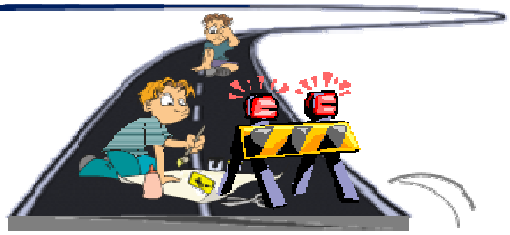
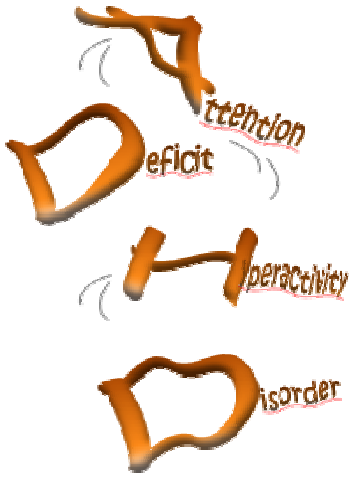
NEWSLETTER





INDICE:

MARIONEGRI
ISTITUTO DI RICERCHE FARMACOLOGICHE

BIBLIOGRAFIA ADHD MARZO 2012

Acad Pediatr. 2012;12:110-16.

TRENDS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER AMBULATORY DIAGNOSIS AND MEDICAL TREATMENT IN THE UNITED STATES, 2000-2010.

Garfield CF, Dorsey ER, Zhu S, et al.

Objectives: Because of several recent clinical and regulatory changes regarding attention deficit-hyperactivity disorder (ADHD) in the United States, we quantified changes in the diagnosis of ADHD and its pharmacologic treatment from 2000 through 2010.

Methods: We used the IMS Health National Disease and Therapeutic Index, a nationally representative audit of office-based providers, to examine aggregate trends among children and adolescents younger than 18 years of age. We also quantified how diagnosis and treatment patterns have evolved on the basis of patient and physician characteristics and the therapeutic classes used.

Results: From 2000 to 2010, the number of physician outpatient visits in which ADHD was diagnosed increased 66% from 6.2 million (95% confidence interval 5.5-6.9M) to 10.4 million visits (95% confidence interval 9.3-11.6 million). Of these visits, psychostimulants have remained the dominant treatment; they were used in 96% of treatment visits in 2000 and 87% of treatment visits in 2010. Atomoxetine use decreased from 15% of treatment visits upon product launch in 2003 to 6% of treatment visits by 2010. The use of potential substitute therapies - clonidine, guanfacine, and bupropion - remained relatively constant (between 5% and 9% of treatment visits) during most of the period examined. During this period, the management of ADHD shifted away from pediatricians and towards psychiatrists (from 24% to 36% of all visits) without large changes in illness severity or the proportion of ADHD treatment visits accounted for by males (73%-77%).

Conclusions: In 10 years, the ambulatory diagnosis of ADHD increased by two-thirds and is increasingly managed by psychiatrists. The effects of these changing treatment patterns on children's health outcomes and their families are unknown.

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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;4:11-23.

NEUROCOGNITIVE TRAINING FOR CHILDREN WITH AND WITHOUT AD/HD.

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

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

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ADHD Atten Deficit Hyperact Disord. 2012;4:25-35.

HEALTH-RELATED QUALITY OF LIFE IN ADHD: A POOLED ANALYSIS OF GENDER DIFFERENCES IN FIVE ATOMOXETINE TRIALS.

Wehmeier PM, Schacht A, Escobar R, et al.

Attention-deficit/hyperactivity disorder (ADHD) is associated with considerable impairment in health-related quality of life (HR-QoL). Atomoxetine has been found to improve HR-QoL in both children and adolescents. However, there is scarcity of data on gender differences in treatment responses to ADHD medications. This pooled analysis of five atomoxetine trials aimed to evaluate treatment differences with respect to HR-QoL and ADHD symptoms across genders. Data from 5 clinical atomoxetine trials (4 from Europe and 1 from Canada) with similar inclusion and exclusion criteria and similar durations (8- to 12-week follow-up) were included in the pooled analysis. All studies included the Child Health and Illness Profile-Child Edition (CHIP-CE) Parent Report Form. In addition, correlations between HR-QoL and ADHD core symptoms were compared between girls and boys. Data from 136 girls and 658 boys (mean age: 9. 6 and 9. 7 years, respectively) were pooled. Boys and girls were similarly impaired at baseline with minor differences in some of the subdomains. Treatment effect of atomoxetine was significant in both groups for the Risk Avoidance domain and its subdomains. No gender effect with both clinical and statistical significance was found for treatment outcome. Correlations between ADHD Rating Scale and CHIP-CE scores were similar in both genders and were generally low at baseline and moderate at endpoint and for the change from baseline to endpoint. Atomoxetine was effective in improving some aspects of HR-QoL in both genders without any significant differences across genders. Correlations between core symptoms of ADHD and HR-QoL were low to moderate in both boys and girls.

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ADHD Atten Deficit Hyperact Disord. 2012;4:37-39.

SAFE AND EFFECTIVE METHYLPHENIDATE THERAPY IN A PEDIATRIC PATIENT WITH GLAUCOMA.

Lewis H, Lewis J.

Stimulant medications used as first-line treatment in attention deficit hyperactivity disorder (ADHD) are contraindicated in patients with glaucoma. We present the first reported case of using methylphenidate therapy to safely and effectively treat ADHD in a pediatric patient with glaucoma.

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Afr J Psychiatry (South Africa). 2011;14:286-89.

ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOM SELF-REPORT AMONG MEDICAL STUDENTS IN ELDORET, KENYA.

Atwoli L, Owiti P, Manguro G, et al.

Objective: To determine the prevalence of self-reported attention deficit hyperactivity disorder (ADHD) symptoms among medical students in Eldoret, Kenya.

Method: A cross-sectional descriptive study of all medical students who gave consent to participate in the study. Undertaken at Moi University's School of Medicine in Eldoret, Kenya. Comprising two hundred and fifty three (253) undergraduate medical students, with a mean age of 23.7 years (19-42, s.d. 4.1), of whom 51% were female. Measuring ADHD symptomatology using the Adult ADHD Self-Report Scale (ASRS v1.1).

Results: The prevalence rate of self-reported ADHD symptoms using the ASRS screener was 23.7%. This was significantly associated with being in the age-group 17-20 years compared ($p<0.05$). The prevalence rate was higher among females (25.6%) than among males (21.8%), but this difference was not statistically significant. Preclinical students had a higher prevalence rate of ADHD symptoms (28.7%) compared to clinical students (19.6%), but this was also not statistically significant. Using a modification of the ASRS full symptom checklist to approximate a Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR) ADHD diagnosis yielded a 'possible ADHD' prevalence rate of 8.7%. Of these, the inattentive type was the most common (40.9%).

Conclusion: The prevalence rate of self-reported ADHD symptoms among medical students in Eldoret is very high and possibly interferes with the students' social and academic functioning. Further studies are suggested to generate information on the real ADHD prevalence in the general population and in special populations such as schools and colleges.

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Am J Drug Alcohol Abuse. 2012;38:93-100.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SUBTYPES IN ADOLESCENTS WITH COMORBID SUBSTANCE-USE DISORDER.

Tamm L, Adinoff B, Nakonezny PA, et al.

Background: Little is known about the relationship between attention-deficit/hyperactivity disorder (ADHD) subtypes and substance-use disorder (SUD). As there is literature suggesting different subtype phenotypes, there may be subtype differences in regard to the risk for developing SUD and substance treatment response.

Objectives: To characterize the sample in a Clinical Trials Network (CTN) study according to ADHD subtypes and baseline psychosocial and substance-use characteristics and to compare subtypes on response to treatment. Methods: Secondary analyses on data collected from adolescents (n = 276) diagnosed with ADHD and SUD (non-nicotine) and treated with stimulant medication or placebo and cognitive behavioral therapy (CBT) for substance use. Participants were characterized as inattentive or combined ADHD subtype and compared on baseline characteristics and treatment outcome.

Results: The combined subtype presented with more severe SUDs and higher rates of conduct disorder. There were a greater proportion of boys with inattentive subtype. The inattentive subtype appeared less ready for treatment (greater University of Rhode Island Change Assessment precontemplation scores) with poorer coping skills (poorer problem-solving and abstinence focused coping) at baseline. However, the two subtypes responded equally to treatment even after controlling for baseline differences.

Conclusions: Findings from this large community sample indicate that there were no subtype differences in treatment response, although there were differences in terms of substance use, antisocial behavior, readiness for treatment, and gender prior to treatment. Scientific Significance: This study is the first to report on subtype differences for treatment response for non-nicotine SUD in a comorbid ADHD-SUD population. Despite some baseline differences, both subtypes responded equally to treatment, suggesting limited relevance for subtype designation on treatment planning.

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Am J Epidemiol. 2011;173:S65.

PERSISTENCE OF ADHD SYMPTOMS FROM CHILDHOOD THROUGH ADOLESCENCE IN A COMMUNITY SAMPLE OF BOYS AND GIRLS.

Holbrook JR, McKeown RE, Cuffe SP, et al.

Attention-Deficit Hyperactivity Disorder (ADHD) is most common in childhood, but symptoms often persist into adolescence. This communitybased study examined ADHD symptom persistence and factors associated with elevated symptom counts. Elementary school children in a SC school district were screened with the teacher report Vanderbilt ADHD scale. High scorers and a random sample of remaining children were invited for interviews. Data were collected on ADHD symptom presence via the Diagnostic Interview Schedule for Children. We interviewed 481 parents at baseline (children aged 5-13 years) and invited them to three waves of follow-up, with 352 parents (73%) seen at least once over the next 3-6 years. Descriptive statistics and models were fit using SUDAAN to account for statistical weights and sampling design. A majority of baseline participants had at least one inattentive or hyperactive/impulsive symptom. Inattentive and hyperactive/impulsive symptom counts (greater-than or equal to) 6 (part of ADHD criteria) were present in 10.4% (95% CI: 8.3-13.1) and 24.4% (95% CI: 20.4-28.9) of the sample, respectively. In two waves of follow-up data, mean inattentive symptom count did not change ($t = 0.66$, $p = 0.51$), while mean hyperactive/impulsive symptom count decreased through developmental stages ($t = 4.73$, $p < 0.001$). Impairment domains showed a similar pattern. Adding the third wave of follow-up data will allow marginal models to identify the rate of symptom count decline and changes in impairment domains while adjusting for significant symptom predictors. ADHD symptoms, especially inattentive symptoms, persisted into adolescence. Understanding the rate and pattern of decline in different groups is important for understanding the natural course of ADHD and for treatment planning.

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Am J Epidemiol. 2011;173:S160.

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

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

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

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

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

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

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Am J Psychiatry. 2011;168:1164-70.

CHILDHOOD TRAJECTORIES OF INATTENTION AND HYPERACTIVITY AND PREDICTION OF EDUCATIONAL ATTAINMENT IN EARLY ADULTHOOD: A 16-YEAR LONGITUDINAL POPULATION-BASED STUDY.

Pingault JB, Tremblay RE, Vitaro F, et al.

Objective: Literature clearly documents the association between mental health problems, particularly attention deficit hyperactivity disorder (ADHD), and educational attainment. However, inattention and hyperactivity are generally not considered independently from each other in prospective studies. The aim of the present study was to differentiate the unique, additive, or interactive contributions of inattention and hyperactivity symptoms to educational attainment.

Method: The authors randomly selected 2,000 participants from a representative sample of Canadian children and estimated developmental trajectories of inattention and hyperactivity between the ages of 6 and 12 years using yearly assessments. High school graduation status, at age 22-23 years, was obtained from official records.

Results: Four trajectories of inattention and four trajectories of hyperactivity were observed between the ages of 6 and 12 years. After controlling for hyperactivity and other confounding variables, a high inattention trajectory (compared with low inattention) strongly predicted not having a high school diploma at 22-23 years of age (odds ratio=7.66, 95% confidence interval [CI]=5.06-11.58). To a lesser extent, a declining or rising trajectory of inattention also made a significant contribution (odds ratios of 2.67 [95% CI=1.90-3.75] and 3.87 [95% CI=2.75-5.45], respectively). Hyperactivity was not a significant predictor once inattention was taken into account.

Conclusions: Inattention rather than hyperactivity during elementary school significantly predicts long-term educational attainment. Children with attention problems, regardless of hyperactivity, need preventive intervention early in their development.

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Am J Psychiatry. 2011;168:1154-63.

GRAY MATTER VOLUME ABNORMALITIES IN ADHD: VOXEL-BASED META-ANALYSIS EXPLORING THE EFFECTS OF AGE AND STIMULANT MEDICATION.

Nakao T, Radua J, Rubia K, et al.

Objective: Structural neuroimaging studies in attention-deficit hyperactivity disorder (ADHD) have been relatively inconsistent and have mainly been conducted with pediatric samples. Furthermore, there is evidence that stimulant medication may have an effect on brain structure. The authors conducted a meta-analysis of voxel-based morphometry studies in children and adults with ADHD and examined the potential effects of age and stimulant medication on regional gray matter volumes.

Method: The PubMed, ScienceDirect, Web of Knowledge, and Scopus databases were searched for articles published between 2001 and 2011. Manual searches were also conducted, and authors of studies were contacted for additional data. Coordinates were extracted from clusters of significant gray matter difference between ADHD patients and healthy comparison subjects. Metaregression methods were used to explore potential age and stimulant medication effects.

Results: Fourteen data sets comprising 378 patients with ADHD and 344 healthy subjects met inclusion criteria. The ADHD group had global reductions in gray matter volumes, which were robustly localized in the right lentiform nucleus and extended to the caudate nucleus. Both increasing age and percentage of patients taking stimulant medication were found to be independently associated with more normal values in this region. Patients also had slightly greater gray matter volumes in the left posterior cingulate cortex.

Conclusions: These findings confirm that the most prominent and replicable structural abnormalities in ADHD are in the basal ganglia. They furthermore suggest that ADHD patients may progressively catch up with their developmental delay with advancing age and that use of stimulant medication may be associated with normalization of structural abnormalities in ADHD, although longitudinal studies are needed to confirm both observations.

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Am J Psychiatry. 2012;169:167-77.

BLOOD PRESSURE AND HEART RATE OVER 10 YEARS IN THE MULTIMODAL TREATMENT STUDY OF CHILDREN WITH ADHD.

Vitiello B, Elliott GR, Swanson JM, et al.

Objective: It is unknown whether prolonged childhood exposure to stimulant medication for the treatment of attention deficit hyperactivity disorder (ADHD) increases the risk for developing abnormalities in blood pressure or heart rate. The authors examined the association between stimulant medication and blood pressure and heart rate over 10 years.

Method: A total of 579 children, ages 7-9, were randomly assigned to 14 months of medication treatment, behavioral therapy, the combination of the two, or usual community treatment. The controlled trial was followed by naturalistic treatment with periodic assessments. Blood pressure and heart rate data were first analyzed with linear regression models based on an intent-to-treat approach, using raw data and the blood pressure categories of prehypertension and hypertension. Currently medicated patients were then compared with never or previously medicated patients. Associations between cumulative stimulant exposure and blood pressure or heart rate were assessed.

Results: No treatment effect on either systolic or diastolic blood pressure could be detected. Children who were treated with stimulants had a higher heart rate (mean=84.2 bpm [SD=12.4] on medication alone and mean=84.6 bpm [SD=12.2] on medication plus behavioral therapy) than those who were treated with behavioral therapy alone (mean=79.1 bpm [SD=12.0]) or those who received usual community treatment (mean=78.9 bpm [SD=12.9]) at the end of the 14-month controlled trial, but not thereafter. Stimulant medication did not increase the risk for tachycardia, but greater cumulative stimulant exposure was associated with a higher heart rate at years 3 and 8.

Conclusions: Stimulant treatment did not increase the risk for prehypertension or hypertension over the 10-year period of observation. However, stimulants had a persistent adrenergic effect on heart rate during treatment.

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Am J Psychiatry. 2012;169:160-66.

STIMULANT MEDICATION USE IN CHILDREN: A 12-YEAR PERSPECTIVE.

Zuvekas SH, Vitiello B.

Objective: The authors examined the utilization of stimulant medications for the treatment of ADHD in U.S. children during the period 1996-2008 to determine trends by age, sex, race/ethnicity, family income, and geographic region.

Method: The 1996-2008 database of the Medical Expenditure Panel Survey, a nationally representative annual survey of U.S. households, was analyzed for therapeutic stimulant use in children age 18 and younger. The data for 1987 were also recalculated for reference.

Results: An estimated 3.5% (95% confidence interval=3.0-4.1) of U.S. children received stimulant medication in 2008, up from 2.4% in 1996. Over the period 1996-2008, stimulant use increased consistently at an overall annual growth rate of 3.4%. Use increased in adolescents (annual growth, 6.5%), but it did not significantly change in 6- to 12-year-olds, and it decreased in preschoolers. Use remained higher in boys than in girls, and it remained consistently lower in the West than in other U.S. regions. While differences by family income have disappeared over time, use of stimulants in ADHD treatment is significantly lower in racial/ethnic minorities.

Conclusions: Overall, pediatric stimulant use has been slowly but steadily increasing since 1996, primarily as a result of greater use in adolescents. Use in pre-schoolers remains low and has declined over time. Important variations related to racial/ethnic background and geographic region persist, thus indicating a substantial heterogeneity in the approach to the treatment of ADHD in U.S. communities.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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ANAE Approche Neuropsychol Apprentiss Enfant. 2011;23:487-93.

SENSITIVITY AND SPECIFICITY OF CHILDHOOD EXECUTIVE FUNCTIONING INVENTORY (CHEXI) IN CHILDREN WITH ATTENTION DISORDERS.

Catale C, Lejeune C, Merbah S, et al.

Thorell and Nyberg (2008) have recently developed the Childhood Executive Functioning Inventory (CHEXI), a new rating inventory of executive functioning for children that can be divided into four a priori subscales: working memory, planning, inhibition, and regulation The major goals of our study is to present a French adaptation of this questionnaire and to discuss its clinical interests in terms of sensibility and specificity with children with attentional deficits.

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

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

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

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

Methods: A random clustered sample of elementary students was selected from schools in Tabriz, Iran. Students were screened by Conner's teacher rating scale for ADHD and a detailed history from parents and teachers for the presence of any type of tic was obtained. Next, a clinical interview based on the Kiddie Schedule for Affective Disorders and Schizophrenia-Present and Lifetime Version (K-SADS-PL), and an interview with parents lead to the definitive diagnosis.

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

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

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Arch Pediatr Adolesc Med. 2012;166:224-31.

DOCTOR-OFFICE COLLABORATIVE CARE FOR PEDIATRIC BEHAVIORAL PROBLEMS: A PRELIMINARY CLINICAL TRIAL.

Kolko DJ, Campo JV, Kilbourne AM, et al.

Objectives: To evaluate the feasibility and clinical benefits of an integrated mental health intervention (doctoroffice collaborative care [DOCC]) vs enhanced usual care (EUC) for children with behavioral problems.

Design: Cases were assigned to DOCC and EUC using a 2:1 randomization schedule that resulted in 55 DOCC and 23 EUC cases.

Setting: Preassessment was conducted in 4 pediatric primary care practices. Postassessment was conducted in the pediatric or research office. Doctor-office collaborative care was provided in the practice; EUC was initiated in the office but involved a facilitated referral to a local mental health specialist.

Participants: Of 125 referrals (age range, 5-12 years), 78 children participated.

Interventions: Children and their parents were assigned to receive DOCC or EUC.

Main Outcome Measures: Preassessment diagnostic status was evaluated using the Schedule for Affective Disorders and Schizophrenia for School-aged Children. Preassessment and 6-month postassessment ratings of behavioral and emotional problems were collected from parents using the Vanderbilt Attention-Deficit/Hyperactivity Disorder Diagnostic Parent Rating Scale, as well as individualized goal achievement ratings forms. At discharge, care managers and a diagnostic evaluator completed the Clinical Global Impression Scale, and pediatricians and parents completed satisfaction and study feedback measures.

Results: Group comparisons found significant improvements for DOCC over EUC in service use and completion, behavioral and emotional problems, individualized behavioral goals, and overall clinical response. Pediatricians and parents were highly satisfied with DOCC.
Conclusion: The feasibility and clinical benefits of DOCC for behavioral problems support the integration of collaborative mental health services for common mental disorders in primary care.

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Arq Neuro-Psiquiatr. 2012;70:180-84.

LOW QUALITY OF LIFE SCORES IN SCHOOL CHILDREN WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER RELATED TO ANXIETY.

Zambrano-Sanchez E, Martinez-Cortes JA, del Rio-Carlos Y, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is an alteration that begins early in infancy and whose cardinal symptoms are inattention, hyperactivity and impulsivity. There are few studies for specific tests to measure Quality of Life (QoL) in children with ADHD.
Methods: We evaluated QoL of 120 children from 7-12 years of age with ADHD and of a group of 98 healthy control children. To measure QoL, we utilized the Questionnaire of Quality of Life for Children in Pictures (AutoQuestionnaire Qualite de Vie Enfant Image, AUQUEI). We evaluated anxiety in children by the Childrens Manifest Anxiety Scale-Revisited (CMAS-R). We compared results among groups and employed the calculation of correlation between the AUQUEI questionnaire and the CMAS-R scale.
Results: The total average of the AUQUEI questionnaire in children with ADHD was 45.2, while in the control group it was 54.3 ($p<0.05$). We also observed significant differences between the control group and groups of children with ADHD in the CMAS-R scale. We found significant correlations between AUQUEI questionnaire and CMAS-R scale.
Conclusion: The main result was to the disclosure that low QoL scores in ADHD children was anxiety-related.

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Bahrain Med Bull. 2012;34:1-6.

THE IMPACT OF MULTIMODAL PSYCHOSOCIAL INTERVENTION AMONG CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

al Ansari A, Asiri MM.

Objective: Evaluation of the effectiveness of psychosocial intervention in comparison to outpatient management.
Setting: Child and Adolescent Psychiatric Unit, Psychiatric Hospital, Ministry of Health, Bahrain. Design: Retrospective/cross sectional study.
Method: Group 1 (ROM) consist of twenty children from outpatient and group 2 (MPI) consist of 15 children from day-care, aged 4-16 years, diagnosed with DSM IV ADHD were recruited for the study after four weeks of treatment from 2006-2009.
Result: Twelve (80%) children from daycare group were from non-intact family (P>.036). Fourteen mothers (70%) from ROM and 9 mothers (60%) from MPI reported marked improvement in both groups. Blind investigator and therapist/nurse found more improvement among those received more intense psychosocial intervention, group 2 (MPI) (P>.018).
Conclusion: Group 2 (MPI) had more psychopathology compared to Group 1 (ROM). The staff and blind investigator reported better improvement among children in Group 2 (MPI). Difficult ADHD cases benefit more from intense psychosocial intervention in Group 2 (MPI).

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Biol Psychol. 2012;89:606-08.

CAFFEINE EFFECTS ON RESTING-STATE ELECTRODERMAL LEVELS IN AD/HD SUGGEST AN ANOMALOUS AROUSAL MECHANISM.

Barry RJ, Clarke AR, McCarthy R, et al.

The effect of a single oral dose of caffeine was examined in a randomised double-blind placebo-controlled repeated-measures cross-over study. Eighteen children with AD/HD, aged between 8 and 13 years, were individually age- and gender-matched with a control group. All children participated in two sessions, one week apart. Skin conductance level (SCL) from a 3. min eyes-closed epoch, commencing 30. min after ingestion of caffeine or placebo, was examined. Across conditions, mean SCL was lower in the AD/HD group than controls, confirming hypoarousal in AD/HD. Caffeine produced an increase in SCL, and this increase did not differ between the groups. However, arousal increases were dose-dependent in controls, but not in AD/HD. Rather, caffeine-induced arousal increases in the AD/HD group were positively related to their hyperactivity/impulsivity levels. This suggests an anomalous arousal mechanism in AD/HD functionally related to impairment in one symptom dimension.

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Bipolar Disord. 2012;14:52.

ATTENTION DEFICIT/HYPERACTIVITY DISORDER COMORBID WITH BIPOLAR DISORDER DOES NOT ENHANCE COGNITIVE IMPAIRMENT.

Akkaya C, Gunduz C, Cangur S, et al.

Introduction: Bipolar disorder (BD) is a chronic, severe, and highly disabling psychiatric disorder. Cognitive impairment is frequently observed among individuals with BD during acute and euthymic phases of the disorder. Attention deficit/hyperactivity disorder (ADHD) is one of the most common childhood psychiatric disorder. About 50% of the affected children, the disorder continues to adulthood, which corresponds to a 4-5% prevalence rate for adult ADHD in the community and 9-35% in the BD patients. The aim of this study is to determine the frequency of adult ADHD comorbidity with lifetime BD, and the influence of this comorbidity on cognitive impairment.

Methods: Between 18 and 65 years old patients who are regularly followed up at Uludag University Psychiatry Department, Mood Disorder Unit and had already received a diagnosis of BD according to DSM-IV criterions were recruited. Inclusion criteria requires remission for at least 1 month at the time of enrollment to the study, as corroborated with the Young Mania Rating Scale ((greater-than or equal to)8) and Hamilton Depression Scale ((greater-than or equal to)7) scores. All patients were also assessed for the presence of ADHD according to DSM-IV criterions, and also completed the Turkish version of the Wender Utah Rating Scale-25 (WURS) and adult attention-deficit/ hyperactivity disorder self report scale (ASRS) for confirmation of the diagnosis. Wisconsin Card Sorting Test (WCST), Stroop Test and Trail Making Test were applied to all patients by a specialist psychologist to establish cognitive impairment.

Results: Sixty nine consecutive bipolar patients (39 female, 22 male) were evaluated. Of the 69, 8 (%11.6) patients had comorbid adult ADHD. There is no significant difference in WCST, Stroop Test and Trail Making Test between BD and BD comorbid adult ADHD groups.

Conclusions: This study concluded that adult ADHD comorbid with BD has no unfavorable effects on cognitive impairment, but the data presented here has to be verified with further studies with increased number of cases.

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Bipolar Disord. 2012;14:53.

ADULT ATTENTION DEFICIENCY-HYPERACTIVITY DISORDER WITH BIPOLAR DISORDER: THE GOOD CLINICAL OUTCOMES OF A CASE WITH STIMULANT TREATMENT.

Aksoy Coban A, Eraslan'zt'rk D.

Introduction: It is still being a discussion that stimulant treatments are not safe for childs, adolescents and adults with Attention Deficiency-Hyperactivity Disorder (ADHD) because they cause sensitivity for risk of a substance abuse, especially cocaine, but many of the results of studies suggested that there is no causal relationship between stimulant treatment and further substance abuse.

Case Presentation: 24 years old, single, male patient. He has attended with substance abuse problems. He has been taking methamphetamine as 'ecstasy' every day and in huge doses. He had started to abuse substances at age of 15. He had many depressive and hypomanic episodes from early adolescence and sometimes these were rapid cycling, especially in early adolescence. He had a severe ADHD story in his childhood and still has adult ADHD. After detoxification, he had put on mood stabilizers, antipsychotic treatment, than methylphenidate treatment started at a dosage of 10 mg/day. He reported that he started to 'live' because he could catch the time, could organize his daily living, could talk to his family without any argument, and could do all these without taking any substance. His mood regulation has been better than ever with these treatments.
Discussion: Substance abuse may be the consequence of inattentiveness or impulsiveness in adult ADHD, but substance abuse alone may contribute to depression or hypomania/mania. We know that the lifetime prevalence of ADHD in Bipolar Disorder is approximately 20% which means that patients with ADHD with a substance abuse are under a very high risk of developing an affective dysregulation. Many of the studies suggested on using stimulants in ADHD to prevent substance abuse which would also contribute the prevention of affective dysregulation, very closely related with ADHD. In our case, mood regulation has been better after stimulant treatment contrary to worried expectations. He didn't abuse anything till today after treatment.

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Bipolar Disord. 2012;14:58.

THE FREQUENCY OF ADULT ATTENTION-DEFICIT HYPERACTIVITY AND BIPOLAR DISORDERS IN PARENTS OF ADHD CHILDREN.

Kolat U, Bakim B, Sertcelik S, et al.

Background: ADHD is one of the most common mental disorders of childhood and adolescence, and characterized by inattention, hyperactivity, and impulsivity symptomatology. In addition to increased rates of ADHD and bipolar disorder in the offspring of parents and siblings of children with ADHD, family studies resulted in a high risk for ADHD and bipolar disorder in the offspring of parents with ADHD.
Methods: 132 parents (67 mother and 65 father) of 90 ADHD children; aged between 6 and 12, and 67 parents (34 mother and 33 father) of 45 non-ADHD children; aged between 6 and 12, were recruited in the study. Control parents were matched to ADHD children parents according to age, gender and educational status. Wender Utah Rating Scale and Turgay's Adult ADD/ADHD DSM-IV Based Diagnostic and Rating Scale were administered to the participants. SCID-I/CV (Structured Clinical Interview for DSM-IV Axis I Disorder, Clinical Version) was used to evaluate the psychopathology in probands' and controls' parents.
Results: Rate of childhood ADHD were significantly higher among parents ofADHDchildren compared to the parents of control group (p = 0.039). Rate of adultADHD(p = 0.076) and bipolar disorder (p = 0.277) were not significantly higher among parents of ADHD children compared to the parents of control group. Rate of bipolar disorder were significantly higher among fathers of ADHD children compared to the mothers of ADHD children group (p = 0.032). Rate of repeating the year in school (p = 0.025) and entering in trouble with the police (p = 0.046) and having any mood disorder (p = 0.014) were significantly higher among parents of ADHD children compared to the control group.
Conclusion: This is a study that evaluates the prevalence of adult ADHD and bipolar disorder in the parents of children with ADHD. Under the highlight of our findings, assessing adult ADHD and bipolar disorder in patients with having a child with ADHD is important for treatment and prognosis.

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Bipolar Disord. 2012;14:48.

BRAIN-DERIVED NEUROTROPHIC FACTOR IN JUVENILE BIPOLAR DISORDER AND ATTENTION-DEFICIT HYPERACTIVITY DISORDER: DIFFERENTIATION USING BDNF SERUM LEVELS, AND VAL66MET POLYMORPHISM.

Zeni CP, Tramontina S, Aguiar BW, et al.

Background: Frontiers between Juvenile Bipolar Disorder (JBD) and Attention-Deficit/Hyperactivity Disorder (ADHD) are not well defined. Few studies have addressed potentially different neurobiological factors between the two disorders. Brain-Derived Neurotrophic Factor (BDNF) has been increasingly recognized for its etiologic and prognostic role in adult BD studies. We assessed transmission of the

Val66Met polymorphism at BDNF gene and BDNF serum levels in children and adolescents with BD comorbid with ADHD (BD+ADHD), ADHD alone, and healthy subjects.
Methods: Children and adolescents were extensively assessed for psychiatric diagnoses by K-SADS-PL and clinical evaluation. The val66met polymorphism at BDNF was genotyped, and BDNF protein serum levels were measured in drug-free patients.
Results: No preferential transmission of the Val allele was observed in BD (n = 66; Z = 0.52 p = 0.60) or ADHD (n = 144; Z = 0.12 p = 0.91). In the ANCOVA, we detected a significant group effect (patients with BD+ADHD had higher serum levels than those with ADHD - F80,7 = 4.09, p = 0.03), after adjusting for severity (CGI-S) scores. We did not observe significant effects of the Val66Met polymorphism and any significant difference between both ADHD/BD groups and healthy controls on BDNF serum levels.
Discussion and Conclusion: Although BDNF gene does not seem to play a significant role in differentiating children and adolescents with ADHD + BD from those with ADHD, BDNF serum levels deserve further attention in future research on neurobiological aspects of BD and ADHD.

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BMC Psychiatry. 2012;21.

PSYCHOMETRIC ANALYSIS OF THE NEW ADHD DSM-V DERIVED SYMPTOMS.

Ghanizadeh A.

Background: Following the agreements on the reformulating and revising of ADHD diagnostic criteria, recently, the proposed revision for ADHD added 4 new symptoms to the hyperactivity and Impulsivity aspect in DSM-V. This study investigates the psychometric properties of the proposed ADHD diagnostic criteria.
METHOD: ADHD diagnosis was made according to DSM-IV. The parents completed the screening test of ADHD checklist of Child Symptom Inventory-4 and the 4 items describing the new proposed symptoms in DSM-V.
Results: The confirmatory factor analysis of the ADHD DSM-V derived items supports the loading of two factors including inattentiveness and hyperactivity/impulsivity. There is a sufficient reliability for the items. However, confirmatory factor analysis showed that the three-factor model is better fitted than the two-factor one. Moreover, the results of the exploratory analysis raised some concerns about the factor loading of the four new items.
Conclusions: The current results support the two-factor model of the DSM-V ADHD diagnostic criteria including inattentiveness and hyperactivity/impulsivity. However, the four new items can be considered as a third factor.

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Brain Dev. 2012.

EEG CHARACTERISTICS AND VISUAL COGNITIVE FUNCTION OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Shi T, Li X, Song J, et al.

Using visual and auditory continuous performance tests (CPT) and EEG, cognitive function and EEG power were investigated in patients with attention deficit hyperactivity disorder (ADHD). CPT and EEG were conducted for 44 ADHD children and 44 healthy controls of comparable age and sex. The EEG power tests include relative power of theta, alpha, and beta, and theta/beta and theta/alpha ratios. ADHD patients showed significantly higher theta relative power, lower beta relative power, and higher theta/beta ratio ($p < 0.05$). ADHD patients showed a significantly lower score of auditory CPT ($p < 0.05$). The EEG power characteristics were correlated significantly with the visual attention function in ADHD children ($p < 0.01$). Higher-order level cognitive dysfunction affects ADHD pathogenesis. Cortical hypoarousal effects on several mechanisms including the fronto-striatal circuitry may be implicated in the inhibition of prepotent and premature responses.

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Brain Res. 2012.

BRAIN ACTIVATION TO CUES PREDICTING INESCAPABLE DELAY IN ADOLESCENT ATTENTION DEFICIT/HYPERACTIVITY DISORDER: AN FMRI PILOT STUDY.

Lemiere J, Danckaerts M, Van Hecke W, et al.

Background: The choice of small immediate over large delayed rewards (i.e., impulsive choice) is a signal marker of motivational style in Attention Deficit/Hyperactivity Disorder (ADHD). The delay aversion model proposes that, in part, this is a conditioned delay avoidance response. Here we test the prediction derived from this model that, in ADHD, cues predicting inescapable delay differentially activate brain regions shown previously to be responsive to motivationally salient, negatively valenced environmental events.

Methods: Ten adolescents with ADHD and 10 age matched controls performed a simple speeded reaction time task under two conditions. On Escape Delay trials slow responses only were punished by the imposition of post-response delay periods. On No Escape Delay trials post-response delay occurred on all trials irrespective of response speed. Using functional Magnetic Resonance Imaging (fMRI) BOLD responses were acquired to compare anticipatory brain activation following the two cue types. ROI analyses found significant ADHD-related hyperactivation following No Escape compared to Escape Delay trial cues in the insula, amygdala, ventral striatum and orbito-frontal cortex.

Conclusion: The results of this pilot study provide further evidence for the role of altered motivational systems in ADHD and the most direct evidence for a biological basis of delay aversion.

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Cardiol Young. 2012;22:158-61.

EFFECTS OF ATOMOXETINE ON CARDIOVASCULAR FUNCTIONS AND ON QT DISPERSION IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Sert A, Gokcen C, Aypar E, et al.

Background: Atomoxetine is a central norepinephrine reuptake inhibitor used to treat attention deficit/hyperactivity disorder. The effects of atomoxetine on cardiovascular functions and QT dispersion in children with attention deficit/hyperactivity disorder have not been previously reported. The aim of this study was to analyse cardiovascular functions and QT dispersion on the surface electrocardiogram of children with attention deficit/hyperactivity disorder during atomoxetine therapy.

Methods: A total of 40 children - with a mean age of 8.6 plus or minus 2.3 years and a median age of 11 years; ranged from 8 to 14 years - with attention deficit/hyperactivity disorder - with six girls and 34 boys - were included in the study. We recorded the mean systolic and diastolic blood pressure, heart rate, corrected QT interval, QT dispersion, and left ventricular systolic functions at baseline and 5 weeks after atomoxetine therapy.

Results: Atomoxetine decreased baseline mean systolic and diastolic blood pressure; baseline mean heart rate decreased; and baseline mean corrected QT interval and QT dispersion mildly increased. Atomoxetine decreased baseline mean ejection fraction and baseline mean shortening fraction.

Conclusion: The results of our study suggest that atomoxetine does not cause clinically significant alterations in QT dispersion, systolic and diastolic blood pressure, heart rate, corrected QT interval, and left ventricular systolic functions during short-term treatment in children with attention deficit/hyperactivity disorder.

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Child Adolesc Ment Health. 2012.

TEACHERS' RECOGNITION OF CHILDREN WITH ADHD: ROLE OF SUBTYPE AND GENDER.

Moldavsky M, Groenewald C, Owen V, et al.

Background: This study investigates the ability of primary school teachers to recognise Attention Deficit/Hyperactivity Disorder (ADHD), and the impact of subtype and child gender on recognition and proposed management.

Method: Primary school teachers read one of four types of vignette describing the behaviour of a 9-year-old child: either a boy or a girl with inattentive or combined subtype of ADHD. Teachers were asked about their conceptualisation of the child's difficulties and their thoughts about need for specialist referral and other interventions.

Results: Of 496 teachers, 99% identified the presence of a problem. Subtype (combined) of ADHD influenced teachers' recognition of ADHD and agreement that medication might be helpful. Only 13% of teachers thought that medication might be helpful.
Conclusions: Results suggest a need for better teacher awareness about inattentive subtype of ADHD.

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Child Adolesc Psychiatr Clin North Am. 2012;21:145-59.
STRATEGIES FOR IMPLEMENTING EVIDENCE-BASED PSYCHOSOCIAL INTERVENTIONS FOR CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Eiraldi RB, Mautone JA, Power TJ.

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Chin J Contemp Pediatr. 2012;14:89-92.
CO-MORBIDITY OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH EPILEPSY.
Han Y, Qin J, Jiang YW, et al.
Objective: To estimate the prevalence of attention deficit hyperactivity disorder (ADHD) in children with epilepsy, and the factors that may contribute to the prevanlence of co-morbidity between ADHD and epilepsy.
Methods: A total of 256 children aged 6-15 years old who were diagnosed with epilepsy were enrolled. The prevalence of ADHD in children with epilepsy, and the factors that may contribute to the development of co-morbidity between ADHD and epilepsy were explored.
Results: The systematic evaluation in 192 patients was completed. Of the 192 children, 81 (42.2%) were diagnosed with ADHD. The earlier the epilepsy onset, the higher the frequency of the co-morbidity of ADHD occurring. The longer the period of antiepileptic medication, the higher the prevalence of the co-morbidity of ADHD. Epileptic children receiving a combination of antiepileptic drugs had a higher prevalence of ADHD. ADHD was more common in children with some specific types of epilepsy, such as Lannox-Gastaut syndrome and generalized tonic-clonic epilepsy, or epilepsy with multifocal epileptic discharges in the EEG record.
Conclusions: ADHD occurs frequently in children with epilepsy. The factors associated with increased risk of ADHD include the onset age of epilepsy, the types of seizures or epileptic syndromes, the epileptiform EEG discharges, and the effects of antiepileptic drugs.

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Cogn Emot. 2012;26:176-85.
EARLY INFORMATION PROCESSING BIASES IN SOCIAL ANXIETY.
Miskovic V, Schmidt LA.
Considerable controversy persists regarding the nature of threat-related attention biases in social anxiety. Previous studies have not considered how variations in the temporal and energetic dimensions of affective stimulus delivery interact with anxiety-related individual differences to predict biased attention. We administered a visual dot-probe task, using faces that varied in affective intensity (mild, moderate, strong) and presentation rate (100, 500, 1,250 ms) to a selected sample. The high, compared to the low, socially anxious group showed vigilance towards angry faces and emotionally ambiguous faces more generally during rapid (100 ms) presentations. By 1,250 ms, there was only a non-specific motor slowing associated with angry faces in the high socially anxious group. Findings suggest the importance of considering both chronometric and energetic dimensions of affective stimuli when examining anxiety-related attention biases. Future studies should consider using designs that more closely replicate aspects of real-world interaction to study processing biases in socially anxious populations.

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

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

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

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

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European Child & Adolescent Psychiatry. 2012 Jan;21:39-49.

EXAMINING THE RELATIONSHIP BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND OVERWEIGHT IN CHILDREN AND ADOLESCENTS.

Erhart M, Herpertz-Dahlmann B, Wille N, et al.

Although a higher prevalence of overweight/obesity was reported in clinical samples of patients with Attention-Deficit/Hyperactivity Disorder (ADHD), an association between overweight and ADHD has yet not been established in the general population in childhood. As both disorders are common and significantly affect psychosocial functioning, we investigated the prevalence of ADHD in overweight/obese youth and vice versa. In a cross-sectional nationally representative and community based survey 2,863 parents and their children aged 11–17 years rated symptoms on the Diagnostic and Statistical Manual of Mental Disorders-based German ADHD Rating scale. Weight and height were assessed by professionals. Body mass index was categorized according to national age and sex specific reference values. Overall, 4.2% of the respondents met criteria for ADHD. The prevalence of ADHD was significantly higher for overweight/obese (7%) than for normal weight (3.5%) and underweight (4.9%) children. In a logistic regression analysis controlling for age, gender, and socio-economic status, overweight/obese children were twice as likely to have an ADHD diagnosis (OR = 2.0). Vice versa, adjusting for all covariates, children with ADHD had an OR of 1.9 for overweight/obesity status. For all weight-status groups, children with ADHD more frequently reported eating problems as compared to their non-clinical counterparts. Overweight/obese respondents with ADHD displayed the highest level of health services utilization. A clinician should be aware of the significant risk for a child with ADHD to become overweight and for an overweight child to have ADHD. Longitudinal studies are needed to better understand the mechanisms underlying the association between ADHD and overweight/obesity.

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Eur Child Adolesc Psychiatry. 2012;1-8.

EFFICACY AND SAFETY OF ARIPIPRAZOLE IN CHILD AND ADOLESCENT PATIENTS.

Kirino E.

Aripiprazole (APZ) has a unique pharmacological profile, as a partial agonist at the dopamine D2 and serotonin 5HT1A receptors and an antagonist at the serotonin 5HT2A receptor; this drug has few side effects (such as extrapyramidal syndrome, hyperprolactinemia, weight gain, metabolic disorders, and sedation) which are typical problems with other antipsychotic drugs. Due to its high tolerability, it is possible

to safely administer it to children and adolescents. Efficacy and tolerability of APZ in children and adolescents have been well demonstrated in many clinical studies, which supported approvals granted by the US Food and Drug Administration (FDA) for schizophrenia, bipolar diseases, and irritability associated with autistic disorder in children and adolescents. APZ is expected to exert sedative, anti-depressive, and anti-anxiety effects, and stabilize emotion. APZ is an antipsychotic drug which could be useful for a wider spectrum of psychiatric disorders in children and adolescents. There is little risk of deterioration (such as disinhibition and acting out) and rapid stabilization is easy to achieve in children and adolescents without definitive diagnoses or with a combination of more than one spectrum of disorders. The effectiveness of APZ in children and adolescents is reviewed and discussed, given its pharmacological profile and the outcomes of various clinical studies. However, randomized or blind studies are still limited, and the majority of reports referenced here are open-label studies and case reports. Conclusions drawn from such studies must be evaluated with caution, and a further accumulation of controlled studies is thus needed.

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Eur J Paediatr Neurol. 2012.

THE RCBF BRAIN MAPPING IN ADOLESCENT ADHD COMROBID DEVELOPMENTAL COORDINATION DISORDER AND ITS CHANGES AFTER MPH CHALLENGING.

Yeh CB, Huang WS, Lo MC, et al.

Background: Cormobid developmental coordination disorder (DCD) in the patients with attention-deficit hyperactivity disorder (ADHD) often complicated the treatment strategy. Methylphenidate (MPH) improves the coordination problem in patients with ADHD.

Aim: The study intended to investigate the pathophysiology and the mechanisms of MPH in comorbid DCD of the adolescents with ADHD.

Methods: Brain images using technetium-99m ethyl cysteinate dimmer (99mTc-ECD) single photon emission computed tomography (SPECT) were done in 10 drug-naive adolescents with ADHD without DCD and 5 adolescents with ADHD comorbid DCD. The baseline rCBF and changes of rCBF after 10 mg MPH challenge between two groups were compared using statistical parametric mapping (SPM99) analysis.

Results: Lower rCBF of bilateral frontal lobe, inferior parental lobe, and increased rCBF of right posterior cingulate gyrus, anterior lobe of cerebellum were found in ADHD comorbid DCD group compared to ADHD without DCD group. Decreased rCBF in the right occipital, inferior temporal lobe was found in ADHD comorbid DCD group after MPH while ADHD alone group revealed increased rCBF in bilateral occipital lobe.

Conclusions: The results help us understand the pathophysiology of DCD in ADHD adolescents. The different rCBF response to MPH provides a clue for future intervention of DCD in ADHD adolescents.

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Headache. 2012;52:374-84.

ATTENTION IN CHILDREN AND ADOLESCENTS WITH HEADACHE.

Riva D, Usilla A, Aggio F, et al.

Objective. The previous studies reporting consistent visual reaction times slowing in patients with migraine prompted us to verify if headache could be associated to a broader impairment of attention. This study aims to undertake a thorough investigation of attentional performance by extending the evaluation to children with primary headache of different types.

Methods. We compared 62 children with headache (14 migraineurs with aura, 29 without aura and 19 with tension type headache) and 52 controls without headache, matched for age, sex, and intelligence using Conners' Continuous Performance Test.

Results. The 3 clinical groups did not differ in attentional measures. The headache patients, collapsed in 1 single sample, had mean scores in Hit Reaction Time significantly different from those of controls and also had a higher percentage of atypical scores in 2 indices of the Conners' Continuous Performance Test (faster mean reaction time and more commissions).

Conclusions. Our results confirm the presence of an association between attentional problems and headache that may impact academic learning and daily activities on the long term. The finding that the 3

clinical groups did not show significant differences in attentional performance supports the hypothesis that migraine and tension headache form a continuum that may share the same pathophysiological mechanisms. These results are discussed considering that neurotransmitters and the cerebral circuits subserving headache, personality profile, and attention could overlap, thus predisposing these children to even mild attention malfunctioning.

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Int J Behav Dev. 2012;36:157-66.

GENDER DIFFERENCES IN CONSEQUENCES OF ADHD SYMPTOMS IN A COMMUNITY-BASED ORGANIZATION FOR YOUTH.

Vitulano ML, Fite PJ, Wimsatt AR, et al.

Attention-Deficit/Hyperactivity Disorder (ADHD) has been linked to disruptive behavior and disciplinary consequences; however, the variables involved in this process are largely unknown. The current study examined rule-breaking behavior as a mediator of the relation between ADHD symptoms and disciplinary actions 1 year later during after-school care at a community-based organization in a sample of 147 school-age children (M = 8.22 years; 54.4% male). Additionally, gender was examined as a moderator of these relations. Total ADHD symptoms positively predicted rule-breaking behavior at 1-year follow-up, which in turn was positively associated with disciplinary actions also at 1-year follow-up. Gender moderated these relations, such that the mediated effect of rule-breaking behavior on the association between total ADHD symptoms and disciplinary actions was significant for boys but not for girls. Further, when ADHD symptom dimensions were simultaneously included in the model, only hyperactive/impulsive symptoms were a positive predictor of rule-breaking behavior, and rule-breaking behavior mediated this link between hyperactive/impulsive symptoms and disciplinary actions. However, when examining ADHD symptom dimensions, no gender differences emerged. Implications for findings and future directions are discussed.

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Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2012 Feb;40:177-88.

SYMPTOMS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND SOCIAL AND SCHOOL ADJUSTMENT: THE MODERATING ROLES OF AGE AND PARENTING.

Kawabata Y, Tseng WL, Gau SS-F.

This study examined the associations between symptoms of attention-deficit/hyperactivity disorder (ADHD) and social and school adjustment (academic performance, peer relationships, school social problems) and the moderating roles of children's age and maternal parenting (affection and overprotection) in these associations. The sample consisted of 2,463 students who were in the first to ninth grade in northern Taiwan. Results from the linear mixed models demonstrated that ADHD symptoms were inversely associated with academic performance and positively associated with social adjustment problems. Further, children's age and maternal parenting moderated the associations between ADHD symptoms and school and social adjustment. For example, maternal overprotection moderated the relation between hyperactivity and negative peer relationships (i.e., difficulty forming and maintaining friendships), such that this relation was stronger for children who experienced higher levels of overprotection than children who did not. Moreover, children's age moderated the association between attention problems and decreased academic performance, such that this association was stronger for older children and adolescents than for younger children. Furthermore, children's age and maternal affection interacted to influence the association between attention problems and school social problems (i.e., bullying, aggression, and peer rejection) with maternal affection acting as a buffer for older children (grades 4–6) only. These findings are discussed from a developmental psychopathology perspective.

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Journal of Abnormal Child Psychology: An official publication of the International Society for Research in Child and Adolescent Psychopathology. 2012 Feb;40:165-75.

ASSOCIATION OF POSITIVE AND NEGATIVE PARENTING BEHAVIOR WITH CHILDHOOD ADHD: INTERACTIONS WITH OFFSPRING MONOAMINE OXIDASE A (MAO-A) GENOTYPE.

Li JJ, Lee SS.

Relatively little is known about the potential interplay between genetic and environmental influences on attention-deficit/hyperactivity disorder (ADHD), including gene-environment interaction (G×E). There is evidence that parenting behavior interacts with offspring genotype in the development of externalizing problems, but studies have largely focused on explicit maltreatment rather than differentiated measures of parenting behavior, including positive and negative parenting. We tested the interactive effects of the 30-base pair variable number tandem repeat (VNTR) polymorphism of the monoamine oxidase A gene (MAO-A) with positive and negative parenting behavior on parent- and teacher ratings of inattention and hyperactivity symptoms among 150 6–9 year-old boys with and without ADHD. Negative parenting predicted parent and teacher ratings of inattention symptoms, but only among boys with high-activity MAO-A genotype. MAO-A genotype did not moderate the association of positive parenting and parent- and teacher ratings of ADHD. We discuss the potential role of interactive exchanges between parenting behavior and child genotype in the development and persistence of ADHD and related behavior problems.

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J Adolesc Health. 2012.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SUBTYPE DIFFERENTIALLY PREDICTS SMOKING EXPECTANCIES IN ADOLESCENTS.

Foster I, Racicot S, McGrath JJ.

Purpose: Attention deficit hyperactivity disorder (ADHD) is an established risk factor for smoking; however, no studies have considered whether precursors to smoking behavior differ among adolescents with ADHD. Smoking expectancies are beliefs about the potential consequences of smoking, and they develop before smoking initiation. ADHD characteristics may contribute to the formation of expectancies and eventual smoking behavior. We evaluated whether clinical levels of ADHD subtypes differentially predicted smoking expectancies.

Methods: Adolescents (n = 221; age mean = 12.67 years) completed the Smoking Expectancy Scale for Adolescents, answered standardized questions about their smoking behavior, and provided expired breath samples to verify never-smoking status. Parents completed the Conners' Parent Rating Scale for ADHD symptoms of inattention and hyperactivity/impulsivity.

Results: Adolescents with clinical levels of inattention were significantly less likely to endorse negative consequences, including Expected Costs (odds ratio [OR] = .16), Appearance-Presentation Costs (OR = .29), Social Costs (OR = .19), Health Costs (OR = .21), and Addiction Costs (OR = .39). Inattentive female adolescents were significantly more likely to endorse Weight Control as a consequence. Adolescents with clinical levels of hyperactivity/impulsivity were more likely to endorse positive consequences, including Expected Benefits (OR = 5.31), Affect Control (OR = 2.60), and Boredom Reduction (OR = 3.14); they were less likely to endorse Social Costs (OR = .27).

Conclusions: ADHD subtype differentially predicted smoking expectancies. Adolescents with ADHD may be more vulnerable to developing pro-smoking expectancies due to subtype-related deficits in neurocognitive processing. These findings have potential implications for developing targeted smoking prevention programs.

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J Affective Disord. 2012;138:479-84.

DIFFERENTIAL EXPRESSION OF PROSTAGLANDIN D2 SYNTHASE (PTGDS) IN PATIENTS WITH ATTENTION DEFICIT-HYPERACTIVITY DISORDER AND BIPOLAR DISORDER.

Marin-Mendez JJ, Patino-Garcia A, Segura V, et al.

Background: As marker genes for bipolar disorder (BP) and attention deficit hyperactivity disorder (ADHD) are not fully identified, we carried out a complete genome analysis to search for genes differentially expressed in ADHD and BP.

Materials and methods: We recruited 39 patients (30 ADHD, 9 BP), aged 7 to 23 years. For evaluation of the psychiatric diagnosis, we used a semi-structured interview based on the K-SADS-PL (DSM-IV). RNA was extracted from peripheral blood and analyzed with the GeneChip (registered trademark) Human Genome U133-Plus 2.0 (Affymetrix). For the validation of differentially expressed genes, real-time PCR was used.
Results: Hybridization and subsequent statistical analysis found 502 probe-sets with significant differences in expression in ADHD and BP patients. Of these, 82 had highly significant differences. Neuregulin (NRG1), cathepsins B and D (CTSB, CTSD) and prostaglandin-D2-synthase (PTGDS) were chosen for semi-quantitative mRNA determination. The expression of PTGDS was statistically increased in ADHD relative to BP patients ($p = 0.01$). We found no such differential expression with NRG1, CTSB and CTSD genes ($p > 0.05$).
Conclusions: The gene coding for PTGDS was found to be more expressed in patients with ADHD relative to patients with BP, indicating a possible link with the differential etiology of ADHD. The experimental approach we have used is, at least in part, validated by the detection of proteins directly concerned with brain functions, and shows a possible way forward for studies of the connection between brain function genes and psychiatric disorders. Limitations: Confirmation of our findings requires a larger sample of patients with clearly-defined phenotypes.

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J Child Neurol. 2012;27:383-88.

A TRIANGULAR MODEL FOR DIAGNOSIS AND MANAGEMENT OF PRESCHOOL ADHD: SYMPTOM OR SYNDROME?

Zuckerman J, Diamond G, Shuper A.

Attention deficit/hyperactivity disorder (ADHD) is a common, well-defined, developmental disorder with a recognized genetic-neurologic basis. Studies report pathogenic involvement of the dopaminergic and serotonergic pathways. Its presentation in the preschool years is variable and can be mistaken for other common behavioral and developmental problems. The aim of this work is to propose an interactive "triangular model" based on the temperamental-genetic, emotional-behavioral, and developmental-genetic pathways of ADHD to explain the evolution of the clinical picture and serve as a guide to appropriate management, particularly in the preschool years. The model can also be used in parental counseling. This article describes 3 illustrative cases of preschool children with hyperactive and inattentive behaviors who were diagnosed with ADHD by standardized developmental and psychological batteries and followed at 2 child developmental centers. By applying the model, treatment could be targeted at the predominant area of difficulty for each child.

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Journal of Child Psychology and Psychiatry. 2012 Mar;53:243-51.

GENE BY ENVIRONMENT INTERACTIONS INFLUENCING READING DISABILITY AND THE INATTENTIVE SYMPTOM DIMENSION OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER.

Rosenberg J, Pennington BF, Willcutt EG, et al.

Background: Reading disability (RD) and attention deficit/hyperactivity disorder (ADHD) are comorbid and genetically correlated, especially the inattentive dimension of ADHD (ADHD-I). However, previous research indicates that RD and ADHD enter into opposite gene by environment (G × E) interactions.
Methods: This study used behavioral genetic methods to replicate these opposite G × E interactions in a sample of same-sex monozygotic and dizygotic twin pairs from the Colorado Learning Disabilities Research Center (CLDRC; DeFries et al., 1997) and to test a genetic hypothesis for why these opposite interactions occur.
Results: We replicated opposite G × E interactions for RD (bioecological) and ADHD-I (diathesis-stress) with parental education in the same sample of participants. The genetic hypothesis for this opposite pattern of interactions is that only genes specific to each disorder enter into these opposite interactions, not the shared genes underlying their comorbidity. To test this hypothesis, we used single models with an exploratory three-way interaction, in which the G × E interactions for each disorder were moderated by comorbidity. Neither three-way interaction was significant. The heritability of RD did not vary as a function

of parental education and ADHD-I. Similarly, the heritability of ADHD-I did not vary as a function of parental education and RD.
Conclusions: We documented opposite G × E interactions in RD and ADHD-I in the same overall twin sample, but the explanation for this apparent paradox remains unclear. Examining specific genes and more specific environmental factors may help resolve the paradox.

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Journal of Child Psychology and Psychiatry. 2012 Mar;53:292-303.
THE HIERARCHICAL FACTOR MODEL OF ADHD: INVARIANT ACROSS AGE AND NATIONAL GROUPINGS?
Toplak ME, Sorge GB, Flora DB, et al.
Objective: To examine the factor structure of attention-deficit/hyperactivity disorder (ADHD) in a clinical sample of 1,373 children and adolescents with ADHD and their 1,772 unselected siblings recruited from different countries across a large age range. Hierarchical and correlated factor analytic models were compared separately in the ADHD and sibling samples, across three different instruments and across parent and teacher informants. Specific consideration was given to factorial invariance analyses across different ages and different countries in the ADHD sample.
Method: A sample of children and adolescents between 5 and 17 years of age with ADHD and their unselected siblings was assessed. Participants were recruited from seven European countries and Israel. ADHD symptom data came from a clinical interview with parents Parental Account of Childhood Symptoms and questionnaires from parents and teachers (Conners Parent and Teacher).
Results: A hierarchical general factor model with two specific factors best represented the structure of ADHD in both the ADHD and unselected sibling groups, and across informants and instruments. The model was robust and invariant with regard to age differences in the ADHD sample. The model was not strongly invariant across different national groups in the ADHD sample, likely reflecting severity differences across the different centers and not any substantial difference in the clinical presentation of ADHD.
Conclusions: The results replicate previous studies of a model with a unitary ADHD component and separable specific traits of inattention and hyperactivity/impulsivity. The unique contribution of this study was finding support for this model across a large developmental and multinational/multicultural sample and its invariance across ages.

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Journal of Child Psychology and Psychiatry. 2012 Mar;53:304-12.
AN EPIDEMIOLOGICAL STUDY OF ADHD SYMPTOMS AMONG YOUNG PERSONS AND THE RELATIONSHIP WITH CIGARETTE SMOKING, ALCOHOL CONSUMPTION AND ILLICIT DRUG USE.
Gudjonsson GH, Sigurdsson JF, Sigfusdottir ID, et al.
Background: This study investigates the relationship between attention deficit hyperactivity disorder (ADHD) symptoms and cigarette smoking, alcohol use and illicit drug use.
Method: The participants were 10,987 pupils in the final three years of their compulsory education in Iceland (ages 14–16 years). The participants completed questionnaires in class relating to anxiety, depression and antiestablishment attitudes, ADHD symptoms, smoking, alcohol consumption and illicit drug use.
Results: Of the total sample, 5.4% met screening criteria for ADHD. Smoking, alcohol and illicit drug use were significantly related to ADHD symptoms. In addition, the number of different illicit drugs consumed was significantly higher among the ADHD symptomatic than the nonsymptomatic participants, including the illicit use of sedatives. The main distinguishing illicit drug substances were lysergic acid diethylamide (odds ratio or OR = 8.0), cocaine (OR = 7.5), mushrooms (OR = 7.1) and amphetamines (OR = 6.5). Logistic multiple regressions showed that after controlling for gender and school grade, ADHD symptoms predicted smoking, alcohol use and illicit drug use independent of anxiety, depression and antiestablishment attitudes. In addition, poly-substance use was linearly and incrementally related to ADHD symptoms with a large effect size.

Conclusions: The findings underscore the vulnerability of young persons with ADHD symptoms to smoking, alcohol and illicit drug use, possibly as a means of self-medication, and emphasize a need for early identification and treatment to reduce the risk of escalation.

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Journal of Child Psychology and Psychiatry. 2012 Mar;53:234-42.

A LONGITUDINAL TWIN STUDY ON THE ASSOCIATION BETWEEN ADHD SYMPTOMS AND READING.

Greven CU, Rijsdijk FV, Asherson P, et al.

Background: Attention deficit hyperactivity disorder (ADHD) and reading disability commonly co-occur because of shared genetic risk factors. However, the stability and change of these genetic influences and the predictive relationships underlying this association longitudinally remain unclear.

Methods: ADHD symptoms and reading were assessed as continuous dimensions in a UK general population sample of approximately 7,000 twin pairs. Parent ratings of ADHD symptoms and teacher ratings of reading were obtained at two ages: middle childhood (ages 7–8 years) and early adolescence (ages 11–12 years). Cross-lagged quantitative genetic analyses were applied.

Results: ADHD symptoms and reading significantly predicted each other over time. However, ADHD symptoms were a significantly stronger predictor of reading than vice versa. Inattentive and hyperactive-impulsive symptoms of ADHD both contributed to the prediction of reading, but inattentiveness was a significantly stronger predictor. Furthermore, ADHD symptoms and reading were highly heritable, and their association was primarily attributable to shared genetic influences. Despite notable genetic innovation for each trait, genetic factors involved in the association of ADHD symptoms and reading over time were highly stable.

Conclusions: ADHD symptoms may put children at increased risk for reading problems and vice versa. Moreover, enduring genetic mechanisms appear to be important in the association of ADHD symptoms and reading over time.

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J Clin Psychopharmacol. 2012;32:300-02.

STATUS EPILEPTICUS ASSOCIATED WITH THE ADMINISTRATION OF LONG-ACTING METHYLPHENIDATE IN A 7-YEAR-OLD GIRL.

Goetz M, Surman CBH, Mlynarova E, et al.

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J Clin Psychopharmacol. 2012;32:302-03.

ATOMOXETINE FOR ENCOPRESIS IN 2 CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER.

Herguner S, Herguner A.

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J Clin Psychopharmacol. 2012;32:291.

SAPOPHAGIA (COMPULSIVE SOAP EATING) AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN A CHILD RESPONSIVE TO CLONIDINE.

Saddichha S, Vibha P, Vishnuvardhan G.

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J Hosp Med. 2012;7:S239.

CLONIDINE WITHDRAWAL IN A CHILD WITH ADHD.

Lewis K.

Case Presentation: An 8-year-old female with past medical history significant for bipolar disorder and ADHD presented to an emergency department for evaluation of four days of vomiting and diffuse abdominal pain. The patient had been unable to take her routine medications including Risperidone 1 mg

BID, Dextroamphetamine and Amphetamine (Adderall) 50 mg Qday, and Clonidine 0.4 mg Qhs during this time period. Family history was significant for adult-onset hypertension in her father. On physical exam, the patient was hypertensive with an initial blood pressure reading of 141/90 (>99%ile for age and height). The remainder of her vitals were within normal limits. She was uncomfortable, but nontoxic appearing, with a diffusely tender abdomen, but no peritoneal signs. Aside from concentrated urine with ketones present, basic lab evaluation including chemistry, cbc, lfts, and pancreatic enzymes were without significant abnormalities. Abdominal plain film was consistent with a mild ileus. The patient was admitted to the hospital for IV fluid hydration, serial abdominal exams, pain control, and blood pressure monitoring. Despite pain control measures, the patient's course in the hours following admission was characterized by hypertension as severe as 179/117. This was treated with IV hydralazine, with improvement to 157/92. The patient subsequently experienced a 2-3 min generalized tonic-clonic seizure prompting transfer to the intensive care unit for continuous IV nicardipine administration and blood pressure monitoring. With subsequent improvement in the patient's vomiting, and resolution of her presumed viral syndrome, her home clonidine was resumed and she was rapidly weaned off of the nicardipine drip. Her blood pressures returned to normal for the remainder of her hospital stay. Additional evaluation including head ct, four-extremity blood pressures, EKG, renal ultrasound, and laboratory assessment for secondary causes of hypertension, was negative. Discussion with the patient's primary care physician confirmed previous normal blood pressure readings both prior to the initiation of and while taking her stimulant and clonidine.
Discussion: The prevalence of ADHD in the US pediatric population is estimated at 3-5%. Clonidine is a commonly prescribed medication in this population, both as monotherapy, and in combination with stimulants. The side effect of rebound hypertension in patients in whom clonidine is abruptly discontinued has been well documented. In this patient, the abrupt discontinuation of a relatively high dose of clonidine resulted in malignant hypertension with seizure.
Conclusions: Patients in whom clonidine is abruptly discontinued, especially at high doses, and when used in combination with high doses of stimulants, should be monitored closely and treated aggressively for rebound hypertension. Whenever possible, abrupt discontinuation should be avoided.

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J Neurother. 2012;16:12-31.

EVENT-RELATED POTENTIAL STUDY OF ATTENTION REGULATION DURING ILLUSORY FIGURE CATEGORIZATION TASK IN ADHD, AUTISM SPECTRUM DISORDER, AND TYPICAL CHILDREN.

Sokhadze EM, Baruth JM, Sears L, et al.

Autism spectrum disorders (ASD) and attention deficit/hyperactivity disorder (ADHD) are very common developmental disorder that share some similar symptoms of social, emotional, and attentional deficits. This study is aimed to help understand the differences and similarities of these deficits using analysis of dense-array event-related potentials (ERP) during an illusory figure recognition task. Although ADHD and ASD seem very distinct, they have been shown to share some similarities in their symptoms. Our hypothesis was that children with ASD will show less pronounced differences in ERP responses to target and nontarget stimuli as compared to typical children and, to a lesser extent, ADHD. Participants were children with ASD (N=16), ADHD (N=16), and controls (N=16). EEG was collected using a 128-channel EEG system. The task involved the recognition of a specific illusory shape, in this case a square or triangle, created by three or four inducer disks. There were no between-group differences in reaction time (RT) to target stimuli, but both ASD and ADHD committed more errors; specifically, the ASD group had statistically higher commission error rate than controls. Posterror RT in ASD group was exhibited in a posterror speeding rather than corrective RT slowing typical for the controls. The ASD group also demonstrated an attenuated error-related negativity as compared to ADHD and controls. The fronto-central P200, N200, and P300 were enhanced and less differentiated in response to target and nontarget figures in the ASD group. The same ERP components were marked by more prolonged latencies in the ADHD group as compared to both ASD and typical controls. The findings are interpreted according to the "minicolumnar" hypothesis proposing existence of neuropathological differences in ASD and ADHD, specifically minicolumnar number/width morphometry spectrum differences. In autism, a model of local hyperconnectivity and long-range hypoconnectivity explains many of the behavioral and cognitive deficits present in the condition, whereas the inverse arrangement of local hypoconnectivity and long-range hyperconnectivity in ADHD explains some deficits typical for this disorder. The current ERP study supports the proposed suggestion

that some between-group differences could be manifested in the frontal ERP indices of executive functions during performance on an illusory figure categorization task.

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J Psychiatry Neurosci. 2012;37:129-37.

DIFFERENTIAL ASSOCIATION BETWEEN THE NOREPINEPHRINE TRANSPORTER GENE AND ADHD: ROLE OF SEX AND SUBTYPE.

Sengupta SM, Grizenko N, Thakur GA, et al.

Background: Pharmacologic and animal studies have strongly implicated the norepinephrine transporter (NET) in the pathophysiology of attention-deficit/hyperactivity disorder (ADHD). We conducted a family-based study, with stratification based on sex and subtype, to test the association between 30 tag single-nucleotide polymorphisms (SNPs) within the gene encoding NET (SLC6A2) and ADHD.

Methods: Family-based association tests were conducted with the categorical diagnosis of ADHD, as well as quantitative phenotypes of clinical relevance (Conners Global Index for Teachers and Parents, and Child Behavior Checklist measures). Sliding window haplotype analysis was conducted with screening based on conditional power using PBAT.

Results: A previously reported association with rs3785143 was confirmed in this study. Further, extensive association was observed with haplotype blocks, with a differential pattern observed based on sex and subtype. The 5' region of the gene (encompassing haplotype block 1 and including a functional promoter SNP, rs28386840) showed an association with ADHD in girls (irrespective of subtype). A different region of the gene (distributed around haplotype block 2) was associated with distinct behavioural phenotypes in boys. These findings are correlated with previously reported functional studies of gene variants in SLC6A2. Limitations: The most important limitation of the study is the small size of the groups resulting from the stratification based on sex followed by subtype.

Conclusion: The results obtained in this family-based study suggest that haplotype blocks within different regions of SLC6A2 show differential association with the disorder based on sex and subtype. These associations may have been masked in previous studies when tests were conducted with pooled samples.

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J Am Acad Child Adolesc Psychiatry. 2012;51:432-40.

GENOME-WIDE ASSOCIATION STUDY OF INTELLIGENCE: ADDITIVE EFFECTS OF NOVEL BRAIN EXPRESSED GENES.

Loo SK, Shtir C, Doyle AE, et al.

Objective: The purpose of the present study was to identify common genetic variants that are associated with human intelligence or general cognitive ability.

Method: We performed a genome-wide association analysis with a dense set of 1 million single-nucleotide polymorphisms (SNPs) and quantitative intelligence scores within an ancestrally homogeneous family sample of 656 individuals with at least one child affected by attention-deficit/hyperactivity disorder (ADHD).

Results: Haplotype trend regression analysis with sliding four-SNP windows identified haplotypes of genome-wide significance in genes involved in synaptic signaling (KIF16B; p = 1.27E-08) and neurodevelopment (PAX5; p = 3.58E-08), and highlight findings from a recent genetic study of cognitive ability (RXRA; p = 7.7E-08; GYPC; p = 2.5E-07). Further interrogation of SNPs within top haplotypes reveals that the minor alleles are associated with higher intelligence, whereas others are associated with relatively lower (but still average range) intelligence. Effects of the eight genes are additive, as a greater number of the associated genotypes in a given individual predict higher intelligence (p = 5.36E-08) and account for 8% of variance in intelligence.

Conclusions: Analyses that examine additive genetic effects may be useful in identifying regions where the additive effects of SNPs have a significant effect on phenotype. These results describe novel variants and additive effects of genes involved in brain development on variability in intelligence within an ADHD sample. The precise mechanisms of these loci in relation to determining individual differences in general

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J Am Acad Child Adolesc Psychiatry. 2012;51:356-67.

NEUROBIOLOGICAL CIRCUITS REGULATING ATTENTION, COGNITIVE CONTROL, MOTIVATION, AND EMOTION: DISRUPTIONS IN NEURODEVELOPMENTAL PSYCHIATRIC DISORDERS.

Arnsten AFT, Rubia K.

Objective: This article aims to review basic and clinical studies outlining the roles of prefrontal cortical (PFC) networks in the behavior and cognitive functions that are compromised in childhood neurodevelopmental disorders and how these map into the neuroimaging evidence of circuit abnormalities in these disorders.

Method: Studies of animals, normally developing children, and patients with neurodevelopmental disorders were reviewed, with focus on neuroimaging studies.

Results: The PFC provides "topdown" regulation of attention, inhibition/cognitive control, motivation, and emotion through connections with posterior cortical and subcortical structures. Dorsolateral and inferior PFC regulate attention and cognitive/inhibitory control, whereas orbital and ventromedial structures regulate motivation and affect. PFC circuitries are very sensitive to their neurochemical environment, and small changes in the underlying neurotransmitter systems, e.g. by medications, can produce large effects on mediated function. Neuroimaging studies of children with neurodevelopmental disorders show altered brain structure and function in distinctive circuits respecting this organization. Children with attention-deficit/hyperactivity disorder show prominent abnormalities in the inferior PFC and its connections to striatal, cerebellar, and parietal regions, whereas children with conduct disorder show alterations in the paralimbic system, comprising ventromedial, lateral orbitofrontal, and superior temporal cortices together with specific underlying limbic regions, regulating motivation and emotion control. Children with major depressive disorder show alterations in ventral orbital and limbic activity, particularly in the left hemisphere, mediating emotions. Finally, children with obsessive-compulsive disorder appear to have a dysregulation in orbito-fronto-striatal inhibitory control pathways, but also deficits in dorsolateral fronto-parietal systems of attention.

Conclusions: Altogether, there is a good correspondence between anatomical circuitry mediating compromised functions and patterns of brain structure and function changes in children with neuropsychiatric disorders. Medications may optimize the neurochemical environment in PFC and associated circuitries, and improve structure and function.

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Med Sommeil. 2012.

MAZINDOL: AN ALTERNATIVE IN THE TREATMENT OF AWAKENING DISORDERS AND ATTENTION DEFICIT?

Konofal E, Lecendreux M, Jacqz-Aigrain E, et al.

Mazindol is a non-amphetamine central nervous system stimulant. When the amphetamines were withdrawn, mazindol did not dominate the drug landscape in narcolepsy. When modafinil was registred for primary hypersomnias (e.g. narcolepsy), mazindol definitely lost any opportunity to be indicated for hypersomnias, despite clinical studies showing its safety and benefit. The review of the literature about the effects of mazindol at therapeutic doses (1-6 mg/d) confirms its clear efficacy profile in the treatment of excessive daytime sleepiness and cataplexy, with no potential for abuse, no withdrawal syndrome, and rare serious adverse events, even after a long-term exposure. The fact remains that mazindol suffers from limited knowledge of its use and interest in clinical practice. At a time when the depletion of pharmacotherapeutic options extends to orphan diseases in adults, is it possible to consider its therapeutic benefit as extended to attention disorders in children?

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Neural Regen Res. 2011;6:2850-55.

VOXEL-BASED STATISTICAL ANALYSIS OF REGIONAL CEREBRAL GLUCOSE METABOLISM IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Kim JH, Chung YI, Lee JS, et al.

The technique of region of interest-based positron emission tomography is limited by its poor reliability and relatively few examined brain regions. In the present study, we compared brain metabolism assessed using fluorine-18-fluorodeoxyglucose positron emission tomography between 14 attention-deficit hyperactivity

disorder (ADHD) patients and 15 normal controls with scoliosis at resting state by statistical parametric mapping. Glucose metabolism was decreased in the left parahippocampal gyrus, left hippocampus, left anterior cingulate gyrus, right anterior and posterior lobes of the cerebellum, left superior temporal gyrus, left insula, left medial and middle frontal gyri, right medial frontal gyrus, and left basal ganglia (putamen, amygdala, and caudate nucleus) in children with ADHD. These data suggest that children with ADHD exhibit hypometabolism in various brain regions compared to controls, indicating that ADHD symptoms are unlikely the result of abnormalities in specific areas.

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Neuroendocrinol Lett. 2011;32:790-98.

CIRCADIAN RHYTHMS OF SALIVA MELATONIN IN ADHD, ANXIOUS AND NORMAL CHILDREN.

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

BACKGROUND: Attention-deficit/hyperactivity disorder (ADHD) and anxiety disorders are the most frequent psychiatric disorders in children. Changes in rhythms of symptoms during the day may be influenced by genetic, biological and psychological factors. Some changes of melatonin rhythm may hypothetically change the activity of ADHD by changing arousal or in anxiety children by changing their emotional state. In our present study we identify one group of ADHD children combine type without comorbids, one group of anxiety children and a control group. Most changes of melatonin daily rhythm are supposed in the anxiety group, especially in sleeping time, and more prominent change in the ADHD group with prominent hyperactivity and conduct disorder symptoms.

METHODS: Thirty-four ADHD and forty-three control children and eleven anxiety children, all 6-12 years old, participated in the study. The saliva specimens were collected in four different sessions during the school year, around the time of the spring and autumn equinox, when the natural light lasted 11.2 h (plus or minus) 0.9 h.

RESULTS AND CONCLUSIONS: In our study more symptoms of conduct disorder elevated positive or negative correlations between psychopathology and saliva level of melatonin in ADHD and anxiety samples. We hypothesize that co-morbidity of ADHD or anxiety with impulsivity and conduct disorders might have elevated correlations between psychopathology of ADHD or anxiety and plasma melatonin level.

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Neuropsychiatr Enfance Adolesc. 2012.

PREVALENCE OF ATTENTION DEFICIT HYPERACTIVITY DISORDER IN SCHOOLCHILDREN IN SFAX, TUNISIA: CROSS SECTIONAL STUDY.

Khemakhem K, Yaich S, Ayedi H, et al.

Introduction: Attention deficit-hyperactivity disorder (ADHD) is a problem of public health because of its frequency and impact. The objective of our work was to study the prevalence of ADHD in school population in the region of Sfax.

Population and methods: The study was cross running from 1/4/2008 until 1/10/2008, caring on 513 students, 240 boys and 273 girls. They were enrolled in the first year of teaching basis until 5th year of basic education. Schools were randomly selected from a list provided by the Regional Directorate education in all schools of communal areas in the region of Sfax. The Conners scale of teachers and parents was used as a screening tool. Children who had at least one pathological test have benefited clinical evaluation with their parents. The diagnoses were according to DSM-IV-TR.

Results: The award of the Conners scale has identified 404 students for high scores were normal in the two versions of the scale for hyperactivity, impulsiveness and inattention, and 109 students who had a pathological score on at least one of the Conners scales. The interview with the 109 students, allowing clinical evaluation of children with reference to DSM-IV-TR, has enabled us to carry at least one diagnosis nosographic for 92 pupils of whom 51 had ADHD. Of a total of 513 students, 51 students were affected by ADHD DSM-IV. Thus, the prevalence of ADHD in schools in our study was 9.94%. In our study, ADHD was 5.26% in mixed-type cases, inattention prevalent in 2.7% and hyperactivity in impulsive 1.94% cases.

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Neuropsychology. 2012 Mar;26:165-71.

SPECIFICITY OF DYSPRAXIA IN CHILDREN WITH AUTISM.

MacNeil LK, Mostofsky SH.

Objective: To explore the specificity of impaired praxis and postural knowledge to autism by examining three samples of children, including those with autism spectrum disorder (ASD), attention-deficit hyperactivity disorder (ADHD), and typically developing (TD) children.

Method: Twenty-four children with ASD, 24 children with ADHD, and 24 TD children, ages 8–13, completed measures assessing basic motor control (the Physical and Neurological Exam for Subtle Signs; PANESS), praxis (performance of skilled gestures to command, with imitation, and tool use) and the ability to recognize correct hand postures necessary to perform skilled gestures (the Postural Knowledge Test; PKT).

Results: Children with ASD performed significantly worse than TD children on all three assessments. In contrast, children with ADHD performed significantly worse than TD controls on PANESS but not on the praxis examination or PKT. Furthermore, children with ASD performed significantly worse than children with ADHD on both the praxis examination and PKT, but not on the PANESS.

Conclusions: Whereas both children with ADHD and children with ASD show impairments in basic motor control, impairments in performance and recognition of skilled motor gestures, consistent with dyspraxia, appear to be specific to autism. The findings suggest that impaired formation of perceptual-motor action models necessary to development of skilled gestures and other goal directed behavior is specific to autism; whereas, impaired basic motor control may be a more generalized finding.

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Pediatr Ann. 2011;40:556-62.

TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Pierce K.

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Pediatr Neonatol. 2012.

AUDITORY EVENT-RELATED POTENTIALS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Tsai ML, Hung KL, Lu HH.

Background: Recording of event-related potentials (ERPs) from the scalp is a noninvasive technique reflecting the sensory and cognitive processes associated with attention tasks. Attention deficit hyperactivity disorder (ADHD) is a disorder involving deficits in attention and behavioral control. The aim of this study was to investigate the difference in ERPs between normal children and those with ADHD.

Methods: We examined 50 children with ADHD and 51 age-matched controls. All children with ADHD met the full criteria for ADHD according to Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV). The auditory oddball paradigm was applied, and event-related long-latency components (N1, P2, N2 and P3) from Fz, Cz and Pz were measured in each test subject.

Results: Children with ADHD showed a significantly longer latency and a lower amplitude of P3 compared to normal control children ($p < 0.01$). Delayed N2 latency at the Pz electrode was shown in children with ADHD compared to normal controls ($p < 0.01$). No differences in other ERP indices were found between children with ADHD and controls. When divided into four age groups, the latency of P3 was significantly increased in all age groups and a significantly smaller amplitude in P3 over the central region was found in children with ADHD > 10 years of age ($p < 0.05$).

Conclusion: We found that the endogenous ERPs (P3 and N2) were significantly affected in children with ADHD, compared to exogenous ERPs (N1 and P2). Increased latency of P3 suggests a slower processing speed, and decreased P3 amplitude is interpreted as disruption of inhibitory control in children with ADHD. These results indicate a neurocognitive abnormality in ADHD, as presented by a reduction in ERP response.

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Psychiatr Serv. 2012;63:115-21.

MEDICATION USE AND SPENDING TRENDS AMONG CHILDREN WITH ADHD IN FLORIDA'S MEDICAID PROGRAM, 1996-2005.

Fullerton CA, Epstein AM, Frank RG, et al.

Objective: How the introduction of new pharmaceuticals affects spending for treatment of children with attention-deficit hyperactivity disorder (ADHD) is unknown. This study examined trends in use of pharmaceuticals and their costs among children with ADHD from 1996 to 2005.

Methods: This observational study used annual cohorts of children ages three to 17 with ADHD (N=107,486 unique individuals during the study period) from Florida Medicaid claims to examine ten-year trends in the predicted probability for medication use for children with ADHD with and without psychiatric comorbidities as well as mental health spending and its components. Additional outcome measures included average price per day and average number of days filled for medication classes.

Results: Overall, the percentage of children with ADHD treated with ADHD drugs increased from 60% to 63%, and the percentage taking antipsychotics more than doubled, from 8% to 18%. In contrast, rates of antidepressant use declined from 21% to 15%, and alpha agonist use was constant, at 15%. Mental health spending increased 61%, with pharmaceutical spending representing the fastest-rising component (up 192%). Stimulant spending increased 157%, mostly because of increases in price per prescription. Antipsychotic spending increased 588% because of increases in both price and quantity (number of days used). By 2005, long-acting ADHD drugs accounted for over 90% of stimulant spending.

Conclusions: Long-acting ADHD drugs have rapidly replaced short-acting stimulant use among children with ADHD. The use of antipsychotics as a second-tier agent in treating ADHD has overtaken traditional agents such as antidepressants or alpha agonists, suggesting a need for research into the efficacy and side effects of second-generation antipsychotics among children with ADHD.

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Psychiatr Serv. 2012;63:122-29.

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

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

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

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

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

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

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Psychiatry Res. 2010;178:137-41.

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

Edel MA, Juckel G, Brune M.

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

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Psychiatry Res. 2012.

MOTOR IMPAIRMENT IN CHILDREN WITH ANXIETY DISORDERS.

Skirbekk B, Hansen BH, Oerbeck B, et al.

This study examined the frequency and degree of motor impairment in referred children with anxiety disorders (AnxDs), compared with children with attention deficit/hyperactivity disorder (ADHD), children with comorbid AnxDs and ADHD, and nonreferred controls. All participants (n = 141; 90 males, 51 females; mean age: 10 years, 1 month; range: 7-13 years) had an IQ greater than 70. Diagnoses of mental disorders were established using the Schedule for Affective Disorders and Schizophrenia for School-Aged Children (Kiddie-SADS). Motor ability was assessed using the Movement Assessment Battery for Children (M-ABC). We found that children with AnxDs exhibited significantly higher total impairment scores on the M-ABC than controls, but were not significantly different from children with ADHD or children with comorbid AnxDs and ADHD. All clinical groups exhibited similar profiles of motor impairment. A total of 19 (46%) children with AnxDs scored below the 5th percentile on the M-ABC, indicating that motor function is impaired in many children with AnxDs to a degree that probably interferes with their activities of daily living. These results support the notion that assessment of motor function is important in understanding the daily challenges of children with AnxDs.

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Psychiatry Res. 2012.

ASSOCIATION OF COMORBID ANXIETY WITH SOCIAL FUNCTIONING IN SCHOOL-AGE CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD).

Lee SS, Falk AE, Aguirre VP.

Although attention-deficit/hyperactivity disorder (ADHD) is frequently comorbid with disruptive behavior disorders, less is known about ADHD and comorbid anxiety. To improve understanding about the association of anxiety and social functioning, we studied 223 6 to 9 year-old ethnically diverse boys and girls (M = 7.4 years) with and without ADHD. According to parents, children with ADHD and anxiety (n = 46) and ADHD only (n = 71) were consistently less socially competent than comparison children (i.e., no anxiety and ADHD: n = 80) and children with anxiety only (n = 26), who did not differ from one another. A similar pattern emerged for teacher ratings where youth with ADHD only and ADHD with anxiety exhibited the most social problems, but they did not differ from each other. These data suggest that comorbid anxiety does not exacerbate social dysfunction among 6 to 9 year-old children with ADHD. We consider findings within a developmental psychopathology framework to further understand social development in children with ADHD and anxiety.

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Psychiatry Res. 2012.

THE QEEG THETA/BETA RATIO IN ADHD AND NORMAL CONTROLS: SENSITIVITY, SPECIFICITY, AND BEHAVIORAL CORRELATES.

Ogrim G, Kropotov J, Hestad K.

The purpose of the present study was to determine if the theta/beta ratio, and theta and beta separately, correlate with behavioral parameters, and if these measures discriminate between children and adolescents with ADHD and normal gender- and age-matched controls. Sixty-two patients and 39 controls participated in the study. A continuous performance test (CPT), a GO/NOGO test and two rating scales were used to measure behavior in the patient group. EEG spectra were analyzed in eyes-closed and eyes-opened conditions, and in a GO/NOGO task in both groups. Neither the theta/beta ratio at CZ, nor theta and beta separately discriminated significantly between patients and controls. When each person was compared with the database significant elevations of theta were found in 25.8% of the patients and in only one control subject (2.6%). In the ADHD group, theta at CZ was positively correlated with inattention and executive problems and negatively correlated with hyperactivity/impulsivity. Beta correlated with good attention level in the control group, but with ADHD symptoms in the patients. Omission errors in the GO/NOGO test discriminated between patients and controls with an accuracy of 85%. For theta at CZ, the accuracy was 62%. Significantly elevated theta characterized a subgroup of ADHD and correlated with inattention and executive problems.

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Psychiatry Res. 2012.

THE RESPONSE TO STRESS IN BRAZILIAN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Palma SMM, Fernandes DRM, Muszkat M, et al.

This study assessed the function of the hypothalamic-pituitary-adrenal (HPA) axis, during response to stress, through the measurement of salivary cortisol in 38 children with attention deficit hyperactivity disorder (ADHD) and its subtypes, who were matched to 38 healthy control subjects. These measures were made at four time intervals: 15 min before exposing the subjects to a stressor - the Continuous Performance Test (CPT), and 20, 40, and 60 min after such exposure. The baseline cortisol levels were statistically similar in both groups. The mean values of cortisol at the four time intervals were not statistically different between the three subtypes of ADHD (inattentive, hyperactive-impulsive and combined); thus, the ADHD group was treated as a single group. Following the stressor test, the ADHD group had significantly higher levels of salivary cortisol than the control group at time intervals of 20 and 40 min, whereas in this latter group exposure to the CPT did not induce an increase of cortisol. These results suggest that the increased cortisol levels in the ADHD group could be due to the lack of comorbidities. In addition, these patients facing a computerized test, might have responded with a motivational pathway with an increase of cortisol.

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Psychological Medicine: A Journal of Research in Psychiatry and the Allied Sciences. 2012 Mar;42:639-46.

DEFICIENT EMOTIONAL SELF-REGULATION AND PEDIATRIC ATTENTION DEFICIT HYPERACTIVITY DISORDER: A FAMILY RISK ANALYSIS.

Biederman J, Spencer T, Lomedico A, et al.

Background: Although deficient emotional self-regulation (DESR) is associated with attention deficit hyperactivity disorder (ADHD), little research investigates this association and little is known about its etiology. Family studies provide a method of clarifying the co-occurrence of clinical features, but no family studies have yet addressed ADHD and DESR in children.

Method: Subjects were 242 children with ADHD and 224 children without ADHD. DESR was operationalized using an aggregate score =180 and <210 in the anxious/depressed, attention and aggression scales (AAA profile) of the Child Behavior Checklist (CBCL), termed the CBCL-DESR profile. The CBCL-bipolar (CBCL-BP) profile was defined as =210 on the CBCL-AAA scale. We examined the familial transmission of ADHD and the CBCL-AAA scale in families selected through probands with and without these conditions.

Results: We found a linear increase in the prevalence of CBCL-DESR in siblings as indexed by the Control, ADHD, ADHD + CBCL-DESR and ADHD+CBCL-BP proband groups. While the ADHD siblings were at elevated risk for both the CBCL-DESR and CBCL-BP compared with non-ADHD siblings, a significantly higher rate of CBCL-BP in the siblings of ADHD + CBCL-BP probands was found compared with siblings of the Control probands.
Conclusions: ADHD shows the same degree of familial transmission in the presence or absence of DESR. CBCL-DESR and CBCL-BP are familial, but further work is needed to determine if these definitions are distinctly familial or represent a continuum of the same psychopathology.

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Psychol Addict Behav. 2012 Mar;26:124-32.

ARE SYMPTOMS OF ADHD RELATED TO SUBSTANCE USE AMONG COLLEGE STUDENTS?

Glass K, Flory K.

Attention-deficit/hyperactivity disorder (ADHD) is a common childhood disorder that often persists into adolescence and adulthood and has been associated with an increased risk for substance use. Due to improved treatment and educational policies, more students with high levels of ADHD symptoms are attending college despite continued ADHD symptoms. Little research has examined whether college students with higher levels of ADHD symptoms are at increased risk for heavy substance use compared to college students with few ADHD symptoms. The current study examined the relation of ADHD symptoms to substance use (e.g., cigarette smoking, alcohol use, marijuana use, and cocaine use). We hypothesized that greater ADHD symptomatology (inattentive, hyperactive/impulsive, and total ADHD) would be related to higher rates of cigarette smoking, alcohol use, alcohol-problems, and illicit drug use. Participants were 889 college undergraduates who completed an online survey. Results suggest that ADHD symptoms, particularly inattentive symptoms, were positively associated with cigarette smoking and problems associated with alcohol after controlling for conduct disorder (CD) symptoms. ADHD symptoms were not significantly associated with alcohol use or illicit drug use after the effects of CD symptoms were accounted for. Results have important implications for prevention and treatment of college student substance use. Limitations and future directions are discussed.

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Res Dev Disabil. 2012;33:1287-93.

PSYCHIATRIC DISORDERS AMONG CHILDREN WITH CEREBRAL PALSY AT SCHOOL STARTING AGE.

Bjorgaas HM, Hysing M, Elgen I.

The aim of the present population study was to estimate the prevalence of psychiatric disorders in children with cerebral palsy (CP), as well as the impact of comorbid conditions. A cohort of children with CP born 2001-2003, and living in the Western Health Region of Norway were evaluated at school starting age. Parents were interviewed with the diagnostic instrument Kiddie-SADS, to find the prevalence of psychiatric disorders. Sixty-seven children participated, 43 boys, with mean age 88 months (SD 6,8 months). Most children had spastic CP, Gross Motor Function Classification System (GMFCS) levels I and II were found in 2/3 of the group. We found the diagnostic instrument appropriate for GMFCS levels I-IV. Child psychiatric disorders were found in 57% of the children, including 28 children meeting criteria for an attention deficit disorder, which was the most common. Communication problem was significantly associated with having a psychiatric disorder, whereas intellectual disability, type of CP and functional level did not account for significant differences. Subthreshold symptoms were found in 33 children, and 42 children (75%) met criteria for either psychiatric disorder, or mental health symptoms. One in four (14 children) were considered well-functioning from a mental health point of view. We conclude with a recommendation for early psychiatric evaluation of all children with CP.

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Revista Brasileira de Psiquiatria. 2012;34:114-15.

HYPOPLASTIC SPLENIUM OF THE CORPUS CALLOSUM AND CO-OCCURRENCE OF ATTENTION DEFICIT/HYPERACTIVITY AND LANGUAGE DISORDERS: A CASE REPORT.

Nunes E, Schneider B, Dursun S, et al.

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Rev Mex Neuroceinc. 2011;12:358-64.

USE AND ABUSE OF HEAD COMPUTED TOMOGRAPHY IN AMBULATORY PEDIATRIC NEUROLOGY.

Motta Ramirez GA, Jimenez-Parra JL, Limas-Santos NI, et al.

Introduction: Although the risks associated with radiation exposure during imagenological studies are considered low in modern times, their use is justified only when it is expected to obtain useful information for decision-making.

Objective: To describe the most frequent indications for head computed tomography (CT) in pediatric patients.

Methods: Head CT studies and their indications performed from January 2008 and March 2010 in the Department of Radiology of the Unit of Medical Specialties of the Ministry of National Defense were reviewed.

Results: A total of 668 head CT studies performed to pediatric patients (age range: 1 month to 18 years) were reviewed: 403 (60.3%) boys and 265 (39.7%) girls. The most frequent indications for head CT were study of headache (39.1%), seizures/ epilepsy (32.2%), investigation of structural abnormalities (13.9%), neurodevelopmental retardation (10%) and attention deficit hyperactivity disorder (4.9%). Only 5% of the head CT studies were abnormal.

Conclusion: A minority of the patients of this study had an abnormal head CT study with findings potentially changing the decision-making process.

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

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

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

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

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

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

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

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Tijdschr Psychiatr. 2012;54:294-95.
ELIMINATION DIET IN CHILDREN WITH ADHD.
Pelsser LMJ .

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Transl Psychiatry. 2012;2.
PRENATAL EXPOSURE TO CIGARETTE SMOKE OR ALCOHOL AND CEREBELLUM VOLUME IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND TYPICAL DEVELOPMENT.
De Zeeuw P, Zwart F, Schrama R, et al.
Prenatal exposure to teratogenic substances, such as nicotine or alcohol, increases the risk of developing attention-deficit/hyperactivity disorder (ADHD). To date, studies examining this relationship have used symptom scales as outcome measures to assess the effect of prenatal exposure, and have not investigated the neurobiological pathways involved. This study explores the effect of prenatal exposure to cigarettes or alcohol on brain volume in children with ADHD and typically developing controls. Children with ADHD who had been exposed prenatally to either substance were individually matched to children with and without ADHD who had not been. Controls who had been exposed prenatally were also individually matched to controls who had not been. For prenatal exposure to both smoking and alcohol, we found a pattern where subjects with ADHD who had been exposed had the smallest brain volumes and unexposed controls had the largest, with intermediate volumes for unexposed subjects with ADHD. This effect was most pronounced for cerebellum. A similar reduction fell short of significance for controls who had been exposed to cigarettes, but not alcohol. Our results are consistent with an additive effect of prenatal exposure and ADHD on brain volume, with the effects most pronounced for cerebellum.

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World J Biol Psychiatry. 2012;13:223-31.
BRAIN IRON LEVELS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A PILOT MRI STUDY.
Cortese S, Azoulay R, Castellanos FX, et al.
Objective. Brain iron deficiency has been supposed to be involved in the pathophysiology of ADHD. Available studies assessing iron in ADHD are based on serum ferritin, a peripheral marker of iron status. To what extent serum ferritin correlates with brain iron (BI) is unclear. The main aim of this study was to compare BI, estimated with magnetic resonance imaging (MRI) in the putamen, pallidum, caudate, and thalamus, between children with and without ADHD. The secondary aim was to assess the correlation between serum ferritin and BI levels.
Methods. Thirty-six children (18 with and 18 without ADHD, the latter including nine healthy controls and nine psychiatric controls) completed MRI and blood sampling. Brain iron levels were estimated by imaging T2 *.
Results. Children with ADHD showed significantly lower estimated BI in right and left thalamus compared to healthy controls. Estimated BI did not differ significantly between children with ADHD and psychiatric controls. Children with ADHD had significantly lower levels of serum ferritin than healthy as well as psychiatric controls. Serum ferritin and T2 * values did not correlate significantly in most regions.
Conclusions. Low iron in the thalamus may contribute to ADHD pathophysiology.

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World J Biol Psychiatry. 2012;13:211-22.
GENOME-WIDE ASSOCIATION STUDY OF MOTOR COORDINATION PROBLEMS IN ADHD IDENTIFIES GENES FOR BRAIN AND MUSCLE FUNCTION.
Fliers EA, Vasquez AA, Poelmans G, et al.
Objectives. Motor coordination problems are frequent in children with attention deficit/hyperactivity disorder (ADHD). We performed a genome-wide association study to identify genes contributing to motor coordination problems, hypothesizing that the presence of such problems in children with ADHD may identify a sample of reduced genetic heterogeneity.

Methods. Children with ADHD from the International Multicentre ADHD Genetic (IMAGE) study were evaluated with the Parental Account of Children's Symptoms. Genetic association testing was performed in PLINK on 890 probands with genome-wide genotyping data. Bioinformatics enrichment-analysis was performed on highly ranked findings. Further characterization of the findings was conducted in 313 Dutch IMAGE children using the Developmental Coordination Disorder Questionnaire (DCD-Q).
Results. Although none of the findings reached genome-wide significance, bioinformatics analysis of the top-ranked findings revealed enrichment of genes for motor neuropathy and amyotrophic lateral sclerosis. Genes involved in neurite outgrowth and muscle function were also enriched. Among the highest ranked genes were MAP2K5, involved in restless legs syndrome, and CHD6, causing motor coordination problems in mice. Further characterization of these findings using DCD-Q subscales found nominal association for 15 SNPs.
Conclusions. Our findings provide clues about the aetiology of motor coordination problems, but replication studies in independent samples are necessary.

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

DEFICIENT ADAPTIVE REGULATION OF EMOTION IN CHILDREN WITH ADHD .

Schmitt K, Gold A, Rauch WA.

Objectives: The current study investigates whether children with and without ADHD differ in their implementation of emotion-regulation strategies. In addition, it explores whether the regulation patterns of ADHD children are related to co-occurring behavioral and emotional problems.
Methods: A group of 21 children with ADHD and a group of 20 children without ADHD (ages 10-13) completed the Questionnaire on Emotion Regulation in Children and Adolescents (FEEL-KJ, Grob & Smolenski, 2005). Furthermore, we employed the parent-rated Strengths and Difficulties Questionnaire (Woerner, Becker & Rothenberger, 2004) to assess the socioemotional problems of ADHD children.
Results: Self-reports revealed group differences in terms of adaptive emotion regulation, though no group differences were found in terms of maladaptive emotion regulation. Specifically, children with ADHD reported less frequently applying the strategies "Cognitive Problem Solving," "Problem-Oriented Acting," "Mood Enhancement," "Reevaluation," and "Distraction." Children with ADHD also reported seeking social support less frequently than the controls. Moreover, significant negative correlations were found between adaptive coping and co-occurring behavioral and emotional problems.
Conclusions: Children with and without ADHD specifically differ in their application of problem-oriented emotion-regulation strategies, especially those ADHD children suffer from co-occurring problems who particularly infrequently apply adaptive emotion regulation strategies.

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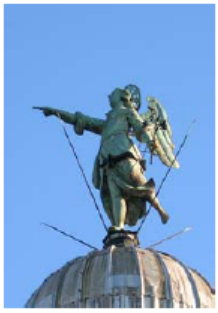
SYSTEMIC APPROACH TO ADHD CHILDREN AND THEIR FAMILIES: A NPIA TERRITORIAL SERVICE EXPERIENCE

Silvana Cremaschi[1], Elisa Cidin[2], Marzona Federico[6], Giuseppe Zappulla[1], Barbara Bortolossi[2], Graziella Sartor[3], Fabrizia Martignon[4], Chiara D'Angelo[5]



1 Medical doctor SOC NPIA Udine- 2 Psychologist SOC NPIA Udine - 3 Neuro-psychomotor therapist SOC NPIA Udine - 4 Language therapist SOC NPIA Udine - 5 Nurse SOC NPIA Udine - 6 Medical doctor Clinic of Pediatrics AOU Udine

Background

The aim of this study is to present the clinical experience at NPIA Territorial Service based on a Relational Systemic Approach to children with ADHD diagnosis and to share the questions aroused by the review of our last year of activity.

The Relational Systemic Approach is based on the belief that personal development results from the interaction between genotype, phenotype and "ecotype". According to this view, the observation and evaluation space must be guaranteed for the individual aspects (cognitive, neuropsychological, meta-cognitive, emotional and relational), for the environment and for the interaction between these different factors (e.g.: how environment answers to the "different" child functioning).

Multimodal therapy based on Relational Sistemic Approach is focused to help both the children to improve their skills (as attention, concentration, planning skills, impulsivity control, self effectiveness and self esteem) and to help families and environment.

Objectives

In this study we try to demonstrate the clinical value of the Relational Sistemic Approach on diagnostic and therapeutic practise with ADHD children.

In 2011 our NPIA Territorial Service is responsible for 134 children and teenagers (100 males and 34 females) aged from 6 to 18 years with ADHD diagnosis. Our evalutation has shown that: 29 of these patients have an associated behavior disorder, 1 has drug abuse, 2 show self-injury, 36 have anxiety or mood disorders, 19 have language disorders, 16 have learning disorders, 4 have dyspraxia or other movement disorders, 4 are mentally retarded, 2 have epilepsy. Moreover 8 children were recently immigrated, 2 were adopted after experience of institutionalization, 5 have lived moments of stress because of serious familiar tensions and adverse life events, 3 have a story of child abuse.
Critical analysis of our data brought us to the creation of our internal diagnosis and taking charge guidelines. We want now to analyze them through the 75 first contact patients clinical history review.

Materials

75 ADHD children diagnosed on the basis of ICD 10 and DSM IV R criteria;
Psycho-diagnosis has been focused on nuclear internalized end exteriorized symptoms, functional impairment, cognitive and neuropsychological skills, self esteem level and social skills.
75 ADHD children's families;
Quality of Families interactions has been measured with PIR GAS.
10 teacher team involved in managing severe impaired ADHD children in their classrooms (impairment levels: 6^{th} axis/ICD 10>4).

Methods

Family Psychotherapy in families with PIR GAS < 70.
Parent training (based on cognitive-behavioral approach with additional special focus on systemic context and interaction) in families with PIR GAS between 40 and 70. Trainers: psychologist and psychiatric nurse.
Family counseling in families with PIR GAS >70
Teacher training based on cognitive-behavioral approach with additional special focus on systemic context and interaction (impairment levels: 6^{th} axis/ICD 10 > 4). Trainers: psychologist and psychiatric nurse.
Autoregulation training and pedagogic intervention focused on children from 6 to 8 years old and 8 to 11 years old (in smalls groups of children). Trainers: neuro-psychomotor therapist and speech therapist with pedagogic competences.

Neuropsychological training in smalls groups of children (3-4 subjects) focused on children aged 6 to 8 and 8 to 11 years old. Trainers: neuro-psychomotor therapist and speech therapist with pedagogic competences.
Individual psychotherapy centered both on personal experience, self attribution and mood disorders and on specific ADHD social problems.
Psychopharmacologic therapy administered only to severely impaired children (impairment levels; 6th axis/ICD 10> 5) after psychotherapy or specific training.

Results and Discussion

Our Relational Systemic Approach and Multimodal Therapeutic Approach involves:

1. A listening space for parents and a therapeutic space for the whole family
   - Family listening

     At least 3 semi-structured interviews: what do they say about themselves and about the child? How they define the "problem" which has brought them to our attention? What member of the family decided to ask for help? Who and why has send them to our Service? Why at this particular moment? What did the family/school/doctor do to solve the problem and why it didn't succeed? How other members of the family function? What is the role of the affected child in his family (defense of the "weak" parent, warning for a far parent, "scapegoat" boy or part of a conflicting three-person relation?) What difficulties do the family face in trying to "get on well"? What do the parents and the families think about other people's "judgment"? In their opinion, what can be helpful in their search for happiness? (See ICF interview)

     At the end of the interviews (and occasionally during the following meetings) we apply the PIR GAS.
   - PIR GAS results

     75 families with first contact in 2011: 7 scored < 40 (serious family relation disorder/child which required report to the Social Services and Legal Authority); 52 scored between 70 and 40 (intra-familiar relation disorder treatable with familiar psychotherapy); 16 scored > 70 (appropriate functioning families and/or families with mild problem in handling complex situations).
   - Our answers

     - The 7 families with serious family relation disorder (PIR GAS < 40) were followed together with social services, with family, social educational support, both at home and at school.

- The 52 families with intra-familiar relation disorder (PIR GAS 40-70) were followed in 41 cases with familiar psychotherapy (in more difficult situations) and in 11 cases with parent training. Families treated with familiar psychotherapy could benefit from a parent training during next year.
- The 16 appropriate functioning families followed a short period of counseling about the disorder of the child in order to improve their relational and educational expertise and to avoid ADHD associated problems.

- Open questions

  We meet the families at a time of difficulty in managing the problem. Those who show a serious degree of relationship disorder are involved in a circular interaction among parents character, educational models and styles, familiar tensions and conflicts, typical of the family support net, and the cognitive and behavioral style of the child. Is an early intervention possible?

2. A listening space for the child and a therapeutic rehabilitative individual space
   - Child listening

     At least 3 semi-structured interviews: what does he say about himself? What meaning does he give to his symptom/s? What does he think his parents "see" in him in his opinion? What does he think his relatives/teachers/schoolmates "see" in him? What difficulties does he find in trying to "feel well"? What could help him according to the child? (see ICF interview). After the interviews with family and child, we suggest a structured evaluation with neuro-psychological and psycho-diagnostic tests.
   - Results of clinical observation and neuropsychological and psycho-diagnostic evaluation.

     Among the 75 children with first contact in 2011 with exteriorized disorder and posite results of the SDAG and CONNERS scale, 45 presented neuro-cognitive disorders evaluated with neuro-psychological tests: (16 presented behavioral impulsiveness and planning deficit, 29 attention and short-term memory); 28 presented internalized disorders: (11 suffer from anxiety, 17 suffer from depression), 16 had language disorders (specially in comprehension), 17 were mentally retarded or had a cognitive level in lower quartile o norm (4 had a IQ < or = to 70, 13 had a IQ between 70 e 85).
   - Our answers.

- Neuro-cognitive training: addressed to the children with attention, memory and planning disorders, carried out by speech therapist and psychomotor therapist (26 children) ;
- Auto-regulation training and pedagogic intervention : focused on children aged 6 to 8 years old and 8 to 11 years old (12 children);
- Individual Psychotherapy: children and adolescents with internalized disorder or behavior disorder received familiar psychotherapy followed or together with individual psychological support (25 children or adolescents);
- Psychopharmacological treatment: we proposed it only in association with our multimodal treatment with the child and the family only in the case of children who followed the entire diagnostic procedure, who received auto-regulation training and/or rehabilitative neuro-cognitive training but who presented disorder level >4 at 6th Axis in ICD 10 Classification, a very low tolerance level of the disorder in any aspect of his life (self, family, class). 24 children (among the 134 followed in 2011) with age between 8 and 16 years (mean age 13.5 years) take Ritalin (5/75 in first year of follow up); 5 adolescents with disorders excessively interfering with the psychotherapy and the quality of life take Risperdal (mean age 15.2 years).

- Open questions

  Internalized symptoms are involved in a circular relation with the exteriorized disorder. In several cases the exaggerated behavior caused experiences of anxiety and depression for the inevitable frustrations. It sometimes seems that the internalized disorder (manifested with irritability, behavioral instability, aggressiveness) could have caused, as an answer to the environment, an aggressive, impulsive and inattentive behavioral style as an answer to the environment. Could an early diagnosis of internalized disorder have helped the parents in avoiding the following establishing of pathological relational dynamics? Language disorders and mental retard are relevant factors in structuring impulsive answers, poorly internalized both from a cognitive and a behavioral/relational point of view. Could an early diagnosis of language disorders and mental retard and the consequent involvement of the parents in better educational and communicational abilities “prevent” the establishing of exteriorized disorders? 60% of children presents significant neuropsychological, attention, planning and memory disorders “measurable” with tests. With these children it is necessary to organize a specific rehabilitation and maybe further clinical, neuro-physiological, genetic, neuro-imaging research.

3. A listening space for the life background and a space for sharing of thoughts and intervention ideas
   - Contest listening
     Teachers, educators, relatives have a space for sharing their thoughts, their strategies in solving the child's problems in the family or school setting.
   - Results
     Problematic issues highlighted by teachers, educators and relatives involve cognitive aspects, but especially behavioral aspects and group relationships (school, scout, sport)
   - Our answers
     - Teachers are invited to the Teacher training (10 class groups)
     - Grandparents and other relatives can be involved in meetings with the clinicians team together with the parents and, sometimes they can be involved in some sessions of familiar therapy
     - Educators and teachers can be involved in meetings with the team in the presence of the parents or can be invited to conference or public discussions.
   - Open question
     How much does the expression of the disorders vary in the different settings? How much does the acceptance of the hyperactive behavior in the different kinds and orders of school vary? How much can a "stable and authoritative" behavior help the control of the child's emotion, impulsiveness and behavior?

Conclusion

Our Multimodal Terapeutic Approach can be articulated in the following interventions: parent training, teacher training, familiar psychotherapy, neuropsychological training, autoregulation training, individual psychotherapy and psychopharmacological treatment. Different interventions can be chosen and associated accotrding to personal, familiar and environmental impariment and resources.

Our Multimodal Approach is still taking place: parents and children relationship and family interactions will be avaluated one year after th end of the parent

training and/or familiar psychotherapy. Attention, memory and planning abilities will be evaluated at the end of individual autoregulation training, autoregulation and neurocognitive rehabilitation in small groups. Impulsiveness and conflict solving abilities will be evaluated at the end of educative training in small groups. The abilities in behavioral problem management and the child's empowerment in his classroom will be evaluated one year after the end of teacher training.

Preliminary data suggest us the opportunity to keep together, within a unique clinical service diagnostic assessment, familiar and individual psychotherapeutic interventions, neuropsychological and autoregulation training, pharmacologic intervention and environmental interventions.

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Research Submission

Attention in Children and Adolescents With Headache

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Objective.—The previous studies reporting consistent visual reaction times slowing in patients with migraine prompted us to verify if headache could be associated to a broader impairment of attention. This study aims to undertake a thorough investigation of attentional performance by extending the evaluation to children with primary headache of different types.

Methods.—We compared 62 children with headache (14 migraineurs with aura, 29 without aura and 19 with tension type headache) and 52 controls without headache, matched for age, sex, and intelligence using Conners' Continuous Performance Test.

Results.—The 3 clinical groups did not differ in attentional measures. The headache patients, collapsed in 1 single sample, had mean scores in Hit Reaction Time significantly different from those of controls and also had a higher percentage of atypical scores in 2 indices of the Conners' Continuous Performance Test (faster mean reaction time and more commissions).

Conclusions.—Our results confirm the presence of an association between attentional problems and headache that may impact academic learning and daily activities on the long term. The finding that the 3 clinical groups did not show significant differences in attentional performance supports the hypothesis that migraine and tension headache form a continuum that may share the same pathophysiological mechanisms. These results are discussed considering that neurotransmitters and the cerebral circuits subserving headache, personality profile, and attention could overlap, thus predisposing these children to even mild attention malfunctioning.

Key words: children, adolescent, headache, attention

Abbreviations: C controls, CPT Conners' Continuous Performance Test, H group with headache, HRT Hit Reaction Time, M migraineurs, MA migraine with aura, MoA migraine without aura, MRI magnetic resonance imaging, TTH tension headache patients

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Headache is a common neurological condition. Although a high prevalence is estimated in adulthood,[1] headache is also frequent in pediatric age groups,[2] increasing progressively from preschool age to adolescence.[3] The diagnostic criteria were classified by the International Headache Society in 1988,[4] but an accurate definition of various forms of headache (for developmental age, too) was provided only by the subsequent revision,[5] proposing a more careful differential diagnosis between migraine and tension headache.

The frequency and chronicity of the disorder have drawn attention not only to the diagnostic and therapeutic issues but also to prognosis, particularly to the possible cognitive and behavioral consequences. However, the findings have been rather

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contradictory and often scarcely comparable, because of the use of different inclusion criteria and neuropsychological measures.

Numerous studies of adults with migraine showed neuropsychological impairment in tasks such as psychomotor speed,[6-8] attention,[6,8,9] language,[10] verbal and visual memory,[8,11] and executive functioning.[12] Other studies failed to confirm these results finding no neuropsychological dysfunction in migraineurs (M) compared with controls (C).[13-19]

On adult tension headache patients (TTH) there is only 1 longitudinal neuropsychological study that identified no cognitive impairments in TTH compared with M and C.[20]

Although numerous studies have investigated the role of clinical variables such as the frequency, duration and intensity of attacks on the neuropsychological performance of M, few have found significant correlation between neuropsychological deficits and higher frequency of attacks or longer history of the disease.[21]

Concerning developmental age, several studies identified an emotional and behavioral profile in children with headache, characterized by a greater prevalence of internalization disorders such as anxiety and mood disorders,[22-30] whereas only a few (and even then, scarcely conclusive) contributions investigated the headache impact on neurocognitive performance.[10,22,26,31,32] These studies reported impaired short- and long-delay memory in M vs C;[22] in short-term visual memory and visuomotor integration in M vs TTH;[32] and poor verbal abilities, but normal performance in reading, arithmetic or motor and spatial tasks in M vs TTH and C.[10] Only 1 study compared the cognitive performance of M children with their healthy siblings and found no significant difference in sequential and simultaneous information processing.[31]

In a previous study we assessed general cognition and several neuropsychological functions (short-term auditory and visuospatial memory, visual attention and speed of information processing) in 17 migraineurs with aura (MA) and 31 migraineurs without aura (MoA) children finding that both groups performed within normal range, except for a significant delay in simple reaction times (RT).[26]

Because of the different neuropsychological functions investigated and the different clinical groups considered, the previously referenced works are unable to define specific cognitive profiles in headache patients, but they consistently identified an adequate global intellectual functioning[22,26,31,32] and slower information processing both in M adults[8,33] and children.[26]

On the basis of previous studies reporting consistent RT slowing in the population with migraine, we hypothesized that headache could be associated to a broader dysregulation of attention. We used the Conners' Continous Performance Test to compare a larger sample of migraineurs with and without aura to children with tension headache and controls.

METHODS

Participants.—We undertook a single-institution, prospective, study conducted from January 2007 to December 2008 at the Developmental Neurology Division of the Fondazione IRCCS Istituto Neurologico C. Besta in Milan, Italy. During the study period, 98 children were assessed for primary headache.

The following exclusion criteria were considered: (1) any other systemic diseases or major psychiatric disorders; (2) different types of headache in association; (3) significantly altered neuroradiological and/or neurophysiological and/or blood chemistry findings; (4) anomalies emerging on neurological examination.

None of the patients were taking any medication during the study, and were without previous or current use of migraine prophylaxis.

The test sessions were held on a symptom-free day at least 2 days after the latest attack in order to rule out the risk of the subject being in the postdrome phase. The fact that patients reported neither discomfort nor pain at the time of the assessment enabled us to rule out any effects of hangover on their neuropsychological performance.

After this selection, the study involved 62 patients (33 males, range 6-17 years), comprising 29 cases of MoA (18 males, range 6 years, 6 months-16 years, 10 months), 14 cases of MA (6 males, range

RESULTS

MA, MoA, and TTH groups were comparable for gender (chi-square = 1.777, d.f. = 2, $P = .411$), age ($F = 0.640$, $P = .531$), and intelligence ($F = 2.207$, $P = .639$).

The frequency of the attacks and the duration of the disorder did not significantly differ among the 3 groups with headache (duration: MA mean 28 months, range 6-126; MA- mean 39.42 months, range 6-102; TTH mean 29.86 months, range 6-108 months; frequency: MA mean 2.79, range 1-5 attacks for month; MA- mean 6, range 2-20 attacks for month; TTH mean 6.79, range 1-20 attacks for month).

One-way analysis of variance was used to compare the mean performance and chi-square test was computed to compare the observed frequencies of moderately and markedly atypical scores in MA, MoA, and TTH groups (see Table 1).

As no significant difference was recorded in attentional performance among the 3 clinical samples, the subsequent statistical analyses were performed collapsing all the patients into a combined Headache group (H) whose scores are reported in Table 2.

H and C samples were comparable for gender (chi-square = 0.074, d.f. = 1, $P = .851$), age ($t = 0.536$, $P = .593$), and intelligence ($t = -1.219$, $P = .225$).

Analysis of covariance was computed to compare the H and C using intelligence as covariate as the mean Full IQ was higher in C than H although the difference was not statistically significant. Only the mean score of HRT, ie, the mean reaction time for all target responses, was significantly different between the 2 groups ($F = 8.248$, $P = .005$), also after Bonferroni correction for multiple comparisons (alpha = 0.05/9 = 0.006). Moreover, the H obtained higher frequency of atypical scores than C in HRT (chi-square = 28.39, d.f. = 4, exact $P < .001$), and in Commissions, ie, the number of times the individual responds to a non-target (chi-square = 9.84, d.f. = 2, exact $P = .004$). Table 2 shows the evident prevalence of moderately atypical scores in H. A significant negative relationship was found between the HRT and Commissions in CPT ($r = -0.624$; $P < .001$) (see Figure). This result suggests that quick go–no go response times to visual stimuli are related to higher number of false positives, which means that faster patients are less accurate.

Finally, we did not find any relationship between the duration of headache and the attack frequency and attention performance. In our sample we had children with a history of headache ranging from 6 months to 9 years and with attack frequency ranging from 1 to 20 crises per month and, despite this, all patients showed consistent performance in attention tasks. This was an unexpected finding even if previous studies[9,11] have already reported similar conclusions.

DISCUSSION

The main results of this study were as follows: (1) MA, MoA, and THH did not differ in attentional measures; and (2) H had mean scores in HRT significantly different from those of C and got also higher percentage of atypical scores in HRT and Commissions than those observed in C.

Nevertheless, we found higher percentage of atypical scores of CPT indices HRT and Commission compared to percentage observed in C. These findings denote a style of response characterized by more rapid reaction times and more numerous false positive responses than C. These results are consistent with Villa et al's findings,[9] who found great number of action errors suggesting an impulsive response style in children with migraine.

Our data thus indicate a style of response characterized by faster responses (at the expense of accuracy) in complex tasks such as the CPT, which involves signal detection but also response inhibition and sustained attention.

In children and adolescents with migraine, we found normal intelligence and visual selective and divided attention in paper-and-pencil tasks but significantly reduced information processing speed, which has been interpreted as an early sign of a subclinical neuropsychological dysfunction, correlated with the frequency of headache attacks and interictal period.[26]

Moreover, the fact that neither the mean CPT scores nor the incidence of atypical performance are different among the 3 groups with headache is in

7 years, 8 months-17 years, 2 months), and 19 cases of TTH (9 males, range 6 years, 10 months-17 years, 9 months), according to the diagnostic criteria of the International Headache Society.[5]

All patients underwent brain magnetic resonance imaging, comprehensive neurological examination, and a specific protocol of blood chemistry analyses for headache as described in our previous paper,[26] with normal results in all patients. The frequency of attacks and the duration of different types of headache were also recorded. Frequency was calculated as the average number of attacks per month in the last 6 months; duration was recorded as the number of months since the onset of the disorder (which was at least 6 in all patients).

The control group (C) was collected from among the patients' healthy classmates of the same gender and socio-economic status, with no known psychiatric or neurological problems. After assessing their intelligence, we excluded patients with Full IQ significantly lower or higher than the patient's and selected 52 controls (29 males, range 6 years, 11 months to 14 years, 8 months). Neither patients nor controls had learning difficulties and their school record was within the normal range for their class.

None of the children were taking medications with action in the central nervous system.

Informed consent was obtained from parents or tutors and the study was approved by our local research ethics committee.

Cognitive and Computerized Attention Assessment.—Patients and controls were assessed in a quiet room at the Istituto Neurologico C. Besta by examiners who had specific training on the neuropsychological assessment of children. All patients were tested during an interictal period (between 2 successive attacks).

The following were investigated:

- Intellectual abilities using the Raven Progressive Matrices.[34,35] Scored were compared with normative data recollected on the developmental Italian population.
- Sustained attention and response inhibition using Conners' CPT,[36] which measures the variability and the decline in attentional performance during the test, as well as other components of the attentional process: arousal or alertness, selective attention and response inhibition (detailed description of this test is reported in the Appendix). We considered the American norms for the CPT as this test would not be influenced by language or cultural factors as also confirmed by our ongoing data collection. The non-clinical sample includes 1920 individuals for CPT enrolled from the general population aged from 6 years to adults. For children and teenagers, the age groups are 2-year intervals.

Statistical Analysis.—SPSS 10.0 for Windows (SPSS Inc., Chicago, IL, USA) was used to analyze all data. The IQ scores were assessed using the Raven Progressive Matrices. All the CPT measures were converted into T scores, with a mean of 50 and a standard deviation of 10.

For the CPT indices, the manual considers scores $T \geq 65$, outside 90% of the normal distribution, as markedly atypical, and scores $60 \leq T \leq 64$, between 85 and 89% of the normal distribution, as moderately atypical. For the Hit Reaction Time (HRT) and Response Style, we also considered scores $T \leq 34$ as markedly atypical and scores $35 \leq T \leq 39$ as moderately atypical to indicate unusually fast reaction times, and impulsive responses style, respectively.

The independent-sample *t*-test and analysis of variance were computed to compare the mean scores of age, intelligence, and different attentional indices. The Bonferroni correction was used for multiple comparisons.

The non-parametric chi-square test, adjusted using the exact method, was used to compare the observed frequencies of normal, moderately, and markedly atypical scores.

Finally, the Pearson correlation was computed to study the relationship between neuropsychological measures, and between clinical data (duration of disorder and frequency of attacks) and cognitive variables.

All statistic analyses were 2-tailed and *P* values of .05 or lower were considered significant.

Table 1.—Mean and Standard Deviation (SD) of Age and Raven Progressive Matrices (PM) in 3 Groups With Headache

		MA	MoA	TTH	Analysis of variance	MA		MoA		TTH		Chi-square
		Mean (SD)	Mean (SD)	Mean (SD)	*P*	Mod	Mark	Mod	Mark	Mod	Mark	*P*
Age (years.months)		12.9 (2.10)	11.9 (2.8)	12 (2.11)	.531							
Raven PM (IQ)		108.79 (13.97)	104.97 (14.06)	105 (11.06)	.639							
Conners' CPT												
Omissions		47.11 (4.85)	47.19 (6.12)	49.09 (6.52)	.510	0	0	0	1	0	1	1.000
Commissions		52.72 (11.77)	52.38 (9.43)	49.72 (11.07)	.630	5	1	6	2	4	1	.828
HRT		44.42 (11.06)	44.11 (9.77)	45.52 (8.27)	.882	7	1	5	5	2	3	.092
	Rapid HRT					1	1	2	1	0	0	
	Slow HRT											
Variability		46.93 (7.59)	46.26 (8.79)	48.18 (10.35)	.772	1	0	3	0	0	2	.209
Detectability		54.32 (8.27)	51.14 (8.95)	50.99 (8.54)	.474	3	1	1	2	3	0	.212
Response style	Hurried	50.42 (11,55)	46.85 (6.57)	48.36 (6.86)	.394	1	0	2	1	2	0	.929
	Accurate					1	1	2	0	2	0	
Perseveration		47.66 (4.01)	51.36 (11.27)	47.12 (4.27)	.173	0	0	1	2	0	0	.764
HRT block change		48.41 (7.03)	50.40 (7.20)	48.05 (10.75)	.588	0	0	1	1	1	1	1.000
HRT ISI change		46.01 (9.15)	42.82 (6.80)	45.01 (6.61)	.354	0	1	0	0	0	0	.226

For CPT variables, both mean and SD, and frequencies of moderately atypical (Mod) and markedly atypical (Mark) scores are reported.
CPT = Conners' Continuous Performance Test; HRT = Hit Reaction Time; ISI = Interstimulus Interval Change.

Table 2.—Mean and Standard Deviation (SD) of Age and Raven Progressive Matrices (PM) in the Combined Headache Group (H) and Controls (C)

		H	C		H		C		
		Mean (SD)	Mean (SD)	*t*-test	Mod	Mark	Mod	Mark	*P*
Age (years.months)		12.1 (2.9)	11.10 (2.1)	.593					
Raven PM (IQ)		105.84 (13.08)	108.54 (10.56)	.225					
Conners' CPT				Analysis of covariance					Chi-square
Omissions		47.75 (5.96)	47.54 (7.71)	.937	0	2	0	4	.409
Commissions		51.64 (10.40)	48.31 (11.74)	.123	15	4	4	0	.004
HRT	Rapid HRT	44.61 (9.51)	49.54 (8.76)	.005	14	0	0	0	<.001
	Slow HRT				3	0	2	0	
Variability		47.00 (8.95)	47.15 (12.21)	.884	4	2	3	2	.153
Detectability		51.81 (8.64)	51.46 (10.14)	.993	5	3	4	2	.175
Response Style	Hurried	48.12 (8.01)	47.54 (8.15)	.917	4	1	3	0	.284
	Accurate				4	1	5	0	
Perseveration		49.22 (8.44)	48.62 (7.58)	.710	1	2	0	4	.409
HRT block change		49.23 (8.35)	47.08 (7.86)	.205	2	2	4	0	.309
HRT ISI change		49.21 (7.34)	50.31 (9.19)	.832	0	1	0	2	.176

For CPT variables, both mean and SD, and frequencies of moderately atypical (Mod) and markedly atypical (Mark) scores are reported.
CPT = Conners' Continuous Performance Test; HRT = Hit Reaction Time; ISI = Interstimulus Interval Change.

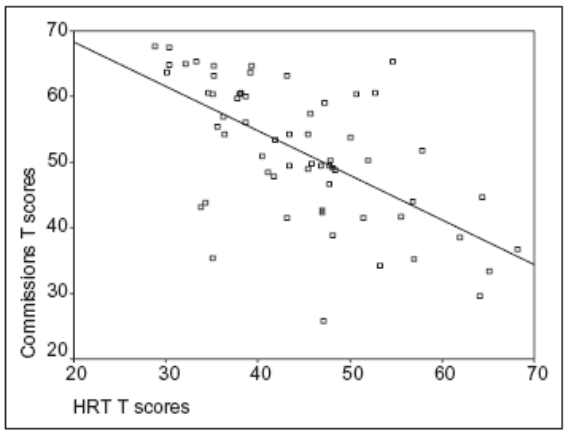

Figure.—Correlation between the Hit Reaction Time (HRT) and the Commissions in Conners' Continuous Performance Test.

favor of an uniform cognitive and attentional phenotype in H children and adolescent, confirming already published data on adults.[8,11]

These results suggest that M and THH are part of the same disorder;[37-42] they probably share the same pathophysiological mechanisms[38,39] and are distinguishable in terms of severity with TTH at the mild end of the severity continuum and M at the severe end,[42,43] as suggest by severity theory.[44]

This attentional impairment can be explained in the context of the neurochemical mechanisms underlying both migraine and attentional processing.[9] Dopamine and noradrenaline play an important role in the genesis of the migraine attacks: noradrenaline limits the hyperexcitability of the trigeminal system if normal,[45] or facilitates migraine or syncope if low,[46] whereas dopamine takes part in the generation of prodromic symptoms.[47] According to Posner model,[48] attention is the capacity to focus and adequately respond to more salient stimuli suppressing the others. The complexity of this function is subserved by a complex anatomical network involving brainstem, cerebral cortex and limbic system, where numerous neurotransmitters, mainly noradrenaline and dopamine, act.[49] Noradrenaline acts in the cortex and in subcortical structures maintaining alertness and continuous attention over time, whereas dopamine acts in the prefrontal cortex and its connections with striatum and cingulated gyrus, modulating selective and sustained attention.[49]

Furthermore, different types of attention are subserved by different neural networks.[50-60] Specifically for the task used in this study, positron emission tomography and fMRI studies have demonstrated an extensive activation of a neural network, including areas in the frontal, cingulate, parietal, temporal and occipital cortices, and the cerebellum.[55-60]

The greater prevalence of anxiety and mood disorders reported in children[22-30] and adults[61] with H might also influence the processing of the attentional tasks.

The relationship between anxiety and attentional control was initially theorized by Eysenck[62] and has been confirmed by recent neuroimaging studies.[63-66] They have found an under-recruitment of cognitive executive brain regions, including the cingulate and prefrontal cortices, linked to dysregulation of emotion,[63] poor control of attention to threat-related stimuli,[64] and anxiety-inducing reduced inhibition of distractors.[66]

Hence, anxiety would be linked to malfunctioning of prefrontal attentional control mechanisms to inhibit distractor processing, as observed in the CPT. Pediatric mood and anxiety disorders are characterized by core deficits in executive functions and commonly co-occur with attention malfunctioning, both involving prefrontal cortex. In our previous study we found a behavioral phenotype characterized by internalizing problems on the Child Behavior Check List in children and adolescent with MoA and MA,[26] and this has also been confirmed by our ongoing data collection on a larger pediatric population with headache.

Some limitations should be considered in the present study. First, our referred sample cannot be considered representative of pediatric headache patients because of selection bias because of the fact that we studied only a small group of children and adolescents with headache collected at our institute. Additionally, although attack frequency was not associated to attention measures, the presence of a number of ≥20 attacks per month in the TTH and MA- group suggests difficulty of assessing the children during the 48-hour headache-free period. Further studies on larger samples with lower fre-

quency headaches could add evidence to reliability and specificity of attentional profile in children with headache.

CONCLUSIONS

The attentional CPT performance of children and adolescents with MA, MoA, and TTH did not differ in this study. We found generally faster reaction times in tasks demanding the inhibition of a highly activated response and denoting a rather impulsive response style. This deficit is mild, and can be highlighted only by an accurate laboratory neuropsychological assessment. Alternatively, it can also be seen as an early marker of a subclinical neuropsychological dysfunction, as it has been seen in another types of attention.[9,26] This condition could in the long-term impact on learning and daily activities. The same pathophysiological mechanisms and neural circuits that underlie headache are also involved in the personality profiles and in the attentional mechanisms, predisposing these children to more or less severe attention malfunctioning, which should be evaluated early to improve possible treatment planning.

APPENDIX

Test Description.—The standard version of the CPT consists in requesting a rapid response over a prolonged period of time (14 minutes). Target and non-target visual stimuli are presented on the screen, one at a time, in random order and with a variable time interval between 1 stimulus and the next, every 1, 2, or 4 seconds. The subject is asked to press the space bar every time a letter (the target stimulus) appears in the middle of the computer screen, but not to do so (ie, to inhibit any automated response) when the letter X (non-target stimulus) appears.

CPT Measures:

- *Omissions*: the number of targets to which the individual did not respond.
- *Commissions:* the number of times the individual responded to a non-target ("X").
- *Hit Reaction Time (HRT)*: the mean reaction time (in milliseconds) for all target responses over all 6 time blocks. A high T-score reflects a slow response time.
- *Variability of standard error:* the variability of the standard deviations of the standard error values for each sub-block can alternatively be considered to calculate the consistency of reaction times.
- *Detectability:* measures the subject's ability to discriminate between target and non-target stimuli.
- *Response Style (B)*: indicates an individual's style of response. High scores indicate a tendency to be slow or cautious, low scores indicate a tendency to give more hurried and less accurate responses when not providing a response to non-targets.
- *Perseverations:* a response in which the reaction time was less than 100 ms; these responses are assumed to be anticipatory, perseverative, random, or slow/inattentive, because it is physiologically impossible to respond accurately in so short a time.
- *HRTs Block Change (HRT Block Change):* variation in reaction times of correct responses to targets in blocks. It indicates a tendency for reaction times to change across the 6 blocks.
- *HRTs Interstimulus Interval Change (HRT ISI Change)*: this indicates the change in the reaction times over the 3 Interstimulus Intervals (ISI; 1, 2, or 4 seconds).

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