



NEWSLETTER



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**PREVALENZA DELL'ADHD IN UNA POPOLAZIONE PEDIATRICA
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http://www.medicoebambino.com/?id=RIC1210_10.html.

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**CARDIOVASCULAR MEASURES IN CHILDREN AND ADOLESCENTS
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J Child Adol Psychopharmacol 2012;22:423-431.

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3. Segnalazioni

Corso di Alta Formazione

**"L'alunno con ADHD (disturbo dell'attenzione e/o iperattività)
a scuola: Costruzione del Piano Didattico Personalizzato
e gestione in classe"**

Facoltà di Psicologia, SPAEE – Università Cattolica Sacro Cuore

8 marzo e 10 maggio 2013; Brescia (BS)

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BIBLIOGRAFIA ADHD DICEMBRE 2012

ADHD Atten Deficit Hyperact Disord. 2012;4:189-97.

PARENTAL EFFICACY AND CHILD BEHAVIOR IN A COMMUNITY SAMPLE OF CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD).

Primack BA, Hendricks KM, Longacre MR, et al.

Most studies of attention-deficit hyperactivity disorder (ADHD) youth have obtained data from the perspective of either children or parents, but not both simultaneously. The purpose of this study was to examine child and parent perspectives on parenting in a large community-based sample of children with and without ADHD. We identified children in grades 4-6 and their parents through surveys administered to a random sample of public schools. We used multivariable logistic regression to determine independent associations between child and parent characteristics and the presence of ADHD while controlling for covariates and clustering by school. Sufficient data were achieved for 2,509 child/parent dyads. Ten percent of youths (n = 240) had been diagnosed with ADHD. Compared with those without ADHD, those with ADHD were more commonly male (67.9 vs. 48.0 %, p <.001) and age 12 or over (16.3 vs. 10.3 %). After adjusting for covariates and clustering, compared to children without ADHD, children with ADHD were significantly more likely to report lower self-regulation (OR = 0.68, 95 % CI = 0.53, 0.88) and higher levels of rebelliousness (OR = 2.00, 95 % CI = 1.52, 2.69). Compared with parents whose children did not have ADHD, parents of children with ADHD rated their overall parental efficacy substantially lower (OR = 0.23, 95 % CI = 0.15, 0.33). However, child assessment of parenting style was similar by ADHD. Despite the internal challenges community-based youth with ADHD face, many parents of ADHD youth exhibit valuable parental skills from the perspective of their children. Feedback of this information to parents may improve parental self-efficacy, which is known to be positively associated with improved ADHD outcomes.

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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.

ADHD Atten Deficit Hyperact Disord. 2012;4:205-12.

ANALYSIS OF BRAIN METABOLISM BY PROTON MAGNETIC RESONANCE SPECTROSCOPY (1H-MRS) IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SUGGESTS A GENERALIZED DIFFERENTIAL ONTOGENIC PATTERN FROM CONTROLS.

Arcos-Burgos M, Londono AC, Pineda DA, et al.

Attention-deficit/hyperactivity disorder (ADHD) is the most common behavioral disorder of childhood. Preliminary studies with proton magnetic resonance spectroscopy (1H-MRS) of the brain have reported differences in brain metabolite concentration-to-Cr ratios between individuals with ADHD and unaffected controls in several frontal brain regions including anterior cingulate cortex. Using multivoxel 1H-MRS, we compared 14 individuals affected with ADHD to 20 individuals without ADHD from the same genetic isolate. After controlling by sex, age, and multiple testing, we found significant differences at the right posterior cingulate of the Glx/Cr ratio density distribution function between ADHD cases and controls ($P < 0.05$). Furthermore, we found several interactions of metabolite concentration-to-Cr ratio, age, and ADHD status: Ins/Cr and Glx/Cr ratios at the left posterior cingulate, and NAA/Cr at the splenius, right posterior cingulate, and at the left posterior cingulate. We also found a differential metabolite ratio interaction between ADHD cases and controls for Ins/Cr and NAA/Cr at the right striatum. These results show that: (1) NAA/Cr, Glx/Cr, and Ins/Cr ratios, as reported in other studies, exhibit significant differences between ADHD cases and controls; (2) differences of these metabolite ratios between ADHD cases and controls evolve in specific and recognizable patterns throughout age, a finding that replicates previous results obtained by structural MRI, where is demonstrated that brain ontogeny follows a different program in ADHD cases and controls; (3) Ins/Cr and NAA/Cr ratios, at the right striatum, interact in a differential way between ADHD cases and controls. As a whole, these results replicate previous 1H-MRS findings and add new intriguing differential metabolic and ontogeny patterns between ADHD cases and controls that warrant further pursue.

ADHD Atten Deficit Hyperact Disord. 2012;4:199-204.

FATTY ACIDS IN ADHD: PLASMA PROFILES IN A PLACEBO-CONTROLLED STUDY OF OMEGA 3/6 FATTY ACIDS IN CHILDREN AND ADOLESCENTS.

Johnson M, Mansson JE, Ostlund S, et al.

The aim of this study was to assess baseline levels and changes in plasma fatty acid profiles in children and adolescents with ADHD, in a placebo-controlled study with Omega 3/6 supplementation, and to compare with treatment response. Seventy-five children and adolescents aged 8-18 years with DSM-IV ADHD were randomized to 3 months of Omega 3/6 (Equazen eye q) or placebo, followed by 3 months of open phase Omega 3/6 for all. n-3, n-6, n-6/n-3 ratio, EPA and DHA in plasma were measured at baseline, 3 and 6 months. Subjects with more than 25 % reduction in ADHD symptoms were classified as responders. At baseline, no significant differences in mean fatty acid levels were seen across active/placebo groups or responder/non-responder groups. The 0-3 month changes in all parameters were significantly greater in the active group ($p < 0.01$). Compared to non-responders, the 6-month responders had significantly greater n-3 increase at 3 months and decrease in n-6/n-3 ratio at 3 and 6 months ($p < 0.05$). Omega 3/6 supplementation had a clear impact on fatty acid composition of plasma phosphatidyl choline in active versus placebo group, and the fatty acid changes appear to be associated with treatment response. The most pronounced and long-lasting changes for treatment responders compared to non-responders were in the n-6/n-3 ratio.

ADHD Atten Deficit Hyperact Disord. 2012;4:167-77.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER AND CARDIAC VAGAL CONTROL: A SYSTEMATIC REVIEW.

Rash JA, Aguirre-Camacho A.

Attention-deficit hyperactivity disorder (ADHD) is characterized by behavioural disinhibition, deficient emotional self-regulation, inattention, and hyperactivity. The constellation of deficits found in children with ADHD implicates autonomic dysregulation characterized by deficient control of the heart by parasympathetic influences. While it is generally assumed that autonomic regulation of the heart is

impaired during ADHD, the information pertaining to this dysregulation is limited. A systematic review of three databases was conducted between January and March 2012 for peer reviewed publications examining the relationship between cardiac vagal control (CVC) and ADHD without comorbid psychopathology. 19 articles were reviewed with only 6 meeting inclusion criteria. Findings were not unanimous but suggested that children with unmedicated ADHD experienced lower levels of CVC than did healthy controls. It was difficult to evaluate whether children with ADHD exhibited a different pattern of withdrawal and application of CVC than did normal controls. Findings suggested CVC reactivity depended on the task employed but children with ADHD experienced dampened CVC reactivity during tasks that involved self-regulation and emotion regulation. Finally, medication acted to correct the autonomic imbalance experienced by children with ADHD but did not bring this imbalance into normal levels. Given that so few studies were identified, no firm conclusions can be made, and there is a clear need for additional research in this area. Recommendations for future research are discussed.

ADHD Atten Deficit Hyperact Disord. 2012;4:179-87.

TO WHAT EXTENT ARE TASK-SWITCHING DEFICITS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER INDEPENDENT OF IMPAIRED INHIBITION?

Rauch WA, Gold A, Schmitt K.

Executive functions, higher-order cognitive functions needed for goal-directed behavior, have been studied extensively in the search for endophenotypes for ADHD, yet results have been inconclusive. We examine the performance of children with ADHD in task switching as an as yet understudied potential endophenotype. A group of 20 children with ADHD and a group of 23 children without ADHD (ages 7-12) performed a task-switching paradigm and a Go/No-Go Task. Children with ADHD displayed significantly greater specific switch costs, that is, compared to control children they were especially impaired directly after task switches. There were no group differences with respect to the general switch costs, which are estimated by comparing performance on single task blocks to the block where both tasks are intermixed. Specific switch costs and Go/No-Go error rate were significantly correlated; yet, group differences in the task-switching paradigm remained significant even when inhibition was controlled for. This pattern of results suggests that children with ADHD are neither generally impaired in executive function nor only impaired with respect to inhibition. Instead, they display a highly specific deficit with regard to the flexible suppression and amplification of different task rules according to the context. Our conclusion that task switching has the potential to be added to the list of ADHD endophenotypes is strengthened by the independence of task-switching deficits and inhibition.

Arch Gen Psychiatry. 2012;69:1295-303.

CLINICAL AND FUNCTIONAL OUTCOME OF CHILDHOOD ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER 33 YEARS LATER.

Klein RG, Mannuzza S, Ramos Olazagasti MA, et al.

Context: Prospective studies of childhood attention-deficit/hyperactivity disorder (ADHD) have not extended beyond early adulthood.

Objective: To examine whether children diagnosed as having ADHD at a mean age of 8 years (probands) have worse educational, occupational, economic, social, and marital outcomes and higher rates of ongoing ADHD, antisocial personality disorder (ASPD), substance use disorders (SUDs), adult-onset psychiatric disorders, psychiatric hospitalizations, and incarcerations than non-ADHD comparison participants at a mean age of 41 years.

Design: Prospective, 33-year follow-up study, with masked clinical assessments.

Setting: Research clinic.

Participants: A total of 135 white men with ADHD in childhood, free of conduct disorder, and 136 men without childhood ADHD (65.2% and 76.4% of original cohort, respectively).

Main Outcome Measures: Occupational, economic, and educational attainment; marital history; occupational and social functioning; ongoing and lifetime psychiatric disorders; psychiatric hospitalizations; and incarcerations.

Results: Probands had significantly worse educational, occupational, economic, and social outcomes; more divorces; and higher rates of ongoing ADHD (22.2% vs 5.1%, $P < .001$), ASPD (16.3% vs 0%, $P < .001$), and SUDs (14.1% vs 5.1%, $P = .01$) but not more mood or anxiety disorders ($P = .36$ and $.33$) than did comparison participants. Ongoing ADHD was weakly related to ongoing SUDs ($\phi = 0.19$, $P = .04$), as well as ASPD with SUDs ($\phi = 0.20$, $P = .04$). During their lifetime, probands had significantly more ASPD and SUDs but not mood or anxiety disorders and more psychiatric hospitalizations and incarcerations than comparison participants. Relative to comparisons, psychiatric disorders with onsets at 21 years or older were not significantly elevated in probands. Probands without ongoing psychiatric disorders had worse social, but not occupational, functioning.

Conclusions: The multiple disadvantages predicted by childhood ADHD well into adulthood began in adolescence, without increased onsets of new disorders after 20 years of age. Findings highlight the importance of extended monitoring and treatment of children with ADHD.

Arts Psychother. 2013;40:37-44.

SOCIAL COMPETENCE INTERVENTION PROGRAM (SCIP): A PILOT STUDY OF A CREATIVE DRAMA PROGRAM FOR YOUTH WITH SOCIAL DIFFICULTIES.

Guli LA, Semrud-Clikeman M, Lerner MD, et al.

This study explored the effects of participation in the Social Competence Intervention Program (SCIP), an innovative creative drama-based group intervention, of children diagnosed with autism spectrum disorder (ASD), nonverbal learning disability (NLD) and/or attention deficit hyperactivity disorder (ADHD). Eighteen participants in SCIP were compared to a clinical control group of 16 on changes in measures of social perception, social competence, and naturalistic observed social behavior. Hierarchical multiple regression model was used for all primary quantitative analyses. Interviews were conducted post-treatment to provide qualitative data. The treatment group showed significant improvement in key domains of observed social behavior in a natural setting compared to the clinical control group. Parents and children in the SCIP condition reported multiple positive changes in social functioning. These findings provide preliminary support for the use of a creative drama program for children with social competence deficits related to social perception problems.

Behav Ther. 2012 Dec;43:862-75.

DOES A POSITIVE BIAS RELATE TO SOCIAL BEHAVIOR IN CHILDREN WITH ADHD?

Linnea K, Hoza B, Tomb M, et al.

This study examines whether positively biased self-perceptions relate to social behaviors in children with attention-deficit/hyperactivity disorder (ADHD) as compared to control children. The social behaviors of children with ADHD ($n = 87$) were examined relative to control children (CTL; $n = 38$) during a laboratory-based dyadic social interaction task. Children with ADHD were sub-grouped into those with a positive illusory bias (PIB) in their self-perceptions (ADHD+PIB) versus those without such a bias (ADHD PIB). Using a behavioral coding system adapted for this study, ADHD+PIB, ADHD PIB, and CTL participants were compared on objectively coded social behaviors occurring within the context of the social interaction task. Whereas both ADHD groups displayed more disruptive behavior than controls, only the ADHD + PIB group displayed less prosocial behavior and less effortful behavior. This study breaks new ground by examining positively biased self-perceptions as they relate to social behavior in children with ADHD and provides promising new insight into the social problems experienced by these children.

Behav Brain Funct. 2012;8.

POSSIBLE EFFECT OF NOREPINEPHRINE TRANSPORTER POLYMORPHISMS ON METHYLPHENIDATE-INDUCED CHANGES IN NEUROPSYCHOLOGICAL FUNCTION IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER .

Park S, Kim JW, Yang YH, et al.

Background: Dysregulation of noradrenergic system may play important roles in pathophysiology of attention-deficit/hyperactivity disorder (ADHD). We examined the relationship between polymorphisms in the norepinephrine transporter SLC6A2 gene and attentional performance before and after medication in children with ADHD.

Methods: Fifty-three medication-naïve children with ADHD were genotyped and evaluated using the continuous performance test (CPT). After 8-weeks of methylphenidate treatment, these children were evaluated by CPT again. We compared the baseline CPT measures and the post-treatment changes in the CPT measures based on the G1287A and the A-3081T polymorphisms of SLC6A2.

Results: There was no significant difference in the baseline CPT measures associated with the G1287A or A-3081T polymorphisms. After medication, however, ADHD subjects with the G/G genotype at the G1287A polymorphism showed a greater decrease in the mean omission error scores ($p = 0.006$) than subjects with the G/A or A/A genotypes, and subjects with the T allele at the A-3081T polymorphism (T/T or A/T) showed a greater decrease in the mean commission error scores ($p = 0.003$) than those with the A/A genotypes.

Conclusions: Our results provide evidence for the possible role of the G1287A and A-3081T genotypes of SLC6A2 in methylphenidate-induced improvement in attentional performance and support the noradrenergic hypothesis for the pathophysiology of ADHD.

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Behav Brain Sci. 2012;35:362-63.

POSTGENOMICS AND GENETIC ESSENTIALISM.

Dar-Nimrod I.

Traditional lay perceptions of genetics are plagued with essentialist biases leading to some unfortunate consequences. Changes in the scientific understanding of heredity in general, and in genotype-phenotype relationships more specifically, provide a vital basis for shifting public understanding of genetics. Facilitating postgenomic literacy among the public has the potential to have translational implications in diminishing deleterious attitudes, beliefs, and behaviors.

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Behav Neurosci. 2012 Dec;126:762-71.

PHYSICAL EXERCISE AND CATECHOLAMINE REUPTAKE INHIBITORS AFFECT ORIENTING BEHAVIOR AND SOCIAL INTERACTION IN A RAT MODEL OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Robinson AM, Eggleston RL, Bucci DJ.

The effects of methylphenidate (MPH), atomoxetine (ATMX), and/or physical exercise (EX) on orienting behavior and social interaction were examined in spontaneously hypertensive rats (SHRs), a commonly used animal model of attention-deficit/hyperactivity disorder (ADHD). During the orienting procedure, rats received repeated presentations of a nonreinforced visual stimulus. As observed previously, orienting behavior (rearing up on the hind legs) habituated across trials in normo-active control rats (Wistars) but not in SHRs, suggesting that SHRs have difficulty ignoring irrelevant behavioral stimuli. Treatment with MPH (0.125 mg/kg), ATMX (0.125 mg/kg), or EX (3 weeks of access to a running wheel), alone or in combination, reduced rearing behavior in SHRs to the level observed in the Wistar control group. Similarly, drug treatment and/or EX reduced the number of social interactions exhibited by SHRs, while having no effects on locomotor activity. It is important to note that EX was just as effective as MPH or ATMX in reducing orienting behavior and social interaction. In contrast to the SHRs, neither MPH nor ATMX affected orienting or social behavior in Wistar rats. Together, these findings support the growing literature that EX may be useful as an adjunctive or replacement therapy in ADHD.

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BMC Med Genomics. 2012;5.

CORRELATIONS OF GENE EXPRESSION WITH RATINGS OF INATTENTION AND HYPERACTIVITY/IMPULSIVITY IN TOURETTE SYNDROME: A PILOT STUDY.

Tian Y, Stamova B, Ander BP, et al.

Background: Inattentiveness, impulsivity and hyperactivity are the primary behaviors associated with attention-deficit hyperactivity disorder (ADHD). Previous studies showed that peripheral blood gene expression signatures can mirror central nervous system disease. Tourette syndrome (TS) is associated with inattention (IA) and hyperactivity/impulsivity (HI) symptoms over 50% of the time. This study determined if gene expression in blood correlated significantly with IA and/or HI rating scale scores in participants with TS.

Methods. RNA was isolated from the blood of 21 participants with TS, and gene expression measured on Affymetrix human U133 Plus 2.0 arrays. To identify the genes that correlated with Conners Parents Ratings of IA and HI ratings of symptoms, an analysis of covariance (ANCOVA) was performed, controlling for age, gender and batch.

Results: There were 1201 gene probesets that correlated with IA scales, 1625 that correlated with HI scales, and 262 that correlated with both IA and HI scale scores ($P < 0.05$, $|\text{Partial correlation } (r_p)| > 0.4$). Immune, catecholamine and other neurotransmitter pathways were associated with IA and HI behaviors. A number of the identified genes ($n=27$) have previously been reported in ADHD genetic studies. Many more genes correlated with either IA or HI scales alone compared to those that correlated with both IA and HI scales.

Conclusions: These findings support the concept that the pathophysiology of ADHD and/or its subtypes in TS may involve the interaction of multiple genes. These preliminary data also suggest gene expression may be useful for studying IA and HI symptoms that relate to ADHD in TS and perhaps non-TS participants. These results will need to be confirmed in future studies.

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BMC Pediatr. 2012;12.

FACTORS ASSOCIATED WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER AMONG US CHILDREN: RESULTS FROM A NATIONAL SURVEY.

Lingineni RK, Biswas S, Ahmad N, et al.

Background: The purpose of this study was to investigate the association between Attention Deficit/Hyperactivity Disorder (ADHD) and various factors using a representative sample of US children in a comprehensive manner. This includes variables that have not been previously studied such as watching TV/playing video games, computer usage, family member's smoking, and participation in sports.

Methods: This was a cross-sectional study of 68,634 children, 5-17 years old, from the National Survey of Children's Health (NSCH, 2007-2008). We performed bivariate and multivariate logistic regression analyses with ADHD classification as the response variable and the following explanatory variables: sex, race, depression, anxiety, body mass index, healthcare coverage, family structure, socio-economic status, family members' smoking status, education, computer usage, watching television (TV)/playing video games, participation in sports, and participation in clubs/organizations.

Results: Approximately 10% of the sample was classified as having ADHD. We found depression, anxiety, healthcare coverage, and male sex of child to have increased odds of being diagnosed with ADHD. One of the salient features of this study was observing a significant association between ADHD and variables such as TV usage, participation in sports, two-parent family structure, and family members' smoking status. Obesity was not found to be significantly associated with ADHD, contrary to some previous studies.

Conclusions: The current study uncovered several factors associated with ADHD at the national level, including some that have not been studied earlier in such a setting. However, we caution that due to the cross-sectional and observational nature of the data, a cause and effect relationship between ADHD and the associated factors can not be deduced from this study. Future research on ADHD should take into consideration these factors, preferably through a longitudinal study design.

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BMC Psychiatry. 2012;219.

PERSISTENCE OF PHARMACOLOGICAL TREATMENT INTO ADULTHOOD, IN UK PRIMARY CARE, FOR ADHD PATIENTS WHO STARTED TREATMENT IN CHILDHOOD OR ADOLESCENCE.

McCarthy S, Wilton L, Murray ML, et al.

Background: ADHD guidelines in the UK suggest that children and adults who respond to pharmacological treatment should continue for as long as remains clinically effective, subject to regular review. To what extent patients persist with treatment from childhood and adolescence into adulthood is not clear. This study aims to describe, in UK primary care, the persistence of pharmacological treatment for patients with ADHD who started treatment aged 6--17 years and to estimate the percentage of patients who continued treatment from childhood and adolescence into adulthood.

Methods: The Health Improvement Network (THIN) database was used to identify patients with ADHD who received their first prescription for methylphenidate/ dexamfetamine/atomoxetine, aged 6--17 years. Patients were monitored until their 'censored date' (the earliest of the following dates: date the last prescription coded in the database ended, end of the study period (31st December 2008), date at which they transferred out of their practice, date of death, the last date the practice contributed data to the database). Persistence of treatment into adulthood was estimated using Kaplan Meier analysis.

Results: 610 patients had follow-up data into adulthood. 213 patients (93.4% male) started treatment between 6--12 years; median treatment duration 5.9 years. 131 (61.5%) stopped before 18 years, 82 (38.5%) were still on treatment age ≥ 18 years. 397 patients (86.4% male) started treatment between 13--17 years; median treatment duration was 1.6 years. 227 (57.2%) stopped before 18 years, 170 (42.8%) were still on treatment age ≥ 18 years. The number of females in both age categories was too small to formally test for differences between genders in persistence of treatment.

Conclusion: Persistence of treatment into adulthood is lower (~40%) compared with published rates of persistence of the condition (~65% when symptomatic definition of remission used). Due to the limited number of patients with data past 18 years, it is important that ongoing monitoring of prescribing into later adulthood is undertaken, particularly to observe the effects of recommendations in new guidelines.

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BMC Psychiatry. 2012;212.

CONTRIBUTIONS OF CIRCADIAN TENDENCIES AND BEHAVIORAL PROBLEMS TO SLEEP ONSET PROBLEMS OF CHILDREN WITH ADHD.

Gruber R, Fontil L, Bergmame L, et al.

Background: Children with attention-deficit/hyperactivity disorder (ADHD) are two to three times more likely to experience sleep problems. The purpose of this study is to determine the relative contributions of circadian preferences and behavioral problems to sleep onset problems experienced by children with ADHD and to test for a moderation effect of ADHD diagnosis on the impact of circadian preferences and externalizing problems on sleep onset problems.

Methods: After initial screening, parents of children meeting inclusion criteria documented child bedtime over 4 nights, using a sleep log, and completed questionnaires regarding sleep, ADHD and demographics to assess bedtime routine prior to PSG. On the fifth night of the study, sleep was recorded via ambulatory assessment of sleep architecture in the child's natural sleep environment employing portable polysomnography equipment. Seventy-five children (26 with ADHD and 49 controls) aged 7--11 years (mean age 8.61 years, SD 1.27 years) participated in the present study.

Results: In both groups of children, externalizing problems yielded significant independent contributions to the explained variance in parental reports of bedtime resistance, whereas an evening circadian tendency contributed both to parental reports of sleep onset delay and to PSG-measured sleep-onset latency. No significant interaction effect of behavioral/circadian tendency with ADHD status was evident.

Conclusions: Sleep onset problems in ADHD are related to different etiologies that might require different interventional strategies and can be distinguished using the parental reports on the CSHQ

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BMJ Open. 2012;2.

PREVALENCE, DETERMINANTS AND SPECTRUM OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD) MEDICATION OF CHILDREN AND ADOLESCENTS IN GERMANY: RESULTS OF THE GERMAN HEALTH INTERVIEW AND EXAMINATION SURVEY (KIGGS).

Knopf H, Holling H, Huss M, et al.

Objective: To investigate the prevalence, determinants and spectrum of attention-deficit hyperactivity disorder (ADHD) medication and its associations with socioeconomic status (SES), health-related behaviour and living conditions.

Design: Observational cross-sectional study.

Setting: Germany.

Participants: Representative population-based sample of non-institutionalised youth aged between 0 and 17 years (n=17 450) and examined between 2003 and 2006.

Main outcome measure: Prevalence and spectrum of ADHD medication (Anatomical Therapeutic Chemical (ATC) code N04BA) measured by standardised computer-assisted personal interview (CAPI) on drug use.

Results: The overall prevalence of ADHD medication (stimulants including atomoxetine) was 0.9% (95% CI 0.7% to 1.1%). Boys used these drugs (1.5%, 1.2% to 1.8%) five times more than girls 0.3% (0.2% to 0.5%). The highest prevalence rates were for boys aged 6-10 years (2.3%, 1.7% to 3.1%) and 11-13 (2.7%, 2.0% to 3.7%). Boys from families with no immigration background used ADHD medication almost 6 times as frequently as boys with an immigration background (1.7% vs 0.3%). Multivariate analysis (binary logistic regression) showed boys (OR 5.16, 95% CI 3.15 to 8.47), 11-year-olds to 13-year-olds (2.24, 1.28 to 3.49), children in large cities (2.18, 1.13 to 4.22), children with no immigration background (3.06, 1.34 to 6.99), and children with only a good (vs excellent) parent-rated health status (1.91, 1.18 to 3.08) being more likely to be using ADHD medication. A visit to the doctor in the last month or last quarter was associated with a higher probability for ADHD medication (3.18, 1.29 to 7.95 and 3.59, 1.45 to 8.90, respectively).

Conclusions: Results show prevalence rates of ADHD medication use for the German child and adolescent population that are considerably lower than published prevalence rates from the USA, but comparable with those of western European and Scandinavian countries. Lower use rates in rural versus urban regions may point to differential healthcare access. The inverse association of ADHD medication use with immigration status suggests potentially restricted access to healthcare services for immigrants or may reflect culture-specific differences in attitudes towards symptoms of ADHD.

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Brain Res. 2012.

EXOGENOUS ORIENTING OF VISUAL-SPATIAL ATTENTION IN ADHD CHILDREN.

Ortega R, Lopez V, Carrasco X, et al.

Visual spatial orienting of attention towards exogenous cues has been one of the attentional functions considered to be spared in ADHD. Here we present a design in which 60 (30 ADHD) children, age: 10.9(plus or minus)1.4, were asked to covertly orient their attention to one or two (out of four) cued locations, and search for a target stimulus in one of these locations, while recording behavioral responses and EEG/ERP. In all conditions, ADHD children showed delayed reaction times and poorer behavioral performance. They also exhibited larger cue-elicited P2 but reduced CNV in the preparation stage. Larger amplitude of CNV predicted better performance in the task. Target-elicited N1 and selection negativity were also reduced in the ADHD group compared to non-ADHD. Groups also differed in the early and late P3 time-windows. The present results suggest that exogenous orienting of attention could be dysfunctional in ADHD under certain conditions. This limitation is not necessarily caused by an impairment of the orienting process itself, but instead by a difficulty in maintaining the relevant information acquired during the early preparation stage through the target processing stage, when it is really needed.

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Child Psychiatry Hum Dev. 2012 Dec;43:958-67.

PARENTAL AUTONOMY SUPPORT MODERATES THE LINK BETWEEN ADHD SYMPTOMATOLOGY AND TASK PERSEVERANCE.

Thomassin K, Suveg C.

The current study investigated the moderating role of mother and father autonomy support in the link between youth Attention-Deficit Hyperactivity Disorder (ADHD) symptoms and task perseverance. ADHD symptomatology was assessed using a multi-informant composite of mother, father, and teacher ratings, and youth perseverance and parental support of autonomy were examined using a behavioral observation paradigm (i.e., difficult puzzle task). Results indicated that youth who were rated as exhibiting more symptoms of ADHD persevered less on a difficult puzzle task and that this relationship was moderated by parental level of autonomy support. In the context of high parental autonomy support, the negative relation between ADHD and perseverance became nonsignificant. Findings indicate that supporting youth autonomy may have significant implications for their development and that it would be valuable to aid parents in developing the appropriate skills necessary for them to successfully support their child's autonomy.

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Compr Psychiatry. 2013;54:7-10.

AGREEMENT BETWEEN DIAGNOSTIC AND STATISTICAL MANUAL OF MENTAL DISORDERS, FOURTH EDITION, AND THE PROPOSED DSM-V ATTENTION DEFICIT HYPERACTIVITY DISORDER DIAGNOSTIC CRITERIA: AN EXPLORATORY STUDY.

Ghanizadeh A.

Background: There is no empirical literature about the American Psychiatry Association proposed new diagnostic criteria for attention deficit hyperactivity disorder (ADHD). This study examined the agreement between ADHD diagnosis derived from Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), and DSM-V diagnostic criteria. It also reports sensitivity, specificity, and agreement for ADHD diagnosis.

Methods: A clinical sample of 246 children and adolescents were interviewed face to face using both ADHD diagnostic criteria for DSM-V and DSM-IV by interviewing clinician. Comorbid psychiatric disorders were screened using DSM-IV criteria.

Results: The rate of ADHD diagnosis using DSM-V was significantly higher than the rate detected by using DSM-IV diagnostic criteria. The sensitivity of DSM-V diagnostic criteria was 100%, while its specificity was 71.1%. The kappa agreement between DSM-IV and DSM-V was 0.75. In addition, positive predictive value was 85.1%. All the four newly added symptoms to ADHD diagnostic criteria are statistically more common in the children with ADHD than those in the comparison group. However, these symptoms are also very common in the children without ADHD.

Conclusion: It is expected that the rate of ADHD would increase using the proposed ADHD DSM-V criteria. Moreover, the newly added symptoms have a low specificity for ADHD diagnosis.

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Dev Cognitive Neurosci. 2012.

PRELIMINARY DATA SUGGESTING THE EFFICACY OF ATTENTION TRAINING FOR SCHOOL-AGED CHILDREN WITH ADHD.

Tamm L, Epstein JN, Peugh JL, et al.

A pilot randomized clinical trial was conducted to examine the initial efficacy of Pay Attention!, an intervention training sustained, selective, alternating, and divided attention, in children diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD). After a diagnostic and baseline evaluation, school-aged children with ADHD were randomized to receive 16 bi-weekly sessions of Pay Attention! (n = 54) or to a waitlist control group (n = 51). Participants completed an outcome evaluation approximately 12 weeks after their baseline evaluation. Results showed significant treatment effects for parent and clinician ratings of ADHD symptoms, child self-report of ability to focus, and parent ratings of executive functioning. Child performance on neuropsychological tests showed significant treatment-related improvement on strategic

planning efficiency, but no treatment effects were observed on other neuropsychological outcomes. Treatment effects were also not observed for teacher ratings of ADHD. These data add to a growing body of literature supporting effects of cognitive training on attention and behavior, however, additional research is warranted.

Dev Neurorehabilitation. 2013;16:52-57.

EXTERNALIZING AND TANTRUM BEHAVIOURS IN CHILDREN WITH ASD AND ADHD COMPARED TO CHILDREN WITH ADHD.

Tureck K, Matson JL, May A, et al.

Objective: Compare rates of externalizing in children with autism spectrum disorder (ASD) and attention deficit/hyperactivity disorder (ADHD) symptoms to children with ADHD.

Method: Parents/caregivers of 85 children with ASD and/or ADHD were surveyed about their children's behaviours using the Autism Spectrum Disorders-Comorbidity for Children and the Autism Spectrum Disorders-Behaviour Problem for Children.

Results: Specific main effects analyses were then conducted. Children with ASD exhibited a higher number of externalizing ($F(1,83)83.34, p<0.001$) and tantrum behaviours ($F(1,83)781.86, p<0.001$) than children without ASD.

Conclusions: ASD exacerbates the externalizing symptoms of ADHD during childhood. This study adds to the literature on the importance of assessing for a wide-range of possible behaviour problems in children presenting with ADHD symptomatology. The implications of these findings are discussed in the context of other research.

Eth Human Psychol Psychiatry. 2012;14:5-14.

THE RISKS ASSOCIATED WITH STIMULANT MEDICATION USE IN CHILD AND ADOLESCENT POPULATIONS DIAGNOSED WITH ATTENTION- DEFICIT/HYPERACTIVITY DISORDER.

Stolzer JM.

Throughout human history, psychiatric dysfunction in child and adolescent populations has been rare. However, over the last 2 decades, psychiatric diagnoses have reached epidemic proportions-particularly in the United States. Currently, attention-deficit/hyperactivity disorder (ADHD) is the most commonly diagnosed psychiatric illness in child and adolescent populations with an estimated 10-12 million children diagnosed in the United States. Over the last 2 decades, behavior patterns that were once perceived as typical, normative developmental stages have been systematically redefined by those promoting the mass labeling and drugging of children as a "chemical imbalance of the brain." Grounded in bioevolutionary theory, this article will challenge the existing medical model and will explore in-depth the risks associated with the ADHD label and the use of stimulant medication in pediatric populations. In addition, this article will examine the cultural, physical, neurological, psychological, and social correlates as they relate to the diagnosis of ADHD in America.

Eur J Integr Med. 2012;4:73-74.

CLASSICAL HOMEOPATHY HELPS HYPERACTIVE CHILDREN-A 10-YEAR FOLLOW-UP OF HOMEOPATHIC AND INTEGRATED MEDICAL TREATMENT IN CHILDREN SUFFERING FROM ATTENTION DEFICIT DISORDER WITH AND WITHOUT HYPERACTIVITY.

Klaus VA, Ursula S, Heiner F, et al.

Aim: To investigate long-term clinical and cost effectiveness of individualised homeopathic and medical treatment of children with attention deficit hyperactivity disorder (ADHD).

Methods: An open pilot study had revealed sufficient data to develop a randomised, double-blind, placebo-controlled trial (RCT), embedded in a prospective observational study of children with ADHD diagnosis,

according to established neuropsychiatric criteria (Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV)). After a screening run-in phase of homeopathic treatment, the crossover RCT was followed by open-label long-term follow-up. At diagnosis, beginning of, and after each crossover period, and five times in long-term follow-up, parents reported Conners' Global Index (CGI, 10 items, rated 0-3 points each primary variable) and patients underwent neuropsychological testing (secondary variables) until the end of RCT. Cost comparison (tertiary variable) was done after the clinical trial and during long-term follow-up.

Results: A total of 83 children between 7 and 15 years were treated with individually prescribed homeopathic remedies. As 13 patients did not improve at least 50% in CGI values (inclusion criterion), the remaining 62 children (84%) participated in, and 58 finished a double-blind cross-over RCT. During this RCT, CGI ratings were significantly lower (average 1.67 points) under verum than under placebo ($p = 0.0479$). After 17 and 115 months of treatment, long-term global CGI reached 8/30 points, resembling an improvement of more than 50% ($p < 0.0001$). Specific CGI results (range) after 10 years for children without any therapy, children with homeopathy and children with methylphenidate (MPD) as a single or a combined therapy will be given. Cognitive performance (global visual perception, impulsivity/hyperactivity and learning/attention) and social behaviour improved highly significantly and were stable during follow-up ($p = 0.0001$ - $p = 0.0004$). Homeopathy costs are 75% of average stimulant therapy (20 mg MPD) in the first, and 50% of 10 mg MPD in following years summing up to CHF 2120 (D 1705) compared to CHF 3650 (D 2920) for the single child with stimulant therapy (average 20 mg day⁻¹) during 10 years.

Conclusion: In children with ADHD, individualised homeopathic therapy has both, a clinically significant and specific long-lasting effect with duration over 10 years, and may reduce costs to an amount of up to 50%.

Eur J Neurol. 2012;19:210.

CLUMSINESS IN CHILDREN WITH ADHD COMPARED WITH NORMAL CHILDREN BASED ON THE LINCOLN OZERETSKI SCALE.

Kazemi A, Khaledi F, Kazemi M.

Introduction: Clumsiness is a syndrome that has a pathological meaning. It is mainly concerned with the motor activities of children. The children who are suffering from such a problem are not able to perform normal motor skills even if they do not show any neurological symptoms in laboratory tests. The object of the present study is the evaluation of clumsiness in children with ADHD compared with normal children based on Lincoln Ozeretski Scale.

Methods: The statistical sample consisted of 30 boys with ADHD, who were selected according to an available sampling method and 30 boys without ADHD, selected through random sampling, at the age of six. Measurement tools consisted of Motor Development Lincoln-Ozeretski Scale. Data were analyzed using T-Test.

Results: The results showed that there is a significant difference between the kids' motor skills and the dependent variables ($t=10.43$).

Conclusion: Children with ADHD compared to normal children are at a lower level of motor skills, and suffer from clumsiness. In other words, children suffering from this syndrome, show incompetent and abnormal motor-skills in learning and doing an activity expected from them.

Eur J Neurol. 2012;19:577.

MILD MOVEMENT AND MENTAL DISORDERS IN CHILDREN. THE IMPACT OF EEG BIOFEEDBACK FOR VOLUNTARY AND INVOLUNTARY MOVEMENTS AND ADHD COMPARED TO INTENSIVE CLASSICAL NEUROREHABILITATION.

Ziakova E, Bartko D, Klobucka S.

Introduction: EEG biofeedback belongs to the new attractive neurorehabilitation methods. Its efficacy on motor skills and ADHD and/or ADD in children is not well known. Aim of this study was to compare efficacy of this method with intensive classical neurorehabilitation.

Material and methods: Material consists of 60 children with mild central movement disorders in combination with ADHD/ ADD. Whole material was divided into two groups: 1st group: 30 children, mean age 8.9yrs, underwent 30 EEG biofeedback procedures. 2nd group: 30 children, mean age 8.5yrs, underwent intensive classical neurorehabilitation 2-3 times a week. The length of one procedure was 30-45 minutes in both groups. All children were tested using PANESS test before and after procedures (PANESS test was used for assessment of various movement variables: lateral preference, standing, walking, balance, coordination, overflow movements, dysrhythmia, repetitive and pattern movements). Achieved total time in repetitive and pattern movements was also evaluated.

Results: Significant improvement in total score of all variables of PANESS test: before (M=58.57) and after (M=25.87) biofeedback rehabilitation was documented ($p=0.000$). Sum of achieved time of repetitive and pattern movements was (Mdn=101.60) vs. (Mdn=88.95, $p=0.000$) after procedures. In the 2nd group (intensive classical neurorehabilitation) improvement in motor skills was also found out but these changes did not reach statistical significance. Achieved time: (Mdn=137.06) vs. (Mdn=107.85, $p=0.000$) was significantly shorter but less marked. Significant improvement was found also in total time of repetitive and pattern movements.

Conclusion: EEG biofeedback neurorehabilitation significantly improved not only motor skills but also ADHD/ADD parameters. Comparing results of both groups, showed significantly better results in motor skills in the 1st group and similar significant results in total time of repetitive and pattern movements in the 2nd group.

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Eur J Neurol. 2012;19:207.

NEUROPHYSIOLOGICAL PERSPECTIVES OF ELECTROENCEPHALOGRAPHY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Dube A, Yadav K, Gupta A, et al.

Objective: The present study was undertaken to digitally evaluate the electroencephalographic signature in children with Attention Deficit Hyperactivity Disorder (ADHD).

Method: 30 children in the age range of 3-11 years were included in the present study and power spectral analysis of electroencephalographic (EEG) output from the central EEG electrode pair location (preferably the Cz - Vertex pair) was run to test the hypothesis that cortical slowing in the prefrontal region can serve as a basis for differentiating children with ADHD from healthy children.

Results: Quantitative electroencephalographic findings indicated significant increased theta power and decreased delta power seen in patients with ADHD with lack of suppression of Mu-waves which suggested significant maturational dysfunction in cortical arousal in the prefrontal cortex, cortical slowing and dysfunctional mirror neuron system in children with ADHD.

Conclusion: These findings constituted a positive initial test of a QEEG- based neurometric test for use in the assessment of ADHD and the significance of the mirror neuron system in the disorders of the social mind.

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Eur J Neurol. 2012;19:212.

NEUROPHYSIOLOGICAL PERSPECTIVES OF ELECTROENCEPHALOGRAPHY IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Gupta A.

The present study was carried out in the Department of Pediatrics & Dept. of Physiology in collaboration with the Departments of Neurology, SMS Medical College, Jaipur. 30 children in the age group of 3 to 11 years (median age range of 7-10 years) with an intelligence quotient (IQ) of more than 70, suffering from ADHD (male : female ratio being 3:1), diagnosed as per DSM IV criteria, were included in the study. An equal number of children matched for age and sex acted as the control cohort. 18 to 20 epochs were selected for Power Spectral Analysis, each lasting 2-3 seconds, the time duration representing confocal and frequency matched neuronal pool based on the theory of analysis of sharp changes or rapid transitional processes (RTP) reflected in quasi-stationary segments of local EEGs Epochs with more than

100v on the electroencephalogram representing artifacts were excluded from the mean. However no significant difference could be seen in the absolute powers of beta and alpha waves. The increased theta/beta ratio in ADHD children and absence of Mu-wave suppression [a characteristic feature of the mirror neuron's operational architectonics (Oberman et al, 2005)] give an insight into the features of the disease process of ADHD, namely cerebral dysmaturation (Monstra et al, 1996) and broken mirrors. In the present study no significant difference could be seen in the absolute powers of alpha and beta waves in ADHD children and the control group.

Eur J Neurol. 2012;19:554.

EFFECTIVENESS OF VESTIBULAR STIMULATION ON VISUAL AND AUDITORY ATTENTION IN 7- TO 12-YEAR-OLD CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Haghighoo HA, Hosseini SA, Salamati A, et al.

Introduction: Inadequate processing of sensory information especially equilibrium leads to typical behaviors in attention deficit hyperactivity (ADHD) children which manifested as inattentive behaviors. In this research we aimed to study the effects of vestibular stimulation on visual and auditory attention in 7- to 12-year-old ADHD children, using IVAPLUS- CPT (Integrated Visual and Auditory Continuous Performance Test).

Methodology: 30 Children diagnosed with ADHD (7- to 12-year-old), which were right handed and had normal IQ based on Wechsler test participated in this research following their consent and divided randomly in the intervention and control groups. All participants were assessed using IVA-PLUS-CPT, then the intervention group participated in normal occupational therapy activities plus vestibular stimulation while the control group was recruited only in normal occupational therapy activities. Intervention continued for 10 sessions, twice a week for 5 weeks. At the end, all participants were evaluated again using IVA-PLUS-CPT. The collected data was analysed using SPSS software version 16 and differences in pre- and post-test were comprised between the two groups using independent T-Test.

Results: Vestibular stimulation led to significantly differences in attention, visual attention, auditory attention, impulse control and auditory impulse control ($p < 0.05$) but visual impulse control did not show significant differences amongst the two groups.

Conclusion: Vestibular stimulation can affect meaningfully visual and auditory attention in ADHD children. Hence it can be used as a therapeutic technique in treating these children.

Eur J Radiol. 2012;81:4119-22.

ASSESSMENT OF MEMORY/ATTENTION IMPAIRMENT IN CHILDREN WITH PRIMARY NOCTURNAL ENURESIS: A Voxel-BASED MORPHOMETRY STUDY.

Yu B, Kong F, Peng M, et al.

Aim: Assessment of memory/attention impairment and related exploration of the gray matter differential MR density variations between children with and without primary nocturnal enuresis (PNE) using voxel-based morphometry (VBM) methodology is the aim of the present study.

Methods: A total of 75 right-handed PNE children (M/F = 39:36, average age 10.4 (plus or minus) 1.3 years) and 72 age-matched, right-handed, healthy controls (M/F = 40:32, 10.0 (plus or minus) 1.2 years) were recruited for the study. First, intelligence tests were performed using the China-Wechsler Intelligence Scale for Children (C-WISC) in both PNE and control children. The full intelligence quotient (FIQ), verbal IQ (VIQ), performance IQ (PIQ), and memory/caution (M/C) factor were measured. Voxel-based morphometry (VBM) was performed using high resolution 3 Tesla T1-weighted MR images, processed using VBM5 in the PNE and control children. Student's t-test or Mann-Whitney U test were performed to analyze the difference in the gray matter density (GMD) between the PNE and control children.

Results: The FIQ, VIQ, and PIQ in the PNE group were within the normal range and did not significantly differ from the control group, though the M/C factor was statistically lower in the PNE group. Compared with normal controls, PNE children exhibited lower GMD in the right dorsolateral prefrontal cortex (DLPFC) and the left cerebellum ($P < 0.001$).

Conclusion: Impairment in memory/attention was detected in PNE children, and the structural abnormalities of the right DLPFC and left cerebellum are likely to be implicated in these deficits.

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Eur Neuropsychopharmacol. 2012.

REWARD CIRCUIT CONNECTIVITY RELATES TO DELAY DISCOUNTING IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Costa Dias TG, Wilson VB, Bathula DR, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent psychiatric disorder that has poor long-term outcomes and remains a major public health concern. Recent theories have proposed that ADHD arises from alterations in multiple neural pathways. Alterations in reward circuits are hypothesized as one core dysfunction, leading to altered processing of anticipated rewards. The nucleus accumbens (NAcc) is particularly important for reward processes; task-based fMRI studies have found atypical activation of this region while the participants performed a reward task. Understanding how reward circuits are involved with ADHD may be further enhanced by considering how the NAcc interacts with other brain regions. Here we used the technique of resting-state functional connectivity MRI (rs-fcMRI) to examine the alterations in the NAcc interactions and how they relate to impulsive decision making in ADHD. Using rs-fcMRI, this study: examined differences in functional connectivity of the NAcc between children with ADHD and control children; correlated the functional connectivity of NAcc with impulsivity, as measured by a delay discounting task; and combined these two initial segments to identify the atypical NAcc connections that were associated with impulsive decision making in ADHD. We found that functional connectivity of NAcc was atypical in children with ADHD and the ADHD-related increased connectivity between NAcc and the prefrontal cortex was associated with greater impulsivity (steeper delayed-reward discounting). These findings are consistent with the hypothesis that atypical signaling of the NAcc to the prefrontal cortex in ADHD may lead to excessive approach and failure in estimating future consequences; thus, leading to impulsive behavior.

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Front Integr Neurosci. 2012.

ELECTROPHYSIOLOGICAL CORRELATES OF FEARFUL AND SAD DISTRACTION ON TARGET PROCESSING IN ADOLESCENTS WITH ATTENTION DEFICIT-HYPERACTIVITY SYMPTOMS AND AFFECTIVE DISORDERS.

Singhal A, Shafer AT, Russell M, et al.

In this study we used event-related brain potentials (ERP) as neural markers of cognitive operations to examine emotion and attentional processing in a population of high-risk adolescents with mental health problems that included ADHD, anxiety, and depression. We included a healthy control group for comparison purposes, and employed a modified version of the emotional oddball paradigm, consisting of frequent distracters (scrambled pictures), infrequent distracters (sad, fearful, and neutral pictures) and infrequent targets (circles). Participants were instructed to make a right hand button press to targets and a left hand button press to all other stimuli. EEG/ERP recordings were taken using a high-density 256-channel recording system. Behavioral data showed that for both clinical and non-clinical adolescents, reaction time was slowest in response to the fearful images. Electrophysiological data differentiated emotion and target processing between clinical and non-clinical adolescents. In the clinical group we observed a larger P100 and Late Positive Potential (LPP) in response to fearful compared to sad or neutral pictures. There were no differences in these ERPs in the healthy sample. Emotional modulation of target processing was also identified in the clinical sample, where we observed an increase in P300 amplitude, and a larger sustained LPP in response to targets that followed emotional pictures (fear & sad) compared to targets that followed neutral pictures or other targets. There were no differences in these target ERPs for the healthy participants. Taken together, we suggest that these data provide important and novel evidence of affective and attention dysfunction in this clinical population of adolescents, and offer an example of the disruptive effects of emotional reactivity on basic cognition.

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Front Syst Neurosci. 2012;1-36.

NETWORK, ANATOMICAL, AND NON-IMAGING MEASURES FOR THE PREDICTION OF ADHD DIAGNOSIS IN INDIVIDUAL SUBJECTS.

Bohland JW, Saperstein S, Pereira F, et al.

Brain imaging methods have long held promise as diagnostic aids for neuropsychiatric conditions with complex behavioral phenotypes such as Attention-Deficit/Hyperactivity Disorder. This promise has largely been unrealized, at least partly due to the heterogeneity of clinical populations and the small sample size of many studies. A large, multi-center dataset provided by the ADHD-200 Consortium affords new opportunities to test methods for individual diagnosis based on MRI-observable structural brain attributes and functional interactions observable from resting state fMRI. In this study, we systematically calculated a large set of standard and new quantitative markers from individual subject datasets. These features (> 12,000 per subject) consisted of local anatomical attributes such as cortical thickness and structure volumes, and both local and global resting state network measures. Three methods were used to compute graphs representing interdependencies between activations in different brain areas, and a full set of network features was derived from each. Of these, features derived from the inverse of the time series covariance matrix, under an L1-norm regularization penalty, proved most powerful. Anatomical and network feature sets were used individually, and combined with non-imaging phenotypic features from each subject. Machine learning algorithms were used to rank attributes, and performance was assessed under cross-validation and on a separate test set of 168 subjects for a variety of feature set combinations. While non-imaging features gave highest performance in cross-validation, the addition of imaging features in sufficient numbers led to improved generalization to new data. Stratification by gender also proved to be a fruitful strategy to improve classifier performance. We describe the overall approach used, compare the predictive power of different classes of features, and describe the most impactful features in relation to the current literature.

Harv Rev Psychiatry. 2012 Dec;20:309-17.

PSEUDO-ADHD IN A CASE OF FIRST-EPISODE SCHIZOPHRENIA: DIAGNOSTIC AND TREATMENT CHALLENGES.

Freedman JL, Zimmet SV, Duckworth K, et al.

Presents the case of TC, a 16-year-old male of Colombian descent with a prior history of attention-deficit/hyperactivity disorder (ADHD) and depression who initially presented to our outpatient treatment program following his first hospitalization in the context of suicidal gestures and increasing psychotic symptomatology. TC had been hospitalized at a local community adolescent inpatient unit after holding a knife to his throat while experiencing command auditory hallucinations to kill himself. TC entered our specialized program for adolescents and young adults with psychotic illnesses following discharge from his first inpatient hospitalization. While he responded well to individual therapy sessions, TC's participation in our program's recovery and psychoeducation groups was limited at times. While still participating in our program, the patient has been able to return to his high school, where, following an individualized educational plan, he is now in a half-day program in a smaller classroom with additional staff support. His psychotic negativism and cognitive impairment remain but are less severe than on initial evaluation, and the patient has noted improvement in academics. Although TC's recovery from first-episode schizophrenia is incomplete on his current regimen of haloperidol, his trajectory remains promising.

HealthMED. 2012;6:3482-87.

CASE STUDY: SCHOOL EXPERIENCE OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Knezevic-Floric O, Zukovic S, Ninkovic S.

Understanding subjective school experiences of children with attention deficit hyperactivity disorder (ADHD), as well as educational experiences of their mothers is the aim of this paper, as well as the interest of the author. In the research of case study draft eight children with ADHD and their mothers participated (included in work of the Clinic of developmental paediatrics, Novi Sad, Serbia). Data are collected by two unstructured interviews constructed for the needs of this study. Material collected is processed by

procedures of quantitative analysis. The most striking finding of this study shows that mothers of children with ADHD are familiar with models of educational processes that are adapted to ADHD symptoms, which should be a basis in education of teachers for work with ADHD children. Analysis of material collected has also shown that teachers by their behaviour (criticism and punishments) contribute negative experiences of hyperactive children at school. In that sense, familiarity of teachers with ADHD children's experiences could contribute to redirecting of teacher's attention to creation of school environment that would facilitate educational success of children with ADHD.

Iranian Journal of Psychiatry and Clinical Psychology. 2012;17:332-35.

ASSOCIATION BETWEEN POLAND SYNDROME AND AUTISTIC DISORDER: A CASE REPORT.

Shooshtari MH, Elyasi F, Tavasoli A.

Objectives: The aim of the current study was to report associated problems of Poland Syndrome in a patient.

Method: A 5 years old son affected to Poland Syndrome was accurately assessed.

Results: The results showed the patient had communication, verbal and behavioral problems besides Poland Syndrome. Also, he received attention deficit hyperactivity disorder diagnosis and had seizure history. After accurate assessment, autistic disorder was diagnosed and occupational and speech therapy was prescribed besides treating seizure and symptoms of other problems.

Conclusion: When a patient is being referred because of hyperactivity, she should be accurately evaluated and assessed for other psychiatric problems.

J Adolesc Health. 2012;51:593-600.

ADHD KNOWLEDGE, PERCEPTIONS, AND INFORMATION SOURCES: PERSPECTIVES FROM A COMMUNITY SAMPLE OF ADOLESCENTS AND THEIR PARENTS.

Bussing R, Zima BT, Mason DM, et al.

Purpose: The chronic illness model advocates for psychoeducation within a collaborative care model to enhance outcomes. To inform psychoeducational approaches for ADHD, this study describes parent and adolescent knowledge, perceptions, and information sources and explores how these vary by sociodemographic characteristics, ADHD risk, and past child mental health service use.

Methods: Parents and adolescents were assessed 7.7 years after initial school district screening for ADHD risk. The study sample included 374 adolescents (56% high and 44% low ADHD risk) aged, on average, 15.4 (standard deviation = 1.8) years, and 36% were African American. Survey questions assessed ADHD knowledge, perceptions, and cues to action and elicited used and preferred information sources. Multiple logistic regression was used to determine potential independent predictors of ADHD knowledge. McNemar tests compared information source utilization against preference.

Results: Despite relatively high self-rated ADHD familiarity, misperceptions among parents and adolescents were common, including a sugar etiology (25% and 27%, respectively) and medication overuse (85% and 67%, respectively). African American respondents expressed less ADHD awareness and greater belief in sugar etiology than Caucasians. Parents used a wide range of ADHD information sources, whereas adolescents relied on social network members and teachers/school. However, parents and adolescents expressed similar strong preferences for the Internet (49% and 51%, respectively) and doctor (40% and 27%, respectively) as ADHD information sources.

Conclusions: Culturally appropriate psychoeducational strategies are needed that combine doctor-provided ADHD information with reputable Internet sources. Despite time limitations during patient visits, both parents and teens place high priority on receiving information from their doctor.

J Affective Disord. 2012 Dec;141:143-59.

AN UPDATE ON THE DEBATED ASSOCIATION BETWEEN ADHD AND BIPOLAR DISORDER ACROSS THE LIFESPAN.

Skirrow C, Hosang GM, Farmer AE, et al.

Diagnostic formulations for attention deficit hyperactivity disorder (ADHD) and bipolar disorder (BD) both include symptoms of distractibility, psychomotor agitation and talkativeness, alongside associated emotional features (irritability and emotional lability). Treatment studies suggest the importance of accurate delineation of ADHD and BD. However, boundaries between the two disorders are blurred by the introduction of broader conceptualisations of BD. This review attempts to elucidate whether associations between ADHD and BD are likely to be driven by superficial symptomatological similarities or by a more meaningful etiological relationship between the disorders. This is achieved by outlining findings on comorbidity, temporal progression of the disorders, familial co-variation, and neurobiology in ADHD and BD across the lifespan. Longitudinal studies fail to consistently show developmental trajectories between ADHD and BD. Comparative research investigating neurobiology is in its infancy, and although some similarities are seen between ADHD and BD, studies also emphasise differences between the two disorders. However, comorbidity and family studies appear to show that the two disorders occur together and aggregate in families at higher than expected rates. Furthermore close inspection of results from population studies reveals heightened co-occurrence of ADHD and BD even in the context of high comorbidity commonly noted in psychopathology. These results point towards a meaningful association between ADHD and BD, going beyond symptomatic similarities. However, future research needs to account for heterogeneity of BD, making clear distinctions between classical episodic forms of BD, and broader conceptualisations of the disorder characterised by irritability and emotional lability, when evaluating the relationship with ADHD.

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J Affective Disord. 2012.

THE COMORBIDITY OF ANXIETY AND DEPRESSIVE SYMPTOMS IN OLDER ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A LONGITUDINAL STUDY.

Michielsen M, Comijs HC, Semeijn EJ, et al.

Background: Comorbidity between Attention-Deficit/Hyperactivity Disorder (ADHD) and depression and anxiety disorders in children and young to middle-aged adults has been well documented in the literature. Yet, it is still unknown whether this comorbidity persists into later life. The aim of this study is therefore to examine the comorbidity of anxiety and depressive symptoms among older adults with ADHD. This is examined both using cross-sectional and longitudinal data.

Methods: Data were used from the Longitudinal Aging Study Amsterdam (LASA). Participants were examined in three measurement cycles, covering six years. They were asked about depressive and anxiety symptoms. To diagnose ADHD, the DIVA 2.0, a diagnostic interview was administered among a subsample (N=231, age 60-94). In addition to the ADHD diagnosis, the association between the sum score of ADHD symptoms and anxiety and depressive symptoms was examined. Data were analyzed by means of linear regression analyses and linear mixed models.

Results: Both ADHD diagnosis and more ADHD symptoms were associated with more anxiety and depressive symptoms cross-sectionally as well as longitudinally. The longitudinal analyses showed that respondents with higher scores of ADHD symptoms reported an increase of depressive symptoms over six years whereas respondents with fewer ADHD symptoms remained stable.

Limitations: The ADHD diagnosis is based on the DSM-IV criteria, which were developed for children, and have not yet been validated in (older) adults.

Conclusions: It appears that the association between ADHD and anxiety/depression remains in place with aging. This suggests that, in clinical practice, directing attention to both in concert may be fruitful.

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J Affective Disord. 2012 Dec;141:382-89.

PEDIATRIC BIPOLAR DISORDER AND ADHD: FAMILY HISTORY COMPARISON IN THE LAMS CLINICAL SAMPLE.

Arnold LE, Mount K, Frazier T, et al.

Background: Transgenerational association of bipolar spectrum disorder (BPSD) and attention deficit/hyperactivity disorder (ADHD) has been reported, but inconclusively.

Method: Children ages 6–12 were systematically recruited at first outpatient visit at 9 clinics at four universities and reliably diagnosed; 621 had elevated symptoms of mania (>12 on the Parent General Behavior Inventory 10-Item Mania Scale); 86 had scores below 12. We analyzed baseline data to test a familial association hypothesis: compared to children with neither BPSD nor ADHD, those with either BPSD or ADHD would have parents with higher rates of both bipolar and ADHD symptoms, and parents of comorbid children would have even higher rates of both.

Results: Of 707 children, 421 had ADHD without BPSD, 45 BPSD without ADHD, 117 comorbid ADHD+BPSD, and 124 neither. The rate of parental manic symptoms was similar for the comorbid and BPSD-alone groups, significantly greater than for ADHD alone and “neither” groups, which had similar rates. ADHD symptoms in parents of children with BPSD alone were significantly less frequent than in parents of children with ADHD (alone or comorbid), and no greater than for children with neither diagnosis. Family history of manic symptoms, but not ADHD symptoms, was associated with parent-rated child manic-symptom severity over and above child diagnosis.

Limitations: The sample was not epidemiologic, parent symptoms were based on family history questions, and alpha was 0.05 despite multiple tests.

Conclusions: These results do not support familial linkage of BPSD and ADHD; they are compatible with heritability of each disorder separately with coincidental overlap.

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J Affective Disord. 2012.

EMOTIONAL LABILITY, COMORBIDITY AND IMPAIRMENT IN ADULTS WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Skirrow C, Asherson P.

Background: Adults with attention-deficit hyperactivity disorder (ADHD) frequently report emotional lability (EL). However, it is not known whether EL may be accounted for by comorbid psychiatric conditions or symptoms. This study evaluates the influence of comorbid clinical symptoms on EL, and investigates the relationship between EL and impairment.

Methods: Over 500 consecutive male adult referrals at the ADHD Clinic for adults at the South London and Maudsley Hospital (U.K) were screened. 41 individuals with ADHD without comorbidity, current medication or frequent substance were identified, and compared with 47 matched healthy male control participants. Measures included IQ, clinical interview and self-reported ADHD symptoms, EL, impairment and antisocial behaviour.

Results: ADHD participants reported elevated EL, showing good case-control differentiation in receiver operating curve analysis. EL was most strongly predicted by hyperactivity-impulsivity rather than subsyndromal comorbid symptoms, and contributed independently to impairment in daily life.

Limitations: Results may not generalise to children with ADHD, or many adults with ADHD, who are frequently affected by comorbid psychiatric conditions and substance use disorders.

Conclusions: EL in adults with ADHD appears to be primarily associated with ADHD itself rather than comorbid conditions, and helps to explain some of the impairments not accounted for by classical features of the disorder. Results indicate that adults presenting with long-term problems with EL should routinely be screened for the presence of ADHD.

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J Allergy Clin Immunol. 2012.

MENTAL HEALTH COMORBIDITY IN PATIENTS WITH ATOPIC DERMATITIS.

Yaghmaie P, Koudelka CW, Simpson EL.

Background: Recent data, primarily from Europe, suggest that children with atopic dermatitis (AD) might be at increased risk of mental health disorders.

Objective: We aimed to quantify the mental health burden associated with pediatric AD in the United States.

Methods: A cross-sectional study design was used analyzing data from the 2007 National Survey of Children's Health, a survey reporting on the health status of 92,642 noninstitutionalized children aged 0 to 17 years. The lifetime prevalence of various provider-diagnosed mental health conditions was calculated for those with and without a history of AD.

Results: The odds of having attention deficit hyperactivity disorder was significantly increased in children with AD compared with the odds in control subjects without AD (odds ratio, 1.87; 95% CI, 1.54-2.27), even after controlling for known confounders. The adjusted odds ratios for depression, anxiety, conduct disorder, and autism were 1.81 (95% CI, 1.33-2.46), 1.77 (95% CI, 1.36-2.29), 1.87 (95% CI, 1.46-2.39), and 3.04 (95% CI, 2.13-4.34), respectively, and these estimates were all statistically significant. A clear dose-dependent relationship was observed between the prevalence of a mental health disorder and the reported severity of the skin disease.

Conclusions: Our data reveal a striking association between mental health disorders and AD in the US pediatric population. The severity of the skin disease alters the strength of the association. Prospective cohort studies are needed to verify these associations and to explore underlying mechanisms. Strategies to prevent AD or to aggressively treat early skin inflammation might modify the risk of mental health disorders in at-risk children.

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J Autism Dev Disord. 2012;1-11.

MATCH OR MISMATCH? INFLUENCE OF PARENTAL AND OFFSPRING ASD AND ADHD SYMPTOMS ON THE PARENT-CHILD RELATIONSHIP.

Van Steijn DJ, Oerlemans AM, Van Aken MAG, et al.

Few studies have examined the influence of parental ASD and ADHD symptoms in combination with child pathology on the parent-child relationship as perceived by the child. A sample of 132 families was recruited with one child with ASD (with/without ADHD), and one unaffected sibling. Affected children (regardless of diagnosis) reported lower acceptance and conflict resolution scores than their unaffected siblings, with conflict resolution scores (but not acceptance) being lower than the norm according to both affected and unaffected children in both fathers and mothers. Higher paternal, but not maternal, ASD and ADHD symptoms were related to poorer scores regarding acceptance and conflict resolution, respectively. Treatment targeting conflict resolution skills of parents and the feeling of being less accepted in children with ASD/ADHD may be beneficial.

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J Child Neurol. 2012;27:1547-52.

USING THE TEST OF VARIABLES OF ATTENTION TO DETERMINE THE EFFECTIVENESS OF MODAFINIL IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): A PROSPECTIVE METHYLPHENIDATE-CONTROLLED TRIAL.

Goez HR, Scott O, Nevo N, et al.

The efficacy of modafinil in comparison with methylphenidate in treatment of pediatric attention-deficit hyperactivity disorder (ADHD) has not been thoroughly investigated. This study compared the effect of modafinil versus methylphenidate on continuous attention task in children with ADHD, using the Test of Variables of Attention. Twenty-eight participants completed a baseline test followed by administration of a single dose of either methylphenidate or modafinil, after which the test was repeated. The test was performed a third time, after each subject received a dose of the medication not previously administered. Comparison of scores showed mean baseline, postmethylphenidate, and postmodafinil scores of -2.04,

0.017, and 0.09, respectively. No difference was found between improvements observed with either medication ($P < .05$). Adverse events for both agents were mild and self-limited, including abdominal pain, diarrhea, and hyposomnia. The authors conclude that modafinil is as effective as methylphenidate; however, a larger scale long-term study is required to confirm these results.

J Consult Clin Psychol. 2012 Dec;80:1041-51.

PROSPECTIVE FOLLOW-UP OF GIRLS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER INTO EARLY ADULTHOOD: CONTINUING IMPAIRMENT INCLUDES ELEVATED RISK FOR SUICIDE ATTEMPTS AND SELF-INJURY.

Hinshaw SP, Owens EB, Zalecki C, et al.

Objective: We performed a 10-year prospective follow-up of a childhood-ascertained (6–12 years), ethnically and socioeconomically diverse sample of girls with attention-deficit/hyperactivity disorder (ADHD; $N=140$: combined type [ADHD-C] $n=93$; inattentive type [ADHD-I] $n=47$) plus a matched comparison group ($N=88$). Girls were recruited from schools, mental health centers, pediatric practices, and via advertisements; extensive evaluations confirmed ADHD versus comparison status.

Method: Ten-year outcomes (age range 17-24 years; retention rate=95%) included symptoms (ADHD, externalizing, internalizing), substance use, eating pathology, self-perceptions, functional impairment (global, academic, service utilization), self-harm (suicide attempts, self-injury), and driving behavior.

Results: Participants with childhood-diagnosed ADHD continued to display higher rates of ADHD and comorbid symptoms, showed more serious impairment (both global and specific), and had higher rates of suicide attempts and self-injury than the comparison sample, with effect sizes from medium to very large; yet the groups did not differ significantly in terms of eating pathology, substance use, or driving behavior. ADHD-C and ADHD-I types rarely differed significantly, except for suicide attempts and self-injury, which were highly concentrated in ADHD-C. Domains of externalizing behavior, global impairment, service utilization, and self-harm (self-injury and suicide attempts) survived stringent control of crucial childhood covariates (age, demographics, comorbidities, IQ).

Conclusions: Girls with childhood ADHD maintain marked impairment by early adulthood, spreading from symptoms to risk for serious self-harm. Our future research addresses the viability of different diagnostic conceptions of adult ADHD and their linkages with core life impairments.

J Consult Clin Psychol. 2012 Dec;80:1052-61.

WHEN DIAGNOSING ADHD IN YOUNG ADULTS EMPHASIZE INFORMANT REPORTS, DSM ITEMS, AND IMPAIRMENT.

Sibley MH, Pelham WE Jr, Molina BSG, et al.

Objective: This study examined several questions about the diagnosis of attention-deficit/hyperactivity disorder (ADHD) in young adults using data from a childhood-diagnosed sample of 200 individuals with ADHD (age $M = 20.20$ years) and 121 demographically similar non-ADHD controls (total $N = 321$).

Method: We examined the use of self- versus informant ratings of current and childhood functioning and evaluated the diagnostic utility of adult-specific items versus items from the Diagnostic and Statistical Manual of Mental Disorders (DSM).

Results: Results indicated that although a majority of young adults with a childhood diagnosis of ADHD continued to experience elevated ADHD symptoms (75%) and clinically significant impairment (60%), only 9.6%–19.7% of the childhood ADHD group continued to meet DSM-IV-TR (DSM, 4th ed., text rev.) criteria for ADHD in young adulthood. Parent report was more diagnostically sensitive than self-report. Young adults with ADHD tended to underreport current symptoms, while young adults without ADHD tended to overreport symptoms. There was no significant incremental benefit beyond parent report alone to combining self-report with parent report. Non-DSM-based, adult-specific symptoms of ADHD were significantly correlated with functional impairment and endorsed at slightly higher rates than the DSM-IV-TR symptoms. However, DSM-IV-TR items tended to be more predictive of diagnostic group membership than the non-DSM adult-specific items due to elevated control group item endorsement.

Conclusions: Implications for the assessment and treatment of ADHD in young adults are discussed (i.e., collecting informant reports, lowering the diagnostic threshold, emphasizing impairment, and cautiously interpreting retrospective reports).

J Neural Transm. 2012;119:1417-23.

THE FEASIBILITY AND SAFETY OF S-ADENOSYL-L-METHIONINE (SAME) FOR THE TREATMENT OF NEUROPSYCHIATRIC SYMPTOMS IN 22Q11.2 DELETION SYNDROME: A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL.

Green T, Steingart L, Frisch A, et al.

The goal of this trial was to assess the feasibility and safety of using S-adenosyl-L-methionine (SAME) to treat depressive disorder, attention deficit/hyperactivity disorder (ADHD) and cognitive deficits in individuals with the 22q11.2 deletion syndrome (22q11.2DS). SAME supposedly enhances the activity of the COMT enzyme. Because individuals with 22q11.2DS have only one copy of the gene responsible for the enzyme, COMT haploinsufficiency may be associated with their psychiatric morbidity and cognitive deficits. We assessed twelve 22q11.2DS individuals with depressive disorder or ADHD in a randomized double-blind cross-over placebo-controlled trial, using SAME 800 mg bid. Individuals were evaluated for treatment safety and effectiveness during the trial and upon completion at sixth week. Compared to placebo, there were no significant differences in the rate of reported side effects between SAME and placebo. Despite a general concern that SAME might induce mania in vulnerable individuals, no manic or psychotic symptoms were exhibited during the SAME treatment. Individuals with 22q11.2DS with comorbid depressive disorder with or without psychotic symptoms (n=5) had a larger numerical improvement on relevant clinical scales compared to placebo. No treatment effect was found on ADHD symptoms in subjects who suffered from 22q11.2DS with comorbid ADHD (n=7). Cognitive performance did not improve or deteriorate following treatment with SAME compared to placebo. In conclusion SAME treatment up to 1,600 mg/day for 6 weeks in 22q11.2DS individuals appears to be safe, well tolerated and with no serious side effects. No significant benefit in depressive or ADHD symptoms was detected.

J Neural Transm. 2012;1-7.

ADRENERGIC NEUROTRANSMITTER SYSTEM TRANSPORTER AND RECEPTOR GENES ASSOCIATED WITH ATOMOXETINE RESPONSE IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER CHILDREN.

Yang L, Qian Q, Liu L, et al.

Atomoxetine, a selective inhibitor of the norepinephrine transporter, exerts its therapeutic effect for attention-deficit hyperactivity disorder (ADHD) by increasing the concentration of synaptic norepinephrine. The objective of this study was to evaluate the association of the genetic variants of multiple genes of the noradrenergic neurotransmitter system with atomoxetine response. One hundred and eleven ADHD children and adolescents were enrolled in a prospective, open-label study of atomoxetine for 8-12 weeks. The dose was titrated to 1.2-1.4 mg/kg per day and maintained for at least 4 weeks. The primary efficacy measure was the investigator-rated ADHD Rating Scale-IV. Two categorical evaluations of treatment effects (defined as response and remission) were used. Twelve SNPs in SLC6A2, ADRA2A, and ADRA1A were genotyped to analyze their association with response or remission status. rs3785143 in SLC6A2 was associated with responder status (nominal P = 0.0048; corrected by multiple test, P = 0.0416; OR 2.66, 95 % confidence interval (CI) 1.35-5.26). rs2279805 of SLC6A2 was nominally significantly associated with the remission status. (P=0.0221, OR 2.32, 95 % CI 1.13-4.75, multiple test P=0.2130). The GG haplotype of rs1800544 and rs553668 in ADRA2A achieved nominal significance for association with non-remission (P=0.0219, OR 2.82, 95 % CI 1.16-6.85, multiple test, P=0.2076). The results of this study suggest that DNA variants of both SLC6A2 and ADRA2A in the adrenergic neurotransmitter system might alter the response to atomoxetine, though further replication study in larger sample for validation of these findings is still needed.

J Psychiatr Res. 2012.

DIFFERENTIAL REWARD PROCESSING IN SUBTYPES OF ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Edel MA, Enzi B, Witthaus H, et al.

Objectives: Abnormalities in reward processing have been found in adolescents and adults with ADHD using the 'Monetary Incentive Delay' (MID) task. However, ADHD groups in previous studies were heterogeneous regarding ADHD subtype, gender and, in part, drug treatment status. This study sought to compare neural activations in the ventral striatum (VS) and prefrontal regions during reward processing in homogenous ADHD subtype groups and healthy adults, using the MID task.

Methods: In total, 24 drug-naïve, right-handed male adults with ADHD (12 subjects with combined type (ADHD-ct) and 12 subjects with predominantly inattentive (ADHD-it) type ADHD), and twelve healthy right-handed male control subjects were included.

Results: Compared to ADHD-ct and healthy subjects, ADHD-it subjects showed a bilateral ventral striatal deficit during reward anticipation. In contrast, ADHD-ct subjects showed orbitofrontal hyporesponsiveness to reward feedback when compared with ADHD-it and healthy subjects.

Conclusions: This is the first fMRI study that delineates dysfunctional and subtype-divergent neural and behavioural reward processing in adults with ADHD. (copyright) 2012 Elsevier Ltd. All rights reserved.

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J Psychopathol Behav Assess. 2012;1-11.

FRIENDSHIP INTIMACY EXCHANGE BUFFERS THE RELATION BETWEEN ADHD SYMPTOMS AND LATER SOCIAL PROBLEMS AMONG CHILDREN ATTENDING AN AFTER-SCHOOL CARE PROGRAM.

Becker SP, Fite PJ, Luebke AM, et al.

The friendships of children displaying symptoms of attention-deficit/hyperactivity disorder (ADHD) have been understudied, particularly in comparison to the domain of peer rejection. This study tested whether friendship intimacy exchange buffers the prospective relation between ADHD symptoms and social problems 1 year later in a sample of children attending a community-based after-school program. Children (N = 131; 53 % boys; 66 % African American) ranging from 5 to 13 years of age participated in this study. At baseline, children reported on friendship intimacy exchange with their identified best friend, and program staff rated children on ADHD symptoms and social problems. Staff ratings of children's social problems were collected again 1 year later. Multiple regression analyses indicated that, after controlling for demographic variables and baseline social problems, friendship intimacy exchange significantly moderated the association between ADHD symptoms and social problems at the one-year follow-up. Specifically, the relation between ADHD and social problems was no longer significant for children reporting high levels of friendship intimacy exchange. This moderation was not further qualified by either child age or sex, although boys were more likely than girls to report low rates of friendship intimacy exchange. These findings indicate the importance of friendship intimacy for children displaying ADHD symptoms, who often experience significant peer problems. Friendship quality may be a promising target for prevention and intervention efforts in mitigating some of the long-term social problems associated with ADHD symptomatology, and future research is needed to extend these findings to other domains of friendship quality and clinical samples of children with ADHD.

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J Psychopathol Behav Assess. 2012 Dec;34:510-19.

EMOTION DYSREGULATION AND EMOTIONAL IMPULSIVITY AMONG ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: RESULTS OF A PRELIMINARY STUDY.

Mitchell JT, Robertson CD, Anastopolous AD, et al.

Recent reviews argue that emotion dysregulation is an important feature of attention-deficit/hyperactivity disorder (ADHD) and involves a failure to inhibit negative emotions that leads to negative affectively-driven impulsive behavior (i.e., emotional impulsivity). The goal of the current study was to assess (a) whether emotion dysregulation and emotional impulsivity was higher in a group of adults diagnosed with ADHD and (b) if the relationship between core ADHD symptoms (i.e., inattention and hyperactivity-impulsivity) and emotional impulsivity is mediated by emotion dysregulation symptoms. A group of adults with (n = 18) and

without ($n = 23$) ADHD completed measures of core ADHD symptoms, emotion dysregulation, and emotional impulsivity. A series of one-way analyses of covariance indicated significant between-group differences in emotion dysregulation and emotional impulsivity when current depression and oppositional defiant disorder ratings were covaried. In addition, the relationship between ADHD symptoms and emotional impulsivity was mediated by emotion dysregulation symptoms. These findings suggest that emotion dysregulation and emotional impulsivity are higher in adults diagnosed with ADHD and that emotion dysregulation symptoms have predictive value beyond core ADHD symptoms.

J Subst Abuse Treat. 2013;44:224-30.

PREDICTORS OF TREATMENT RESPONSE IN ADOLESCENTS WITH COMORBID SUBSTANCE USE DISORDER AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Tamm L, Trello-Rishel K, Riggs P, et al.

Attention-Deficit/Hyperactivity Disorder (ADHD) frequently co-occurs with substance use disorder (SUD) and is associated with poor substance-use treatment outcomes. A trial evaluating osmotic-release oral system methylphenidate (OROS-MPH) for adolescents with ADHD and SUD, concurrently receiving behavioral therapy, revealed inconsistent medication effects on ADHD or SUD. Clinical care for this population would be advanced by knowledge of treatment outcome predictors. Data from the randomized placebo-controlled trial ($n = 299$) were analyzed. Significant treatment predictors included: 1) Substance use severity, associated with poorer ADHD and SUD outcomes, 2) ADHD severity, associated with better ADHD and SUD outcomes, 3) comorbid conduct disorder, associated with poorer ADHD outcomes, and 4) court-mandated status, associated with better SUD outcomes but poorer treatment completion. An interaction effect showed that OROS-MPH improved SUD outcomes in adolescents with comorbid conduct disorder compared to placebo. While severe SUD may require more intensive psychosocial treatment, OROS-MPH may improve substance treatment outcomes in adolescents with co-morbid attention and conduct problems.

J Can Acad Child Adolesc Psychiatry. 2012;21:245-52.

PREVENTION OF SUBSTANCE USE IN CHILDREN/ADOLESCENTS WITH MENTAL DISORDERS: A SYSTEMATIC REVIEW.

Salvo N, Bennett K, Cheung A, et al.

Objective: We conducted a systematic review to answer the question: Among youth (less-than or equal to)18 years of age with a mental disorder, does substance use prevention compared to no prevention result in reduced rates of substance use/abuse/ disorder (SUD)? The review was requested by the Ontario Ministry of Health and Long-term Care through the Canadian Institutes for Health Research Evidence on Tap program.

Methods: A four-step search process was used: Search 1 and 2: Randomized controlled trials (RCTs) that evaluated a SUD prevention intervention in individuals with a mental disorder who were: 1) (less-than or equal to)18 years; or, 2) any age. Search 3: Observational studies of an intervention to prevent SUD in those with mental disorder. Search 4: RCTs that evaluated a SUD primary prevention skills-based intervention in high-risk youth (less-than or equal to)18 years.

Results: Searches 1 and 2: one RCT conducted in youth was found; Search 3: two observational studies were found. All three studies reported statistically significant reductions in substance use. Search 4: five RCTs were found with mixed results. Methodological weaknesses including inadequate study power may explain the results.

Conclusions: Little is known about effective interventions to prevent SUD in youth with a mental disorder. Effective SUD primary prevention programs exist and should be evaluated in this high-risk group.

Klin Psikofarmakol Bul. 2011;21:S95.

TREATMENT APPROACHES TO PSYCHIATRIC COMORBIDITIES OF ADHD IN CHILDREN.

Turkbay T.

Attention-deficit hyperactivity disorder (ADHD) is highly comorbid with other psychiatric disorders. Each of the comorbid disorders modifies the overall clinical presentation and treatment response. Sometimes there can be more complex situations. For example, depressed children demonstrate diminished concentration and irritability and it may be difficult to differentiate from the cardinal symptoms of ADHD. Children with ADHD and comorbid disorders have poorer prognoses than those with ADHD alone. Both stimulant medications and atomoxetine markedly reduce symptoms of comorbid oppositional defiant disorder, which often requires adjunctive parent training and behavior management. Severely explosive anger may require the use of atypical antipsychotics. In conduct disorder, stimulant medications and atomoxetine also reduce aggressive behavior and antisocial acts. Atypical psychotics or mood stabilizers may be used for highly aggressive-explosive cases. The majority of children with comorbid ADHD/depression can be managed with a psycho stimulant. However, initial treatment with antidepressant drugs should be saved for treating children with more severe depression. Stimulants can exacerbate symptoms of anxiety disorders. Atomoxetine, SSRIs and behavioral therapies reduce anxiety symptoms. If tic disorders are mild or episodic, they usually require no treatment. Most ADHD/tic disorder patients will not demonstrate an exacerbation of their tics with stimulants. Nevertheless, if tics worsen with stimulant use, an antipsychotic or alpha agonist should be added to the psychostimulant.

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Klin Psikofarmakol Bul. 2011;21:S190.

METHYLPHENIDATE INDUCED THROMBOCYTOPENIA IN A PEDIATRIC PATIENT WITH ADHD AND STUTTERING.

Ozdemir S, Ozdemir FA.

Stuttering and attention deficit hyperactivity disorder (ADHD) can be seen together. Anemia or thrombocytopenia, rarely even pancytopenia may occur as a side effect of medications used to treat both disorders. Thrombocytopenia, although it may be seen in some cases using methylphenidate, occurs rarely. An 8 year-old boy was brought to our outpatient clinic by his family with the complaints of stuttering, attention deficit, and hyperactivity. After the psychiatric evaluation and history were conducted and psychometric tests were applied. One month later methylphenidate 18mg/day was started for the treatment of ADHD. Soon after initiation of medication, petechia developed on both lower extremities of the patient. CBC showed isolated thrombocytopenia and the patient was followed by hematology clinic. On the 6th day upon stopping methylphenidate, the thrombocyte count returned to normal. We also discussed possible mechanisms of thrombocytopenia.

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Klin Psikofarmakol Bul. 2011;21:S57.

ADHD AND MOOD DISORDERS IN CHILDREN.

Diler RS.

Five to 40% of children and adolescents with attention deficit hyperactive disorder (ADHD) also have comorbid major depressive disorders (MDD). Moreover, youths with ADHD have up to a 4 times higher risk of developing depressive disorders than the general adolescent population. Comorbidity with MDD has been associated with elevated impairment and higher rates of hospitalization versus ADHD alone. However, depression in youths with ADHD may be more difficult to diagnose, given that some symptoms overlap between the two disorders. Moreover, many of the medications used to treat ADHD cause side effects resembling symptoms of MDD. Available studies suggest the particular importance of anhedonia, social withdrawal, psychomotor retardation, negative views of self and future, and suicidal thoughts as symptoms that distinguish MDD in youths who have ADHD. Despite ongoing controversy, the view that pediatric bipolar disorder (PBD) is rare or non-existent has been increasingly challenged not only by case reports but also by systematic research; however, a significant portion of bipolar youth, especially children, have high comorbidity with ADHD. Significant debate exists on whether early onset bipolar disorder is mistakenly attributed to attention deficit hyperactivity disorder (ADHD), or whether ADHD is frequently

misdiagnosed as mania. Among pediatric-onset cases of bipolar disorder, comorbid ADHD is frequently seen, and there is strong evidence to suggest that this pattern has a familial and genetic basis. Differentiating bipolarity in children with ADHD is not an academic discussion but also a great concern because of the associated complication of the treatment of these disorders. It is suggested that manic symptoms should represent a distinct change from a child's usual level of functioning (e.g., change or worsening of distractibility during a mood episode in children with ADHD). There are some symptoms that mainly occur in BD youth as compared to other disorders (e.g., ADHD) and may help to differentiate between BD and these disorders, such as clinically relevant euphoria, grandiosity, decreased need for sleep, hypersexuality (without history of sexual abuse or exposure to sex), and hallucinations. We need larger longitudinal studies to better understand the risks and resilience factors of developing BP in ADHD youth.

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Klin Psikofarmakol Bul. 2011;21:S66.

ESSENTIAL FATTY ACIDS IN ADHD TREATMENT.

Durukan I.

Attention deficit hyperactivity disorder (ADHD) is characterized by problems with attention, hyperactivity and impulsivity. These problems often severely affect families, relationships and school performance. Although stimulants and atomoxetine are efficacious in many children, these medications can have side effects such as insomnia, decreased appetite, irritability and impaired growth. The etiology of ADHD is generally accepted to be complex and multifactorial. Little progress has been made in elucidating predisposing biological factors. Related contributory factors for ADHD etiology are diet, nutrition and particular abnormalities in the metabolism of the longchain polyunsaturated fatty acids (LCPUFAs). Essential fatty acids (EFAs) as a complementary or alternative treatment for ADHD have been used as both a primary and an adjunctive treatment in many countries. Humans are unable to synthesize linoleic acid (an omega-6 fatty acid), and α -linolenic acid (ALA), an omega-3 fatty acid. The main dietary sources of linoleic acid and ALA are vegetable oils and their seeds. Both omega-3 and omega-6 LCPUFAs have critical importance for normal brain development and function. Large amounts of both omega-6 and omega-3 LCPUFAs are deposited in the central nervous system during fetal life. During infancy, dietary intake of both omega-3 and omega-6 LCPUFAs continues to be essential for neuronal development. LCPUFAs and their derivatives work as facilitators of dopamine, serotonin and norepinephrine release, as regulators of gene transcription, as modulators of Na⁺-K⁺ ATPase channel function and as the precursors of pro-inflammatory and anti-inflammatory molecular families. The most abundant LCPUFA in the brain is DHA from the omega-3 series, which is concentrated at nerve cell synapses and is important for neural cell signalling and neurotransmitter processes. There is increasing evidence that omega-3 LCPUFAs play a part in many neurodevelopmental and psychiatric disorders. ADHD, dyslexia, developmental coordination disorder and autistic spectrum disorder are suggested to be related to the omega-6/omega-3 spectrum of disturbances. Several studies of LCPUFA supplementation in children with ADHD symptoms have been conducted. Open-label EFA trials in ADHD demonstrate that ADHD symptoms are responsive to EFA supplementation. Despite successful open-label trials, randomized controlled trials of EFA in ADHD have generally been unsuccessful in demonstrating treatment effects and some of them even displayed better results for the placebo group. There are three studies with partial positive results but these studies represent a small minority and two of them have several methodological limitations. The side effects of EFA are generally related to the gastrointestinal system and usually include diarrhea, nausea, fishy aftertaste, belching and indigestion. These side effects seem to be mild, transient and infrequent, and also appear in the placebo groups. Current findings from randomized clinical trials of EFA in children with ADHD are not promising. Most randomized trials have clearly demonstrated lack of superiority compared to placebo. Moreover, the studies that showed positive findings did not use children properly diagnosed with ADHD and none of them demonstrated clinical improvement in more than one setting. This delineation does not support the use of EFA supplements as a treatment for children with ADHD. Future studies should be

planned to consider methodological issues such as proper ADHD diagnosis, blinded controls, adequate sample size and behavioral assessment in more than one setting.

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Klin Psikofarmakol Bul. 2011;21:S57-S58.

ACADEMIC AND OCCUPATIONAL PROBLEMS IN ADHD.

Ozturk M.

Attention Deficit Hyperactivity Disorder (ADHD) is a syndrome of inattention, hyperactivity, impulsiveness and other deficits of executive functions. It's now well known that ADHD often continues into adulthood (1, 2). ADHD is a chronic disorder which leads to a negative impact on functioning throughout the life cycle (3). Children with ADHD are at significant risk of multiple forms of adolescent maladjustment. Approximately up to 60% of childhood cases continue symptomatic into adulthood. In the remaining 40 percent symptoms may remit in early adulthood (4). The manifestation of ADHD changes over the course of life. In some cases the hyperactivity may disappear but decreased attention span and impulse control problems persist (5). Approximately 1 in 25 adults have ADHD, 90% of whom may be currently untreated, with a potentially negative impact on the lives of patients and their families (6). Significant legal, academic, social, and occupational problems have been observed in adults with ADHD (7). Follow up studies suggest that up to 33% of ADHD teens versus 1% to 9% of controls drop out high school. Children with ADHD are at risk of negative academic outcomes. ADHD and similar problems entail a risk of underachievement at school. The results indicate that students with ADHD underachieve in the school situation in relation to their optimal cognitive capacity (3). Adolescents with ADHD complete less education by 2-3 years and demonstrate lower occupational performance at the age of 25 years. Adults with ADHD may struggle with frequent job changes, frequent partner changes, higher rates of divorce, increased motor vehicle accidents, poor money management and higher rates of unwed pregnancy (8). Although their educational performance is lower than people without ADHD, their early employment histories don't differ from those people with similar education (5). Adolescents with ADHD were more likely to smoke cigarettes and use illicit drugs. Their academic attainment was below age norms with more than one fourth repeating grades (9). Studies show that effective treatment significantly improves quality of life (3). Severity of childhood ADHD and treatment significantly predict the persistence of ADHD into adulthood (5). As previously shown by some research for children and adolescents, stimulant medications alone did not eliminate the academic achievement deficit of ADHD undergraduates. ADHD patients who were treated with stimulants were significantly less likely to subsequently develop depressive and anxiety disorders and disruptive behavior and less likely to repeat a grade compared with participants with ADHD who were not treated. Adolescents with ADHD were also significantly more likely to be absent during the academic year, and they were over eight times more likely than adolescents without ADHD to drop out of high school. These findings demonstrate that children with ADHD continue to experience severe academic impairment into high school (10).

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Klin Psikofarmakol Bul. 2011;21:S96-S97.

Treatment of neurological co-morbid disorders in children with ADHD.

Yuce M.

Attention Deficit Hyperactivity Disorder (ADHD) is a neurodevelopmental disorder characterized by inattention, hyperactivity, and impulsive behaviors. ADHD is one of the most common childhood psychiatric disorders. Children with ADHD also have many comorbid disorders and psychiatric symptoms. ADHD may be accompanied with neurological disorders such as epilepsy, headache, and cerebral palsy. Neurological co-morbid conditions can lead to reduction in the level of function, adherence to treatment difficulty, increasing the price of healthcare and medical complications. Therefore, diagnosis and treatment of these neurological co-morbid problems with ADHD are important. ADHD is seen more commonly in children with epilepsy according to the normal population. Approximately 20% of children diagnosed with epilepsy have ADHD as well. Some antiepileptic drugs are known to cause lethargy and impairment of attention. Barbiturates and benzodiazepines may worsen the symptoms of ADHD. It has been reported that some drugs such as tiagabin, zonisamide, and topiramate can cause cognitive slowing and concentration

problems. Psychostimulants are frequently used in the treatment of ADHD. It has been reported that these medications do not severely effect epileptic seizures and may improve cognitive functions. In this presentation treatment approaches for children and adolescents with ADHD and co-morbid neurological disorders will be discussed.

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Klin Psikofarmakol Bul. 2011;21:S97.

DRUG INTERACTIONS OF MEDICATIONS FOR COMORBIDITIES OF ADHD.

Abali O.

ADHD is a very common psychiatric disorder in childhood. Children with ADHD have frequently another psychiatric disorder. Conduct disorder, learning disorder, addiction, and mood disorders are frequently seen in children with ADHD. It has been estimated that 23%- 42% of youth receiving psychiatric drugs are receiving multiple drugs (1). Recently drug interactions have been emphasized in these patients. Stimulant drugs and atomoxetine, which is a non stimulant drug, are used in patients with ADHD. Interactions between these drugs and other psychotropic drugs are important for treatment quality. Drug interactions should be considered to prevent adverse effects and increase treatment quality. Possible drug interactions could impact on liver, intestine, or plasma. There are a lot of important risks due to drug interactions in patients with ADHD. Drug plasma levels can change due to CYP-P450 system interactions. It is estimated that approximately 7% of the population may be poor metabolizers, causing slow metabolism(2). Also inhibitors of the cytochrome P450 can increase drug levels by several folds. Some drugs inhibit these systems very potently so that concentration of drug can reach very high levels. Important complications such as neuroleptic malignant syndrome, serotonergic syndrome, and hallucinations can be seen during these interactions. Treatment strategies should be reviewed from this perspective. Possible drug interactions couldn't be exactly predicted by the clinicians for every patient. But potential drug interactions should be considered for every patient. Drug interactions will be discussed at this presentation. The treatment strategies will be updated for long term good quality treatment based on the literature.

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Klin Psikofarmakol Bul. 2011;21:S96.

TREATMENT APPROACHES TO PSYCHIATRIC COMORBIDITIES OF ADHD IN ADOLESCENTS.

Semerci B.

Adolescences with ADHD, who suffer from social problems, are under risk of depression, anxiety, destructive conduct disorder, and drug addiction. If there are co-morbid disorders associated with ADHD, it makes the treatment difficult and causes some other complications. The fundamental treatment principles of the psychiatric co-morbidities of ADHD are also effective for adolescence period. However, especially, we should be careful about the conditions that have high prevalence during adolescence period and the conditions which affect prognosis in a negative way. These situations need to be assessed in diagnosis and treatment plan. Anxiety Disorders: Some researches indicate that a stimulant treatment has small effects on anxiety disorder. The treatment of ADHD without anxiety disorder gets more successful results. However, according to recent research, treatment is also effective on anxiety disorder. In general, considering the effect of CBT on the anxiety disorder treatment, it is suggested that CBT beside medication treatment is effective on ADHD having co morbidity with anxiety disorder. If there is co morbidity, it is suggested that the priority needs to be given to ADHD and that if the anxiety symptoms continue, another medication treatment should be considered. Mood Disorders: Depression is an important problem in adolescence period. The important point in treatment is to identify that if ADHD causes to depressive findings or major depression. If ADHD cooccurs with major depression, both of them need to be treated. The treatment may be done either by stimulants or atomoxetine or only by SSRIs or tricyclic anti depressants. The last option is to use the two methods both. When there is co-morbid depression and ADHD, the efficacy of antidepressants is lower than when it is depression alone. In clinical observation, depression findings in adolescence period should be assessed attentively. If there is major depression, the treatment should be carried out together with ADHD. Selective serotonin reuptake inhibitors (SSRI) may be used with stimulants. Conduct Disorders: If ADHD is not treated, it may possibly turn to conduct disorder. In

many studies, the use of stimulants for the treatment of co-morbid ADHD and conduct disorder is investigated. The results of these studies show that stimulants are effective when the morbidities are both separate or together. However, if there are co-morbid ADHD and conduct disorder, the effectiveness of stimulants on aggression is lower. If there are co-morbid ADHD and aggression and if the typical ADHD treatment does not work, it may be useful to add atypical antipsychotics to the treatment. If ADHD is co-morbid with conduct disorder, working with adolescents, using behavioural approaches, supporting families and to providing them education about the problem may be helpful. If ADHD co occurs with drug addiction, both disorders should be treated. Stimulants can be used in a controlled way. However, due to addiction, prescribing stimulants may be cause legal problems. Atomoxetine and bupropion could be other options. Eventhough, antidepressants are effective in ADHD, their effectiveness in addiction is limited.

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Klin Psikofarmakol Bul. 2011;21:S148.

INFLUENCE OF POLYMORPHISM OF THE NOREPINEPHRINE TRANSPORTER GENE (SLC6A2) AND ALPHA-2 ADRENERGIC RECEPTOR GENE (ADRA2A) ON REGIONAL CEREBRAL BLOOD FLOW IN A KOREAN ADHD SAMPLE: A PRELIMINARY STUDY.

Yang Y, Kim J, Kim B, et al.

Some genes related to the noradrenergic system have been investigated as candidate genes in Attention Deficit Hyperactivity Disorder (ADHD). Through functional brain imaging studies, it has been reported that brain areas such as the prefrontal cortex (PFC), dorsal anterior cingulate cortex, and striatum show abnormal findings in ADHD patients. We have investigated whether there was an association between polymorphism of the noradrenergic system related genes (SLC6A2 and ADRA2A) and regional cerebral blood flow (rCBF) in a Korean ADHD sample. Methods: A total of thirty-six children (31 boys and 5 girls, mean age: 8.9 ((plus or minus) 1.84) years) participated in this study. Subjects were recruited from the outpatient's clinic of child and adolescent psychiatry in the Seoul National University Hospital. The diagnosis of ADHD was made based on the DSM-IV-TR. All patients were drug naive at the time of image acquisition. Genotyping of SLC6A2 (G1287A, -3081(A/T)) and ADRA2A (DraI, MspI) was done. SPM8 (Statistical parametric mapping 8) was used to compare images between the two groups divided by each genotype. Results: Children with the G/A and A/A genotypes at the SLC6A2 G1287A polymorphism showed decreased rCBF in the right inferior temporal gyrus and the left middle temporal gyrus compared to children with G/G genotype (uncorrected p-value< 0.001). In ADRA2A MspI polymorphism, children with the C/G and C/C genotypes showed increased rCBF in the left striatum and the left cingulate gyrus and decreased rCBF in the left cerebellar vermis compared to children with G/G genotype. There were no significant rCBF alterations across genotypes in the SLC6A2 -3081(A/T) and ADRA2A MspI genes. Conclusion: This study showed that the noradrenergic system related genes might be associated with functional brain abnormalities in children with ADHD.

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Klin Psikofarmakol Bul. 2012;22:325-31.

EFFECT OF FERRITIN ON SHORT-TERM TREATMENT RESPONSE IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Oner P, Oner O, Cop E, et al.

Objectives: Several studies have shown that iron deficiency and ferritin levels are associated with parent and teacher Attention Deficit Hyperactivity Disorder (ADHD) ratings. Although there are conflicting results, it has also been reported that iron supplementation may help to decrease ADHD symptoms. When all these previous studies are taken into account, it is clear that a large study investigating the effects of iron deficiency and ferritin levels on routine pharmacological treatment of ADHD with stimulants would be helpful to elucidate this treatment from a clinical point of view.

Methods: A total of 345 subjects with combined or predominantly hyperactive-impulsive (PHI) subtypes of ADHD were included. All diagnoses were based on the DSM-IV criteria and ascertained by direct interviews conducted by the authors, who are experienced child psychiatrists certified in the use of the Schedule for Affective Disorders and Schizophrenia for School-Age Children - Present and Lifetime Version (K-SADS-PL) semi-structured interview. The two treatment response criteria were: 1) 25% or more

decrease in pre-treatment Conners Parent Rating Scale (CPRS) and Conners Teacher Rating Scale (CTRS) Hyperactivity (HA) and Total Problems scores; 2) CPRS and CTRS HA scores lower than the cut-off point ("very improved").

Results: A total of 255 (73.9%) patients were on OROS-methylphenidate (OROS-MPH) and 90 (26.1%) were on immediate release methylphenidate (IR-MPH). The mean(plus or minus)sd of OROS-MPH and IR-MPH doses were 28.8(plus or minus)8.1 and 20.9(plus or minus)7.1 mg, respectively. More than half (52.5%) of the subjects were previously drug-naïve at treatment inception. Two hundred and seventy eight (80.6%) subjects had combined subtype ADHD and the remainder had predominantly hyperactive-impulsive subtype. Only 60 (17.4%) of the subjects had no comorbid disorders, while 38.3% had one comorbid disorder, 32.8% had two comorbid disorders, and 11.6% had three or more comorbid disorders. The most frequent comorbidity was Oppositional Defiant Disorder/Conduct Disorder (ODD/CD, 51.6%), followed by Learning Disabilities (LD, 35.4%) and Anxiety Disorders (AD, 15.9%). Logistic regression analysis showed that subjects with comorbid ODD/CD and LD were less likely to respond to treatment. Ferritin levels and iron deficiency were not associated significantly with outcomes.

Conclusions: In a large sample of subjects with combined or predominantly hyperactive-impulsive subtypes of ADHD, after controlling for several factors, we found that neither iron deficiency (ferritin <12 ng/ml) nor ferritin levels were associated with less favorable short-term treatment outcomes with stimulants. Subjects with comorbid ODD/CD and LD were less likely to have a 25% or more decrease in CTRS Total score. The presence of ODD/CD was also a negative predictor of treatment response in terms of CPRS Total and HA scores. The lack of a negative treatment response in ADHD subjects with iron deficiency and lack of a negative association with ferritin levels suggest that the relationship between iron metabolism and ADHD, a highly heterogeneous disorder, may be more complicated than previously believed.

Liver Int. 2012.

INCREASED RISKS OF EPILEPSY AND NEUROPSYCHIATRIC DISEASES IN CHILDREN OF MOTHERS WITH ALCOHOLIC LIVER DISEASE.

Stokkeland K, Ebrahim F, Hultcrantz R, et al.

Background: Pregnancy in women with liver disease may increase the risk of fetal complication. Data on disease frequencies in children born to mothers with alcoholic liver disease do not exist, although we do know that prenatal alcohol exposure may affect the fetus negatively.

Aims: The aim of this study was to assess the relative risk of neuropsychiatric diseases in children who were born to mothers with chronic liver diseases.

Methods: We linked the Hospital Discharge Register, Medical Birth Register and Pharmaceutical Register in Sweden between 1969 and 2009 to identify women with liver disease. We identified their children, up to the age of 16 in the Medical Birth Register, born between 1973 and 2009. Between 2005 and 2009, we identified every prescription that was dispensed to these children.

Results: We identified 5 124 children of mothers with alcoholic liver disease. There were 22 960 children of mothers with non-alcoholic liver disease. For controls, we used 10 sex-, age- and birthplace-matched children. There were more children born to mothers with alcoholic liver disease before the birth who had been dispensed antiepileptics ($n = 11$, $RR = 3.2$ (1.6-6.4)), neuroleptics ($n = 7$, $RR = 5.0$ (2.0-12.5)) and drugs to treat attention deficit hyperactivity disorders ($n = 22$, $RR = 5.9$ (3.7-9.4)) compared with sex-, age- and regionally adjusted controls. Children born to mothers with non-alcoholic liver disease had significantly increased risk of being dispensed drugs to treat attention deficit disorders ($RR = 2.2$ (1.8-2.6)).

Conclusions: Mothers with alcoholic liver disease have increased risks of having children with severe neurological and psychiatric disorders.

NeuroImage. 2012 Dec;63:1833-40.

PARADOXICAL RESULTS OF ADAPTIVE FALSE DISCOVERY RATE PROCEDURES IN NEUROIMAGING STUDIES.

Reiss PT, Schwartzman A, Lu F, et al.

Adaptive false discovery rate (FDR) procedures, which offer greater power than the original FDR procedure of Benjamini and Hochberg, are often applied to statistical maps of the brain. When a large proportion of the null hypotheses are false, as in the case of widespread effects such as cortical thinning throughout much of the brain, adaptive FDR methods can surprisingly reject more null hypotheses than not accounting for multiple testing at all—i.e., using uncorrected p-values. A straightforward mathematical argument is presented to explain why this can occur with the q-value method of Storey and colleagues, and a simulation study shows that it can also occur, to a lesser extent, with a two-stage FDR procedure due to Benjamini and colleagues. We demonstrate the phenomenon with reference to a published data set documenting cortical thinning in attention deficit/hyperactivity disorder. The paper concludes with recommendations for how to proceed when adaptive FDR results of this kind are encountered in practice.

Neuropharmacology. 2012 Dec;63:1327-34.

THE SPONTANEOUSLY HYPERTENSIVE AND WISTAR KYOTO RAT MODELS OF ADHD EXHIBIT SUB-REGIONAL DIFFERENCES IN DOPAMINE RELEASE AND UPTAKE IN THE STRIATUM AND NUCLEUS ACCUMBENS.

Miller EM, Pomerleau F, Huettl P, et al.

The most widely used animal model of attention-deficit/hyperactivity disorder (ADHD) is the spontaneously hypertensive rat (SHR/NCrl), which best represents the combined subtype (ADHD-C). Recent evidence has revealed that a progenitor strain, the Wistar Kyoto from Charles River Laboratories (WKY/NCrl), is useful as a model of the inattentive subtype (ADHD-PI) and the Wistar Kyoto from Harlan Laboratories (WKY/NHsd) and the Sprague Dawley (SD) have been suggested as controls. Dopamine (DA) dysfunction in the striatum (Str) and nucleus accumbens core (NAc) is thought to play a significant role in the pathophysiology of ADHD but data obtained with the SHR is equivocal. Using high-speed chronoamperometric recordings with carbon fiber microelectrodes, we found that the SHR/NCrl displayed decreased KCl-evoked DA release versus the WKY/NCrl model of ADHD-PI in the dorsal Str. The WKY/NCrl and the WKY/NHsd control did not differ from each other; however, the control SD released less DA than the WKY/NCrl model of ADHD-PI in the dorsal Str and less than the control WKY/NHsd in the intermediate Str. The SHR/NCrl had faster DA uptake in the ventral Str and NAc versus both control strains, while the WKY/NCrl model of ADHD-PI exhibited faster DA uptake in the NAc versus the SD control. These results suggest that increased surface expression of DA transporters may explain the more rapid uptake of DA in the Str and NAc of these rodent models of ADHD.

Neuropharmacology. 2013 Jan;64:321-28.

A SELECTIVE DOPAMINE REUPTAKE INHIBITOR IMPROVES PREFRONTAL CORTEX-DEPENDENT COGNITIVE FUNCTION: POTENTIAL RELEVANCE TO ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Schmeichel BE, Zemlan FP, Berridge CW.

Drugs used to treat attention deficit hyperactivity disorder (ADHD) improve prefrontal cortex (PFC)-dependent cognitive function. The majority of ADHD-related treatments act either as dual norepinephrine (NE) and dopamine (DA) reuptake inhibitors (psychostimulants) or selective NE reuptake inhibitors (SNRIs). Certain benztrapine analogs act as highly selective DA reuptake inhibitors while lacking the reinforcing actions, and thus abuse potential, of psychostimulants. To assess the potential use of these compounds in the treatment of ADHD, we examined the effects of a well-characterized benztrapine analog, AHN 2-005, on performance of rats in a PFC-dependent delayed-alternation task of spatial working memory. Similar to that seen with all drugs currently approved for ADHD, AHN 2-005 dose-dependently improved performance in this task. Clinically-relevant doses of psychostimulants and SNRIs elevate NE and DA preferentially in the PFC. Despite the selectivity of this compound for the DA transporter, additional microdialysis studies demonstrated that a cognition-enhancing dose of AHN 2-005 that lacked locomotor activating effects increased extracellular levels of both DA and NE in the PFC. AHN 2-005 produced a

larger increase in extracellular DA in the nucleus accumbens, although the magnitude of this was well below that seen with motor activating doses of psychostimulants. Collectively, these observations suggest that benztropine analogs may be efficacious in the treatment of ADHD or other disorders associated with PFC dysfunction. These studies provide a strong rationale for future research focused on the neural mechanisms contributing to the cognition-enhancing actions and the potential clinical utility of AHN 2-005 and related compounds.

Neuropsychopharmacology. 2012;38:S219.

PHARMACOGENETIC MODERATORS OF METHYLPHENIDATE AND GUANFACINE RESPONSE IN CHILDREN AND ADOLESCENTS WITH ADHD.

Nurmi EL, Mallya KS, McGough J, et al.

Background: Pharmacogenetic influences may explain differential response to commonly prescribed psychiatric medications. The consideration of pharmacogenetic factors has shown clinical utility in medical specialties such as oncology, cardiovascular medicine, and pulmonology, improving patient outcomes and reducing morbidity. An expanded understanding of pharmacodynamic factors moderating response to psychiatric medications will allow rapid treatment matching, avoid morbidity, and guide the design of novel therapeutics. While methylphenidate and guanfacine are effective treatments of hyperactive and inattentive symptoms associated with ADHD, variability in individual treatment response is substantial. We sought to determine whether genetic variation in monoamine drug targets could help explain variable treatment outcomes in a randomized, double-blind, placebo-controlled trial of dextmethylphenidate (d-MPH) and guanfacine for pediatric ADHD.

Methods: Subjects were recruited for Project I of the NIMH CIDAR Translational Research to Enhance Cognitive Control (TRECC) Center at UCLA, which aims to develop treatments that specifically remediate executive function deficits as an important path to improve outcomes. Project I was designed to test the short-term efficacy of d- MPH and guanfacine combination pharmacotherapy against standard stimulant or guanfacine monotherapy on both symptom and cognitive endpoints. We further examined the contribution of genetic variation in monoamine candidates on treatment response using the standardized ADHD-Rating Scale IV (ADHD-RS) in this carefully phenotyped sample (n=202). Complete common variation in dopaminergic and adrenergic drug targets was queried, including dopamine (DA) receptors D1-D5 (DRD1, DRD2, DRD3, DRD4, DRD5), alpha-2 adrenergic receptor 2A (ADRA2A), and catabolic enzymes monoamine oxidase A (MAO-A) and B (MAO-B). Known functional and previously associated variants in the DA transporter (SLC3A6), norepinephrine transporter (SLC2A6) and catabolic enzyme catechol- o-methyltransferase (COMT) were also genotyped. Variants were selected using HapMap to identify tag SNPs (tSNPs) that capture the common variability above 10% allele frequency at a minimum r^2 of 0.8. Genotyping was performed on the Life Technologies' TaqMan genotyping platform.

Results: In children receiving d-MPH, two SNPs in DRD2 and a single ADRA2A variant predicted treatment response. None of the 7 homozygotes for the minor allele of a synonymous SNP (His313His, rs6275) met responder criteria, compared to an 80% response rate in 47 common allele carriers ($p=0.0001$). The minor (low expression) allele of the DRD2 Taq1A variant (rs1800497) was associated with an allele dosage-dependent improvement in both groups receiving d-MPH, either alone or in combination with guanfacine ($p=0.001$). Furthermore, haplotypes defined by these 2 DRD2 SNPs showed differential effects on treatment response ($p=0.0017$). Finally, the minor allele of an ADRA2A promoter variant (rs521674) was associated with poor d- MPH response ($p=0.0004$). Guanfacine response was predicted by homozygosity for the minor alleles ($p<0.0001$) of functional variants in DRD1 (rs686) and DRD2 (rs2075654).

Conclusions: Common genetic variation in dopaminergic and adrenergic receptors influenced treatment response to standard ADHD drug therapies in our dataset. These results survive correction for multiple testing (adjusted significance threshold $p<0.002$), and many of these variants have been shown to impact gene expression in functional assays. Monoaminergic candidate genes have been previously examined and received support in small studies of treatment response, though previous studies have not comprehensively evaluated these gene loci. Our study benefits from a randomized, double-blind, placebo-controlled design, an exhaustive genetic approach, a moderate size treatment sample, repeated outcome

measures, and the focus on children and adolescents. Pediatric samples may provide additional power given reduced treatment history, comorbidity (including substance use), and polypharmacy. Our results show promise for eventual personalization of ADHD treatment algorithms and warrant replication in larger samples and prospective treatment studies.

Neuropsychopharmacology. 2012;38:S446.

ASSOCIATION BETWEEN MICROSTRUCTURAL INTEGRITY OF THE FRONTOSTRIATAL TRACTS AND SCHOOL FUNCTIONS: INATTENTION SYMPTOMS AND SUSTAINED ATTENTION AS MEDIATORS.

Fen Gau SS, Merikangas K, Tseng WYI.

Background: Although our prior research demonstrated an association between disturbed frontostriatal circuitry integrity and a wide range of executive dysfunctions in youth with attention-deficit hyperactivity disorder (ADHD) and typically developing youth, its functional significance on school adjustment has not been examined. The goal of this study is to assess links between microstructural integrity of frontostriatal circuitry and school functioning, perhaps the most important functional domain influenced by ADHD diagnosis/symptoms, and to identify the mediating role of specific executive functions and ADHD symptoms on such links.

Methods: We assessed 32 youth with ADHD (mean age=11.4(plus or minus)2.3, Full-scale IQ=109.1(plus or minus)12.2, 29 males) and 32 age-, sex-, IQ-, and handedness-matched typically developing youth by using the Kiddie epidemiologic version of the Schedule for Affective Disorders and Schizophrenia for psychiatric diagnosis, the Social Adjustment Instrument for Children and Adolescents for four domains of school functioning (academic performance, attitude toward school, school social relationship, and school behavioral problems) and the SNAP-IV for inattention and hyperactivity/impulsivity symptoms. The participants received the tasks involving executive functions in the Cambridge Neuropsychological Test Automated Battery: Intra-dimensional/Extra-dimensional Shifts, Spatial Working Memory, Rapid Visual Information Processing (RVP), and Stocking of Cambridge. The frontostriatal tracts were reconstructed by diffusion spectrum imaging tractography and were subdivided into four functionally distinct segments, including dorsolateral, medial prefrontal, orbitofrontal, and ventrolateral tracts. Tract-specific analysis was used and generalized fractional anisotropy values were computed along individual targeted fiber tracts to investigate alterations in microstructure integrity. All the analyses were controlled for the participants' sex and age.

Results: Youth with ADHD had lower generalized fractional anisotropy of all the bilateral frontostriatal fiber tracts; poorer academic performance, more negative attitude, less social interactions, and more behavioral problems at school; and worse performance in set-shifting, sustained attention, attention control, and spatial planning than typically developing youth. Due to small sample size and no group difference in the correlations between frontostriatal tracts and four domains of school functions, we did not stratify our analysis for the two groups. We found that bilateral orbitofrontal tracts integrity was positively correlated with all four domains of school functioning and the eight frontostriatal tracts were significantly associated with school behavioral problems. Mediator analyses of the associations between bilateral orbitofrontal tracts and school functioning revealed that these associations were mediated by sustained attention as measured by the RVP and by inattentive symptoms; however, these associations were not mediated by other executive functions such as setshifting, working memory, and spatial planning or hyperactivity/impulsivity symptoms.

Conclusion: Our findings demonstrate a direct association of the frontostriatal circuitry, particularly bilateral orbitofrontal tracts, with attention and functional impact on academic performance and school behaviors. The links, supported by our findings, are mediated by inattention symptoms as observed by the parents and sustained attention as measured by the CANTAB. The similarity of these associations in youth with and without ADHD suggests that ADHD may be a severe manifestation of a common pathway of attentional functioning in youth rather than emerging from a distinct pathological mechanism.

Neuropsychopharmacology. 2012;38:S240-S241.

DOPAMINERGIC NETWORKS: BRAIN MATURATION AND ADHD.

Tomasi D, Volkow ND.

Background: Developmental changes in dopaminergic networks likely contribute to the dramatic increase in risk-taking behaviors and the emergence of various psychiatric disorders in the transition from childhood into adolescence. Several PET studies documented a significant decline in DA neurotransmission (receptors, transporters, DA synthesis) with age but the use of radioactive tracers precludes their application to the study of healthy children. Here we use nullrestingstatenull functional connectivity (RFC) measures derived from seeds in VTA and SN (main DA nuclei) to study changes in DA neurotransmission in the transition from childhood to adulthood. Our working hypothesis was that typically developing children (TDC) and healthy adults would show differential midbrain connectivity in regions of the nigrostriatal, mesolimbic and mesocortical DA pathways. In order to assess the sensitivity of these pathways to developmental disorders we also evaluated the connectivity of VTA and SN in ADHD children and tested the nulldelayed maturationnull hypothesis in ADHD.

Methods: A total of 1420 open-access nullresting-statenu magnetic resonance imaging datasets were included: 247 ADHD (12(plus or minus)3 years old; 197 boys) and 459 TDC (12 (plus or minus)3 years old; 244 boys) from the nullADHD-200null initiative and 714 (23(plus or minus)3 years old; 321 males) healthy adults from the null1000 functional connectomesnull project. After standard image preprocessing steps (realignment, removal of motion-related and global signal fluctuations, spatial normalization), seed-voxel correlation with Gram-Schmidt orthogonalization was used to compute the VTA and SN connectivity patterns. Voxelwise ANOVA (with age, gender and mean motion covariates) with a conservative statistical threshold (PFEW<0.05, family-wise error corrected for multiple comparisons in whole brain) was used to evaluate the statistical significance of group differences in functional connectivity.

Results: TDC demonstrated lower VTA-connectivity in left NAc, amygdala, hippocampus, parahippocampus, vermis, insula, PFC, ACC, OFC, SMA, temporal pole and middle temporal cortex, but higher VTA-connectivity in subthalamic nucleus and thalamus than adults. TDC demonstrated higher SN-connectivity than adults in NAc, amygdala, hippocampus, parahippocampus, insula, subthalamic nucleus, globus pallidus, vermis, temporal pole, anterior and middle cingulum, PFC, OFC, SMA, and Rolandic operculum. Voxelwise SPM correlations revealed significant age-related VTAconnectivity increases in NAc, caudate, vermis, insula, DMN and temporal pole. Age-related SN-connectivity decreases were significant in caudate, motor and premotor cortices, temporal pole, Rolandic operculum, occipital cortex, and postcentral gyrus. ADHD children had higher VTA-connectivity in amygdala, hippocampus, globus pallidus, thalamus, vermis and insula, and higher SNconnectivity in amygdala and insula than TDC. A delayed maturation was found in thalamus, subthalamic nucleus and globus pallidus (VTA-connectivity), left amygdala and insula (SN-connectivity) and accelerated maturation in hippocampus, amygdala, vermis, left caudate, right NAc and right insula (VTA-connectivity) in ADHD children compared to TDC.

Conclusions: Here we identify overlapping as well as distinct connectivity patterns for SN and VTA that are consistent with their neuroanatomical projections and with the role of DA in the modulation of brain functional connectivity. We also identify strong connectivity with regions that are not traditionally associated with DA pathways and age-related connectivity changes during childhood/adolescence, as well as prominent differences in functional connectivity between ADHD children and TDC. Overall these findings suggest maturation strengthening of VTA-connectivity with DMN regions and maturation pruning of SNconnectivity with motor and medial temporal cortices during the transition from childhood to adulthood. This transition is characterized by age-related VTA-connectivity increases in limbic and DMN regions and with SN-connectivity decreases in motor and medial temporal cortices. The changes from a predominant influence of SN in childhood/adolescence to a combined influence of SN and VTA in young adulthood might explain the increased vulnerability to psychiatric disorders, such as ADHD, early in life. These findings also demonstrate the feasibility of using RFC and fMRI for studying DA networks in childhood when the increase sensitivity to adverse effects of radioactivity limits the use of PET methods.

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Neuropsychopharmacology. 2012;38:S254-S255.

REGIONAL BRAIN VOLUME IN ADHD AND ITS RELATIONSHIP TO ATAXIA AND INTRASUBJECT VARIABILITY.

Valera E, Zeffiro T, Spencer R, et al.

Background: Motor coordination problems in ADHD have long been recognized in ADHD, and studies have found that up to 50% of ADHD children have motor difficulties. These difficulties can have a detrimental impact on their lives. Although these issues are addressed in a literature for ADHD children, there do not appear to be any analogous reports regarding detailed motor assessment of coordination in ADHD adults or any examination of how these motor abnormalities may relate to structural brain volume or other behavioral variables.

Methods Using a modified version of the International Cooperative Ataxia Rating Scale (MICARS), we obtained an objective assessment of ataxia severity in 22 ADHD adults and 22 matched controls. We used voxel based morphometry incorporating the SUIT cerebellar spatial normalization technique to examine ataxia scores in relation to regional brain volumes. We also used a tapping task to examine ataxia scores in relation to intrasubject variability.

Results: Relative to controls, ADHD adults showed significantly higher scores for total ataxia, posture and gait disturbances, and limb/kinetic measures. Ataxia scores were negatively correlated with regions in middle and superior frontal gyri as well as the posterior cerebellum (trend level). Ataxia scores were also positively correlated with tapping intrasubject variability, which was also higher in the ADHD adults. Total and clock, but not motor, variance were associated with ataxia scores.

Conclusions: These data show that motor abnormalities in ADHD persist into adulthood and can be detected by clinical motor examination. These data also show that ataxia is associated with localized volume reductions in frontal gyri, with a trend in a region of the secondary motor representation of the cerebellum. Associations between frontal regions and ataxia are consistent with previous reports implicating regions of the frontal cortex in ataxia. Finally, measures of ataxia are related to clock but not motor intrasubject variability, providing additional support for timing abnormalities contributing to the clinical phenomenology of ADHD. Overall, these findings provide additional evidence for the involvement of frontocerebellar abnormalities in the pathophysiology of ADHD.

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Neuropsychopharmacology. 2012;38:S349.

ASSOCIATION BETWEEN THE CHANGE IN ELECTRODERMAL ACTIVITY AFTER ACUTE TRYPTOPHAN DEPLETION AND MOOD, AGGRESSION AND VENTURESOMENESS IN YOUNG PEOPLE WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Von Polier G, Biskup C, Kotting WF, et al.

Background: The neurotransmitter serotonin (5-HT) has been shown to play an important role in the underlying neurobiological processes of aggressive behavior, with evidence coming from animal and human studies. However, few studies have been conducted in young people. The current pilot study was set out to investigate the influence of acute tryptophan depletion (ATD) on physiological arousal in young people with attention deficit hyperactivity disorder (ADHD), a population at risk for aggressive behavior. Here we aimed to explore if ATD, a physiological neurodietary method of decreasing central nervous 5-HT synthesis in humans, would result in changed physiological arousal in young people subjected to a task designed to elicit aggressive behavior when compared to a tryptophan (TRP) balanced control amino acid mixture (BAL).

Methods: ATD Moja-De is a physiological method of decreasing plasma levels of TRP, the physiological precursor amino acid (AA) of 5-HT. The administration of an AA beverage lacking TRP leads to a temporary decrease in 5-HT synthesis in the human brain as relevant AAs use the same L-1 transport system to overcome the blood brain barrier (BBB). Competitive antagonism of the AAs at L-1 leads to decreased substrate availability for tryptophan hydroxylase 2 (TPH-2), the rate-limiting enzyme for central nervous 5-HT synthesis. As a consequence of decreased substrate availability for TPH-2 central nervous 5-HT synthesis is diminished. The Moja-De ATD protocol differs from classic ATD mixtures previously used in neuropsychiatric and pharmacological research. It involves a body weight-adapted dosing regime of relevant amino acids and also involves modified AA quantities. ATD Moja-De was proven to have acceptable tolerability while other AA mixtures previously used in ATD research were associated with side

effects such as vomiting and nausea, thus allowing the use of ATD Moja-De in young people. The study design for this pilot study was a double-blind within-subject repeated measures crossover design. Participants were 9 to 15 year old boys (n=10) and girls (n=10) with a confirmed diagnosis of ADHD. Pregnancy tests (in female subjects) and drug screening tests were obtained in advance of each study day. The amino acid mixtures (ATD/BAL) were administered after an overnight protein fast on two separate study days. Reactive aggression was provoked using a point-subtraction aggression game (PSAG) 2.5 hours (time point marking a significant decrease in TRP influx across the BBB) after administration of ATD or the BAL control condition (AA mixture with TRP) on two separate study days. Externalizing behavior was assessed using the Child Behavior Checklist (CBCL). Impulsivity, venturesomeness and empathy were assessed using the IVE questionnaire (adapted German version of the Eysenck impulsivity questionnaire for young people). Mood states after administration of ATD/BAL were assessed using the ASTS mood questionnaire repeatedly during and after administration of the PSAG. While participating in the PSAG subjects' electrodermal activity (EDA) was recorded, serving as a biophysiological marker of sympathetic activity and physiological arousal. Numbers and extent of skin conductance responses (SCR) were evaluated.

Results: Significant positive correlations between the mean EDA difference from ATD to BAL ((Delta) EDAATD-BAL) and positive mood states were observed in both male and female participants. (Delta) EDAATD-BAL was negatively correlated with anger and venturesomeness in both males and females, and with aggression in males. No significant differences in SCR were observed during the PSAG when comparing the ATD and the BAL condition.

Conclusions: The preliminary findings of the present investigation are somewhat in line with previous research indicating a potential link between amygdala activation and central nervous serotonin function. The correlation between (Delta) EDAATD-BAL and positive mood could be seen as indicative for increased amygdala activity, in particular as previous research supports an association between increased amygdala activity and physiological arousal as indexed by SCR. As opposed to positive mood states, anger was negatively correlated with (Delta) EDAATD-BAL as was aggressiveness. The latter findings might be interpreted in the contextual framework of the low arousal theory, suggesting that subjects with reduced physiological arousal tend to show elevated externalizing behavior. Because of the limited sample size the present findings must be considered preliminary and should be replicated in future large scale studies.

Noropsikiyatr Ars. 2012;49:260-65.

VIOLENT BEHAVIOR IN ADOLESCENCE: INDIVIDUAL AND FAMILIAL FACTORS.

Zinnur Kilic E.

Objective: In this study, a group of violent male adolescents aged 12-15 years old, who were students of a primary school located in a district where families with low socioeconomic status (SES) live was compared with a non-violent peer group in terms of self and family variables, in an aim to understand the risk factors related to adolescent violent behavior.

Methods: Data were gathered about the family relations, presence of domestic violence, and other environmental risk factors for a group of adolescents who show violent behavior at school (n: 22) and compared to their non-violent peers (n: 19) from the same school by getting information both from the adolescents themselves and their mothers. The Self-Perception Profile for Adolescents, Rosenberg Self-Esteem Scale, Children's Depression Inventory and the Connors' Rating Scales were used to measure the relevant variables. Family characteristics were investigated by direct interviews with the mothers and by using the General Health Questionnaire and the Family Assessment Device for both mothers and fathers.

Results: The results of this study showed that adolescents who were violent at school were similar to non-violent ones in terms of domestic violence and self-perception and self-esteem. The violent group perceived themselves as being worse in terms of academic performance and showed higher levels of attention deficit hyperactivity symptoms.

Conclusion: The results suggest that the violent behaviour at school for some adolescents may be a way of proving themselves and being accepted by their peers.

Pediatr Ann. 2012;41:456-58.

A 10-YEAR-OLD BOY WITH ADHD SYMPTOMS.

Cosme Cruz RM, Clark CM, Shin L.

Pediatrics. 2012;130:1012-18.

AGE, ACADEMIC PERFORMANCE, AND STIMULANT PRESCRIBING FOR ADHD: A NATIONWIDE COHORT STUDY.

Zoega H, Valdimarsdottir UA, Hernandez-Diaz S.

BACKGROUND: We evaluated whether younger age in class is associated with poorer academic performance and an increased risk of being prescribed stimulants for attention-deficit/hyperactivity disorder (ADHD).

METHODS: This was a nationwide population-based cohort study, linking data from national registries of prescribed drugs and standardized scholastic examinations. The study population comprised all children born in 1994-1996 who took standardized tests in Iceland at ages 9 and 12 (n = 11 785). We estimated risks of receiving low test scores (0-10th percentile) and being prescribed stimulants for ADHD. Comparisons were made according to children's relative age in class.

RESULTS: Mean test scores in mathematics and language arts were lowest among the youngest children in the fourth grade, although the gap attenuated in the seventh grade. Compared with the oldest third, those in the youngest third of class had an increased relative risk of receiving a low test score at age 9 for mathematics (1.9; 95% confidence interval [CI] 1.6-2.2) and language arts (1.8; 95% CI 1.6-2.1), whereas at age 12, the relative risk was 1.6 in both subjects. Children in the youngest third of class were 50% more likely (1.5; 95% CI 1.3-1.8) than those in the oldest third to be prescribed stimulants between ages 7 and 14.

CONCLUSIONS: Relative age among classmates affects children's academic performance into puberty, as well as their risk of being prescribed stimulants for ADHD. This should be taken into account when evaluating children's performance and behavior in school to prevent unnecessary stimulant treatment.

Personality and Individual Differences. 2012 Dec;53:963-68.

ITEM RESPONSE THEORY ANALYSES OF ADOLESCENT SELF-RATINGS OF THE ADHD SYMPTOMS IN THE DISRUPTIVE BEHAVIOR RATING SCALE.

Gomez R.

The graded response model (GRM) was used to evaluate the item response theory properties of the ADHD inattention and hyperactivity/impulsivity symptoms in the Disruptive Behavior Rating Scale-Self Report (DBRS-SR). This measure was completed by 363 adolescents, between 12 and 17 years of age. The findings showed that all symptoms were generally good for discriminating their respective latent traits. For most symptoms, their threshold values suggested that they were good at representing the appropriate traits from the mean trait levels, and their information values began to increase substantially from around ± 1 SD from the mean. These findings indicate good psychometric properties for the DBRS-SR. The practical and clinical implications of the findings are discussed.

Pharmacoepidemiol Drug Saf. 2012;21:135-36.

A POPULATION-BASED STUDY OF STIMULANT DRUG TREATMENT FOR ADHD AND ACADEMIC PROGRESS IN CHILDREN.

Zoega H, Rothman KJ, Huybrechts KF, et al.

Background: Evidence is sparse regarding long-term effects of stimulant treatment on academic progress among children with attention-deficit/hyperactivity disorder (ADHD).

Objectives: We evaluated the hypothesis that later start of stimulant treatment for ADHD adversely affects academic progress in mathematics and language arts among 9-to 12-year old children.

Methods: We linked nationwide data from the Icelandic Medicines Registry and the Database of National Scholastic Examinations. The study population comprised 11,872 children born 1994-1996 who took standardized tests in both 4th and 7th grade. We estimated the probability of academic decline (drop of (greater-than or equal to)5.0 percentile points) according to drug exposure and timing of treatment start between examinations. To limit confounding by indication we concentrated on children who started treatment either early or later, but at some point between 4th grade and 7th grade standardized tests.

Results: In contrast with non-medicated children, children starting stimulant treatment between their 4th and 7th grade tests were more likely to decline in test performance. The crude probability of academic decline was 72.9% in mathematics and 42.9% in language arts for children with a treatment start 25-36 months after the 4th grade test. Compared with those starting treatment earlier ((less-than or equal to)12 months after tests), the multivariable adjusted risk ratio (RR) for decline was 1.7 (95% confidence interval [CI] 1.2-2.4) in mathematics and 1.1 (95% CI 0.7-1.8) in language arts. The adjusted risk ratio of mathematics decline with later treatment was higher among girls (RR, 2.7; 95% CI 1.2-6.0), than boys (RR, 1.4; 95% CI 0.9- 2.0).

Conclusions: Later start of stimulant drug treatment for ADHD is associated with academic decline in mathematics.

Pharmacoepidemiol Drug Saf. 2012;21:149.

ANALYSIS OF ADHD (ATTENTION-DEFICIT/HYPERACTIVITY DISORDER) AMONG FLU-VACCINATED PEDIATRIC POPULATION IN THE UNITED STATES MEDICAL CLAIMS DATABASE.

Tsai K.

Background: To better understand the reports of ADHD after the flu vaccinations in adolescence, an US claims database study was planned.

Objectives: The purpose of this study was to describe the rates of ADHD before/after the index date of flu vaccination among adolescent population in the 2009 Thomson Reuters MarketScan(registered trademark) Commercial and Encounters Research Databases.

Methods: The flu vaccination groups were defined by ICD-9 CPT codes: 90655-90658 and 90650 for TIV (trivalent inactivated influenza vaccine) and LAIV (live attenuated influenza vaccine), respectively. The conditions of ADHD were defined by ICD-9 diagnosis codes (314.0). The unvaccinated group "a" and "b" was defined as subjects who have "not had" and "had" any medical/pharmacy claims recorded for any types of health care utilizations during the 3 months prior to the flu season (July 1st-September 31st), respectively.

Results: During 2009, the LAIV vaccinated only boys aged 9-18 years has the higher rates of ADHD (1-30 days before: 51.5 per 1,000 person-month vs. 1-30 days after: 68.0 per 1,000 person-month) than the TIV vaccinated only boys of similar ages (1-30 days before: 13.1 per 1,000 person-month vs. 1-30 days after: 43.6 per 1,000 person-month). Among the 2 unvaccinated groups, the unvaccinated "a" boys aged 9-18 years has slightly lower rates of ADHD (1-30 days before: 11.3 per 1,000 person-month vs. 1-30 days after: 12.7 per 1,000 person-month) than the unvaccinated "b" boys of similar ages (1-30 days before: 17.2 per 1,000 person-month vs. 1-30 days after: 21.3 per 1,000 person-month).

Conclusions: In conclusion, the limitations with claims database analysis such as parenting-preferences/physician preferences in choosing/deciding health care options specially for the pediatric population which can not be measured as channelling bias may have confounded the results. Alternative approach such as self-control comparisons before/after the index date of flu vaccination are planned as the next step to explore the current findings further.

PLoS ONE. 2012;7.

FOLATE METABOLISM GENE 5,10-METHYLENETETRAHYDROFOLATE REDUCTASE (MTHFR) IS ASSOCIATED WITH ADHD IN MYELOMENINGOCELE PATIENTS.

Spellicy CJ, Northrup H, Fletcher JM, et al.

The objective of this study was to examine the relation between the 5, 10-methylenetetrahydrofolate reductase (MTHFR) gene and behaviors related to attention-deficit/hyperactivity disorder (ADHD) in individuals with myelomeningocele. The rationale for the study was twofold: folate metabolizing genes, (e.g. MTHFR), are important not only in the etiology of neural tube defects but are also critical to cognitive function; and individuals with myelomeningocele have an elevated incidence of ADHD. Here, we tested 478 individuals with myelomeningocele for attention-deficit hyperactivity disorder behavior using the Swanson Nolan Achenbach Pelham-IV ADHD rating scale. Myelomeningocele participants in this group for whom DNAs were available were genotyped for seven single nucleotide polymorphisms (SNPs) in the MTHFR gene. The SNPs were evaluated for an association with manifestation of the ADHD phenotype in children with myelomeningocele. The data show that 28.7% of myelomeningocele participants exhibit rating scale elevations consistent with ADHD; of these 70.1% had scores consistent with the predominantly inattentive subtype. In addition, we also show a positive association between the SNP rs4846049 in the 3'-untranslated region of the MTHFR gene and the attention-deficit hyperactivity disorder phenotype in myelomeningocele participants. These results lend further support to the finding that behavior related to ADHD is more prevalent in patients with myelomeningocele than in the general population. These data also indicate the potential importance of the MTHFR gene in the etiology of the ADHD phenotype.

PLoS ONE. 2012;7.

DEFICITS IN COGNITIVE CONTROL, TIMING AND REWARD SENSITIVITY APPEAR TO BE DISSOCIABLE IN ADHD.

De Zeeuw P, Weusten J, van Dijk S, et al.

Recent neurobiological models of ADHD suggest that deficits in different neurobiological pathways may independently lead to symptoms of this disorder. At least three independent pathways may be involved: a dorsal frontostriatal pathway involved in cognitive control, a ventral frontostriatal pathway involved in reward processing and a frontocerebellar pathway related to temporal processing. Importantly, we and others have suggested that disruptions in these three pathways should lead to separable deficits at the cognitive level. Furthermore, if these truly represent separate biological pathways to ADHD, these cognitive deficits should segregate between individuals with ADHD. The present study tests these hypotheses in a sample of children, adolescents and young adults with ADHD and controls. 149 Subjects participated in a short computerized battery assessing cognitive control, timing and reward sensitivity. We used Principal Component Analysis to find independent components underlying the variance in the data. The segregation of deficits between individuals was tested using Loglinear Analysis. We found four components, three of which were predicted by the model: Cognitive control, reward sensitivity and timing. Furthermore, 80% of subjects with ADHD that had a deficit were deficient on only one component. Loglinear Analysis statistically confirmed the independent segregation of deficits between individuals. We therefore conclude that cognitive control, timing and reward sensitivity were separable at a cognitive level and that deficits on these components segregated between individuals with ADHD. These results support a neurobiological framework of separate biological pathways to ADHD with separable cognitive deficits.

PLoS ONE. 2012;7.

ANATOMICAL BRAIN IMAGES ALONE CAN ACCURATELY DIAGNOSE CHRONIC NEUROPSYCHIATRIC ILLNESSES.

Bansal R, Staib LH, Laine AF, et al.

Objective: Diagnoses using imaging-based measures alone offer the hope of improving the accuracy of clinical diagnosis, thereby reducing the costs associated with incorrect treatments. Previous attempts to use brain imaging for diagnosis, however, have had only limited success in diagnosing patients who are independent of the samples used to derive the diagnostic algorithms. We aimed to develop a classification algorithm that can accurately diagnose chronic, well-characterized neuropsychiatric illness in single

individuals, given the availability of sufficiently precise delineations of brain regions across several neural systems in anatomical MR images of the brain.

Methods: We have developed an automated method to diagnose individuals as having one of various neuropsychiatric illnesses using only anatomical MRI scans. The method employs a semi-supervised learning algorithm that discovers natural groupings of brains based on the spatial patterns of variation in the morphology of the cerebral cortex and other brain regions. We used split-half and leave-one-out cross-validation analyses in large MRI datasets to assess the reproducibility and diagnostic accuracy of those groupings.

Results: In MRI datasets from persons with Attention-Deficit/Hyperactivity Disorder, Schizophrenia, Tourette Syndrome, Bipolar Disorder, or persons at high or low familial risk for Major Depressive Disorder, our method discriminated with high specificity and nearly perfect sensitivity the brains of persons who had one specific neuropsychiatric disorder from the brains of healthy participants and the brains of persons who had a different neuropsychiatric disorder.

Conclusions: Although the classification algorithm presupposes the availability of precisely delineated brain regions, our findings suggest that patterns of morphological variation across brain surfaces, extracted from MRI scans alone, can successfully diagnose the presence of chronic neuropsychiatric disorders. Extensions of these methods are likely to provide biomarkers that will aid in identifying biological subtypes of those disorders, predicting disease course, and individualizing treatments for a wide range of neuropsychiatric illnesses.

PLoS ONE. 2012;7.

FAMILY-ENVIRONMENTAL FACTORS ASSOCIATED WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHINESE CHILDREN: A CASE-CONTROL STUDY.

du Prel Carroll X, Yi H, Liang Y, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is one of the most common psychiatric disorders, affecting an estimated 5 to 12% of school-aged children worldwide. From 15 to 19 million Chinese children suffer from ADHD. The aim of this study was to investigate the association between family-environmental factors and ADHD in a sample of Chinese children.

Methods: A pair-matched, case-control study was conducted with 161 ADHD children and 161 non-ADHD children of matching age and sex, all from 5-18 years of age. The ADHD subjects and the normal controls were all evaluated via structured diagnostic interviews. We examined the association between family-environmental factors and ADHD using the conditional multiple logistic regression with backward stepwise selection to predict the associated factors of ADHD.

Results: Having experienced emotional abuse and being a single child were both significant factors associated with children diagnosed with ADHD. ADHD subjects were more likely to have suffered from emotional abuse (OR=11.09, 95% CI=2.15-57.29, P=0.004) and have been a single child in the family (OR=6.32, 95% CI=2.09-19.14, P=0.001) when compared to normal controls. The results were not modified by other confounding factors.

Conclusion: Our findings provide evidence that family-environmental factors are associated with ADHD among children in China. These findings, if confirmed by future research, may help to decrease ADHD by increasing the awareness of the effects of childhood emotional abuse.

Proc Natl Acad Sci U S A. 2012;109:20089-94.

LONG-TERM INFLUENCE OF NORMAL VARIATION IN NEONATAL CHARACTERISTICS ON HUMAN BRAIN DEVELOPMENT.

Walhovd KB, Fjell AM, Brown TT, et al.

It is now recognized that a number of cognitive, behavioral, and mental health outcomes across the lifespan can be traced to fetal development. Although the direct mediation is unknown, the substantial variance in fetal growth, most commonly indexed by birth weight, may affect lifespan brain development. We investigated effects of normal variance in birth weight on MRI-derived measures of brain development in 628 healthy children, adolescents, and young adults in the large-scale multicenter Pediatric Imaging, Neurocognition, and Genetics study. This heterogeneous sample was recruited through geographically

dispersed sites in the United States. The influence of birth weight on cortical thickness, surface area, and striatal and total brain volumes was investigated, controlling for variance in age, sex, household income, and genetic ancestry factors. Birth weight was found to exert robust positive effects on regional cortical surface area in multiple regions as well as total brain and caudate volumes. These effects were continuous across birth weight ranges and ages and were not confined to subsets of the sample. The findings show that (i) aspects of later child and adolescent brain development are influenced at birth and (ii) relatively small differences in birth weight across groups and conditions typically compared in neuropsychiatric research (e.g., Attention Deficit Hyperactivity Disorder, schizophrenia, and personality disorders) may influence group differences observed in brain parameters of interest at a later stage in life. These findings should serve to increase our attention to early influences.

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Prog Neurol Psychiatry. 2012;16:16-17.

A CASE OF ADHD IN A PATIENT WITH NOONAN SYNDROME.

Mushtaq I, Matras B.

Noonan syndrome is a genetic disorder characterised by several features including short stature, congenital heart defects and learning problems. Here, Dr Mushtaq and colleagues describe how they managed a case of ADHD in a patient with Noonan syndrome.

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Psychol Assess. 2012 Dec;24:913-24.

DIMENSIONALITY, HIERARCHICAL STRUCTURE, AGE GENERALIZABILITY, AND CRITERION VALIDITY OF THE GAIN'S BEHAVIORAL COMPLEXITY SCALE.

Conrad KJ, Conrad KM, Mazza J, et al.

This study used Rasch measurement model criteria and traditional psychometric strategies to examine key psychometric properties of the Behavioral Complexity Scale (BCS), a widely used measure of externalizing disorders that focuses on attention deficit, hyperactivity, and conduct disorders. With a sample of 7,435 persons being screened for substance use disorders, the BCS was found to (a) be unidimensional, (b) have a hierarchical severity structure, (c) be generalizable to both youths and adults, and (d) meet hypothesized correlations with criterion variables. The BCS performed well as a unidimensional measure. The Rasch severity hierarchy of attention deficit to hyperactivity to conduct disorders provided a perspective that suggested that a dimensional measure could be used as an alternative and, in some ways, as an improvement to categorical diagnosis and common dimensional approaches. The finding of 3 low-severity conduct disorder items also supported a revision of categorical criteria, especially in substance use disorders.

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Western Journal of Nursing Research. 2012 Dec;34:999-1001.

ROLE OF THE RPS IN ALLEVIATING SYMPTOMS OF ACUTE AND CHRONIC RDD.

Conn VS.

Almost all of us have heard about attention deficit disorder (ADD) and the negative effects this learning disability can have on an affected individual's success in school and the workplace. RDD, short for "researcher distractibility disorder," is characterized by a compulsive tendency to dabble in areas of investigation that are either tangential to or completely unrelated to one's declared program of research. Like ADD, uncontrolled RDD can have a devastating effect on one's professional success as an investigator and scholar. Although there is no cure for RDD, a powerful antidote exists to combat its effects. A diagnosis of RDD can be devastating, as there is no cure for this potentially disabling disease. But if treatment is begun early via activation of an RPS, symptoms can be successfully controlled. With an actively functioning RPS on board, even the most severely afflicted individuals among us can expect to lead satisfying and successful professional lives.

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Dicembre 2012

http://www.medicoebambino.com/?id=RIC1210_10.html

MEDICO E BAMBINO PAGINE ELETTRONICHE

RICERCA

Prevalenza dell'ADHD in una popolazione pediatrica e sua esposizione al trattamento psico-comportamentale e farmacologico

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Prevalence of ADHD in the Italian paediatric population and rate of exposition to pharmacological and behavioural treatment

Key words

ADHD, Prevalence, Multimodal treatment, Register

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Abstract

Objective: to assess the prevalence of ADHD in the Italian paediatric population and to evaluate the rate of exposition to pharmacological treatment in children and adolescents affected by ADHD.

Method: observational post-marketing study, 4th phase. Assessment of the drugs prescribed to children and adolescents aged between 6-18 with ADHD in child psychiatry unit of San Donà di Piave.

Results: the population aged 6-18 years amount to 24,000 inhabitants. 2,503 (10.8%) were examined in 2007 for suspected developmental disorders and 286 (1.2%) were diagnosed positive for ADHD. 20 out of 286 (7.0%) patients had received the multimodal treatment and 186 the behavioural treatment alone. In 2010, the subjects suffering from ADHD were 263 (1.1 %) on a population aged 6-18 of 24,650 individuals. 44 (16.7 %) were in multimodal treatment and 153 received behavioural treatment.

Conclusions: the survey was carried out in a small population. Nevertheless this cohort is quite representative of Italian paediatric population. The observed prevalence of ADHD corresponds to that expected on the basis of the data of previous epidemiological Italian surveys but considerably lower than the one reported in international literature. The rate of exposure to pharmacological treatment is similar to that of other European countries.

RIASSUNTO

Obiettivo: stimare la prevalenza dell'ADHD nella popolazione pediatrica e valutare il tasso di esposizione al trattamento farmacologico nei bambini e negli adolescenti affetti da ADHD.

Metodo: studio osservazionale post-marketing, fase IV. Valutazione della prescrizione del farmaco a bambini ed adolescenti affetti da ADHD e di età compresa tra i 6 e i 18 anni nell'Unità Operativa di Neuropsichiatria Infantile di San Donà di Piave.

Risultati: La popolazione di età compresa tra i 6 e i 18 anni della Azienda sanitaria locale di San Donà di Piave in Veneto ammonta a circa 24.000 individui. Nel 2007 sono stati esaminati 2503 soggetti (10,8% della popolazione) per valutazione clinica per sospetti disturbi dello sviluppo e in 286 (1,2%) è stato diagnosticato l'ADHD. 20 su 286 pazienti (7,0%) hanno ricevuto il farmaco nell'ambito di un trattamento multimodale e 186 solo il trattamento psico - comportamentale. Nel 2010 i soggetti affetti da ADHD erano 263 (1,1%) su una popolazione di età 6-18 anni di 24.650 individui. 44 (16,7%) erano in trattamento multimodale e 153 hanno ricevuto terapie psico - comportamentali.

Conclusioni: 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.

INTRODUZIONE

La **Sindrome da iperattività e deficit di attenzione** (ADHD)¹ è uno dei più frequenti disturbi dello sviluppo nell'infanzia e colpisce dal 2% al 14% dei bambini in età scolare². In Italia la prevalenza attesa, sulla base di vari studi effettuati negli ultimi dieci anni, è dell'1% ([Tabella I](#)). La prevalenza dell'ADHD nella popolazione pediatrica italiana di età compresa tra i 6 ed i 18 anni è tuttavia molto variabile³⁻⁸, perché gli studi effettuati in passato hanno utilizzato procedure diagnostiche differenti.

Il miglior trattamento per il paziente affetto da ADHD richiede una gestione multidisciplinare e multimodale a lungo termine e consiste nell'associazione del farmaco con una terapia comportamentale⁹⁻¹¹.

Lo scopo dell'intervento comportamentale è quello di migliorare le funzioni psicosociali ed educative nei bambini e negli adolescenti affetti da questa sindrome¹²⁻¹⁵. Il controllo dei sintomi si ottiene anche con il trattamento farmacologico che è sintomatico e dovrebbe essere gestito da specialisti.

Gli stimolanti, metilfenidato e dexamfetamina, sono considerati farmaci di prima scelta¹⁶⁻¹⁸. L'atomoxetina, un inibitore selettivo del re-uptake della noradrenalina, è uno dei composti più recenti per il trattamento dell'ADHD nei bambini¹⁹⁻²¹. Il Metilfenidato ha ricevuto, nel 2007, l'approvazione all'immissione sul mercato dall'Agenzia Italiana del Farmaco e nello stesso periodo l'Atomoxetina otteneva l'autorizzazione, anche a livello europeo, ad essere commercializzata. Questi farmaci sono in commercio in molti altri paesi già da anni e sono disponibili in più di 30 nazioni, la maggior parte delle quali appartiene all'Unione europea.

È importante sottolineare che in Italia la prescrizione del Metilfenidato e dell'Atomoxetina è rigidamente subordinata a precisi test diagnostici²², oltre che all'osservazione clinica e la raccolta strutturata di informazioni provenienti da fonti diverse (genitori, medico, insegnanti), ed è legata all'iscrizione in un apposito registro nazionale la cui principale finalità è la raccolta di informazioni riguardanti la sicurezza di questi farmaci e, in subordine, la stima del tasso di individui affetti da ADHD trattati con farmaci.

Il Registro rappresenta uno strumento unico nel suo genere, atto a garantire la sicurezza dei pazienti e un attento monitoraggio della terapia farmacologica^{23,24}.

Luogo	Contesto	Anno	Casi/ Popolazione	Età	Prevalenza %
Firenze Perugia ³	Scuola	1993	9/250	6 - 12	3,6
Torino ⁸	Pediatria di famiglia	1998	1.203/47.781	6 - 14	2,52
Regione Friuli-Venezia Giulia ⁴	Servizi pediatrici e di salute Mentale	2002	280/64.800	0 - 14	0,43
Roma ⁵	Pediatr di famiglia	1999 - 2003	35/3.305	6 - 15	1,06
Cesena ⁶	Servizio di salute mentale	2003	131/11.980	7 - 14	1,1

Tabella I. Prevalenza dell'ADHD in Italia in contesti differenti

MATERIALI E METODI

Per stabilire la prevalenza dell'ADHD nella popolazione pediatrica italiana e per valutare il tasso di esposizione al trattamento farmacologico nei bambini e adolescenti affetti da ADHD, abbiamo analizzato i dati ricavati dal database del registro dell'ADHD (<http://www.iss.it/adhd/>) cui afferiscono i dati dai Centri per la diagnosi e la gestione della sindrome, accreditati dalle autorità sanitarie regionali.

Il centro di riferimento è responsabile della diagnosi in base ai criteri definiti dal protocollo italiano dell'ADHD che riprende i criteri del Manuale di Diagnostica e Statistica dei Disordini Mentali-IV (DSM-IV) ed è anche responsabile della verifica dell'appropriatezza del piano terapeutico.

Il centro di riferimento assicura l'interfaccia tra il pediatra e il servizio territoriale di neuropsichiatria dell'infanzia e dell'adolescenza (NPiA).

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.

Ogni sei mesi il paziente torna al centro di riferimento per una valutazione sulla sicurezza ed efficacia del trattamento. In base ai risultati, viene stilato un eventuale nuovo piano terapeutico.

Abbiamo analizzato i dati raccolti dal Centro di riferimento regionale di San Donà di Piave in Veneto dal 2007 al 2010. La popolazione pediatrica dai 6 ai 18 anni di età della zona di San Donà corrisponde a circa 24.000 abitanti ed ha una struttura demografica sovrapponibile a quella della popolazione italiana (Tabella II).

Classe d'età	Italia	%	San Donà di Piave	%
6 - 10	2.846.280	38,4	9.466	38,4
11 - 13	1.688.207	22,7	5.743	23,3
14 - 18	2.887.574	38,9	9.441	38,3
Totale	7.422.061	100,0	24.650	100,0

Tabella II. Struttura della popolazione italiana e del comprensorio di San Donà di Piave. Dati ISTAT 2010.

RISULTATI

La Unità Operativa Complessa di Neuropsichiatria Infantile della AULSS 10 di San Donà di Piave nel 2007 ha esaminato 2.503 bambini e adolescenti su una popolazione di 23.067 residenti di età compresa tra i 6 e i 18 anni. Al centro afferiscono tutti i soggetti in età evolutiva con sospetto di patologia neuro-psichiatrica o disturbo dello sviluppo, inviati dal pediatra di libera scelta, dallo psicologo scolastico o dall'insegnante o, direttamente, dalla famiglia.

Abbiamo calcolato la popolazione della fascia d'età 6-18 anni afferente al centro in ciascun anno, la prevalenza di ADHD nella popolazione, il tasso di esposizione al trattamento psico - comportamentale e a quello multimodale dei soggetti con diagnosi di ADHD, l'incidenza (Tabella III). Sono stati esclusi dalle stime i pazienti, seguiti dal centro di San Donà, residenti in altre regioni o in comuni non appartenenti al bacino di riferimento della AULSS 10 della regione Veneto. Nel database del registro nazionale dell'ADHD non risultano bambini, residenti nella AULSS 10, seguiti presso altri centri di riferimento della regione Veneto o di altre regioni.

Durante il 2007, a 286 pazienti è stato diagnosticato l'ADHD, di questi, 186 sono stati trattati solo con il trattamento comportamentale e 20 sono stati sottoposti al trattamento multimodale (Tabella III).

Nel 2008, a 320 bambini è stato diagnosticato l'ADHD, 201 sono stati sottoposti al trattamento psico - comportamentale e 32 sono stati sottoposti al trattamento multimodale (Tabella III). Le diagnosi di ADHD sono state 295 nel 2009: 175 bambini e adolescenti sono stati sottoposti a terapia psico - comportamentale e 44 a trattamento multimodale. Infine, nel 2010 sono

risultati affetti da ADHD 263 individui di cui 153 hanno ricevuto interventi psico – comportamentali e 44 sono stati sottoposti a trattamento multimodale. Ogni anno, circa un quarto (25-28%) dei pazienti con diagnosi di ADHD, caratterizzato da quadro clinico lieve, non è stato sottoposto ad alcun tipo di trattamento. Per questi bambini si è preferito osservare l'evoluzione del quadro clinico riservando un eventuale intervento terapeutico ai casi che manifestassero un peggioramento della sintomatologia. Per ciascun anno preso in esame sono stati calcolati i casi di ADHD presenti nel territorio della ASL 10 di San Donà di Piave e il relativo tasso di prevalenza. È stata calcolata la frazione di soggetti in trattamento psico – comportamentale e il tasso di esposizione ai farmaci specifici, calcolato come rapporto tra i pazienti in trattamento multimodale e il totale dei pazienti con diagnosi di ADHD. È stata calcolata l'incidenza per il 2008, 2009 e 2010, rispettivamente 15 nuovi casi (0,06%), 13 (0,05%) e 8 (0,03%). Sono stati analizzati anche i trattamenti psico – sociali per tipologia e intensità di erogazione (*Tabella IV*). In ciascuno dei quattro anni considerati, il 73% circa dei pazienti con ADHD ha ricevuto un qualche trattamento mentre meno di un terzo non ha ricevuto trattamenti. La distribuzione dell'età alla diagnosi mostra una prevalenza maggiore dell'ADHD tra bambini di età tra i 6 e i 10 anni piuttosto che tra ragazzi di età superiore come atteso dalla letteratura scientifica consultata (*Figura 1*).

Anno	Popolazione 6-18 anni	Pazienti afferenti al centro	Prevalenza di ADHD	Trattamento		
				Psico-comportamentale	Multimodale	Incidenza annuale
2007	23.067	2.503	286 (1,2%)	186 (65,0%)	20 (7,0%)	
2008	24.028	2.115	320 (1,3%)	201 (62,8%)	32 (10,0%)	15(0,06%)
2009	24.370	2.211	295 (1,2%)	175 (59,3%)	44 (14,9%)	13(0,05%)
2010	24.650	2.184	263 (1,1%)	153 (58,2%)	44 (16,7%)	8 (0,03%)

Tabella III. Casi di ADHD (tasso di prevalenza), trattamento multimodale (tasso di esposizione) presso il centro di riferimento per l'ADHD di San Donà di Piave

Trattamento	Pazienti
Parent training	16,7 %
Parent training + Auto – formazione	49,4 %
Terapia cognitivo – comportamentale	24,8%

Tabella IV. Tipo di interventi psico – sociali eseguiti presso il Centro

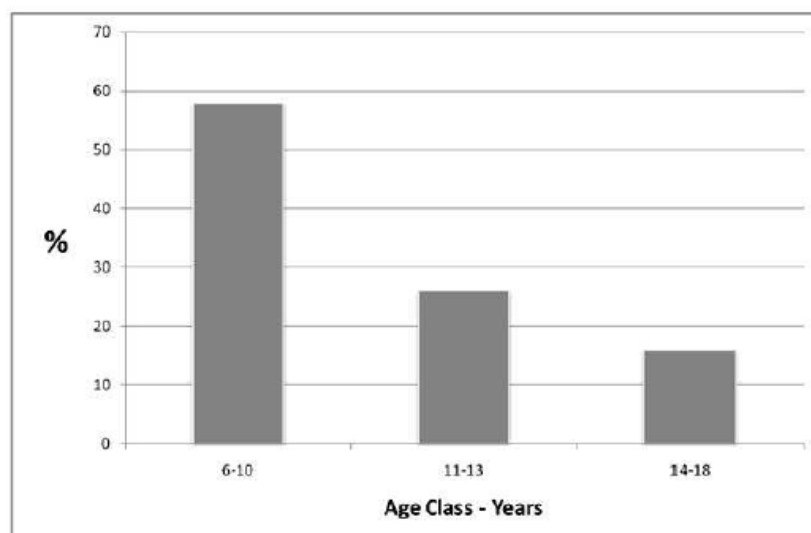


Figura 1. Distribuzione per classe d'età dei casi di ADHD

DISCUSSIONE

La nostra indagine è stata eseguita su un campione rappresentativo della popolazione pediatrica italiana. L'unità di NPIA di San Donà di Piave è il principale centro di riferimento per l'ADHD della regione Veneto ed ha reclutato il 12% dei pazienti afferenti al registro italiano dell'ADHD. La prevalenza media osservata dell'ADHD è 1,2%, non significativamente dissimile dall'1% atteso in base ai risultati di vari studi italiani. Nel nostro studio, l'accuratezza diagnostica è maggiore che in altri studi effettuati negli anni passati in vari contesti regionali³⁻⁸ perché è stato applicato rigorosamente il Protocollo diagnostico e terapeutico della ADHD per il Registro nazionale (<http://www.iss.it/publ/rapp/cont.php?id=23048&lang=1&tipo=5&anno=2009>).

Questo protocollo è stato redatto da un comitato scientifico sulla base dei criteri diagnostici del DSM-IV. La percentuale totale dei bambini esposti al trattamento multimodale è compreso tra il 7% e il 17% di tutti quelli a cui è stato diagnosticata l'ADHD.

L'esposizione al farmaco in Francia è circa il 10% dei bambini affetti da ADHD²⁵. Nel Regno Unito, la percentuale dei bambini esposti a trattamenti farmacologici per ADHD è intorno all'11%. Quindi, il tasso di esposizione ai farmaci specifici per l'ADHD nei principali paesi europei non presenta differenze significative.

La differenza tra i vari paesi è rappresentata dalla prevalenza dell'ADHD: 1,2% nella nostra coorte, 2% in Francia, 5% nel Regno Unito. Queste differenze possono essere spiegate da varie ragioni, ad esempio il modo con cui viene effettuata la diagnosi e chi la effettua (medico generico, pediatra, psichiatra), l'efficienza e la capillarità della rete del servizio sanitario pubblico, l'attitudine a prescrivere farmaci psicotropi, l'efficacia del trattamento comportamentale, l'offerta di opzioni terapeutiche. Sicuramente in Italia la rete territoriale delle neuropsichiatrie infantili svolge un ruolo importante nella corretta gestione dei problemi della sfera psichica. L'attività di questa rete può spiegare un ricorso circoscritto all'uso dei farmaci e un maggiore uso di interventi socio-comportamentali rispetto ad altri paesi europei. Tuttavia, in alcuni casi le strutture non sono in grado di assorbire completamente l'utenza potenziale per i seguenti motivi: casi con quadro clinico moderato, incapacità dei servizi di farsi carico di tutti i pazienti per carenze di organico o sovraccarico di lavoro degli operatori.

CONCLUSIONI

L'indagine è stata effettuata su un campione di popolazione rappresentativo della popolazione pediatrica italiana. La prevalenza di ADHD osservata corrisponde a quella attesa in base agli studi condotti in Italia ma è da due a quattro volte inferiore rispetto a quanto osservato in altri paesi europei ed extraeuropei mentre il tasso di esposizione al trattamento farmacologico è simile a quello osservato in altri contesti europei.

La diagnosi di ADHD è basata su criteri clinici ed è perciò influenzata dalla soggettività dell'osservatore. Tutto ciò porta ad un'ampia variabilità tra paesi, dipendente soprattutto dalla figura professionale cui è affidata la diagnosi. L'accuratezza, nella nostra esperienza, è garantita da un rigido protocollo diagnostico-terapeutico che vincola all'uso di alcune batterie di test diagnostici la cui riproducibilità permette di stimare la concordanza tra osservatori diversi. L'esistenza di una rete di pediatri e neuro-psichiatri, inoltre, permette un'ampia diffusione delle terapie comportamentali e cognitive e potrebbe ridurre proporzionalmente l'uso dei farmaci o il tempo di esposizione agli stessi. Il funzionamento di questa rete dovrebbe essere ottimizzato per permetterle di prendere in carico tutti i casi che necessitano di una qualche forma di trattamento.

Lista delle abbreviazioni

ADHD: Attention deficit hyperactivity disorder

AIFA: Agenzia Italiana del Farmaco

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders-IV

NPIA: Servizio di Neuropsichiatria dell'infanzia e dell'adolescenza

Conflitto di interessi

Gli Autori dichiarano di non avere conflitti di interesse

Contributi degli autori

MD, BE, VC, NF hanno effettuato la diagnosi ADHD, prescritto il tipo di terapia (psicoterapia o trattamento multimodale), raccolto i dati;

NF ha organizzato il database e verificato la congruità interna

GE, PP hanno fatto l'analisi statistica e elaborato il testo

FMR e si è occupata della parte editoriale del manoscritto in base alle linee guida della rivista scientifica

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Cardiovascular Measures in Children and Adolescents with Attention-Deficit/Hyperactivity Disorder Who Are New Users of Methylphenidate and Atomoxetine

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and the Italian Attention-Deficit/Hyperactivity Disorder Regional Reference Centers

Abstract

Objective: The purpose of this study was to assess the cardiovascular effects of drugs used for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents treated in community care centers in Italy.

Methods: This study was an open, prospective, observational study of youth with ADHD treated with atomoxetine (ATX) and methylphenidate (MPH). Measurements of blood pressure and heart rate, and electrocardiogram (ECG) assessment were performed at baseline and at regular intervals up to 24 months.

Results: By June 2010, 1758 youth were enrolled in the Italian ADHD National Registry. Statistically significant increases were observed in cardiovascular measures: in the MPH group after 6 months in heart rate (+2.01, $p=0.01$); in the ATX group after 6 months in diastolic pressure (+1.60, $p=0.01$) and in heart rate (+2.93, $p=0.001$), and after 12 months in heart rate (+3.26, $p=0.003$). Compared with the baseline, 59 patients had an alteration of ECG during the follow-up period. Although at 12 months, the probability of detecting an abnormal ECG was higher in the MPH group than in the ATX group, only 2 out of 30 cases at 6 months with altered ECG were considered to have experienced serious adverse events. One case was treated with ATX and one with MPH, and arrhythmia was the detected abnormality.

Conclusions: Treatment with MPH and ATX in youth appears to have a small but significant impact on the cardiovascular system. The long-term impact of these medications is unknown. Several clinically meaningless ECG alterations were observed mostly in MPH-treated youth. We therefore suggest evaluating cardiovascular risks at baseline.

Introduction

TREATMENT OF PATIENTS with attention-deficit/hyperactivity disorder (ADHD) requires a long-term multimodal, multidisciplinary management, and it is based on pharmacological and/or behavioral therapy (Pliszka et al. 2007). In the last few years, the market for ADHD medications has increased (Scheffler et al. 2007). Stimulant and non-stimulant compounds, such as methylphenidate (MPH) and atomoxetine (ATX) respectively, are the drugs commonly used (Schachter et al. 2001; Cheng et al. 2007). However, despite their efficacy, much attention has been paid to risk/benefit profile assessment. For the cardiovascular system, an increase in blood pressure (BP) and heart rate (HR) has been demonstrated, and cases of stroke, myocardial infarction, and sudden death were reported to the United States Food and Drug

Administration, all in association with stimulant treatment of ADHD patients (Gelperin et al. 2006).

MPH is a sympathomimetic stimulant agent, which has shown to have an effect on HR and BP (Volkow et al. 2003). An open extended trial with Concerta[®] in children reported slight changes in systolic BP (+3.3 mm Hg), diastolic BP (+1.5 mm Hg) and HR (+3.9 bpm) (Wilens et al. 2004). A recent review showed that stimulant medications used in healthy children and adolescents with ADHD are associated with mean elevations in BP (≤ 5 mm Hg) and HR (≤ 10 bpm), without changes in electrocardiographic parameters, and that the expected quota of 5–15% of treated children and adolescents may experience these cardiovascular effects (Hammerness et al. 2011).

ATX is a selective norepinephrine reuptake inhibitor (SNRI), and an effect on the cardiovascular system could be expected. Data

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available from five placebo-controlled trials showed an increase in diastolic BP in children and young boys (Wernicke et al. 2003). The average increase was low, equal to 2.1 mm Hg, and occurred during the first few weeks of treatment. This effect has been confirmed by a recent review, in which a slight increase of BP and HR at the beginning of the treatment had been reported (Stiefel and Besag, 2010). In particular, in children and adolescents within 12 weeks of administration, an increase of diastolic BP (+2–11 mm Hg) and an increase in HR (+5–9 bpm) was reported by controlled studies and one dose-response study.

No evidence of increased cases of QTc interval prolongation in children and adolescents was found for MPH or ATX treatments (Wernicke et al. 2003; Kratochvil et al. 2006; Stiefel and Besag 2010).

Although this alteration of cardiovascular parameter seems to be minor, stimulant or non-stimulant drugs must be used with particular attention in children and adolescents with underlying heart problems. For this reason, before starting a treatment in subjects with ADHD, and during the follow-up period, a cardiovascular physical examination (BP and heart rate measurements, and electrocardiogram [ECG] control) is recommended (American Academy of Pediatrics 2000; EMEA 2009).

In Italy, in March 2007, the Italian Drug Regulatory Agency (AIFA) granted market authorization of immediate-release methylphenidate (IR-MPH) and ATX for treatment of children and adolescents (6–18 years-old) with ADHD, and, simultaneously, funded and activated the Italian ADHD National Registry, an open prospective observational study, managed by the Italian National Institute of Health (Istituto Superiore di Sanità [ISS]) and supervised by a national expert panel, whose main aim is to practice active pharmacovigilance (Panei et al. 2004).

The Italian ADHD National Registry developed a web site (see www.iss.it/adhd), where standard operative procedures and a protocol are available. A screening for cardiovascular disorders, including anamnestic history and measurement of BP and HR for all subjects, was strongly recommended, an ECG assessment was suggested, and a strict monitoring of cardiovascular parameters (BP, heart rate) was recommended during the follow-up.

The first aim of this study was to evaluate the effects of MPH and ATX on BP and HR in a prospective cohort of treated children and adolescents with ADHD, and to detect possible abnormalities of ECG, such as prolongation of the QTc interval.

Patients and Methods

The study was approved by the Ethical Committee of the ISS. It was an observational prospective study conducted in Italy. All children and adolescents treated with ADHD drugs were included in this study and were drug naïve. Children and adolescents ages 6–18 years ($n=1758$), with a diagnosis of ADHD, were recruited between June 2007 and June 2010 across Italy from 87 regional reference centers. The participating centers signed an agreement with the Italian Ministry of Health and were certified to diagnose ADHD and manage patient pharmacological treatment.

All subjects seen in a reference center were referred to the center by the subject's neuropsychiatrist for a suspicion of ADHD, or came on a voluntary basis.

Upon clinical history and clinical interview (95.5% of cases), or semistructured interviews such as Kiddie Schedule for Affective Disorders and Schizophrenia (K-SADS) or Parent Interview for Children Symptoms, Revised for DSM-IV (PICS-IV) tests (in 62.1% and 7.6% of cases, respectively), or other questionnaire (10.1% of cases), or rating scale such Swanson, Nolan, and Pelham,

Version IV (SNAP IV) (49.2% of cases), a diagnosis of ADHD was made according to the American Psychiatric Association, *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) criteria. To be diagnosed with ADHD, all subjects had to present symptoms with the following characteristics: 1) onset before the age of 7 years, 2) duration for at least 6 months, 3) pervasiveness (presence in more than one setting, e.g., at home, at school, at social level), 4) significant functional impairment. All subjects were screened for other mental disorders, and subjects with a different spectrum disorder (e.g., autism) were excluded. Furthermore, for the analysis, subjects with follow-up problems such as only one follow-up visit, or a follow-up of <6 months; or subjects with an altered ECG at baseline and with no ECG assessment; or those with no information on drug therapy, were excluded.

All subjects with ADHD started a multimodal intervention (including at least one of the following: child training, parent training, family therapy, psychodynamic therapy, or counseling), before or simultaneously with the beginning of pharmacological treatment. Moreover, the subjects who accepted the pharmacological treatment signed an informed consent explaining the aim of the study and the tests to be done in order to evaluate the primary parameters.

In Italy, specific guidelines are not available and the choice of treatment was based on current clinical practice. We identified two groups for treatment.

Treatment A

The first group consisted of subjects treated with MPH and with behavior treatment, simultaneously. The drug compound was MPH chlorhydrate 10 mg tablet. Administration was oral at the dosage of 0.3–0.6 mg/kg/dose/day. The total daily dose (mean $18.4 \text{ mg} \pm 10.4 \text{ mg}$) could be administered in two or three doses/daily at the discretion of the subject's neuropsychiatrist. Duration of the renewable prescription was 1 month.

Treatment B

The second group consisted of subjects treated with ATX and with behavior treatment, simultaneously. Patients received ATX chlorhydrate 5 mg, 10 mg, 18 mg, 25 mg, 40 mg, or 60 mg tablets. Administration was oral with the following schedule: started with 0.5 mg/kg/day once a day, for at least 7 days, then increasing the dose 1.2 mg/kg/day to find the optimal dose-response (mean total daily dose $38.6 \text{ mg} \pm 20.5 \text{ mg}$). Duration of the renewable prescription was 1 month.

Data collection

All clinical and relevant information was collected by standard procedures. Cardiovascular screening before the first administration of the drug was performed and included BP (systolic and diastolic values in mm Hg) and HR (in bpm) measurements, and ECG assessment in all subjects (strongly recommended by the Italian National Institute of Health for all Italian reference centers). During the follow-up, clinical assessment was performed monthly, and included measurements of BP and HR. Every 6 months, an ECG assessment was performed. According to guidelines (Blomström-Lundqvist et al. 2003) we defined "sinus bradycardia" as a sinus rate in absolute value <60 bpm, and "sinus tachycardia" as an increase in sinus rate in absolute value >100 bpm.

According to guidelines (Davignon et al. 1979), we defined normal ECG standards for infants and children. Prolongation of QTc interval was defined as any prolongation (in absolute value)

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TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF SUBJECTS STRATIFIED BY SUBJECTS INCLUDED IN THE ANALYSIS AND NOT INCLUDED IN THE ANALYSIS

Variables	Included in the analysis 751 subjects	Not included in the analysis 1007 subjects	Statistic (df), p value
Gender, n (%)			χ^2 (1)=0.01, $p=0.932$
Male	665 (89)	893 (89)	
Female	86 (11)	114 (11)	
Age, years (mean \pm SD)	10.61 \pm 2.71	10.76 \pm 2.86	t (1753)=1.11, $p=0.267$
Age class, n (%)			χ^2 (2)=1.77, $p=0.412$
<11 years	435 (58)	568 (56)	
11 – <15 years	262 (35)	351 (35)	
≥ 15 years	52 (7)	87 (9)	
Type of ADHD, n (%)			χ^2 (2)=0.54, $p=0.762$
ADHD-I	42 (6)	52 (5)	
ADHD-H	34 (4)	52 (5)	
ADHD-C	673 (90)	886 (90)	
Presence of comorbidity			
At least one	545 (73)	704 (71)	χ^2 (1)=0.86, $p=0.353$
Oppositional defiant disorder	307 (41)	403 (40)	χ^2 (1)=0.04, $p=0.834$
Conduct disorder	35 (5)	76 (8)	χ^2 (1)=6.30, $p=0.412$
Depression	50 (7)	64 (6)	χ^2 (1)=0.04, $p=0.837$
Anxiety	99 (13)	164 (16)	χ^2 (1)=3.54, $p=0.060$
Learning disorder	343 (46)	405 (41)	χ^2 (1)=4.54, $p=0.033$

with respect to detected value at the screening before the first administration of the drug, in accordance with the main objective of active pharmacovigilance of the study. ECGs with alterations or pathological aspects were read by pediatric cardiologists.

According to guidelines (Surawicz et al. 2009), we defined an incomplete right bundle branch block a rsr', rsR', or rSR' in leads V1 or V2 with a QRS duration between 90 and 100 ms in children and adolescents between 8 and 16 years of age, and between 86 and 90 ms in children <8 years of age.

The clinical monitoring of the register consisted of regular checking, via the web. All clinical data (relative to recruitment and follow-up) of each enrolled subject was entered in an electronic case report form (eCRF) that was located in a protected area of the web site (www.iss.it/adhd). Centers, child neuropsychiatry services, and pediatricians can access this protected area through user id and password.

The register database was based at the Italian National Institute of Health, Rome, which was also responsible for its protection and management. Data management was implemented by an infrastructure named "Advanced Multicenter Research" (AMR) and developed by Consorzio Inter-universitario per il Calcolo Automatico dell'Italia nord-orientale (CINECA). This application allowed the checking of any informative flow, the imputing of data, and the monitoring of information up to the analysis of the results. The access to the dedicated web site, www.farmacovigilanza.iss.it, followed security procedures RC4 ISO-8859-1.

Statistical analysis

ECG controls were performed at baseline and every 6 months from enrolment. BP and HR were measured at baseline and then monthly from enrolment.

Categorical variables are presented as absolute and percent frequencies, whereas quantitative variables are summarized as means \pm standard deviations (SD). Data have been analyzed separately according to three reference periods: from enrolment (time 0) to 6 months, from 0 to 12 months, and from 0 to 24 months of follow-up. As for treatment, subjects were divided into three groups according to the drug(s) received during the reference period under examination:

those receiving MPH only (MPH group), those receiving ATX only (ATX group), and those receiving both drugs, but not simultaneously (MIXED group). The other subjects not receiving either MPH or ATX in the reference period, but receiving other psychotropic drugs, were excluded from the following analyses.

For any reference period, only subjects with data at baseline and at least one measurement during the follow-up period (for ECG) or at the end of the period (in case of BP and pulse) were included in the statistical analyses.

Comparisons between MPH and ATX treatment groups in relation to frequency of ECG abnormalities were performed by χ^2 test. Relative risk (RR) with 95% confidence interval (95% CI) was computed as effect size estimates.

Comparisons within each group in relation to BP and pulse data were performed by paired Student's t -test to assess variations during the reference period, whereas differences between MPH and ATX groups for BP and pulse changes that occurred during the period were tested using Student's t -test for independent samples. Nonparametric tests (Wilcoxon for paired observations and Mann-Whitney U test for independent samples) were used to confirm results of parametric analyses.

Results

At the end of June 2010, 1758 children and adolescents with ADHD were enrolled in the Italian ADHD National Registry; 1558 (88.6%) were males, and 200 (11.4%) were females. The mean age was equal to 10.7 years (SD \pm 2.8 years). In relation to age class analysis, the 10–13-year-old children were the most representative (703 subjects), ~40% of entire population.

Stratified by type of treatment, 840 (47.8%) subjects were treated with MPH, and 918 (52.2%) were treated with ATX. Excluded from the analysis were 1007 enrolled subjects, for the following reasons: Absence of follow-up at 6 months (50.7%), only one follow-up (29.4%), no ECG at baseline (14.0%), an abnormal ECG at baseline (3.7%), and no available information on drug therapy (2.2%). Demographic and clinical characteristics of subjects stratified by subjects included in the analysis and not included

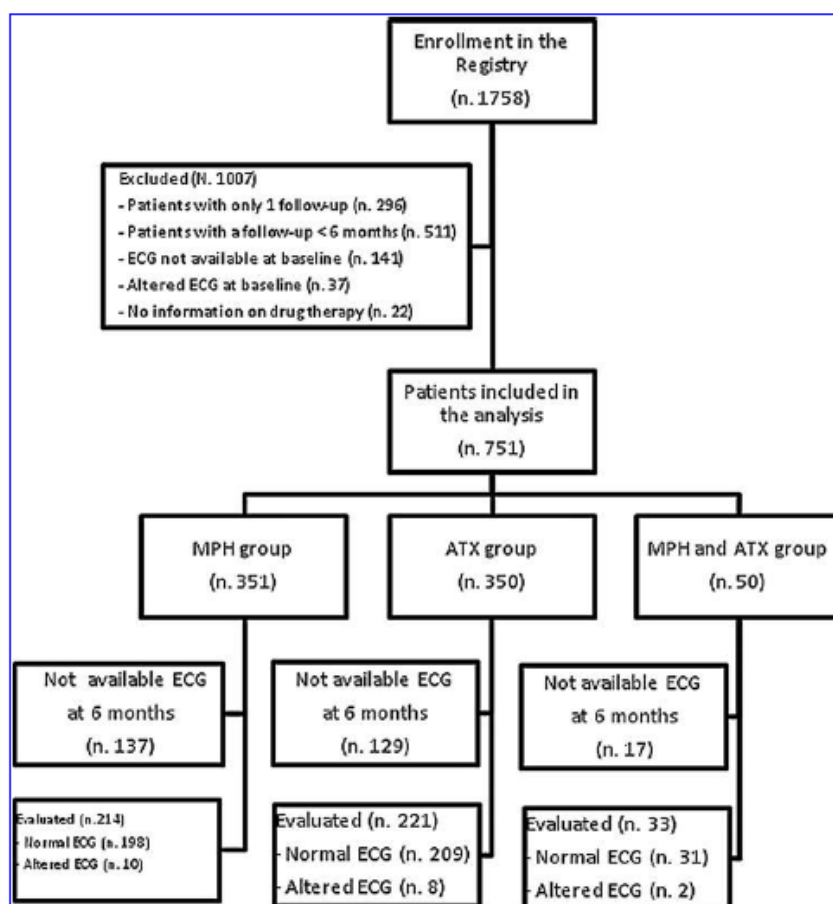


FIG. 1. Flow chart of patients at 6 months of follow-up. The figure reports the number of altered electrocardiograms (ECGs) detected at 6 months of follow-up, stratified for each group of treatment (methylphenidate [MPH] group, atomoxetine [ATX] group, MPH and ATX group). The reasons for which the patients were excluded from analysis are also reported.

in the analysis are described in Table 1. Comparing the two groups, no statistical differences were observed.

ECG evaluation

The follow-up was 0 to 6 months. Three hundred fifty-one (46.7%) subjects were treated with MPH (mean dose 0.4 ± 0.2 mg/

kg/dose/day), 350 (46.6%) with ATX (mean dose 0.7 ± 0.3 mg/kg/day), and 50 (6.7%) with both drugs. ECG at 6 months was not available for some patients in all groups; therefore, only 468 subjects were included in the final analysis, with the following distribution: 214 cases in the MPH group, 221 in the ATX group, and 33 in the MIXED group (see Fig. 1). Demographic and clinical characteristics of subjects included in the three different

TABLE 2. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF SUBJECTS STRATIFIED BY TREATMENT GROUP

Variables	MPH 351 subjects	ATX 350 subjects	Both drugs 50 subjects	Statistic (df) p-value
Gender, n (%)				χ^2 (2) = 2.00, $p = 0.367$
Male	305 (87)	314 (90)	46 (92)	
Female	46 (13)	36 (10)	4 (8)	
Age, years (mean \pm SD)	10.41 ± 2.62	10.82 ± 2.81	10.56 ± 2.55	t (748) = 1.40, $p = 0.140$
Age class, n (%)				χ^2 (4) = 7.45, $p = 0.114$
<11 years	220 (63)	187 (54)	28 (56)	
11 – <15 years	109 (31)	133 (38)	20 (40)	
≥ 15 years	21 (6)	29 (8)	2 (4)	

MPH, methylphenidate; ATX, atomoxetine.

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TABLE 3. DISTRIBUTION OF SUBJECTS WITH AN ALTERED ECG AT 6, 12 AND 24 MONTHS BY TYPE OF TREATMENT

Follow-up	MPH	ATX	MPH and ATX	MPH vs ATX relative risk (95%CI)	p-value
6 months	10/214 (4.7%)	8/221 (3.6%)	2/33 (6.1%)	1.29 (0.52–3.21)	0.58
12 months	19/190 (10.0%)	7/169 (4.1%)	4/53 (7.5%)	2.41 (1.04–5.60)	0.03
24 months	8/77 (10.4%)	–/50 (0.0%)	3/32 (9.4%)	N.A.	

ECG, electrocardiogram; MPH, methylphenidate; ATX, atomoxetine.

treatment group are described in Table 2. Comparing each variable through the three groups, no statistical significant difference was detected, and for this reason the three groups were similar for gender and age.

During this period, 20 out of 468 (4.3%) cases had at least one abnormal ECG. Ten cases were in the MPH group (4.7%), eight in the ATX group (3.6%) and two in the MIXED group (6.1%).

Comparing the MPH group with the ATX group, the MPH group showed an RR > 1, without relevant differences (RR = 1.29, 95% CI: 0.52–3.21; $p = 0.58$).

Follow-up 0–12 months. Four hundred twelve subjects were included in the analysis, with the following distribution: 190 patients in the MPH group, 169 in the ATX group and 53 in the MIXED group. During this period, 30 out of 412 (7.3%) cases presented at least one altered ECG: 19 cases in the MPH group (10.0%), 7 in the ATX group (4.1%), and 4 in the MIXED group (7.5%). Compared with the ATX group, the MPH group showed a significantly higher risk of ECG abnormalities (RR = 2.41, 95% CI: 1.04–5.60; $p = 0.03$).

Follow-up 0–24 months. One hundred fifty-nine subjects were included in the analysis, with the following distribution: 77 cases in the MPH group, 50 in the ATX group, and 32 in the MIXED group. Eleven (6.9%) cases showed at least one altered ECG: eight cases in the MPH group (10.4%), no case in the ATX group, and three cases in the MIXED group (9.4%). The low number of subjects and events makes the point estimate of the relative risk for ECG abnormalities in MPH versus ATX patients unreliable. However, based on these data, we can confidently state that also in this reference period the risk of ECG abnormalities is significantly higher in MPH-treated than in ATX-treated patients (see Table 3).

Qualitative description

Table 4 reports the qualitative description of 59 cases, 38 of which were treated with MPH. Twenty-five right incomplete bundle branch

TABLE 4. DESCRIPTION OF ECG CHANGES BY TYPE OF TREATMENT

ECG changes	Observed cases	Treated patients	
		MPH %	ATX %
Right incomplete bundle branch block	25	64	36
Sinus bradycardia	11	91	9
Sinus tachycardia	12	50	50
Conduction disorders ^a	5	20	80
Lengthened QTc	6	83	17
Total	59	64	36

^aFirst degree atrioventricular block with a PR > 200 msec.

ECG, electrocardiogram; MPH, methylphenidate; ATX, atomoxetine.

block cases, 12 tachycardia cases, 11 bradycardia cases, 6 cases of lengthened QT interval, and 5 conduction disorders were reported. For 12 tachycardia cases, the mean value (\pm SD) of HR was 106.11 (\pm 4.68), with an increment respect to baseline value of 18.89 bpm. For 11 bradycardia cases, the mean value (\pm SD) of HR was 53.67 (\pm 4.93), with a decrease respect to baseline value of 11.83 bpm.

For the prolongation of QTc interval, five out of six cases were treated with MPH, and mean QT interval value was equal to 412 ms (range: 360ms–444ms). In all six cases, QTc values were in the normal range, but were more prolonged with respect to baseline value.

Altered ECGs were reported as being serious adverse events in only 2 out of 30 cases at 6 months. One case was treated with ATX and one was treated with MPH, and arrhythmia was the detected abnormality. In both cases the therapy was interrupted.

Cardiovascular evaluation

We evaluated the BP and HR before the treatment and after 6, 12, and 24 months. Analyzing data separately for each drug, we observed in the MPH group at 6 months a small but not significant increase of systolic pressure ($+0.26 \pm 13.18$) and of diastolic pressure ($+0.82 \pm 10.99$), and a statistically significant increase in pulse ($+2.10 \pm 15.04$). At 12 months, a small (but not significant) increase of diastolic pressure ($+1.35 \pm 12.40$) and in pulse ($+1.25 \pm 12.69$) was confirmed, whereas a small not significant decrease of systolic pressure (-0.49 ± 14.83) was observed in MPH group. After 24 months of treatment with MPH, a small not significant decrease of systolic pressure (-1.00 ± 16.10), and a small statistically significant decrease of diastolic pressure (-3.90 ± 11.23) and in pulse (-3.80 ± 12.82) were observed.

For the ATX group, at 6 months a small not significant increase of systolic pressure ($+0.01 \pm 12.68$), and a small statistically significant increase of diastolic pressure ($+1.61 \pm 11.25$) and in pulse ($+2.94 \pm 13.11$) were observed. At 12 months, small not significant increases of systolic ($+0.36 \pm 13.52$) and diastolic pressure ($+0.13 \pm 10.83$) were confirmed, and a statistically significant increase of HR ($+3.26 \pm 14.32$) was detected. After 24 months, a small not significant increase of systolic pressure ($+2.13 \pm 9.51$), diastolic pressure ($+1.11 \pm 10.76$), and HR ($+0.21 \pm 13.33$) were observed. These data are showed in Tables 5 and 6.

Discussion

There were some factors in the study that limited the conclusions. First, we analyzed 751 children, who matched analysis criteria. To understand the impact on the results, we compared the statistically analyzed population to the one not analyzed, through some parameters, such as age, sex, and type of treatment. No statistical differences were observed. Therefore, we believe that the population analyzed was representative of the patients enrolled in the Italian ADHD National Registry.

Second, we want to emphasize that among the 751 subjects included in the analysis at 6 months ~37% had not been evaluated

TABLE 5. CHANGES OF CARDIOVASCULAR PARAMETERS IN MPH-TREATED SUBJECTS

Parameter	Evaluation 0 months	at 0 and 6 315 subjects 6 months	months p-value ^a	Evaluation 0 months	at 0 and 12 194 subjects 12 months	months p-value ^a	Evaluation 0 months	at 0 and 24 61 Subjects 24 months	months p-value ^a
Systolic pressure (mm Hg)									
Mean ± SD	102.58 ± 13.21	102.84 ± 12.87	0.77	103.01 ± 12.88	102.52 ± 12.75	0.65	100.62 ± 12.32	99.62 ± 12.69	0.63
Median (min, max)	102 (65, 139)	100 (70, 150)		104 (65, 132)	102 (60, 145)		100 (70, 130)	100 (80, 137)	
Diastolic pressure (mm Hg)									
Mean ± SD	63.96 ± 10.22	64.77 ± 9.57	0.19	63.85 ± 10.31	65.20 ± 10.31	0.13	63.18 ± 10.90	59.28 ± 9.66	0.009
Median (min, max)	65 (40, 95)	65 (40, 100)		64.5 (40, 110)	65 (45, 110)		61 (46, 110)	60 (35, 85)	
Heart rate (bpm)									
Mean ± SD	77.76 ± 11.75	79.86 ± 12.51	0.01	77.54 ± 12.33	78.79 ± 11.77	0.17	79.85 ± 12.94	76.05 ± 11.20	0.02
Median (min, max)	78 (51, 120)	80 (43, 120)		77.5 (51, 120)	78 (55, 126)		78 (51, 120)	76 (55, 109)	

^aPaired Student t test.
MPH, methylphenidate.

TABLE 6. CHANGES OF CARDIOVASCULAR PARAMETERS IN ATX-TREATED SUBJECTS

Parameter	Evaluation 0 months	at 0 and 6 316 subjects 6 months	months p-value ^a	Evaluation 0 months	at 0 and 12 166 subjects 12 months	months p-value ^a	Evaluation 0 months	at 0 and 24 38 subjects 24 months	months p-value ^a
Systolic pressure (mm Hg)									
Mean ± SD	104.30 ± 11.50	105.20 ± 11.61	0.21	104.73 ± 10.88	105.09 ± 11.45	0.73	105.84 ± 9.61	107.97 ± 10.81	0.18
Median (min, max)	105 (60, 132)	105 (75, 146)		105 (78, 130)	105 (80, 140)		105 (90, 130)	107.5 (90, 130)	
Diastolic pressure (mm Hg)									
Mean ± SD	66.66 ± 10.20	68.27 ± 9.12	0.01	67.65 ± 10.49	67.78 ± 8.44	0.87	69.34 ± 10.01	70.45 ± 6.30	0.53
Median (min, max)	65 (43, 106)	70 (40, 102)		69.5 (43, 106)	70 (40, 100)		70 (50, 90)	70 (60, 80)	
Heart rate (beats/minute)									
Mean ± SD	78.46 ± 12.52	81.40 ± 12.56	0.001	77.79 ± 12.26	81.05 ± 11.29	0.004	79.58 ± 12.44	79.79 ± 9.58	0.92
Median (min, max)	78 (50, 130)	80 (50, 125)		76 (50, 130)	80 (55, 112)		79.5 (58, 120)	80 (60, 104)	

^aPaired Student t test.
ATX, atomoxetine.

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because an ECG was not available. This likely represents a reality in long-term community treatment centers for chronic conditions. Moreover, adherence to treatment has not been evaluated, because the study was not designed to allow for it, whereas intention to treat analysis was used to analyze the treatment.

Third, after 24 months of treatment there were few observations, and this could have influenced any possible considerations. Further analyses will be performed in order to consolidate our data.

Our study is based on the Italian ADHD National Registry, an observational prospective study with one of the longest follow-up times (> 24 months) reported in the scientific literature, aimed at evaluating the cardiovascular safety of MPH and ATX. All subjects enrolled in the study were drug naïve. This study was performed as a phase IV pharmacovigilance observational study aimed at detecting all changes in the cardiovascular parameters before and during pharmacological treatment. We had also collected and analyzed the variations included in the normal range, because these modifications can represent a clinical warning.

MPH was associated with a mild increase of systolic (+0.26 mm Hg) and diastolic (+0.81 mm Hg) BP and HR, over 6 months of treatment. Only the HR, after 6 months of treatment, showed a statistically significant difference from the baseline (+2 bpm). After 12 months of treatment, this trend for diastolic pressure and HR was confirmed, whereas for systolic pressure a moderate decrease (–0.48 mm Hg) was observed. After 24 months, a slight reduction of all parameters, systolic (–1 mm Hg) and diastolic (–3.90 mm Hg) pressure and HR (–3.80 bpm), was observed, which could have been caused by the fact that a small number of subjects was included in the analysis. These changes, especially those observed in the first period of treatment (0–6 months), have also been reported in a recent study conducted in 114 adolescents with ADHD who were treated with extended-release methylphenidate (OROS-MPH) with a follow-up of 6 months (Hammerness et al. 2009a).

Changes after 24 months were unclear, especially where a decrease of BP and HR was detected. However, these results cannot be conclusive, because the subjects included in the analysis at this step of follow-up were too few. Moreover, we cannot verify the adherence of subjects to the treatment over time. However, a normalization of cardiovascular parameters could be expected, partly because of the increasing age of the subjects.

For ATX, in each study period a mild increase of systolic BP, without statistically significant difference, was observed. The difference was equal to +0.90 mm Hg at 6 months up to +2.13 mm Hg at 24 months. The same trend was detected for diastolic pressure, except at 6 months, when a statistical difference was observed ($p=0.01$). These findings agree with those of two recent publications (Takahashi et al. 2009; Stiefel and Besag 2010), in which an increase in BP was confirmed in the long term. This evidence disagrees with another study, in which an increase of BP occurred in the first weeks of treatment, whereas after >1 year a stabilization of value with no further increase was detected (Wernicke et al. 2003). In our study, the HR showed a statistically significant increase at 6 and 12 months. The variation of pulse was small, between +2.93 bpm and +3.26 bpm, whereas at 24 months a mild not statistically significant increase (+0.21 bpm) was observed. This finding is in agreement with others studies (Wernicke et al. 2003; Takahashi et al. 2009; Stiefel and Besag 2010). Moreover, this effect was expected from the pharmacological action of this drug.

It is important to underline that, for both drugs, no serious clinical implication related to changes of BP and HR was observed.

The study showed some changes in the ECG in a group of subjects treated with MPH or ATX, or both drugs. The proportion of abnormal ECG increased over time, at 6 months it was 4.8% and at 24 months of treatment it was up to 9.9%. The probability to observing an alteration in ECG was higher in the MPH patient group than in the ATX patient group, with the difference increasing over time (RR at 6 months was 1.29; RR at 12 months was 2.41; RR at 24 months not available). After 24 months of treatment with MPH, the probability of detecting ECG changes was 10 times higher than with ATX. Despite these findings, no important clinical changes were observed, except in the two observed cases of arrhythmia, for which the pediatric cardiologist suggested a possible correlation of arrhythmia and the pharmacological treatment, and a permanent discontinuation of treatment was advised.

We observed 25 cases of right incomplete bundle branch block. None of these cases were clinically important.

Twelve tachycardia cases and 11 bradycardia cases were observed, and no clinically meaningful changes were observed; however, in all these cases the treatment was interrupted.

We observed 6 cases of prolonged QTc interval on all detected ECG changes; one subject in the ATX-treated group and five subjects in the MPH-treated group. In all six cases, QTc interval value was in the normal range but was prolonged with respect to baseline value, without clinically meaningful changes. In two recent studies that examined the effect of OROS-MPH on the cardiovascular system, no clinically meaningful changes in ECG parameters were observed (Hammerness et al. 2009 a,b).

For ATX use, we reported only one case of prolongation of QT interval without clinical impact. This agrees with other studies, in which there is no evidence that ATX prolongs QT interval (Wernicke et al. 2003; Hammerness et al. 2009b). However, in one other study, a mild prolongation of QT interval (<5 msec) was detected, but without clinical evidence (Takahashi et al. 2009).

Conclusions

Since 2006, the European Medicines Agency (EMA) required, for both drugs, a “black box” warning on the product information about cardiovascular safety (Strattera [atomoxetine] package insert 2003; Ritalin [methylphenidate] package insert 2007). Our study highlights that the use of MPH and ATX in children and adolescents with ADHD seems not to be the cause of clinical cardiovascular implications. Minor increases in HR and BP were observed, cases of sinus tachycardia were observed in only 2.6% of sample and rare ECG abnormalities (4.3% of sample) were detected. While awaiting future studies of long-term impact, clinicians should continue to monitor and be mindful of ongoing debate about the utility/feasibility of ECG screening. Graham et al. suggest that there is no current evidence to support an incremental benefit for routine ECG assessment of ADHD patients prior to initiation of medication (Graham et al. 2011). Thomas et al., in a retrospective study based on current clinical practice of community pediatricians, studied the impact of ECG assessment on children treated with stimulants and found that only 6.4% of patients had an alteration of ECG prior to initiation of treatment with stimulants, and that only one patient out of four had perceived a significant delay of therapy (Thomas et al. 2011). We believe, in accordance with other authors, that prior to treating children and adolescents with ADHD drugs, it is necessary to evaluate the appropriate individual cardiovascular risk (Hammerness et al. 2011) and to define the best assessment of cardiovascular parameters during the treatment, to increase the safety of treatment in children and adolescents (Elia et al. 2010).

Clinical Significance

Regular monitoring of cardiovascular parameters (anamnesic history and BP and HR measurements) is recommended for all patients, but should be considered mandatory, perhaps at more frequent intervals, for subjects at high risk.

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***L'alunno con ADHD
(disturbo dell'attenzione
e/o iperattività) a scuola:
Costruzione del Piano
Didattico Personalizzato
e gestione in classe***

Corso di Alta Formazione

Facoltà di Psicologia
SPAEE - Servizio di Psicologia
dell'Apprendimento
e dell'Educazione
Formazione Permanente

8 marzo - 10 maggio 2013
Università Cattolica del Sacro Cuore
Contrada Santa Croce 17 - 25122 Brescia



UNIVERSITÀ
CATTOLICA
del Sacro Cuore

con la partecipazione di

NPI Spedali Civili di Brescia

Presentazione

Il corso di alta formazione "L'alunno con ADHD (disturbo dell'attenzione e/o iperattività) a scuola: Costruzione del Piano Didattico Personalizzato e gestione in classe" è strutturato in 8 moduli per un ammontare complessivo di 40 ore, suddivise tra 32 ore di incontri in presenza e 8 ore di attività supervisionata svolta online.

Finalità

Il presente corso ha come finalità la trasmissione di conoscenze relative alle manifestazioni in ambiente scolastico del disturbo dell'attenzione e/o iperattività (ADHD) e di competenze per la gestione in classe degli alunni che presentano tale disturbo. Verranno fornite indicazioni utili ad inquadrare correttamente la patologia e a riconoscerne i principali sintomi ostacolanti l'apprendimento, le relazioni con insegnanti e compagni, la gestione dei compiti. Particolare attenzione sarà dedicata allo sviluppo di competenze che rendano l'operatore capace di intervenire nel rispetto della normativa vigente, di stendere correttamente un Piano Didattico Personalizzato e di sostenere strategie compensative per favorire l'integrazione dell'alunno nel proprio contesto scolastico.

Contenuti

8 marzo 2013

Modulo 1

(A. Antonietti e G. Daffi)

- Introduzione al corso
- Le manifestazioni dell'ADHD in ambito scolastico
- Ipotesi interpretative circa l'origine dei comportamenti problematici
- Il ruolo dell'ambiente scolastico
- I modelli di intervento
- Analisi e discussione di casi

15 marzo 2013**Modulo 2**

(P. Effedri e G. Daffi)

- La diagnosi
- Il contributo della scuola alla raccolta di informazioni
- Aspetti neurobiologici e farmacologici del disturbo
- L'organizzazione dei centri per l'ADHD presso i servizi di Neuropsichiatria infantile: professionalità coinvolte e modalità di intervento
- Il modello di intervento della Lombardia e il progetto regionale ADHD
- La collaborazione richiesta alla scuola
- La collaborazione richiesta alla famiglia
- Esperienze formative dei centri ADHD
- Modalità e criteri di segnalazione e accesso ai centri

22 marzo 2013**Modulo 3**

(M. Prandolini e R. Franchini)

- Modalità di valutazione
- Strumenti e strategie per l'osservazione
- Prove e attività per l'identificazione di aspetti problematici
- Analisi e discussione di casi

5 aprile 2013**Modulo 4**

(E. Zugno e B. Pizzi)

- L'attenzione: definizione e modelli a confronto
- Le difficoltà di attenzione nell'ADHD
- La gestione del bambino disattento in classe
- Analisi di casi

12 aprile 2013**Modulo 5**

(B. Pizzi)

- L'iperattività
- Le difficoltà di controllo nell'ADHD
- La gestione del bambino iperattivo in classe
- Analisi di casi

19 aprile 2013**Modulo 6**

(G. Daffi)

- Funzioni esecutive: Modelli a confronto
- Compromissione delle funzioni esecutive nell'ADHD programmi per il sostegno/sviluppo
- Modelli e protocolli di intervento scolastico sulle funzioni esecutive in ambito nazionale e regionale
- Strategie per favorire la pianificazione e la programmazione di classe
- Strategie per la gestione dei compiti
- L'esperienza dell'Homework Tutor

3 maggio 2013**Modulo 7**

(E. Zugno)

- Aiuti e rinforzi per il bambino con ADHD
- Motivare il bambino con ADHD
- La componente emotiva nella gestione dell'alunno con ADHD
- Le attività ritmico-musicali come strategia di intervento

10 maggio 2013**Modulo 8**

(A. Antonietti e G. Daffi)

- L'intervento in classe
- L'approccio metacognitivo
- Simulazioni e analisi di casi
- Normativa relativa alla gestione dell'alunno con ADHD classe
- La stesura del Piano Didattico Personalizzato
- Adattamenti dei contenuti e delle modalità di presentazione
- La multimedialità come risorsa
- Verifica finale sul percorso svolto

Destinatari

Il corso è rivolto a insegnanti, educatori, formatori, psicologi, pedagogisti e figure sanitarie che operino con soggetti con ADHD.

L'iscrizione è subordinata al preventivo esame del curriculum candidato da parte della direzione del corso.

Struttura e svolgimento

Il corso si svolgerà presso la sede dell'Università Cattolica del Sacro Cuore, sita in Contrada Santa Croce 17 a Brescia.

Tutti gli incontri avranno luogo il venerdì, dalle ore 14.30 alle ore 18.30.

La frequenza, per ottenere l'attestato finale, è obbligatoria per almeno il 75% delle ore in presenza.

Metodologia

Ogni argomento previsto dal programma sarà trattato dal punto di vista dell'inquadramento teorico e operativo. Le attività didattiche saranno svolte in aula secondo i formati della lezione e dell'esercitazione (role-playing, dimostrazione tecnica, discussione di casi, lavoro in piccolo gruppo, question time con il docente, ecc). In specifico, vi saranno momenti a carattere laboratoriale in cui si esamineranno gli strumenti operativi e ci si eserciterà nella loro applicazione.

Il corso prevede anche la richiesta di analizzare un caso e produrre un elaborato sotto forma di Piano Didattico Personalizzato per un alunno con ADHD. Questo compito, quantificato in 8 ore di lavoro personale, sarà svolto online e i partecipanti riceveranno una restituzione rispetto a quanto da loro prodotto.

Ogni partecipante riceverà il materiale didattico.

Una piattaforma online verrà utilizzata per supportare a distanza l'apprendimento.

Un tutor d'aula sarà presente lungo lo svolgimento dell'intero corso e gestirà la piattaforma online e l'interazione a distanza dei corsisti.

Al termine del corso sarà effettuata una verifica dell'apprendimento consistente in una prova scritta relativa ai contenuti del corso e alla loro applicazione. Ai fini del conseguimento dell'attestato è necessario che i partecipanti superino questa prova di verifica.

Docenti

Direzione scientifica

- *Alessandro Antonietti*, Professore di Psicologia Cognitiva Applicata presso la Facoltà di Psicologia dell'Università Cattolica del Sacro Cuore.
Responsabile dello SPAEE e coordinatore del Laboratorio di Psicologia Cognitiva.

Coordinamento didattico

- *Gianluca Daffi*, Collaboratore del Dipartimento di Psicologia dell'Università Cattolica del Sacro Cuore.
Coordinatore formazione Progetto "Condivisione di percorsi diagnostico terapeutici per l'ADHD in Lombardia".

Docenti

- *Alessandro Antonietti*, predetto.
- *Gianluca Daffi*, predetto.
- *Paola Effedri*, Neuropsichiatra Infantile, referente del gruppo di lavoro sull'ADHD della NPI Spedali Civili di Brescia.
- *Roberto Franchini*, Docente di Metodologia delle attività formative e speciali presso la Facoltà di Scienze dell'educazione dell'Università Cattolica del Sacro Cuore, Sede di Brescia.
- *Barbara Pizzi*, Psicologa, collaboratrice dello SPAEE.
- *Maria Cristina Prandolini*, Esperta in Psicopatologia dell'Apprendimento, collabora con la cattedra di Pedagogia Speciale dell'Università Cattolica del Sacro Cuore, Sede di Brescia.
- *Elisa Zugna*, Psicologa, collaboratrice dello SPAEE.

Tutor

- *Maddalena Scolari*, Educatrice specializzata nell'ADHD e collaboratrice del gruppo di lavoro sull'ADHD presso NPI Spedali Civili di Brescia.

Costo

Il costo del corso è di 300 euro (+IVA 21%).

Il Servizio di Psicologia dell'Apprendimento e dell'Educazione (SPAEE) dell'Università Cattolica opera, nelle sedi di Brescia e Milano, in tre settori:

- *servizi psico-educativi e riabilitativi*: si svolgono valutazioni psicodiagnostiche e interventi di riabilitazione e potenziamento per bambini e ragazzi che presentano disabilità intellettive, disturbi specifici dell'apprendimento (DSA: dislessia, disgrafia/disortografia, discalculia) e deficit da disturbo di attenzione e iperattività (ADHD) e che mostrano difficoltà nel far fronte efficacemente alle richieste scolastiche;
- *attività formative*: si propongono attività di formazione, percorsi di ricerca-azione, supervisione e laboratori su queste aree tematiche: metodi e tecniche di apprendimento-insegnamento, professione docente, difficoltà e disturbi di apprendimento, emozioni e comportamento, linguaggi espressivi e creatività, tecnologie in classe. Le attività si rivolgono a insegnanti, dirigenti scolastici, formatori, educatori, riabilitatori, operatori sociali, genitori e studenti;
- *ricerca*: le metodologie di intervento proposte sono accompagnate da studi osservativi e sperimentali per l'elaborazione di test e training, documentati attraverso la pubblicazione di strumenti operativi, volumi in collane dedicate, articoli su riviste specializzate e comunicazioni a congressi.

Il Servizio viene prestato sotto forma di consulenza, percorsi individuali, attività di gruppo, progetti d'intervento e formazione, seminari, da tenersi presso le sedi del Servizio (Milano e Brescia) o presso quelle dei richiedenti o anche a distanza per mezzo di strumenti telematici.

E-mail: spae@unicatt.it

Sito: www.spae.it

Sul sito è possibile iscriversi alla newsletter dello SPAEE e così ricevere notizie sulle attività del Servizio.

Informazioni

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Per ricevere la newsletter iscriversi al seguente indirizzo:

<http://crc.marionegri.it/bonati/adhdnews/subscribe.html>

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

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