verifica dell'appropriatezza del piano terapeutico. La diagnosi si basa sull'uso di più di uno o più test clinici: il colloquio clinico strutturato è usato nel 97% dei casi, seguito dal test K-SADS-PL nel 62%, dallo SNAP_IV nel 51% e dall'ADHD rating scale nel 25%.

Il pediatra è responsabile del paziente per quanto riguarda la visita mensile, la prescrizione dei farmaci in base al piano terapeutico e la rilevazione e segnalazione degli eventi avversi. La terapia comportamentale è assicurata dai servizi territoriali di neuropsichiatria dell'infanzia e dell'adolescenza. Il centro di riferimento fa da interfaccia tra pediatra e servizio territoriale di neuropsichiatria dell'infanzia e dell'adolescenza.

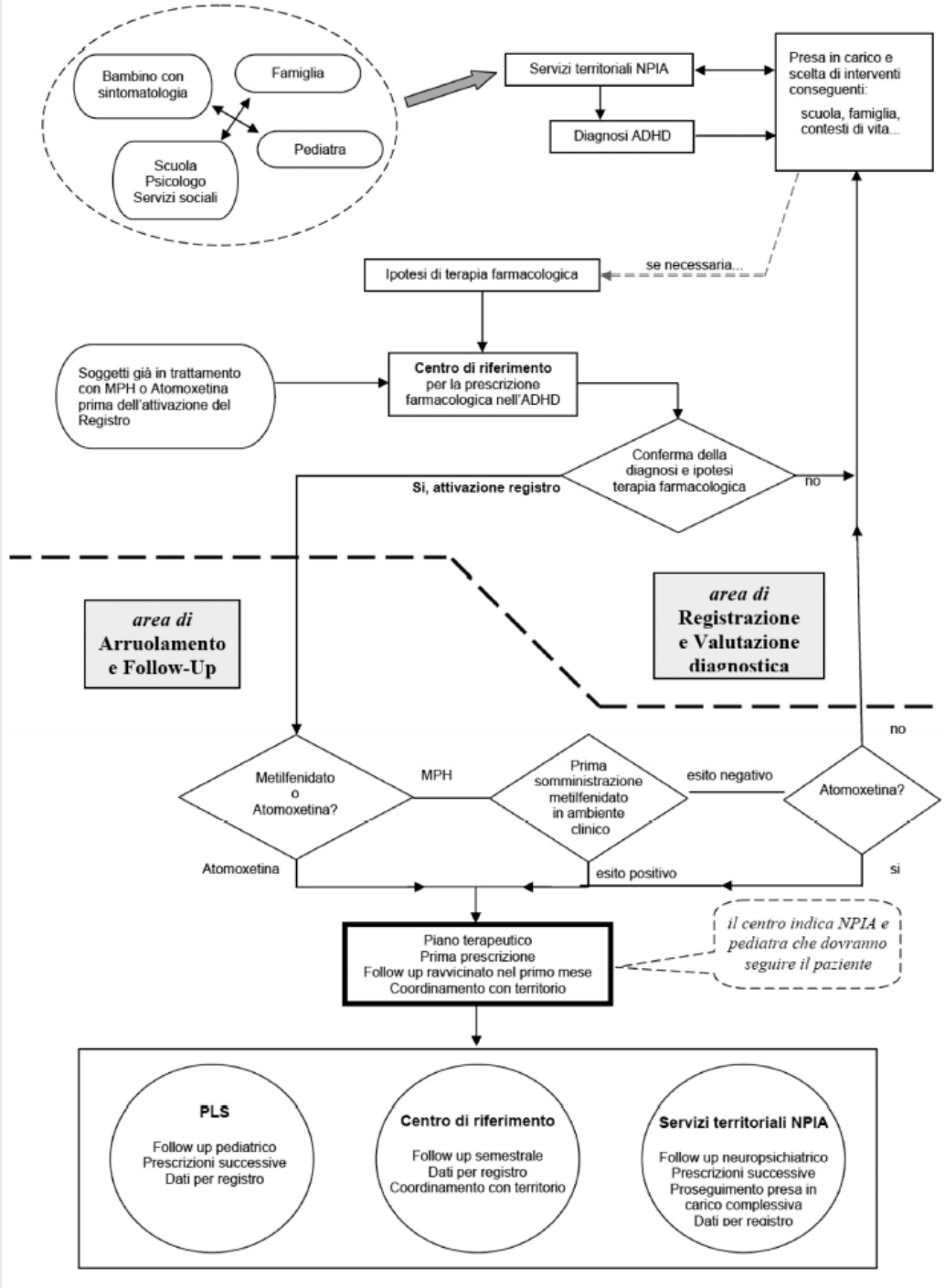

Figura 1. Struttura del modello assistenziale prefigurato per i pazienti con ADHD.

Tabella 1. *Tipologia del trattamento multimodale nei soggetti che hanno ricevuto un trattamento farmacologico*

Intervento*	Farmaco prescritto			
	Metilfenidato	%	Atomoxetina	%
	(n=1098)		(n=951)	
Child training	208	18,9	251	26,4
Parent training	256	23,3	343	36,1
Cognitivo comportamentale	258	23,5	215	22,6
Terapia familiare	68	6,2	89	9,4
Psicoterapia psicodinamica	78	7,1	109	11,5
Counseling	616	56,1	531	55,8
Altro	271	24,7	203	21,3

*La somma delle percentuali di ciascun intervento è maggiore del 100% in quanto un soggetto può avere ricevuto più trattamenti

Risultati

Complessivamente sono stati arruolati nel registro 2049 bambini e adolescenti, di cui 1098 hanno assunto metilfenidato e 951 atomoxetina (tabella 2). I soggetti arruolati sono per l'88,6% maschi e per l'11,4% femmine. La classe d'età 10-13 anni è la più numerosa, con circa il 40% della coorte.

I bambini che afferiscono ai centri di riferimento sono circa il 10% della popolazione residente di 6-18 anni d'età. La prevalenza osservata di ADHD oscilla tra 1,1% e 1,3%. Il tasso di esposizione ai farmaci specifici è compreso tra 7% e 16,7%[25]. Una quota di bambini con diagnosi di ADHD variabile tra il 58,2% e il 65% ha ricevuto terapie psico-sociali. La sintomatologia che fa attivare le procedure diagnostiche è rappresentata dal deficit di attenzione nella totalità dei casi, seguito da iperattività (94%) e impulsività (88%). I problemi scolastici sono presenti nel 64% dei soggetti ai quali è stata diagnosticata la sindrome.

La stratificazione per tipo di trattamento mostra che il 46,4% dei pazienti è stato trattato con atomoxetina e 53,6% con metilfenidato (tabella 3). La prescrizione di questi farmaci è cambiata nel corso degli anni con un progressivo spostamento dall'atomoxetina al metilfenidato. Il dosaggio raccomandato di metilfenidato è di 0,3-0,6 mg/kg/dose per due/tre dosi/die mentre per l'atomoxetina si inizia con un dosaggio di 0,5 mg/kg/die fino a raggiungere un dosaggio medio di mantenimento di 1,2 mg/kg/die. Dai dati del registro osserviamo che la dose media di atomoxetina è 38,5 mg/die (±20,5) e quella di metilfenidato è 18,4 (±10,5) mg/die.

Tabella 2. *Distribuzione degli utilizzatori di atomoxetina e metilfenidato per classi di età*

Classe d'età	Metilfenidato		Atomoxetina		Totale	
	n	%	n	%	n	%
6-7 anni	241	59,9	161	40,1	402	100
8-9 anni	318	57,7	233	42,3	551	100
10-13 anni	427	51,5	403	48,5	830	100
14-17 anni	112	42,1	154	57,9	266	100
Totale	1098	53,6	951	46,4	2049	100

Tabella 3. *Terapia farmacologica per sottotipo di ADHD*

Terapia prescritta	Tipo ADHD						Totale	
	I	%	C	%	H	%	n	%
Atomoxetina	116	12,2	784	82,4	51	5,4	951	100
Metilfenidato	125	11,4	941	85,7	32	2,8	1098	100
Totale	241	11,8	1725	84,2	83	4,0	2049	100

Legenda: I= Inattentivo; C= Combinato; H= Iperattivo

441 (21,5%) soggetti arruolati sono usciti dal registro: 274/951 trattati con atomoxetina pari al 28,8%, e 167/1098 con metilfenidato pari al 15,2%. I motivi di uscita sono rappresentati da: inefficacia, eventi avversi, decisione del paziente e della famiglia, scarsa compliance al follow-up e altri motivi (tabella 4). Un singolo paziente può contribuire anche con più di un motivo di uscita, per es., decisione del paziente ed evento avverso. In questo caso il manifestarsi di un evento avverso, di tipologia tale da non giustificare l'uscita dalla coorte, ha determinato la decisione del paziente di interrompere l'assunzione del farmaco.

La durata del trattamento al momento dell'uscita dal registro, calcolata come tempo medio di ciascun gruppo di trattamento, è di 4,1 mesi per l'atomoxetina e 2 mesi per il metilfenidato.

In 66 casi si è verificata l'interruzione precoce del trattamento, prima del completamento del piano terapeutico, perché si assisteva a un miglioramento significativo e persistente del quadro clinico: 22/1098 casi (2%) erano trattati con metilfenidato e 44/951 (4,6%) con atomoxetina.

Gli effetti collaterali più comuni sono stati inappetenza, irritabilità e cefalea. Complessivamente sono stati registrati 301 eventi in pazienti che assumevano metilfenidato e 273 in quelli esposti all'atomoxetina.

Il numero totale di pazienti con eventi avversi gravi (SAE) osservati è stato 90: 60 (66,7%) trattati con atomoxetina, 26 (28,9%) trattati con metilfenidato e 4 (4,4%) trattati con entrambi i farmaci. Di questi 90 pazienti, 66 hanno interrotto il trattamento farmacologico con uscita dal registro: 14 trattati con metilfenidato e 52 con atomoxetina. Poiché alcuni pazienti hanno manifestato più di un evento avverso, il totale di SAE è di 120. L'atomoxetina ha un RR=1,3 (IC 95% 0,8-1,9) di causare un SAE rispetto al metilfenidato.

Il rischio di eventi cardiovascolari correlati all'uso dei farmaci per ADHD è un argomento dibattuto nella comunità scientifica. Nella coorte del registro italiano si sono verificati 14 eventi clinicamente manifesti (tabella 6) tutti risoltisi positivamente: in 5 casi con la sospensione del farmaco e nei restanti 9 casi con la remissione spontanea. Sono stati riscontrati 69 casi di alterazioni ECG con un RR=2,4 (IC 95% 1,4-4,2) che il metilfenidato provochi l'alterazione rispetto all'atomoxetina (tabella 7). Complessivamente, si può affermare che il rischio di eventi cardiovascolari associati ai farmaci per l'ADHD è basso. In tutti questi casi i pazienti non hanno interrotto il trattamento farmacologico. I casi di blocco di branca erano asintomatici, così come i casi di tachicardia, bradicardia, aritmia sinusale. I casi di allungamento del tratto QT non hanno mai raggiunto livelli patologici (400 msec). In tutti i casi è stata mantenuta la terapia farmacologica con un attento monitoraggio cardiologico.

È stata riscontrata una incidenza di ideazione suicidaria di 4,5‰ casi solo in pazienti trattati con atomoxetina. Le alterazioni epatiche si manifestano con una incidenza dell'1‰ in soggetti trattati con metilfenidato e del 4‰ in quelli che ricevono atomoxetina (tabella 5).

Tabella 4. *Motivi di interruzione del trattamento farmacologico*

	Metilfenidato		Atomoxetina		Totale	
	(n=1098)	%	(n=951)	%	(n=2049)	%
Inefficacia	22	2	36	3,8	58	2,8
Eventi avversi	30	2,7	68	7,2	98	4,8
Decisione del paziente/genitori o del sanitario	63	5,7	122	12,8	185	9
Persi al follow-up	33	3	33	3,5	66	3,2
Altri motivi	19	1,7	15	1,6	34	1,7
Totale	167	15,2	274	28,8	441	21,5

Tabella 5. *Eventi avversi gravi verificatisi per farmaco*

	Metilfenidato		Atomoxetina		RR (95% IC)*
	(n=1098)	%	(n=951)	%	
Ideazione suicidaria	-	-	4	0,4	-
Problemi psichiatrici	5	0,5	19	2,0	3,8 (1,7-8,5)
Problemi epatici	1	0,1	4	0,4	-
Convulsioni	2	0,2	2	0,2	-
Totale	12	1,1	53	5,6	5,1 (2,7-9,5)

* RR = rischio relativo; IC = intervallo di confidenza

Tabella 6. *Eventi avversi cardiovascolari gravi*

SAE Cardiovascolari	Metilfenidato	Atomoxetina
Ipertensione	2	1
Ipotensione	1	-
Tachicardia	2	2
Disturbi della frequenza/ritmo	-	2
Patologie cardiache	-	2
Sincope vaso-vagale	1	-
Embolia aortica	1	-
Totale	7	7

Tabella 7. *Eventi in soggetti che hanno sviluppato un'alterazione all'elettrocardiogramma*

Tipo di alterazione ECG	Metilfenidato		Atomoxetina	
	(n=1098)	%	(n=951)	%
Blocco incompleto di branca dx	16	1,5	4	0,4
Tachicardia sinusale	7	0,6	5	0,5
Bradicardia sinusale	8	0,7	-	
Aritmia sinusale	16	1,5	5	0,5
Allungamento tratto QT	2	0,2	3	0,3
Alterazioni della conduzione	2	0,2	1	0,1
Totale	51	4,6	18	1,9

Discussione

Il registro italiano dell'ADHD ha raggiunto l'obiettivo principale per cui è stato creato: valutare la sicurezza dei farmaci approvati per il trattamento della sindrome mediante un regime di farmacovigilanza attiva nel corso dei due anni successivi all'autorizzazione alla commercializzazione in Italia. Sulla base dei dati raccolti, è emerso che il profilo beneficio/rischio è complessivamente favorevole per entrambi i farmaci e leggermente migliore per il metilfenidato rispetto all'atomoxetina anche se in misura non statisticamente significativa. In particolare, il profilo del rischio cardiovascolare è risultato migliore di quanto atteso sulla base dei dati di letteratura: alcuni degli eventi osservati, quali il blocco di branca destra, sono clinicamente silenti e ininfluenti sulle condizioni generali del soggetto. L'esperienza italiana di effettuare di routine l'ECG a tutti i pazienti prima di iniziare il trattamento farmacologico e, successivamente ogni sei mesi, è stato ripreso dall'Agenzia Europea del Farmaco (European Medicines Agency - EMA) che ha emanato una raccomandazione in tal senso. Abbiamo, altresì, rilevato un'incidenza di ideazione suicidaria, nel gruppo trattato con atomoxetina, simile a quanto segnalato dalla FDA[16]. Il registro ha reso più omogenea la diagnosi attraverso l'uso di procedure operative standard e di un protocollo per la gestione dei soggetti affetti da ADHD. Inoltre, sono stati messi a disposizione dei neuropsichiatri dell'infanzia, via web, i test diagnostici più affidabili. Anche l'appropriatezza nel ricorso al trattamento multimodale è progressivamente cresciuta insieme a una maggiore dimestichezza nell'uso dei farmaci.

Rispetto ad altre esperienze europee, il modello italiano ha il pregio di definire un percorso univoco: dal "segnale d'allarme" - rilevato dalla famiglia, dalla scuola o dal pediatra - attraverso la diagnosi, il trattamento di prima linea (non farmacologico), il trattamento multimodale.

L'esperienza italiana si è rivelata utile anche per l'EMA che ha inserito, nel programma FP 7 della Commissione europea, un bando per la valutazione del profilo di sicurezza globale del metilfenidato, principio attivo di gran lunga più utilizzato per il trattamento dell'ADHD.

Il registro mostra anche numerosi aspetti critici, di cui elenchiamo di seguito i principali. Un numero consistente di bambini e adolescenti è in trat-

tamento con formulazioni di metilfenidato a rilascio prolungato. Tuttora, questi cittadini acquistano i farmaci all'estero e non figurano tra gli arruolati nel registro, determinando così una sottostima della prevalenza dell'ADHD nella popolazione in età evolutiva e del tasso di esposizione al trattamento farmacologico.

Il registro limita il monitoraggio al 18° anno d'età. In realtà ci sono adulti da tempo in trattamento farmacologico e anche gli adolescenti arruolati nel registro non cesseranno l'assunzione del farmaco al compimento della maggiore età. Si tratta di una criticità sul piano regolatorio cui dovrà esser data soluzione in tempi ragionevoli, estendendo l'indicazione d'uso oltre la soglia del 18° anno d'età. Il numero di servizi, le dimensioni e l'efficienza variano notevolmente da regione a regione. In generale la situazione al Centro-Nord è migliore mentre è decisamente critica al Sud e nelle Isole. Non ci sono criteri omogenei di programmazione dei servizi, né linee-guida comuni e condivise da tutte le regioni per la definizione delle attività in base a una scala di priorità.

L'esperienza clinica dei centri si caratterizza per una notevole variabilità cui si aggiunge la novità organizzativa rappresentata dal "modello ADHD". Inoltre, la dotazione di personale, strumenti di lavoro e tecnologie è, spesso, scarsa. Solo in alcune regioni i servizi di neuropsichiatria dell'infanzia e dell'adolescenza sono organizzati per lavorare in rete vasta. Nella maggior parte, il modello organizzativo è quello di unità autonome e, entro certi limiti, autosufficienti. Difficoltà nella messa in rete e nell'accettazione di un modello a matrice doppia: verticale per il percorso diagnostico-terapeutico e orizzontale per la gestione del paziente arruolato nel registro.

Le associazioni di categoria, Federazione Italiana Medici Pediatri e Associazione Culturale Pediatri, hanno fin dall'inizio sostenuto il progetto. Non sempre questa disponibilità ha trovato i singoli pediatri collaboranti. Certamente l'età e, di conseguenza, l'attitudine a utilizzare strumenti informatici gioca un ruolo importante. Ai pediatri, peraltro, sono state rivolte numerose iniziative di formazione, soprattutto a livello locale, in quasi tutte le regioni italiane. L'attività del registro, spesso, si colloca in una situazione già critica per i servizi di neuropsichiatria dell'infanzia e dell'adolescenza, oberati da lunghe liste di attesa cui vanno ad aggiungersi i pazienti "arruolabili" nel registro.

La gestione dei rapporti con i media è stata caratterizzata dalle difficoltà tipiche di persone professionalmente dedicate ad altri compiti e perciò a disagio nel trasmettere messaggi sintetici, chiari e non strumentalizzabili.

Il registro rappresenta il primo esempio di rete nazionale formale in neuropsichiatria infantile. Essere riusciti a creare un network nazionale che include servizi territoriali di neuropsichiatria infantile, pediatri di famiglia, centri ospedalieri, universitari e IRCCS è un successo.

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