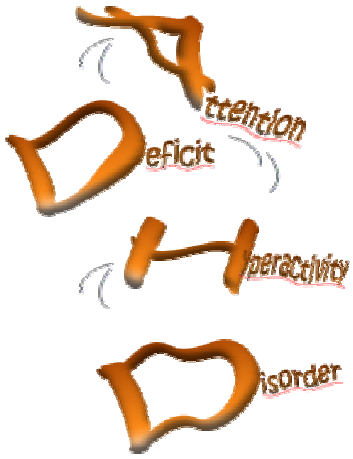
NEWSLETTER



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Learning and Individual Differences 2012;22:896-900. pag. 43

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PARENTS PSYCHOPATHOLOGY OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.
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Ruggiero S, Rafaniello C, Bravaccio C, Gimaldi G, et al.
SAFETY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MEDICATIONS IN CHILDREN: AN INTENSIVE PHARMACOSURVEILLANCE MONITORING STUDY.
J Child Adolesc Psychopharmacol 2012;22:415-22. pag. 56

3. **Segnalazioni**

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MARIONEGRI ISTITUTO DI RICERCHE FARMACOLOGICHE

BIBLIOGRAFIA ADHD GENNAIO 2013

Acta Med Iran. 2012;50:723-28.

BUSPIRONE VERSUS METHYLPHENIDATE IN THE TREATMENT OF CHILDREN WITH ATTENTION- DEFICIT/ HYPERACTIVITY DISORDER: RANDOMIZED DOUBLE-BLIND STUDY.

Mohammadi MR, Hafezi P, Galeiha A, et al.

A recent randomized clinical trial showed buspirone efficacy in the treatment of attentiondeficit/ hyperactivity disorder (ADHD) in children. However, results from a recent multi-site controlled clinical trial of transdermal buspirone failed to separate it from placebo in a large sample of children with ADHD. Therefore, due to these inconsistent findings, this study was designed to assess the efficacy of buspirone in the treatment of children with ADHD compared to methylphenidate in a double blind randomized clinical trial. Forty outpatients with a DSM-IV-TR diagnosis of ADHD were study population of this trial. Subjects were recruited from an outpatient child and adolescent clinic for a 6 week double blind, randomized clinical trial. All study subjects were randomly assigned to receive treatment using tablet of buspirone at a dose of 20-30 mg/day depending on weight (20 mg/day for < 30kg and 30 mg/day for > 30kg) (group 1) or methylphenidate at a dose of 20-30 mg/day depending on weight (20 mg/day for < 30kg and 30 mg/day for > 30kg (group 2) for a 6 week double blind, randomized clinical trial. The principal measure of outcome was the Teacher and Parent ADHD Rating Scale IV. Patients were assessed at baseline and at 21 and 42 days after the medication started. Significant differences were observed between the two groups on the Parent and Teacher Rating Scale scores. The changes at the endpoint compared to baseline were: -8.95(plus or minus)8.73 (mean(plus or minus)SD) and -15.60(plus or minus)7.81 (mean(plus or minus)SD) for buspirone and methyphenidate, for Parent ADHD Rating Scale. The changes at the endpoint compared to baseline were: -9.80 (plus or minus)7.06 (mean(plus or minus)SD) and -22.40(plus or minus)9.90 (mean(plus or minus)SD) for buspirone and methyphenidate, respectively for Teacher ADHD Rating Scale. The difference between the buspirone and methylphenidate groups in the frequency of side effects was not significant except for decreased appetite, headache and insomnia that were observed more frequently in the methylphenidate group. The results of this study suggest that administration of buspirone was less effective than methylphenidate in the treatment of ADHD.

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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.

Act Nerv Super. 2012;54:135-38.

RETAINED PRIMITIVE REFLEXES AND ADHD IN CHILDREN.

Konicarova J, Bob P.

Particularly important postnatal developmental reflexes that diminish in later stages of development are Moro reflex and Galant reflex that belong among the so-called primitive reflexes. According to current evidence persistence of the primitive reflexes is related to certain specific neuropsychiatric disorders. According to current knowledge there is no evidence whether these reflexes play a role in Attention Deficit and Hyperactivity Disorder (ADHD). To develop these findings we have tested a hypothesis whether ADHD children in the school age (8-11 years) will have higher level of persisting primitive reflexes Moro and Galant compared to a control group of children of the same age. Results of this study show that ADHD children have high occurrence of primitive reflexes compared to the control group, which indicates that ADHD symptoms may present a compensation of unfinished developmental stages related to diminishing Moro and Galant reflexes.

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Am J Med Genet Part B Neuropsychiatr Genet. 2013;162:44-54.

PHENOTYPE REFINEMENT FOR COMORBID ATTENTION DEFICIT HYPERACTIVITY DISORDER AND READING DISABILITY.

Sheikhi AR, Martin N, Hay D, et al.

Comorbidity between Attention Deficit Hyperactivity Disorder (ADHD) and reading disability (RD) is common; however, the heritability of this comorbidity is not well understood. This may be due to the complexity and heterogeneity of ADHD and RD phenotypes. Using alternative ADHD-RD sub-phenotypes instead of those arising from the DSM-IV may lead to greater success in the search for comorbid ADHD-RD susceptibility genes. Therefore, this study aims to refine ADHD-RD phenotypes into homogenous informative sub-phenotypes using latent class analysis (LCA). LCA was performed on 2,610 Australian twin families (6,535 individuals) in order to generate probabilistic genetically distinct classes that define ADHD-RD subtypes, including comorbidity, based on related symptom clusters. The LCA separated the phenotypes for ADHD and RD into nine classes. One class was unaffected; three classes demonstrated the three DSM-IV subtypes of ADHD, three subtypes showed different severities of RD, and two classes expressed a combination of RD and ADHD subtypes. LCA proved effective in refining the phenotypes of ADHD alone, RD alone, and ADHD-RD comorbidity, and its ability to classify them into homogenous groups based on clusters of symptoms, suggesting that the latent classes may be robust enough to use in molecular genetic studies.

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Am J Obstet Gynecol. 2013;208:S296.

ASSOCIATION BETWEEN PSYCHOSOCIAL DISORDER DURING PREGNANCY AND CHILDHOOD ATTENTION DEFICIT HYPERACTIVITY DISORDER BY GESTATIONAL AGE AND RACE/ETHNICITY.

Getahun D, Fassett M, Jacobsen S.

OBJECTIVE: Psychosocial distress disorder (PSD) during pregnancy is known to increase the risk of adverse perinatal outcomes. Because stressors during pregnancy may alter development of the fetal nervous system function and behavior later in life, we examined the association between PSD and childhood ADHD and whether the risk varies by gestational age and maternal race/ethnicity. STUDY

DESIGN: A nested case-control study of singleton born children age 3-11 years delivered at >28 weeks of gestation (n=81,678) in Kaiser Permanente Southern California (KPSC) hospitals (1991-2006) was performed using the Perinatal Service System, Hospital Inpatient, Outpatient physician encounter, and Pharmacy records. ICD-9 codes fromhos-pitalizations during pregnancy and infant birth certificates as well as pharmacy records on medication specific for PSD were used to ascertain the exposure and outcomes of interest. Adjusted odds ratio (OR) and 95% confidence interval (CI) were used to quantify the associations.

RESULTS: Five percent of pregnancies were complicated by PSD. Compared with control children, case children were more likely to be male and of White or African-American race/ethnicity. Case children were more likely than control children to be exposed to PSD (OR 1.6, 95%CI 1.4-1.8). A stratified analysis by gestational age revealed that case children born at 34-36, and 37-42 weeks of gestation, were significantly

more likely to be exposed to PSD (1.8-fold [95%CI 1.3, 2.5], and 1.6-fold [95%CI 1.4-1.8], respectively). PSD was associated with increased odds of ADHD across all racial/ethnic groups except Asian/Pacific Islanders.
CONCLUSION: The results suggest that maternal PSD during pregnancy is associated with increased risk of childhood ADHD. Identification of at-risk children may provide the opportunity for early diagnosis and initiate treatment when it is more effective.

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Am J Orthopsychiatry. 2013;83:126-30.
PSYCHOMETRIC PROPERTIES OF A NEW MEASURE TO ASSESS AUTISM SPECTRUM DISORDER IN DSM-5.
Coolidge FL, Marle PD, Rhoades CS, et al.
This article presents preliminary psychometric properties of a new 45-item scale, the Coolidge Autistic Symptoms Survey (CASS), designed to differentiate between children within the autism spectrum (including Asperger's Disorder) and purportedly normal children, in anticipation of DSM-5 changes, in which a single diagnostic category is proposed: autism spectrum disorder. The final sample (N = 72) consisted of 19 children diagnosed with Asperger's Disorder, 19 children who were considered loners by their parents (without an autism diagnosis), and 34 purportedly normal children. The CASS and the 200-item, DSM-IV-TR aligned, Coolidge Personality and Neuropsychological Inventory were completed by a parent. The CASS had excellent internal scale reliability ((alpha)= .97) and test-retest (r = .91) reliability. ANOVA revealed the CASS was able to discriminate significantly among the 3 groups of children. Further research with the CASS appears warranted.

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Behav Ther. 2013.
A RANDOMIZED CONTROLLED TRIAL OF A PARENT TRAINING AND EMOTION SOCIALIZATION PROGRAM FOR FAMILIES OF HYPERACTIVE PRESCHOOL-AGED CHILDREN.
Herbert SD, Harvey EA, Roberts JL, et al.
The present study evaluated the effectiveness of a parent training and emotion socialization program designed specifically for hyperactive preschoolers. Participants were 31 preschool-aged children whose parents were randomly assigned to a parent training (PT) or waitlist (WL) control group. PT parents took part in a 14-week parenting program that involved teaching parenting strategies for managing hyperactive and disruptive behavior as well as emotion socialization strategies for improving children's emotion regulation. Compared to WL mothers, PT mothers reported significantly less child inattention, hyperactivity, oppositional defiance, and emotional lability; were observed using significantly more positive and less negative parenting; and reported significantly less maternal verbosity and unsupportive emotion socialization practices. Results provide some support for the effectiveness of this parenting program for reducing attention-deficit hyperactivity disorder (ADHD) symptoms and associated problems in preschool-aged children.

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Behav Brain Funct. 2013;1.
ASSOCIATION BETWEEN THE GRM7 RS3792452 POLYMORPHISM AND ATTENTION DEFICIT HYPERACITIVEITY DISORDER IN A KOREAN SAMPLE.
Park S, Jung SW, Kim BN, et al.
Background: The purpose of this study was to investigate the association between the ionotropic and glutamate receptors, N-methyl D-asparate 2A (GRIN2A) and 2B (GRIN2B), and the metabotropic glutamate receptor mGluR7 (GRM7) gene polymorphisms and attention-deficit hyperactivity disorder (ADHD) in Korean population.
Methods: We conducted a case--control analysis of 202 ADHD subjects and 159 controls, performed a transmission disequilibrium test (TDT) on 149 trios, and compared scores from the continuous performance

test (CPT), the Children's Depression Inventory (CDI), and the State-Trait Anxiety Inventory for Children (STAIC) according to the genotype of the glutamate receptor genes.
Results: There were no significant differences in the genotype or allele frequencies of the GRIN2A rs8049651, GRIN2B rs2284411, or GRM7 rs37952452 polymorphisms between the ADHD and control groups. For 148 ADHD trios, the TDT analysis also showed no preferential transmission of the GRIN2A rs8049651 or GRIN2B rs2284411 polymorphisms. However, the TDT analysis of the GRM7 rs3792452 polymorphism showed biased transmission of the G allele (chi2 = 4.67, p = 0.031). In the ADHD probands, the subjects with GG genotype in the GRM7 rs37952452 polymorphism had higher mean T-scores for omission errors on the CPT than did those with the GA or AA genotype (t = 3.38, p = 0.001). In addition, the ADHD subjects who were homozygous for the G allele in the GRM7 rs37952452 polymorphism had higher STAIC-T (t = 5.52, p < 0.001) and STAIC-S (t = 2.74, p = 0.007) scores than did those with the GA or AA genotype.
Conclusions: These results provide preliminary evidence of an association between the GRM7 rs37952452 polymorphism and selective attention deficit and anxiety found within the Korean ADHD population.

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BMC Psychiatry. 2013;13.
THE CHILDREN'S ATTENTION PROJECT: A COMMUNITY-BASED LONGITUDINAL STUDY OF CHILDREN WITH ADHD AND NON-ADHD CONTROLS.
Sciberras E, Efron D, Schilpzand EJ, et al.
Background: Attention-Deficit/Hyperactivity Disorder (ADHD) affects approximately 5% of children worldwide and results in significant impairments in daily functioning. Few community-ascertained samples of children with ADHD have been studied prospectively to identify factors associated with differential outcomes. The Children's Attention Project is the first such study in Australia, examining the mental health, social, academic and quality of life outcomes for children with diagnostically-confirmed ADHD compared to non-ADHD controls. The study aims to map the course of ADHD symptoms over time and to identify risk and protective factors associated with differential outcomes.
Methods/design: The sample for this prospective longitudinal study is being recruited across 43 socio-economically diverse primary schools across Melbourne, Australia. All children in Grade 1, the second year of formal schooling (6-8 years), are screened for ADHD symptoms using independent parent and teacher reports on the Conners' 3 ADHD index (~N = 5260). Children screening positive for ADHD by both parent and teacher report, and a matched sample (gender, school) screening negative, are invited to participate in the longitudinal study. At baseline this involves parent completion of the NIMH Diagnostic Interview Schedule for Children IV (DISC-IV) to confirm likely ADHD diagnostic status and identify other mental health difficulties, direct child assessments (cognitive, academic, language and executive functioning; height and weight) and questionnaires for parents and teachers assessing outcomes, as well as a broad range of risk and protective factors (child, parent/family, teacher/school, and socio-economic factors). Families will be initially followed up for 3 years.
Discussion: This study is the first Australian longitudinal study of children with ADHD and one of the first community-based longitudinal studies of diagnostically confirmed children with ADHD. The study's examination of a broad range of risk and protective factors and ADHD-related outcomes has the potential to inform novel strategies for intervention and prevention.

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BMC Psychiatry. 2013;13.
COMORBIDITIES IN ADHD CHILDREN TREATED WITH METHYLPHENIDATE: A DATABASE STUDY.
Kraut AA, Langner I, Lindemann C, et al.
Background: Methylphenidate (MPH) is the most common drug treatment of attention deficit / hyperactivity disorder (ADHD) in children. Treatment with MPH is contraindicated in the presence of certain psychiatric, cerebro- and cardiovascular conditions. We assessed MPH treatment prevalence and incidence and the

frequency of comorbid conditions related to these contraindications in new MPH users compared to a control group without ADHD and ADHD medication.
Methods: We used health care data for the years 2004 to 2006 from the German Pharmacoepidemiological Research Database (GePaRD) which includes about 18% of the German population. MPH treatment prevalence and incidence was assessed based on at least one MPH prescription in the given year. In MPH users, the prevalence of psychiatric and other comorbidities was assessed in the quarter of the first MPH prescription and the three preceding quarters, whereas in controls it was assessed in the earliest four quarters of continuous insurance time starting at 01.01.2004 or the start of insurance if this was later. Differences in the presence of comorbid diagnoses between MPH users and controls were tested by logistic regression.
Results: In 2005, 1.5% of all children and adolescents aged 3 to 17 years (2.3% of males and 0.6% of females) received MPH in Germany. The proportion of children with a record of a psychiatric comorbidity in any of the nine ICD categories of diagnoses was substantially higher in new MPH users (83%) compared to controls (20%). Cerebro- and cardiovascular comorbidities were rare in general. Still, among new MPH users, 2% of males and females had a diagnosis of a pre-existing cardiovascular disorder but only 1.2% of controls.
Conclusions: Besides MPH treatment prevalence we first publish age-specific incidence rates for Germany. A high proportion of children who were started on MPH had a record of a psychiatric comorbidity preceding the first prescription. Cerebro- and cardiovascular conditions were rare in the studied age range, but still higher among children who received MPH than in the control group. Results show that in a substantial subgroup of patients, comorbidities require a thorough weighting of possible risks of MPH medication against the risks of untreated ADHD.

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Brain & Development. 2012 Nov;34:806-11.
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 Dev. 2013.
HIGH INCIDENCE OF SLEEP PROBLEMS IN CHILDREN WITH DEVELOPMENTAL DISORDERS: RESULTS OF A QUESTIONNAIRE SURVEY IN A JAPANESE ELEMENTARY SCHOOL.
Matsuoka M, Nagamitsu S, Iwasaki M, et al.
Objective: The aim of the present school-based questionnaire was to analyze the sleep problems of children with developmental disorders, such as pervasive developmental disorder and attention deficit hyperactivity disorder.
Methods: The sleep problems of 43 children with developmental disorders were compared with those of 372 healthy children (control group). All children attended one public elementary school in Kurume, Japan; thus, the study avoided the potential bias associated with hospital-based surveys (i.e. a high prevalence of sleep disturbance) and provided a more complete picture of the children's academic performance and

family situation compared with a control group under identical conditions. Children's sleep problems were measured with the Japanese version of the Children's Sleep Habits Questionnaire (CSHQ).
Results: Children with developmental disorders had significantly higher total CSHQ scores, as well as mean scores on the parasomnias and sleep breathing subscales, than children in the control group. The total CSHQ score, bedtime resistance, sleep onset delay, and daytime sleepiness worsened with increasing age in children with developmental disorders; in contrast, these parameters were unchanged or became better with age in the control group. In children with developmental disorders, there was a significant association between a higher total CSHQ score and lower academic performance, but no such association was found in the control group. For both groups, children's sleep problems affected their parents' quality of sleep. There were no significant differences in physical, lifestyle, and sleep environmental factors, or in sleep/wake patterns, between the two groups.
Conclusions: Children with developmental disorders have poor sleep quality, which may affect academic performance. It is important for physicians to be aware of age-related differences in sleep problems in children with developmental disorders. Further studies are needed to identify the association between sleep quality and school behavioral performance.

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Brain Injury. 2012 Dec;26:1564-73.
VIRTUAL REALITY AS A SCREENING TOOL FOR SPORTS CONCUSSION IN ADOLESCENTS.
Nolin P, Stipanicic A, Henry M, et al.
Primary objective: There is controversy surrounding the cognitive effects of sports concussion. This study aimed to verify whether the technique of virtual reality could aid in the identification of attention and inhibition deficits in adolescents.
Study design: A prospective design was used to assess 25 sports-concussed and 25 non-sports-concussed adolescents enrolled in a sport and education programme.
Methods and procedures: Participants were evaluated in immersive virtual reality via ClinicaVR: Classroom-CPT and in real life via the traditional VIGIL-CPT.
Main outcomes and results: The neuropsychological assessment using virtual reality showed greater sensitivity to the subtle effects of sports concussion compared to the traditional test, which showed no difference between groups. The results also demonstrated that the sports concussion group reported more symptoms of cybersickness and more intense cybersickness than the control group.
Conclusions: Sports concussion was associated with subtle deficits in attention and inhibition. However, further studies are needed to support these results.

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Brain Topogr. 2013;26:135-51.
DIAGNOSTIC VALUE OF RESTING ELECTROENCEPHALOGRAM IN ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER ACROSS THE LIFESPAN.
Liechti MD, Valko L, Muller UC, et al.
The resting electroencephalogram (EEG) reflects development and arousal, but whether it can support clinical diagnosis of attention-deficit/hyperactivity disorder (ADHD) remains controversial. Here we examined whether theta power and theta/beta ratio are consistently elevated in ADHD and younger age as proposed. Topographic 48-channel EEG from 32 children (8-16 years) and 22 adults (32-55 years) with ADHD and matched healthy controls (n = 30 children/21 adults) was compared. Following advanced artefact correction, resting EEG was tested for increased theta and theta/beta activity due to ADHD and due to normal immaturity. Discriminant analyses tested classification performance by ADHD and age using these EEG markers as well as EEG artefacts and deviant attentional event-related potentials (ERPs). No consistent theta or theta/beta increases were found with ADHD. Even multivariate analyses indicated only marginal EEG power increases in children with ADHD. Instead, consistent developmental theta decreases were observed, indicating that maturational lags of fewer than 3 years would have been detected in children. Discriminant analysis based on proposed simple spectral resting EEG markers was successful for age but not for ADHD (81 vs. 53 % accuracy). Including ERP markers and EEG artefacts improved

discrimination, although not to diagnostically useful levels. The lack of consistent spectral resting EEG abnormalities in ADHD despite consistent developmental effects casts doubt upon conventional neurometric approaches towards EEG-based ADHD diagnosis, but is consistent with evidence that ADHD is a heterogeneous disorder, where the resting state is not consistently characterised by maturational lag.

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Clinical Child and Family Psychology Review. 2012 Dec;15:279-302.

CO-OCCURRING MENTAL HEALTH PROBLEMS AND PEER FUNCTIONING AMONG YOUTH WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A REVIEW AND RECOMMENDATIONS FOR FUTURE RESEARCH.

Becker SP, Luebbe AM, Langberg JM.

It is well established that children and adolescents with attention-deficit/hyperactivity disorder (ADHD) frequently experience co-occurring mental health problems in addition to difficulties in their peer relationships. Although substantial research has focused on the extent to which peer functioning contributes to subsequent co-occurring mental health problems, much less research has considered how co-occurring mental health problems affect peer functioning domains. Therefore, the purpose of this review is to examine the effect of co-occurring mental health problems on the peer functioning of youth with ADHD. The impact of co-occurring externalizing (i.e., oppositional defiant disorder, conduct disorder) and internalizing (i.e., anxiety, depression) symptoms are reviewed, with a focus on whether these co-occurring symptoms exacerbate, attenuate, or have no effect across peer domains of social skills/competence, peer status, and friendship among youth with ADHD. Drawing from a developmental psychopathology framework, this review then draws attention to relevant causal processes and developmental cascades (including social-cognitive, affective, and family and parenting factors) in offering promising avenues for future work.

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Clinical Child and Family Psychology Review. 2012 Dec;15:303-29.

DEVELOPMENTAL CONTEXT AND TREATMENT PRINCIPLES FOR ADHD AMONG COLLEGE STUDENTS.

Fleming AP, McMahon RJ .

Attention-deficit/hyperactivity disorder (ADHD) affects between 2 and 8 % of college students. ADHD is associated with impaired academic, psychological, and social functioning, and with a wide array of negative outcomes including lower GPAs, graduation rates, and self-reported quality of life. The college environment often brings decreased external structure and increased availability of immediate rewards, presenting added demands for behavioral self-regulation—an area in which students with ADHD are already vulnerable. Despite the significant impact of ADHD in college and the unique challenges presented by the college context, virtually no treatment development research has been conducted with this population. In order to provide a framework to guide intervention development, this comprehensive review integrates research from three key domains that inform treatment for college students with ADHD: (1) functional impairment associated with ADHD among college students, (2) etiology of ADHD and the developmental context for ADHD among emerging adults (age 18–24), and (3) treatment outcome research for ADHD among adolescents and adults.A detailed set of proposed treatment targets and intervention principles are identified, and key challenges associated with treatment development in this population are discussed.

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Dev Med Child Neurol. 2013;55:39.

IS METHYLPHENIDATE SAFE FOR CHILDREN WITH EPILEPSY & ADHD?

Sikkander S, Nirmal S, Doddamani L.

Introduction: Epilepsy is one of the common co morbid conditions associated with ADHD. Evidence suggest that around 30% of children with epilepsy can have ADHD, however not all are treated for the ADHD. This is due to concerns around diagnostic issues and possible seizure exacerbations. Problems with inattention and/or impulsivity may arise in children with epilepsy or epilepsy could be seen in children

with ADHD, for any of the following reasons: associated underlying brain damage or dysfunction, adverse effects of medication, or causes related specifically to the epilepsy. It is important to ensure that the management (ie diagnosis, identification of co morbidity, and treatment of symptoms) of the child is appropriate. If epileptiform discharges are causing the ADHD symptoms then child needs optimisation of antiepileptic medication. If ADHD is the problem then appropriate stimulant medication along with antiepileptic should be considered for alleviation of the symptoms. We present to you our experience about managing these complex children reviewed as a part an audit.
Method: Notes analysis of patients with diagnosis of Epilepsy and ADHD.
Results: We had 18 patients on both medication (ie AED &Medication for ADHD). Out of them 17 (95%) had good seizure control. The other patient had epilepsy prior to the diagnosis of ADHD and had no change in seizure frequency after starting on Medication for ADHD.
Discussion: We would like to highlight that methylphenidate did not cause seizure exacerbations in children with epilepsy and ADHD in our study. Treatment with methylphenidate is very likely to be effective and appears to be safe.

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Dev Med Child Neurol. 2013;55:58.

AUDIT ON ASSESSMENT OF GROWTH PARAMETERS IN CHILDREN WITH ADHD ON TREATMENT.

Ganesan S, Omer R, Ikhena E, et al.

Severe symptoms of ADHD (Attention Deficit Hyperactivity Disorder) in children are treated with medications along with behavioural management. However, it has varied side effects including concerns about affecting the growth profile. There are reports in the literature that long term medication can affect the height profile thereby reducing the final adult height. We conducted this audit to find out our practise in managing the children with severe ADHD in Lincolnshire and also to find out any long term effect of medications that can affect the growth. It is a retrospective analysis based on collecting the data from 25 clinical medical records from Grantham ADHD clinics. NICE guideline 2008 for ADHD was taken as the standard. Two-thirds are male and 85%had medications when they were 6 to 10 years old. 92% had plotted growth chart against the recommended standard of 100%. Equasym XL was the preferred drug (50%) for the initial treatment. The average dose ofMethylphenidate (65%) on clinical review was 20 to 40 mg. Growth concerns were observed in 48% during the treatment with height deficit in 16%. No specific correlation to the dose change, preparation of medication noted. Growth faltering was noticed during initial stages of treatment (1-3yr). Management of severe ADHD with medications is challenging. It is essential to actively monitor growth with regular reviews and prompt action to be taken if there are any concerns. Our study findings are consistent with various studies and NICE guidelines on ADHD management. Though height parameters have showed improvement following various active interventions, the true adult height potential is unknown. But it has to be said that height faltering is not a threatening side effect as previously thought. Everyone should be aware of possible growth faltering following medication and it should be discussed with the parents in detail.

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Developmental Science. 2012 Nov;15:791-800.

TEMPORAL DISCOUNTING OF MONETARY REWARDS IN CHILDREN AND ADOLESCENTS WITH ADHD AND AUTISM SPECTRUM DISORDERS.

Demurie E, Roeyers H, Baeyens D, et al.

It has been difficult to differentiate attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) in terms of some aspects of their cognitive profile. While both show deficits in executive functions, it has been suggested that they may differ in their response to monetary reward. For instance, children with ADHD prefer small immediate over large delayed rewards more than typically developing controls. One explanation for this is that they discount the value of rewards to a higher degree as they are moved into the future. The current study investigated whether children with ADHD can be differentiated from those with ASD in terms of reward discounting. Thirty-nine children (8–16 y) with ADHD, 34 children with ASD and 46 typically developing controls performed a hypothetical monetary temporal discounting

task. Participants were instructed to make repeated choices between small variable rewards (0, 5, 10, 20, 30€) delivered immediately and large rewards delivered after a variable delay. Children with ADHD but not ASD discounted future rewards at a higher rate than typically developing controls. These data confirm steeper discounting of future rewards in ADHD and add to a small but growing literature showing that the psychological profile of ADHD can be distinguished from that of ASD in terms of disrupted motivational processes.

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Eur Child Adolesc Psychiatry. 2012;1-7.

PREVALENCE OF ALLERGIC RHINITIS IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A POPULATION-BASED STUDY.

Chou PH, Lin CC, Lin CH, et al.

Allergic rhinitis (AR) is common in children. Characteristic symptoms of AR may result in daytime inattention, irritability, and hyperactivity, which are also components of ADHD. Conflicting data in previous studies exist regarding the relationship between ADHD and AR. The aim of this study was to examine the prevalence and risk of AR in ADHD patients in Taiwan. We conducted a cross-sectional study using the National Health Insurance Research Database in Taiwan. The study subjects included 469 patients who received psychiatric care for ADHD in 2005 and the general population (n = 220,599). Distributions of age, gender, and living areas as well as allergic diseases in the general population and in the ADHD group were examined by (chi)2 tests. Multivariate logistic regression models were used to analyze the risk factors of AR. The prevalence of AR in ADHD group and the general population was 28.4 and 15.2 %, respectively. The prevalence of asthma was 9.6 % in ADHD group and 6.4 % in the general population. Both the prevalence of AR ($p < 0.001$) and asthma ($p = 0.008$) was significantly higher in ADHD group than the general population. The multivariate logistic regression analysis showed that ADHD patients had an increased rate of AR than general population (OR = 1.83; 95 % CI = 1.48-2.27; $p < 0.0001$), and asthma was strongly associated with AR (OR = 9.28; 95 % CI = 8.95-9.63; $p < 0.0001$). Our data showed that ADHD patients had an increased rate of AR. Therefore, psychiatrists should be more aware of the comorbidity of AR when treating ADHD patients.

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Eur Child Adolesc Psychiatry. 2013;1-10.

DIFFERENCES IN PREDICTORS OF TRADITIONAL AND CYBER-BULLYING: A 2-YEAR LONGITUDINAL STUDY IN KOREAN SCHOOL CHILDREN.

Yang SJ, Stewart R, Kim JM, et al.

Traditional bullying has received considerable research but the emerging phenomenon of cyber-bullying much less so. Our study aims to investigate environmental and psychological factors associated with traditional and cyber-bullying. In a school-based 2-year prospective survey, information was collected on 1,344 children aged 10 including bullying behavior/experience, depression, anxiety, coping strategies, self-esteem, and psychopathology. Parents reported demographic data, general health, and attention-deficit hyperactivity disorder (ADHD) symptoms. These were investigated in relation to traditional and cyber-bullying perpetration and victimization at age 12. Male gender and depressive symptoms were associated with all types of bullying behavior and experience. Living with a single parent was associated with perpetration of traditional bullying while higher ADHD symptoms were associated with victimization from this. Lower academic achievement and lower self esteem were associated with cyber-bullying perpetration and victimization, and anxiety symptoms with cyber-bullying perpetration. After adjustment, previous bullying perpetration was associated with victimization from cyber-bullying but not other outcomes. Cyber-bullying has differences in predictors from traditional bullying and intervention programmes need to take these into consideration.

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Eur Neuropsychopharmacol. 2013.

EUROPEAN, RANDOMIZED, PHASE 3 STUDY OF LISDEXAMFETAMINE DIMESYLATE IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Coghill D, Banaschewski T, Lecendreux M, et al.

This study evaluated the efficacy and safety of lisdexamfetamine dimesylate (LDX) compared with placebo in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) in Europe. Osmotic-release oral system methylphenidate (OROS-MPH) was included as a reference arm. Patients (6-17 years old) with a baseline ADHD Rating Scale version IV (ADHD-RS-IV) total score (greater-than or equal to)28 were randomized (1:1:1) to dose-optimized LDX (30, 50, or 70 mg/day), OROS-MPH (18, 36, or 54 mg/day) or placebo for 7 weeks. Primary and key secondary efficacy measures were the investigator-rated ADHD-RS-IV and the Clinical Global Impressions-Improvement (CGI-I) rating, respectively. Safety assessments included treatment-emergent adverse events (TEAEs), electrocardiograms, and vital signs. Of 336 patients randomized, 196 completed the study. The difference between LDX and placebo in least squares mean change in ADHD-RS-IV total score from baseline to endpoint was -18.6 (95% confidence interval [CI]: -21.5 to -15.7) ($p<0.001$; effect size, 1.80). The difference between OROS-MPH and placebo in least squares mean change in ADHD-RS-IV total score from baseline to endpoint was -13.0 (95% CI: -15.9 to -10.2) ($p<0.001$; effect size, 1.26). The proportions (95% CI) of patients showing improvement (CGI-I of 1 or 2) at endpoint were 78% (70-86), 14% (8-21), and 61% (51-70) for LDX, placebo, and OROS-MPH. The most common TEAEs for LDX were decreased appetite, headache, and insomnia. Mean changes in vital signs were modest and consistent with the known profile of LDX. LDX was effective and generally well tolerated in children and adolescents with ADHD.

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Eur Psychiatry. 2013.

SAFETY OF PHOSPHATIDYLSERINE CONTAINING OMEGA3 FATTY ACIDS IN ADHD CHILDREN: A DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL FOLLOWED BY AN OPEN-LABEL EXTENSION.

Manor I, Magen A, Keidar D, et al.

Objective: To evaluate the safety of phosphatidylserine (PS) enriched with omega3 fatty acids, mainly eicosapentaenoic (PS-Omega3) in children with attention-deficit hyperactivity disorder (ADHD).

Methods: Two hundred children diagnosed with ADHD were randomised to receive either PS-Omega3 (300 mg PS-Omega3/day) or placebo for 15 weeks. One hundred and fifty children continued into an open-label extension for an additional 15 weeks in which they all consumed PS-Omega3 (150 mg PS-Omega3/day). Standard blood biochemical and haematological safety parameters, blood pressure, heart rate, weight and height were evaluated. Adverse events and the Side Effect Rating Scale were also assessed.

Results: One hundred and sixty-two participants completed the double-blind phase. No significant differences were noted between the two study groups in any of the safety parameters evaluated. One hundred and forty participants completed the open-label phase. At the end of this phase, no significant changes from baseline were observed in any of the studied parameters among participants who consumed PS-Omega3 for 30 weeks.

Conclusions: Study results demonstrate that consumption of PS-Omega3 by children with ADHD, as indicated in a 30-week evaluation period, is safe and well tolerated, without any negative effect on body weight or growth.

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Front Syst Neurosci. 2012.

DISTINCT NEURAL SIGNATURES DETECTED FOR ADHD SUBTYPES AFTER CONTROLLING FOR MICRO- MOVEMENTS IN RESTING STATE FUNCTIONAL CONNECTIVITY MRI DATA.

Fair DA, Nigg JT, Iyer S, et al.

In recent years, there has been growing enthusiasm that functional MRI could achieve clinical utility for a broad range of neuropsychiatric disorders. However, several barriers remain. For example, the acquisition of large-scale datasets capable of clarifying the marked heterogeneity that exists in psychiatric illnesses will

need to be realized. In addition, there continues to be a need for the development of image processing and analysis methods capable of separating signal from artifact. As a prototypical hyperkinetic disorder, and movement related artifact being a significant confound in functional imaging studies, ADHD offers a unique challenge. As part of the ADHD-200 Global Competition and this special edition of Frontiers, the ADHD-200 Consortium demonstrates the utility of an aggregate dataset pooled across five institutions in addressing these challenges. The work aimed to A) examine the impact of emerging techniques for controlling for "micro-movements," and B) provide novel insights into the neural correlates of ADHD subtypes. Using SVM based MVPA we show that functional connectivity patterns in individuals are capable of differentiating the two most prominent ADHD subtypes. The application of graph-theory revealed that the Combined (ADHD-C) and Inattentive (ADHD-I) subtypes demonstrated some overlapping (particularly sensorimotor systems), but unique patterns of atypical connectivity. For ADHD-C, atypical connectivity was prominent in midline default network components, as well as insular cortex; in contrast, the ADHD-I group exhibited atypical patterns within the dlPFC regions and cerebellum. Systematic motion-related artifact was noted, and highlighted the need for stringent motion correction. Findings reported were robust to the specific motion correction strategy employed. These data suggest that rs-fcMRI data can be used to characterize individual patients with ADHD and to identify neural distinctions underlying the clinical heterogeneity of ADHD.

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Genet Mol Biol. 2012;35:932-38.

THE BRAZILIAN CONTRIBUTION TO ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MOLECULAR GENETICS IN CHILDREN AND ADOLESCENTS.

Genro JP, Roman T, Rohde LA, et al.

Attention-Deficit/Hyperactivity Disorder (ADHD) is a common psychiatric condition of children worldwide. This disorder is defined by a combination of symptoms of inattention and hyperactivity/impulsivity. Diagnosis is based on a sufficient number of symptoms causing impairment in these two domains determining several problems in personal and academic life. Although genetic and environmental factors are important in ADHD etiology, how these factors influence the brain and consequently behavior is still under debate. It seems to be consensus that a fronto-subcortical dysfunction is responsible, at least in part, for the ADHD phenotype spectrum. The main results from association and pharmacogenetic studies performed in Brazil are discussed. The investigations performed so far on ADHD genetics in Brazil and elsewhere are far from conclusive. New plausible biological hypotheses linked to neurotransmission and neurodevelopment, as well as new analytic approaches are needed to fully disclose the genetic component of the disorder.

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HealthMED. 2012;6:3822-25.

PHYSICAL ACTIVITY IN ADHD CHILDREN TREATMENT.

Zivkovic D, Zivanovic N, Zivkovic M, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a chronic condition that affects preor very young schoolchildren. It often persists into adolescence and adulthood - with some changes in symptoms. Basic ADHD symptoms include difficulty sustaining attention, impulsive behavior and hyperactivity. Our research problem was to determine if physical exercising will exert any influence on children's psychological performance, more exactly if physical exercising can eliminate negative effects of ADHD affecting children's behavior and thus enhance their health. Research subject is psychological indicators of behavior (ten indicators according to Iowa Conners Rating Scale) of ADHD children observed prior, during and after the physical exercising treatment. Bearing in mind that up to now ADHD treatment ensued medications with numerous toxic side effects our research aim was to determine ways physical exercising can help young school children with ADHD so as to reduce or eliminate use of medications.

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IEEE Trans Biomed Eng. 2013;60:159-63.

DYNAMICAL NONSTATIONARITY OF RESTING EEGS IN PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (AD/HD).

Latchoumane CFV, Kim IH, Sohn H, et al.

This study applied dynamical nonstationarity analysis (DNA) to the resting EEGs of patients with attention-deficit/hyperactivity disorder (AD/HD). We aimed to assess and characterize AD/HD using features based on the local and global duration of dynamical microstate. We hypothesized that AD/HD patients would have difficulties in maintaining stable cognitive states (e.g., attention deficit and impulsivity) and that they would thus exhibit EEGs with temporal dynamics distinct from normal controls, i.e., rapidly and frequently changing dynamics. To test this hypothesis, we recorded EEGs from 12 adolescent subjects with AD/HD and 11 age-matched healthy subjects in the resting state with eyes closed and eyes open. We found that AD/HD patients exhibited significantly faster changes in dynamics than controls in the right temporal region during the eyes closed condition, but slower changes in dynamics in the frontal region during the eyes open condition. AD/HD patients exhibited a disruption in the rate of change of dynamics in the frontotemporal region at rest, probably due to executive and attention processes. We suggest that the DNA using complementary local and global features based on the duration of dynamical microstates could be a useful tool for the clinical diagnosis of subjects with AD/HD.

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Indian J Psychiatry. 2012;54:S110.

A COMPARATIVE STUDY OF SOCIO-DEMOGRAPHIC PROFLE, PSYCHIATRIC CO-MORBIDITIES AND GLOBAL FUNCTIONING OF ADOLESCENTS WITH OCD AND ADHD.

Rathi A, Sitholey P, Agarwal V, et al.

Aim: Attention-defcit hyperactivity disorder (ADHD) and obsessive compulsive disorder (OCD) are two of the most common childhood and adolescent neuropsychiatric disorders. Adolescents with these disorders have various psychiatric co-morbidities and impairments in various domains of life. This study was conducted to study and compare the socio-demographic profle, psychiatric co-morbidities and global functioning of Indian adolescents suffering from these disorders.

Methods: 57 Adolescents (36 having ADHD and 21 having OCD) between the age group 13 years to less than 18 years were recruited during the study period. Semi-structured proforma for socio-demographic details, K-SADS and clinical interview for psychiatric co-morbidities and CGAS was applied to study the global functioning of these adolescents. The two groups were compared with each other using appropriate statistical methods.

Results: A signifcantly greater number of subjects in the OCD group were from rural areas (42.9%) and had a family income of <6000 INR (47.6%) as compared to the ADHD adolescents (8.3% & 16.7% respectively). Signifcantly greater numbers of adolescents with ADHD had more than one psychiatric co-morbidity (63.9%) as compared to the adolescents with OCD (28.6%). The prevalence of ODD and SLD was signifcantly greater in ADHD adolescents whereas major depressive disorder and conversion disorder was signifcantly greater in adolescents with OCD. The global functioning of ADHD adolescents was signifcantly lower than adolescents with OCD.

Conclusion: The present fndings have implications in the planning of treatment interventions in these adolescents, to make them more cost effective and efficient.

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Indian J Psychiatry. 2012;54:S57.

A CASE REPORT ON ADHD WITH LEARNING DISABILITIES HAVING MINOR PHYSICAL ANOMALIES AND NEUROLOGICAL SOFT SIGNS.

Vijay BG, Arvind N, Nitin S, et al.

Background: ADHD is the commonest psychiatric disorder in children associated with co-morbidities. It used to be called earlier as minimal brain dysfunction, having structural brain changes and neurological soft signs.

Case history: A 10 yr old male child with a family history of celiac sprue in the elder sister and hypothyroidism on the maternal side had complaints of diffculties in motor activities, restlessness, inability to concentrate, inappropriate sociability, diffculty in understanding things, for last 7 years. Personal history showed neonatal jaundice, delayed developmental motor milestones accompanying physical fndings of genu valgus deformity of both legs, ankle eversion, arm length span > height, right retractile testis. Minor physical anomalies of low set ears (Rt > Lt), acromial dimples, deep sacral dimples, wide space between 1st and 2nd toes, Grade 4 power in all muscles of limbs with neurological soft signs (to be shared during presentation). On MSE the child was overfamiliar, hyperactive, over-talkative, distractible, and had a cheerful affect. Investigations revealed bilateral dilated ventricles on CT scan, diffuse cerebral and cerebellar atrophy suggestive of white matter defcits and dilated lateral and 3rd ventricle on MRI. qEEG showed spike and spike slow wave in right temporal as well as bitemporal regions. Biochemical tests showed lowered lipid profle, and raised alkaline phosphatase. Psychological tests- Assessment on NIMHANS Specifc Learning Disability Battery revealed reading level of Lower KG in English and Upper KG in Hindi; also lower KG level in arithmetic. Neuropsychological Test (NEPSY) revealed executive function defcits. Verbal IQ on MISIC was 81.5; Performance IQ could not be done due to inattention. Attention span increased up to 30mins using techniques of grain sorting, coloring within lines, etc and he was later discharged on oral carbamazepine 200 mg and risperidone 1 mg. Genetic and chromosomal studies are planned to rule out the possibility of Williams Syndrome (Q93.8). These details along with management issues will be shared in the case report.
Conclusion: Very few cases having so many neurobiological underpinnings have been reported from India.

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Indian J Psychiatry. 2012;54:S87.

IS ADULT ADHD A VALID DIAGNOSIS?

Johnson J.

Attention defcit hyperactivity disorder is not just a problem in children. ADHD often goes unrecognized throughout childhood and there is a lack of awareness even amongst the psychiatric fraternity. There are far reaching consequences for untreated ADHD with substantial impact on the affected individual's mental health, occupation and relationships. It is also well recognized that patients with untreated ADHD are more likely to abuse illicit drugs with an increased likelihood of coming in contact with the criminal justice system. The subtlety and subjectivity of ADHD symptoms in adults, together with the absence of a single <<gold standard>> for confrming the diagnosis, makes assessment particularly challenging. Evaluation of adults with symptoms of ADHD requires weighing and integrating a range of data, including the patient's history, the patient's self-report of symptoms, collateral history and mental state examination. Moreover most adults with ADHD do not have a <<pure>> form of the disorder. Co-morbidity is more likely to be the rule than the exception. The NICE guidelines recommend that adults with ADHD should also have the beneft of assessment and treatment. This is a far-reaching conclusion, and should lead to a radical change in mental health practice, with adult psychiatry taking on ADHD as part of its remit. Further, NICE recommends that more research is needed on treatments for adults, in particular psychological treatments. The guidance clearly states that transitional arrangements need to be developed. In some parts of the country (UK) adult psychiatrists are comfortable with treating ADHD, in other areas they are not, essentially resulting in a postcode lottery for patients. NICE is therefore recommending that each region should set up a planning group to make the best use of the local resources and ensure a continuing care pathway into adult life for ADHD sufferers. In response to the NICE guidance, we audited existing practice for diagnosis and treatment in children and adults. Based on the audit fndings of a lack of transitional arrangements, we obtained support and fnancial assistance from the commissioners to set up a new <<Transitional and Adult ADHD service>>. Within 12 months we have in excess of 100 patients from our catchment area and referrals from a number of neighboring Trusts where such a service is not available. In summary – although

ADHD is a well established diagnosis in children there is limited awareness of the condition in adults and very limited research in this feld. Our fndings could be replicated in India with immense scope for developing pharmacological and psychosocial treatment pathways in adults.

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Indian J Psychiatry. 2012;54:S63.

BALANCE IMPAIRMENT IN CHILDREN WITH ADHD, ASD, PDD, MBD.

Bajaj P, Chhabria A.

Children with poor academic performance and behavior problems, originally referred for psychiatric assessment and treatment, were evaluated for developmental neurological impairment. Attention defcit and hyperactivity are a given in these children. They were further referred to a physiotherapist for a balance evaluation. Motor defcits such as hypotonia (scapular, trunk, hip, fnger), head tilts, gaze stability defcits (including nystagmus) were also present. It is known that sensory integration disorders: tactile, visual, auditory and vestibular perceptual defcits may be the underlying mechanism for ADHD. The aim of this study is to examine: 1. The incidence of balance impairments (specifcally motor vestibular defcits) in ADHD, ASD, PDD and 2. Outcomes in these children treated for balance impairments.

Methodology: Over a period of 3 years, 40 children in the age group of 3-15 years were evaluated. 30 were evaluated clinically and 10 were evaluated in addition, by computerized dynamic posturography. We focused on vestibular defcits and their treatment over a period of six months. Motor vestibular function includes gaze stability and postural stability.

Results: During evaluation only 2 cases did not show balance impairment while 38 showed some variant of vestibulo- cerebellar defcits. 10 children were non-compliant with treatment. Of the 28 remaining subjects, 25 showed remarkable improvement by treatment of motor vestibular defcits in the felds of: Motor skills [gross (including sports) and fne (including handwriting)] Academics, concentration/ attention defcit improvement Hyperactivity decrease

Conclusion: We have shown that physiotherapy for balance impairments has a large role to play as a therapeutic modality, along with remedial education, as a viable alternative to drug therapy (especially in mild to moderate cases) and as an adjunct in the severe cases.

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Int Clin Psychopharmacol. 2012;28:e44-e45.

BIPOLAR DISORDER AND ADHD. DIFFERENT ASPECTS OF THE SAME PSYCHOPATHOLOGICAL ENTITY OR JUST COMORBIDITIES? AN INTERESTING CASE REPORT.

Bonotis K, Zerdelis A.

Background: Comorbidity between BD and ADHD has been estimated as high while this correlation remains unclear (Faraone et al., 1997; Zepf, 2009; Youngstrom et al., 2010) In this case report we are discussing a case of a 33-years-old male with an interesting psychiatric history tracing back to his juvenile times.

Main clinical features: He was born with the help of forceps. Through his first decade of life failed to develop proper social activities and create interpersonal relationships effectively. It was also noted that he was very inattentive in school activities. At the age of 11, following a head injury with a ball, he presented dizziness, gait disturbance and irritability as he was crying and worrying about past events and experiencing negativism. It is noted that he was unable to distinguish real events of life from his dreams. In these terms he was admitted to the hospital and acute brain infection/inflammation was ruled out which was negative. The EEG was also normal. He was treated with antidepressants with poor response and later on he developed generalized fear and coprolalia. Gilles de la Tourette was suspected and he was started on haloperidol which was not well tolerated. After those events he was transferred to pediatric psychiatry department and there he manifested two-week long mutism. After careful history-taking and observation the diagnosis of bipolar disorder was established. He was started on mood stabilizers and he responded very well. By this time, symptoms of attention deficit and extreme hyperactivity/ impulsivity were observed and the diagnosis of ADHD was also made. Since then he has been hospitalized many times for exacerbations of bipolar disorder, either manic or depressive ones. During the later, he states that he is

somnolent and experiences psychomotor retardation. During the manic diversion and milder during his normothymic state, his main symptomatology stems from his impulsivity and inattentiveness. As a result, he is generally unable to sustain viable interpersonal relationships and this is an additive cause of anxiety to his baseline psychopathology. A recent psychometric evaluation revealed a borderline intelligence (I.Q=80) with deviation between verbal and practical intelligence (V.I>P.I.). During the last 7 years he is experiencing frequent episodes of syncope without objective etiology being identified. The psychopharmacological approaches are summarized in his current treatment which consists of: valproate (1500mg), olanzapine (20mg), quetiapine (400mg), lorazepam (2,5mg), lamotrigine (100mg), thyroxine (100mg history of hypothyroidism). It should be noted that there is no psychiatric history in his family which is very supportive to him whatsoever.
Conclusion: The overlapping symptoms in this patient complicate both the diagnosis and treatment. This case indicates the need for further investigation.

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Int J Eating Disord. 2013;46:39-46.
PARENT REPORTED INATTENTION AND HYPERACTIVITY/IMPULSIVITY AS PREDICTOR OF LONG-TERM WEIGHT LOSS AFTER INPATIENT TREATMENT IN OBESE ADOLESCENTS.
Van Egmond-Froehlich A, Claussnitzer G, Dammann D, et al.
Objective: The long-term success of treatment for pediatric obesity is often unsatisfactory and variable. We aim to elucidate the influence of inattention and hyperactivity/impulsivity on weight loss after inpatient treatment for adolescent obesity.
Method: We included 13-17 year old obese participants treated in three inpatient multidisciplinary treatment centers. At the beginning and end of treatment and at one year follow-up weight and height were measured. Inattention and hyperactivity/impulsivity was assessed with the hyperactivity/inattention (HI) subscale of the parent-rated Strengths and Difficulties Questionnaire. General linear models were used with the standard deviation scores of the &#4;body mass index (BMI-SDS) as dependent variable.
Results: Totally, 253 participants were included (65% female, age: 15.3 (plus or minus) 1.4 years, baseline BMI-SDS: 3.13 (plus or minus) 0.38 kg/m2). HI scores were associated with long-term (p <.001) but not short term (ns) weight loss.
Discussion: This indicates that inattention and hyperactivity/impulsivity is associated with reduced long-term weight loss success in adolescent inpatients.

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Int J Disabil Hum Dev. 2011;10:81-85.
UNINTENTIONAL INTRUSIVE PARTICIPATION IN MULTIMEDIA INTERACTIVE ENVIRONMENTS.
Williams C.
This paper presents data from two independent case studies: a 15-year-old female with cerebral palsy and related profound and multiple learning difficulties, and a 7-year-old male with extreme behaviour associated with autistic spectrum disorder. An audiovisual immersive interactive environment was developed to encourage creative interaction and expression from the participants. In both case studies, there were support workers present and it was the interventions of these support staff which are the main focus of this paper. Results indicated that profuse but unintentional interventions from the staff could have distorted interaction with, dissuaded or diverted participants from meaningful engagements with the reactive feedback provided by the system.

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Invest Clin. 2012;53:353-64.

PREVALENCE OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN VENEZUELAN COLLEGE STUDENTS. PRELIMINARY FINDINGS.

Montiel-Nava C, Leon SO, Medrano AJ, et al.

The aim of this study was to estimate the frequency of the attention deficit/hyperactivity disorder in college students. The sample was constituted by 411 college students, ages between 17 and 47 years, attending the School of Education at the Universidad del Zulia, 1st thru 5th semester. The identification of probable cases was performed by using the ASR-S v1.1 and FASCT as screening instruments. For the second part of the diagnostic process, students with positive scores in both screening measures were selected to be interviewed using the M.I.N.I plus. Results indicated that the estimated prevalence of ADHD in college students is 4.8%, with a behavioral profile which suggests that hyperactivity-impulsivity symptoms were predominant in this sample. Comorbidity related to the ADHD diagnosis was 35%. A prevalence estimate of 4.35% should be considered as an alert sign for the need of diagnostic and treatment of this population.

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J Abnorm Child Psychol. 2012 Nov;40:1289-300.

LONGITUDINAL PREDICTORS OF SCHOOL-AGE ACADEMIC ACHIEVEMENT: UNIQUE CONTRIBUTIONS OF TODDLER-AGE AGGRESSION, OPPOSITIONALITY, INATTENTION, AND HYPERACTIVITY.

Brennan LM, Shaw DS, Dishion TJ, et al.

This project examined the unique predictive validity of parent ratings of toddler-age aggression, oppositionality, inattention, and hyperactivity-impulsivity to academic achievement at school-age in a sample of 566 high-risk children and families. The study also investigated potential indirect effects of the Family Check-Up on school-age academic achievement through changes in child behavior problems. The results demonstrated that toddler-age aggression was most consistently associated with school-age academic achievement, albeit modestly. Moreover, findings showed that the intervention predicted greater decreases in aggression from ages 2–3 to 4–5 compared to controls. The results suggest that in high-risk toddler-aged children, aggression may be a more consistent predictor of school-age academic achievement than other externalizing dimensions, which has implications for early identification and efforts to promote children's adaptation.

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J Abnorm Child Psychol. 2012 Nov;40:1313-26.

A CROSS-LAGGED MODEL OF THE DEVELOPMENT OF ADHD INATTENTION SYMPTOMS AND RAPID NAMING SPEED.

Arnett AB, Pennington BF, Willcutt E, et al.

Although previous research has identified contemporaneous associations between cognitive deficits and symptom phenotypes in Attention Deficit/Hyperactivity Disorder, no studies have as yet attempted to identify direction of effect. The present study used cross-lagged path modeling to examine competing hypotheses about longitudinal associations between rapid naming speed and symptoms of inattention in children. 1,506 school-age twins from Australia and the U.S. were tested for inattention, hyperactivity/impulsivity, and rapid naming speed at three and four time points, respectively. Symptom severity of inattention from Kindergarten to fourth grade is consistently predicted by previous rapid naming, over and above auto-regressive and correlational associations in the model. Likewise, inattention symptoms have a small but significant predictive effect on subsequent rapid naming. The findings support a reciprocal relationship between naming speed and ADHD inattentive symptoms.

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J Abnorm Child Psychol. 2012 Nov;40:1351-62.

EVALUATING A COMPREHENSIVE STRATEGY TO IMPROVE ENGAGEMENT TO GROUP-BASED BEHAVIORAL PARENT TRAINING FOR HIGH-RISK FAMILIES OF CHILDREN WITH ADHD.

Chacko A, Wymbs BT, Chimiklis A, et al.

Behavioral parent training (BPT) is an evidence-based intervention for the treatment of attention-deficit/hyperactivity disorder (ADHD) and related disruptive behavioral disorders of childhood. Despite convincing data on effectiveness, engagement to BPT, particularly for high-risk families, has been a long standing, yet understudied, issue. Data from a clinical trial of a comprehensive BPT approach to enhance engagement and outcomes (the Strategies to Enhance Positive Parenting [STEPP] program) are presented herein. The STEPP program was compared to a traditional group-based BPT program on propensity to attend treatment, propensity to complete homework over the course of treatment, and dropout from BPT. Additionally, factors empirically related to engagement to treatment and targeted by the STEPP program were analyzed to determine whether these factors were enhanced by participation in the STEPP program. In a randomized cohort of 80 single-mothers of school-age children with ADHD, analyses demonstrated that the STEPP program lead to greater propensity to attend treatment over time and a greater propensity to complete homework over the course of treatment. Furthermore, participation in the STEPP Program was associated with a lower rate of dropout. Finally, data suggested that parents assigned to the STEPP program reported significant improvements in factors empirically related to engagement that were targeted within the STEPP program (i.e., amount and quality of social support from their group members, expectations for treatment, and perceived barriers to treatment participation). Results of the study have implications for targeting engagement throughout the process of BPT, particularly for high-risk families.

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J Abnorm Child Psychol. 2012 Nov;40:1301-12.

PARENT-REPORTED ATTENTION DEFICIT/HYPERACTIVITY SYMPTOMATOLOGY IN PRESCHOOL-AGED CHILDREN: FACTOR STRUCTURE, DEVELOPMENTAL CHANGE, AND EARLY RISK FACTORS.

Willoughby MT, Pek J, Greenberg MT.

Although Attention Deficit/Hyperactivity Disorder (ADHD) has increasingly been studied in preschool-aged children, relatively few studies have provided a comprehensive evaluation of the factor structure and patterns of developmental changes in parent-reported ADHD symptomatology across the early childhood period. This study used confirmatory factor analyses to test for longitudinal measurement invariance of ADHD symptoms and semi-parametric finite mixture models to identify prototypic patterns of developmental changes in ADHD symptomatology from 3 to 5 years of age. Participants were 1155 children and their parents who participated in a prospective longitudinal study involving a representative sample of children who resided in six non-metropolitan counties in the United States. Results indicated that (1) ADHD symptomatology was best represented by a single latent factor that exhibited partial measurement invariance from 3 to 5 years of age, (2) 8.5 % of children exhibited sustained high levels of ADHD symptoms from age 3–5 years, and (3) a variety of risk factors differentiated children with sustained high from those with sustained low levels of ADHD, relatively few (most notably caregiver education) were able to differentiate children with sustained high levels of ADHD symptoms from all other groups. Children who exhibit persistent ADHD symptomatology across the early childhood period may define a clinically important group for etiologic research and/or early intervention efforts.

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J Abnorm Child Psychol. 2012 Nov;40:1327-37.

FACTOR STRUCTURE OF A SLUGGISH COGNITIVE TEMPO SCALE IN CLINICALLY-REFERRED CHILDREN.

Jacobson LA, Murphy-Bowman SC, Pritchard AE, et al.

“Sluggish cognitive tempo” (SCT) is a construct hypothesized to describe a constellation of behaviors that includes daydreaming, lethargy, drowsiness, difficulty sustaining attention, and underactivity. Although the construct has been inconsistently defined, measures of SCT have shown associations with symptoms of attention-deficit/hyperactivity disorder (ADHD), particularly inattention. Thus, better characterization of SCT symptoms may help to better predict specific areas of functional difficulty in children with ADHD. The

present study examined psychometric characteristics of a recently developed 14-item scale of SCT (Penny et al., Psychological Assessment 21:380–389, 2009), completed by teachers on children referred for outpatient neuropsychological assessment. Exploratory factor analysis identified three factors in the clinical sample: Sleepy/Sluggish, Slow/Daydreamy, and Low Initiation/Persistence. Additionally, SCT symptoms, especially those loading on the Sleepy/Sluggish and Slow/Daydreamy factors, correlated more strongly with inattentive than with hyperactive/impulsive symptoms, while Low Initiation/Persistence symptoms added significant unique variance (over and above symptoms of inattention) to the predictions of impairment in academic progress.

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J Abnorm Child Psychol. 2012 Nov;40:1223-36.

DIVERSITY IN PATHWAYS TO COMMON CHILDHOOD DISRUPTIVE BEHAVIOR DISORDERS .

Martel MM, Nikolas M, Jernigan K, et al.

Oppositional-Defiant Disorder (ODD) and Attention-Deficit/Hyperactivity Disorder (ADHD) are highly comorbid, a phenomenon thought to be due to shared etiological factors and mechanisms. Little work has attempted to chart multiple-level-of-analysis pathways (i.e., simultaneously including biological, environmental, and trait influences) to ODD and ADHD, the goal of the present investigation. 559 children/adolescents (325 boys) between the ages of 6 and 18 participated in a multi-stage, comprehensive diagnostic procedure. 148 were classified as ODD; 309 were classified as ADHD, based on parent, teacher, and clinician ratings. Children provided buccal or salivary samples of DNA, assayed for select markers in DRD4 and 5HTT. Parents completed the Alabama Parenting Questionnaire and the California Q-Sort. Children completed the Child Perception of Interparental Conflict Scale. Correlational associations consistent with multiple-level-of-analysis pathways to ODD and ADHD emerged. For ODD, children with the short allele of the 5HTT promoter polymorphism had higher neuroticism and ODD symptoms regardless of level of self-blame in relation to inter-parental conflict, whereas children without this allele had more ODD symptoms only in the context of more self-blame for inter-parental conflict. For ADHD (and ODD), children homozygous for the long allele of DRD4 120 bp insertion polymorphism had lower conscientiousness when exposed to inconsistent parenting, whereas children without this genotype were more resilient to effects of inconsistent discipline on conscientiousness. Thus, ODD and ADHD appear to demonstrate somewhat distinct correlational associations between etiological factors and mechanisms consistent with pathway models using a multiple-level-of-analysis approach.

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J Abnorm Child Psychol. 2012 Nov;40:1339-49.

SEMANTIC LANGUAGE AS A MECHANISM EXPLAINING THE ASSOCIATION BETWEEN ADHD SYMPTOMS AND READING AND MATHEMATICS UNDERACHIEVEMENT.

Gremillion ML, Martel MM.

ADHD is associated with academic underachievement, but it remains unclear what mechanism accounts for this association. Semantic language is an underexplored mechanism that provides a developmental explanation for this association. The present study will examine whether semantic language deficits explain the association between ADHD and reading and mathematics underachievement, taking into account alternative explanations for associations, including verbal working memory (WM) impairments, as well as specificity of effects to inattentive and hyperactive-impulsive ADHD symptom domains. Participants in this cross-sectional study were 546 children (54 % male) ages six to twelve (M = 9.77, SD = 1.49). ADHD symptoms were measured via maternal and teacher report during structured interviews and on standardized rating forms. Children completed standardized semantic language, verbal WM, and academic testing. Semantic language fully mediated the ADHD-reading achievement association and partially mediated the ADHD-mathematics achievement association. Verbal WM also partially mediated the ADHD-mathematics association but did not mediate the ADHD-reading achievement association. Results generalized across inattentive and hyperactive-impulsive ADHD symptom domains. Semantic language explained the association between ADHD and reading underachievement and partially explained the association between ADHD and mathematics underachievement. Together, language impairment and WM

fully explained the association between ADHD and reading underachievement, in line with developmental models suggesting that language and WM conjointly influence the development of attention and subsequent academic achievement. This work has implication for the development of tailored interventions for academic underachievement in children with ADHD.

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J Child Adolesc Psychopharmacol. 2012;22:423-31.

CARDIOVASCULAR MEASURES IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WHO ARE NEW USERS OF METHYLPHENIDATE AND ATOMOXETINE.

Arcieri R, Germinario EAP, Bonati M, et al.

Objective: The purpose of this study was to assess the cardiovascular effects of drugs used for attention-deficit/hyperactivity disorder (ADHD) in children and adolescents treated in community care centers in Italy.
Methods: This study was an open, prospective, observational study of youth with ADHD treated with atomoxetine (ATX) and methylphenidate (MPH). Measurements of blood pressure and heart rate, and electrocardiogram (ECG) assessment were performed at baseline and at regular intervals up to 24 months.
Results: By June 2010, 1758 youth were enrolled in the Italian ADHD National Registry. Statistically significant increases were observed in cardiovascular measures: in the MPH group after 6 months in heart rate (+2.01, p=0.01); in the ATX group after 6 months in diastolic pressure (+1.60, p=0.01) and in heart rate (+2.93, p=0.001), and after 12 months in heart rate (+3.26, p=0.003). Compared with the baseline, 59 patients had an alteration of ECG during the follow-up period. Although at 12 months, the probability of detecting an abnormal ECG was higher in the MPH group than in the ATX group, only 2 out of 30 cases at 6 months with altered ECG were considered to have experienced serious adverse events. One case was treated with ATX and one with MPH, and arrhythmia was the detected abnormality.
Conclusions: Treatment with MPH and ATX in youth appears to have a small but significant impact on the cardiovascular system. The long-term impact of these medications is unknown. Several clinically meaningless ECG alterations were observed mostly in MPH-treated youth. We therefore suggest evaluating cardiovascular risks at baseline.

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J Child Adolesc Psychopharmacol. 2012;22:415-22.

SAFETY OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER MEDICATIONS IN CHILDREN: AN INTENSIVE PHARMACOSURVEILLANCE MONITORING STUDY.

Ruggiero S, Rafaniello C, Bravaccio C, et al.

Objective: Our intensive pharmacosurveillance monitoring program was performed to increase the number of adverse drug reactions (ADRs) recorded in the Italian spontaneous reporting database, and to systematically collect more thorough data about atomoxetine (ATX) and methylphenidate (MPH) safety in the pediatric setting.
Methods: From September 2007 to October 2010, 1841 youth were enrolled in the Italian Attention-Deficit/Hyperactivity Disorder Register, but we report here on the 76 children from the five Reference Prescription Centers in Campania, an Italian region where we administered our systematic adverse event checklist.
Results: Among our cohort, 68 children received a prescription of ATX and 8 received a prescription of MPH. Most children were male and between 10 and 13 years of age, had a diagnosis of attention-deficit/hyperactivity disorder-combined (ADHD-C) and had learning disability as the main comorbidity. Most ADRs reported to the Italian spontaneous reporting database occurred in patients from Campania. Twenty-five experienced at least 1 ADR for a total of 40 ADRs reported to the Italian drug agency. Most ADRs were common and not serious, and resolved completely. Weight loss was the most frequently reported ADR. Only two ADRs were unexpected and only one was uncommon. Sixteen ADRs resulted in permanent drug withdrawal. Based on the Naranjo algorithm, 25 ADRs were considered probable and 15 were considered possible.
Conclusions: Although our data provide reassurance of the safety of ATX and MPH, several unexpected or uncommon ADRs (hepatomegaly, suicidal ideation, weight gain, or drug interactions) were identified by

our intensive pharmacosurveillance monitoring program. Our results show that an intensive pharmacosurveillance monitoring program that involves pharmacovigilance centers and clinicians can improve the collection of information on drug safety in children.

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J Child Adolesc Psychopharmacol. 2012;22:452-58.

DRUG TREATMENT PATTERNS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS IN GERMANY: RESULTS FROM A LARGE POPULATION-BASED COHORT STUDY.

Garbe E, Mikolajczyk RT, Banaschewski T, et al.

Objective: Despite a substantial increase in total methylphenidate (MPH) prescriptions in Germany over the last 20 years, and the introduction of modified release MPH (MR MPH) and atomoxetine (ATX), remarkably little is known about treatment patterns of attention-deficit/hyperactivity disorder (ADHD) in individual patients.

Methods: Usage patterns of ADHD drugs in children and adolescents in Germany were analyzed using data from one large German health insurance including >7,200,000 members. Of those, 6210 ADHD patients newly diagnosed in 2005 were followed for a maximum of 4 years. Kaplan-Meier estimates were calculated for onset and discontinuation of ADHD drug treatment. Predictors of time until drug treatment initiation were assessed by Cox regression.

Results: During follow-up, 52.0% of ADHD subjects (53.4% of boys, 47.5% of girls) received ADHD drug treatment. The majority of them (91.6%) were started on MPH, with immediate release MPH (IR MPH) being the initial treatment choice in 75.3%. In these subjects, change to drug treatment with MR MPH in the first year occurred in 48% by switch or addition. Significant predictors of drug treatment were behavioral and emotional disorders (HR=1.13; 95% CI 1.03-1.24) and a diagnosis of ADHD with conduct disorder (HR=1.21, 95% CI 1.12-1.32), whereas young age showed a protective effect. After 6, 12, and 24 months of treatment initiation, 22.4%, 43.4%, and 66.3% of treated girls, and 17.8%, 36.1%, and 54.1% of treated boys had discontinued ADHD treatment.

Conclusion: Drug treatment of ADHD was relatively common in Germany and more frequent in boys than in girls. IR MPH was the predominant treatment choice at treatment initiation. Approximately 20% of treated subjects discontinued drug treatment within the first 6 months, with girls stopping drug treatment earlier than boys. The reasons for early drug discontinuation need to be further explored.

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J Child Neurol. 2013;28:45-49.

ATTENTION SKILLS IN CHILDREN WITH NEUROFIBROMATOSIS TYPE 1.

Isenberg JC, Templer A, Gao F, et al.

Children with neurofibromatosis type 1 are at increased risk for the development of attention problems relative to their unaffected peers. Previous studies have reported deficits in sustained auditory attention, but other aspects of attention, including sustained visual attention, divided attention, response inhibition, and selective attention, have not been consistently documented. In the present study, we specifically investigated attention skills in children with neurofibromatosis type 1 using measures of visual and sustained auditory attention, divided attention, selective attention, and response inhibition. Consistent with previous reports, we confirmed the presence of deficits in sustained visual and auditory attention in children with neurofibromatosis type 1 but also identified deficits in divided attention and response inhibition. Based on the high frequency and wide spectrum of attention system impairments in this at-risk population, we advocate screening children with neurofibromatosis type 1 for attention problems and providing appropriate interventions that address all aspects of their executive functioning.

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J Child Neurol. 2013;28:120-23.

PREVALENCE OF EPILEPSY AND ATTENTION-DEFICIT HYPERACTIVITY (ADHD) DISORDER: A POPULATION-BASED STUDY.

Cohen R, Senecky Y, Shuper A, et al.

Epilepsy and attention-deficit hyperactivity disorder (ADHD) were reported to co-occur at rates higher than expected for coincidental findings. This study investigated the prevalence of both disorders in community-based primary care practice. The central database of the second-largest health maintenance organization in Israel was searched for all children aged 6 to 13 years (n = 284 419; 51.5% males) diagnosed as having ADHD according to the physicians' records and/or the filling of at least 10 prescriptions for antiepileptic medications according to pharmacy records. The prevalence of epilepsy in the total population was 5 out of 1000 children, and the prevalence of ADHD was 12.6%. More than one-fourth (27.7%) of the epileptic children were also diagnosed as having ADHD. On multivariate analysis, children with ADHD had almost twice the risk of epilepsy than children without ADHD. This study supports hospital-based findings of a strong interrelationship between ADHD and epilepsy. The high rate of ADHD in Israeli children warrants further investigation.

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Journal of Child Psychology and Psychiatry. 2012 Dec;53:1277-84.

EFFECTS OF A COMPUTERIZED WORKING MEMORY TRAINING PROGRAM ON WORKING MEMORY, ATTENTION, AND ACADEMICS IN ADOLESCENTS WITH SEVERE LD AND COMORBID ADHD: A RANDOMIZED CONTROLLED TRIAL.

Gray SA, Chaban P, Martinussen R, et al.

Background: Youths with coexisting learning disabilities (LD) and attention deficit hyperactivity disorder (ADHD) are at risk for poor academic and social outcomes. The underlying cognitive deficits, such as poor working memory (WM), are not well targeted by current treatments for either LD or ADHD. Emerging evidence suggests that WM might be improved by intensive and adaptive computerized training, but it remains unclear whether this intervention would be effective for adolescents with severe LD and comorbid ADHD.

Methods: A total of sixty 12- to 17-year olds with LD/ADHD (52 male, 8 female, IQ > 80) were randomized to one of two computerized intervention programs: working memory training (Cogmed RM) or math training (Academy of Math) and evaluated before and 3 weeks after completion. The criterion measures of WM included auditory-verbal and visual-spatial tasks. Near and far transfer measures included indices of cognitive and behavioral attention and academic achievement.

Results: Adolescents in the WM training group showed greater improvements in a subset of WM criterion measures compared with those in the math-training group, but no training effects were observed on the near or far measures. Those who showed the most improvement on the WM training tasks at school were rated as less inattentive/hyperactive at home by parents.

Conclusions: Results suggest that WM training may enhance some aspects of WM in youths with LD/ADHD, but further development of the training program is required to promote transfer effects to other domains of function.

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Journal of Child Psychology and Psychiatry. 2013 Jan;54:3-16.

PRACTITIONER REVIEW: WHAT HAVE WE LEARNT ABOUT THE CAUSES OF ADHD?

Thapar A, Cooper M, Eyre O, et al.

Background: Attention deficit hyperactivity disorder (ADHD) and its possible causes still attract controversy. Genes, pre and perinatal risks, psychosocial factors and environmental toxins have all been considered as potential risk factors.

Method: This review (focussing on literature published since 1997, selected from a search of PubMed) critically considers putative risk factors with a focus on genetics and selected environmental risks, examines their relationships with ADHD and discusses the likelihood that these risks are causal as well as some of the main implications.

Results: No single risk factor explains ADHD. Both inherited and noninherited factors contribute and their effects are interdependent. ADHD is familial and heritable. Research into the inherited and molecular genetic contributions to ADHD suggest an important overlap with other neurodevelopmental problems, notably, autism spectrum disorders. Having a biological relative with ADHD, large, rare copy number variants, some small effect size candidate gene variants, extreme early adversity, pre and postnatal exposure to lead and low birth weight/prematurity have been most consistently found as risk factors, but none are yet known to be definitely causal. There is a large literature documenting associations between ADHD and a wide variety of putative environmental risks that can, at present, only be regarded as correlates. Findings from research designs that go beyond simply testing for association are beginning to contest the robustness of some environmental exposures previously thought to be ADHD risk factors.
Conclusions: The genetic risks implicated in ADHD generally tend to have small effect sizes or be rare and often increase risk of many other types of psychopathology. Thus, they cannot be used for prediction, genetic testing or diagnostic purposes beyond what is predicted by a family history. There is a need to consider the possibility of parents and siblings being similarly affected and how this might impact on engagement with families, influence interventions and require integration with adult services. Genetic contributions to disorder do not necessarily mean that medications are the treatment of choice. We also consider how findings might influence the conceptualisation of ADHD, public health policy implications and why it is unhelpful and incorrect to dichotomise genetic/biological and environmental explanations. It is essential that practitioners can interpret genetic and aetiological research findings and impart informed explanations to families.

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Journal of Child Psychology and Psychiatry. 2013 Jan;54:96-104.
INFANT BRAIN STRUCTURES, EXECUTIVE FUNCTION, AND ATTENTION DEFICIT/HYPERACTIVITY PROBLEMS AT PRESCHOOL AGE. A PROSPECTIVE STUDY.
Ghassabian A, Herba CM, Roza SJ, et al.
Background: Neuroimaging findings have provided evidence for a relation between variations in brain structures and Attention Deficit/Hyperactivity Disorder (ADHD). However, longitudinal neuroimaging studies are typically confined to children who have already been diagnosed with ADHD. In a population-based study, we aimed to characterize the prospective association between brain structures measured during infancy and executive function and attention deficit/hyperactivity problems assessed at preschool age.
Methods: In the Generation R Study, the corpus callosum length, the gangliothalamic ovoid diameter (encompassing the basal ganglia and thalamus), and the ventricular volume were measured in 784 6-week-old children using cranial postnatal ultrasounds. Parents rated executive functioning at 4 years using the Behavior Rating Inventory of Executive Function-Preschool Version in five dimensions: inhibition, shifting, emotional control, working memory, and planning/organizing. Attention Deficit/Hyperactivity Problems were assessed at ages 3 and 5 years using the Child Behavior Checklist.
Results: A smaller corpus callosum length during infancy was associated with greater deficits in executive functioning at 4 years. This was accounted for by higher problem scores on inhibition and emotional control. The corpus callosum length during infancy did not predict Attention Deficit/Hyperactivity Problem at 3 and 5 years, when controlling for the confounders. We did not find any relation between gangliothalamic ovoid diameter and executive function or Attention Deficit/Hyperactivity Problem.
Conclusions: Variations in brain structures detectible in infants predicted subtle impairments in inhibition and emotional control. However, in this population-based study, we could not demonstrate that early structural brain variations precede symptoms of ADHD.

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J Commun Disord. 2013;46:30-52.
PERSONAL FM SYSTEMS FOR CHILDREN WITH AUTISM SPECTRUM DISORDERS (ASD) AND/OR ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD): AN INITIAL INVESTIGATION.
Schafer EC, Mathews L, Mehta S, et al.

The goal of this initial investigation was to examine the potential benefit of a frequency modulation (FM) system for 11 children diagnosed with autism spectrum disorders (ASD), attention-deficit hyperactivity disorder (ADHD), or both disorders through measures of speech recognition performance in noise, observed classroom behavior, and teacher-rated educational risk and listening behaviors. Use of the FM system resulted in significant average improvements in speech recognition in noise for the children with ASD and ADHD as well as large effect sizes. When compared to typically functioning peers, children with ASD and ADHD had significantly poorer average speech recognition performance in noise without the FM system but comparable average performance when the FM system was used. Similarly, classroom observations yielded a significant increase in on-task behaviors and large effect sizes when the FM system was in use during two separate trial periods. Although teacher ratings on questionnaires showed no significant improvement in the average level of educational risk of participants, they did indicate significant improvement in average listening behaviors during two trial periods with the FM system. Given the significantly better speech recognition in noise, increased on-task behaviors, and improved teacher ratings of listening behaviors with the FM system, these devices may be a viable option for children who have ASD and ADHD in the classroom. However, an individual evaluation including audiological testing and a functional evaluation in the child's primary learning environment will be necessary to determine the benefit of an FM system for a particular student.Learning Outcomes: 1. The reader will be able to describe the potential benefit of FM systems for children with ASD and/or ADHD. 2. The reader will be able to identify on-task versus off-task listening behaviors in children with ASD and/or ADHD. 3. The reader will be able to explain the components of a successful pre-fit education program that may be necessary prior to fitting an FM system in children with ASD.

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J Fluency Disord. 2012;37:242-52.

TRAITS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER IN SCHOOL-AGE CHILDREN WHO STUTTER.

Donaher J, Richels C.

Purpose: The purpose of this study was to explore whether parents of CWS reported the presence of ADHD symptoms that would warrant a referral to a psychologist to rule out the disorder. This study also aimed to describe the characteristics of the sample in terms of gender, family history of stuttering, presence of neurological impairment, concomitant diagnoses, and stuttering severity. Finally, this study sought to explore the possible statistical relations among these same variables.

Methods: Participants were 36 school-age CWS (32 males and 4 females) between the ages of 3.9 and 17.2 years (M= 10.4, SD=4.0). Parent responses on the ADHD Rating Scale (Power et al., 2001) were collected via a retrospective chart review.

Results: For this sample 58% (n=21), of the participants met criteria for needing referral for additional evaluation for symptoms related to ADHD. A strong positive relation (r=.720, p< .001) was found between a reported family history of recovered stuttering and the presence of a concomitant diagnosis.

Conclusion: The results of the present study demonstrate the need for further training and education for SLPs working with CWS regarding ADHD.

Educational objectives: The reader will be able to (1) describe the main characteristics of ADHD, (2) discuss the evidence suggesting a possible relationship between ADHD and stuttering and (3) discuss how ADHD characteristics could impact clinical outcomes for CWS.

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J Intellect Disabil Res. 2013;57:191-97.

ASSOCIATION BETWEEN PARENT REPORTS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER BEHAVIOURS AND CHILD IMPULSIVITY IN CHILDREN WITH SEVERE INTELLECTUAL DISABILITY.

Bigham K, Daley DM, Hastings RP, et al.

Background Although children with intellectual disability (ID) seemed to be at increased risk for Attention deficit hyperactivity disorder (ADHD)/hyperactivity problems when assessed with parent report questionnaires and clinical interviews, there has been little attention to the associations between parent reports and observed child behaviours. The purpose of the present study was to compare clinical

symptoms and observed impulsivity in children with ID whose parents reported them as being relatively high and low in ADHD symptoms, and to examine whether any differences were associated with developmental level.
Methods Parents of 28 children with ID completed a behaviour rating scale of hyperactivity symptoms. Parents were also interviewed using a robust clinical interview tool focused on hyperactivity symptoms. The children were all tested by an experimenter to measure their impulsive behaviour.
Results Those children with clinical range scores on parent questionnaire ratings were also reported by parents to have more ADHD symptoms using a parent report clinical interview. Although these children were also more impulsive on an experimental task, when children's developmental ages were statistically controlled impulsivity differences disappeared.
Conclusions Parent reports of ADHD symptoms in children with ID may be positively associated with data derived using clinical interview methods, but they may be less sensitive to developmental expectations when compared with observed child behaviour. Practical implications include the need for multiple sources of information and normative data for children with ID on simple experimental tasks that can be used to aid diagnosis of ADHD in clinical settings.

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Journal of Learning Disabilities. 2013 Jan;46:5-25.
RETHINKING ADHD AND LD IN DSM-5: PROPOSED CHANGES IN DIAGNOSTIC CRITERIA.
Tannock R.
The Diagnostic and Statistical Manual of Mental Disorders (DSM) is currently undergoing revision that will lead to a fifth edition (DSM-5) in 2013. This article first provides a brief synopsis of the DSM-5 administrative structure, procedures, and guiding principles to enhance understanding of how changes are made in the DSM. The next two sections (on attention-deficit/hyperactivity disorder and learning disorders, respectively) highlight the major concerns and controversies surrounding the DSM-IV diagnostic criteria for these two disorders and provide a rationale for the proposed changes to the criteria, along with a commentary on the empirical evidence on which the proposed changes were based.

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Journal of Learning Disabilities. 2013 Jan;46:58-72.
THE PROPOSED CHANGES FOR DSM-5 FOR SLD AND ADHD: INTERNATIONAL PERSPECTIVES—AUSTRALIA, GERMANY, GREECE, INDIA, ISRAEL, ITALY, SPAIN, TAIWAN, UNITED KINGDOM, AND UNITED STATES.
Al-Yagon M, Cavendish W, Cornoldi C, et al.
This article presents an international perspective of the proposed changes to the DSM-5 for learning disabilities (LD) and attention-deficit/hyperactivity disorders (ADHD) across ten countries: Australia, Germany, Greece, India, Israel, Italy, Spain, Taiwan, the United Kingdom, and the United States. We provide perspectives of the present situation for youth with LD and youth with ADHD and describe the legislation, prevalence rates, and educational systems that serve students with disabilities in the respective countries. We also present a discussion of the expected impact of the proposed changes for the diagnosis of LD and ADHD in each country.

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J Managed Care Pharm. 2012;18:676-89.
COMPARATIVE TREATMENT PATTERNS, RESOURCE UTILIZATION, AND COSTS IN STIMULANT-TREATED CHILDREN WITH ADHD WHO REQUIRE SUBSEQUENT PHARMACOTHERAPY WITH ATYPICAL ANTIPSYCHOTICS VERSUS NON-ANTIPSYCHOTICS.
Sikirica V, Pliszka SR, Betts KA, et al.
Background: Although not indicated for attention-deficit/hyperactivity disorder (ADHD), atypical antipsychotics (AAPs) are commonly prescribed for children with ADHD. The treatment patterns, resource

utilization, and costs associated with AAPs relative to non-antipsychotic medications have not been evaluated for children with ADHD.
Objective: To compare treatment patterns, resource utilization, and costs to U.S. third party payers between stimulant-treated ADHD children who switch to or augment their stimulant treatment with AAPs (risperidone, aripiprazole, quetiapine, olanzapine, ziprasidone, paliperidone, and clozapine) compared with non-antipsychotic medications (atomoxetine, clonidine immediate-release (IR), guanfacine IR, dexmethylphenidate, mixed amphetamine salts, methylphenidate, lisdexamfetamine, and dextroamphetamine).
Methods: Patients with at least one ADHD diagnosis (ICD-9-CM codes 314.00 or 314.01) and at least one stimulant medication claim between January 1, 2005 and December 31, 2009, were identified from a large U.S. commercial medical/pharmacy claims database. Patients were classified into the AAP cohort if they had a claim for an AAP following a stimulant fill or into the non-antipsychotic cohort if they had a claim for a nonantipsychotic medication after a stimulant fill and no AAP claims. The index date was defined as the date of the first fill of the AAP or a randomly selected eligible non-antipsychotic medication. Patients were eligible for inclusion if they were aged 6-12 as of the index date and had at least 18 months of continuous eligibility. Patients were excluded if they had a psychiatric diagnosis for which AAPs were approved by the U.S. Food and Drug Administration (FDA) or commonly used. Patients in the non-antipsychotic group were matched 1:1 to patients in the AAP group using a propensity score generated from a logistic regression that included demographics, treatments, resource utilization, and comorbidities during the 6 months prior to the index date. All outcomes were measured during the 12 months following the index date. Treatment patterns were compared using Kaplan-Meier (KM) estimates and Cox proportional hazards models. Annual resource utilization was compared using McNemar's test and Poisson regression. Costs were estimated from the perspective of U.S. third-party payers and were adjusted to 2010 dollars using the medical component of the Consumer Price Index. Both all-cause and mental health-related costs were examined and compared using Wilcoxon signed-rank tests.
Results: Of the 22,622 patients with ADHD identified to have used AAPs after a stimulant, 15,664 (69%) patients did not have a psychiatric diagnosis for which AAPs were FDA-indicated or commonly used. Among the 84,558 patients using non-antipsychotics after a stimulant, 81,397 (96%) did not have such psychiatric diagnoses. A total of 2,127 children in the AAP cohort and 16,508 children in the non-antipsychotic cohort met all of the study inclusion criteria. After propensity score matching, 1,857 children (358 switchers and 1,499 augmenters) were included in each of the matched cohorts. The baseline characteristics were well balanced between the matched cohorts. In the 12 months post-index date, children treated with AAPs were more likely to experience switching (KM: 17.2% vs. 10.4% at 12 months; HR = 1.75) and augmentation (KM: 43.4% vs. 22.4% at 12 months; HR = 2.62) than the non-antipsychotic group (both $P < 0.001$). Rates of discontinuation were similar between groups (KM: 71.8% vs. 71.7% at 12 months; HR = 0.98, P = 0.600). The AAP cohort also had higher mean numbers of hospitalizations, emergency room visits, and outpatient visits (0.08 vs. 0.03, 0.34 vs. 0.25, 14.1 vs. 12.7 per patient, respectively; event rate ratios = 2.61, 1.33, and 1.11, respectively; all $P < 0.001$). The AAP group also incurred higher all-cause mean medical, prescription drug, and total health care costs compared with the non-antipsychotic group ($3,090 vs. $2,238; $3,844 vs. $2,509; $6,934 vs. $4,748, respectively; all $P < 0.001$). Patients in the AAP group also incurred higher mean total, medical, and drug costs related to mental health ($5,057 vs. $2,859; $1,555 vs. $964; $3,502 vs. $1,895, respectively; all $P < 0.001$).
Conclusions: Stimulant-treated children with ADHD who switched to or augmented with AAPs versus non-antipsychotics had significantly greater rates of subsequent augmentation and health care resource utilization as well as higher total health care costs. Further research and/or drug utilization reviews may be warranted to fully evaluate the clinical and economic outcomes of pediatric ADHD patients who are receiving AAPs.

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

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

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

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

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J Neuropsychiatry Clin Neurosci. 2012;24:458-62.

THE EFFECTS OF COMORBID OBSESSIVE-COMPULSIVE DISORDER AND ATTENTION- DEFICIT HYPERACTIVITY DISORDER ON QUALITY OF LIFE IN TOURETTE SYNDROME.

Eddy CM, Cavanna AE, Gulisano M, et al.

Tourette syndrome (TS) is a complex neuropsychiatric disorder affecting patients' quality of life (QoL). The authors compared QoL measures in young patients with "pure" TS (without comorbid conditions) versus those with TS+OCD (obsessive-compulsive disorder), TS+ADHD (attention-deficit hyperactivity disorder), or TS +OCD+ADHD. Age and scores on scales assessing tic severity, depression, anxiety, and behavioral problems were included as covariates. Young patients with both comorbidities exhibited significantly lower Total and Relationship Domain QoL scores, versus patients with pure TS. Across the whole sample, high ADHD-symptom scores were related to poorer QoL within the Self and Relationship domains, whereas high OCD symptom scores were associated with more widespread difficulties across the Self, Relationship, Environment, and General domains. Significant differences in QoL may be most likely when both comorbidities are present, and features of OCD and ADHD may have different impacts on QoL across individual domains.

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J Psychiatr Res. 2012.

1H MRSI OF MIDDLE FRONTAL GYRUS IN PEDIATRIC ADHD.

Tafazoli S, O'Neill J, Bejjani A, et al.

Neuroimaging studies in multiple modalities have implicated the left or right dorsolateral prefrontal cortex (here, middle frontal gyrus) in attentional functions, in ADHD, and in dopamine agonist treatment of ADHD. The far lateral location of this cortex in the brain, however, has made it difficult to study with magnetic resonance spectroscopy (MRS). We used the smaller voxel sizes of the magnetic resonance spectroscopic imaging (MRSI) variant of MRS, acquired at a steep coronal-oblique angle to sample bilateral middle frontal gyrus in 13 children and adolescents with ADHD and 13 age- and sex-matched healthy controls. Within a subsample of the ADHD patients, aspects of attention were also assessed with the Trail Making Task. In right middle frontal gyrus only, mean levels of N-acetyl-aspartate + N-acetyl-aspartyl-glutamate (tNAA),

creatine + phosphocreatine (Cr), choline-compounds (Cho), and myo-inositol (mI) were significantly lower in the ADHD than in the control sample. In the ADHD patients, lower right middle frontal Cr was associated with worse performance on Trails A and B (focused attention, concentration, set-shifting), while the opposite relationship held true for the control group on Trails B. These findings add to evidence implicating right middle frontal cortex in ADHD. Lower levels of these multiple species may reflect osmotic adjustment to elevated prefrontal cortical perfusion in ADHD and/or a previously hypothesized defect in astrocytic production of lactate in ADHD resulting in decelerated energetic metabolism (Cr), membrane synthesis (Cho, mI), and acetyl-CoA substrate for NAA synthesis. Lower Cr levels may indicate attentional or executive impairments.

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J Psychiatr Res. 2012 Nov;46:1398-405.

CORTISOL LEVELS IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Isaksson J, Nilsson KW, Nyberg F, et al.

Regulation of the Hypothalamus-Pituitary-Adrenal axis (HPA-axis) and its end product cortisol differs among persons with certain psychiatric disorders when compared with controls. Some reports concern Attention-Deficit/Hyperactivity Disorder (ADHD) but findings are inconclusive. In this study we collected four saliva samples during a regular weekday in children, 6-17 years old, with ADHD (n = 201) and non-affected comparisons (n = 221). Saliva cortisol was measured with radioimmunoassay technique. Clinical data were collected for diagnostic information. Subtypes and severity of symptoms were determined using parental rating scales. Children with ADHD had lower saliva cortisol levels than comparisons at waking up Median = 9.1 versus 12.7 nmol/L ($p < .001$), 30 min later Median = 15.8 versus 20.1 nmol/L ($p < .001$) and before going to bed Median = 0.8 versus 1.0 nmol/L ($p = .015$). No difference was found for the afternoon sample. When the study group was split into three different age groups similar results were found only for children above 10 years of age. Subtype of ADHD or co-occurring symptoms did not affect the cortisol levels. Degree of severity of ADHD symptoms was not associated with cortisol levels in the study group, other than a weak negative correlation between the afternoon sample and hyperactivity symptoms. The low cortisol levels in children with ADHD may indicate a dysregulation of the HPA-axis, for instance a down-regulation or a phase delay of the diurnal curve. The low levels may be related to the under-arousal possibly underlying several of the core symptoms of ADHD.

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J Am Acad Child Adolesc Psychiatry. 2013;52:12-25.

GENETIC AND ENVIRONMENTAL STABILITY IN ATTENTION PROBLEMS ACROSS THE LIFESPAN: EVIDENCE FROM THE NETHERLANDS TWIN REGISTER.

Kan KJ, Dolan CV, Nivard MG, et al.

Objective: To review findings on attention-deficit/hyperactivity disorder and attention problems (AP) in children, adolescents, and adults, as established in the database of the Netherlands Twin Register and increase the understanding of stability in AP across the lifespan as a function of genetic and environmental influences.

Method: A longitudinal model was fitted on Netherlands Twin Register AP scores from 44,607 child (<12-year-old), adolescent (12- to 18-year-old), and adult (>18-year-old) twins.

Results: Mean AP showed a downward trend with age. Age-to-age correlations ranged from 0.33 (50-(greater-than or equal to)60 years old) to 0.73 (10-12 years old). Stability in individual differences in AP was due to genetic and environmental factors, and change was due primarily to environmental factors. Nonadditive genetic influences were present from childhood to adulthood. Total genetic variance decreased slightly throughout aging, whereas environmental variance increased substantially with the switch from maternal to self-ratings at 12 years of age. As a result, heritability coefficients decreased from 0.70 to 0.74 in childhood (maternal ratings) to 0.51 to 0.56 in adolescence (self-ratings), and 0.40 to 0.54 in adulthood (self-ratings). In childhood, male subjects scored higher than female subjects. After the rater switch at 12 years of age, female subjects tended to score higher than male subjects.

Conclusions: Stability of AP is the result of genetic and environmental stability. The decrease in estimated heritability at 12 years of age is due to an increase in occasion-specific environmental variance and likely reflects a methodologic effect. Because environmental influences have lasting effects on AP, their early detection is crucial.

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J Formos Med Assoc. 2013.

TREATMENT EFFECTS OF COMBINING SOCIAL SKILL TRAINING AND PARENT TRAINING IN TAIWANESE CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Huang YH, Chung CY, Ou HY, et al.

Background/Purpose: Children with attention-deficit/hyperactivity disorder (ADHD) often have problems in social interactions. We investigated the social and behavioral effects of providing both social skill training and parent training to school-aged children with ADHD in Taiwan.

Methods: Seven consecutive 8-week behavioral-based social skill training (SST) group sessions were held for 48 children with ADHD; parallel 8-week parent group sessions were provided simultaneously. Fifty-five children with ADHD were recruited as a control group. All children took medication as prescribed by their doctors. The effects were assessed using the teacher and parent version of the Chinese version of Swanson, Nolan, and Pelham, version IV scale (SNAP-IV), the Chinese version of the Child Behavior Check List (CBCL-C), child and teacher version of the modified Social Skill Rating System (SSRS-C and SSRS-T), at baseline, post-treatment, and 4 months from baseline. The doses of methylphenidate and drug compliance were controlled during the analysis.

Results: The mixed-effects model demonstrated the main effect of group sessions on the Oppositional subscale of SNAP-P, the Anxious/Depressed subscale of CBCL-C, the Self Control subscale of SSRS-C, and the Active Participation subscale of SSRS-T, all in favor of the experimental group. However, the improvement on the Oppositional subscale of SNAP-P and the Self Control subscale of SSRS-C were noted only between baseline and post-treatment period and were not sustained at the end of the follow-up period.

Conclusion: Our study demonstrated that children with ADHD could benefit from this low intensity psychosocial program, although some improvements were not maintained at follow-up assessment.

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Lakartidningen. 2012 Nov;109:2166.

RISK OF ADDH BEING DIAGNOSED ON THE WRONG GROUNDS.

Maler H.

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Learning and Individual Differences. 2012 Dec;22:778-85.

READING MOTIVATIONAL DIFFERENCES AMONG GROUPS: READING DISABILITY (RD), ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD), RD+ADHD, AND TYPICAL COMPARISON.

Lee J, Zentall SS.

This study assessed the reading motivation of 133 students at individual grade levels (2nd–5th), who were divided in subgroups with and without reading disabilities/difficulties (RD) and with and without attention deficit hyperactivity disorder (ADHD). Major findings were that students in the RD subgroup had lower reading motivation (intrinsic, extrinsic, and self-efficacy) and read less for enjoyment than the nondisability (ND) group; students in the combined group (ADHD+RD) showed these motivational deficits in earlier grade levels. However, students with ADHD did not differ from the ND group in reading motivation, and children with RD (with and without ADHD) were equivalent to ND in social motivation up to the 5th grade. Implications of these findings were (a) social reading is an instructional pathway for both groups of students with RD, (b) assessments of reading motivation, in addition to reading skill, may be important in assessing

responses to intervention, and (c)motivational interventions should be implemented early before motivational responses become a motivational style.

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Learning and Individual Differences. 2012 Dec;22:891-95.

AN INVESTIGATION OF COGNITIVE SKILLS AND BEHAVIOR IN HIGH ABILITY STUDENTS.

Alloway TP, Elsworth M.

The purpose of this study was to investigate the cognitive and behavioral profiles of high ability students. Performance on measures of verbal and visuo-spatial working memory and general ability (vocabulary and block design) was compared across the following groups: high, average, and low ability students. The behavioral profile of high ability students was also compared with those with a clinical diagnosis of ADHD. The working memory performance was superior in the high ability students compared to the low and average ability groups, though the relationship between working memory and IQ weakens as a function of increasing ability. The findings are discussed in light of Spearman's law of diminishing returns. The behavioral profile of this group indicates similar features in some respects to those with a clinical diagnosis of ADHD, however, underlying explanations may differ and should be taken into consideration in future research on dual needs in high ability students.

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Learning and Individual Differences. 2012 Dec;22:896-900.

CHILDREN WITH ADHD SYMPTOMS ARE LESS SUSCEPTIBLE TO GAP-FILLING ERRORS THAN TYPICALLY DEVELOPING CHILDREN.

Mirandola C, Paparella G, Re AM, et al.

Enhanced semantic processing is associated with increased false recognition of items consistent with studied material, suggesting that children with poor semantic skills could produce fewer false memories. We examined whether memory errors differed in children with Attention Deficit/Hyperactivity Disorder (ADHD) and controls. Children viewed 18 photographs for each of 4 scripts (e.g., eating at a restaurant). A recognition test followed which included old and new photographs, some of which presenting script consistent information and others depicting the cause (e.g., knocking over a glass of coke) of an effect actually viewed during encoding (wiping the table at the restaurant). Children with ADHD exhibited lower false recognition for script-consistent photographs and were more confident in their errors than controls.

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Learning Disability Quarterly. 2012 Nov;35:248-59.

A READING MOTIVATION INTERVENTION WITH DIFFERENTIAL OUTCOMES FOR STUDENTS AT RISK FOR READING DISABILITIES, ADHD, AND TYPICAL COMPARISONS: 'CLEVER IS AND CLEVER DOES'.

Zentall SS, Lee J.

Past research has failed to recognize motivation for its potential to produce instructional gains, especially for students with reading disabilities/difficulties (RD). To this purpose, a combined motivational intervention was administered to 80 second-grade through fifth-grade students in a randomized pretest–posttest control group design with three population groups and two conditions. The intervention condition described a positive label (e.g., “clever”) associated with specific reading behavior (e.g., answers questions) accompanied by a challenge to perform better than before and better than another (intrinsic and extrinsic goals). While controlling for initial reading differences, the intervention improved the fluency and comprehension for the RD group, with and without attention deficit hyperactivity disorder (ADHD), relative to the no disability (ND) group, even though the ND group also made gains. These findings documented a first-tier empirically based intervention with practical applications for elementary students with RD and their peers, although gains in reading for the ADHD group without RD were not significant.

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Maternal and Child Health Journal. 2012 Dec;16:1771-78.

FACTORS ASSOCIATED WITH A MEDICAL HOME AMONG CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Knapp CA, Hinojosa M, Baron-Lee J, et al.

Providing a medical home to children with Attention-Deficit Hyperactivity Disorder (ADHD) is challenging. Little is known about the factors associated with having a medical home for these children, or how comorbidities affect having a medical home. Our study aims are: (1) identify factors associated with having a medical home and five sub-components of a medical home and (2) determine the effect of medical home on several outcomes for children with ADHD. The sample included 5,495 children with ADHD from the 2007 National Survey of Children's Health. Descriptive and multivariate analyses were conducted. Children with ADHD alone and children with ADHD plus a physical diagnosis had greater frequencies of having a medical home, or meeting the five sub-components, than children with ADHD plus a mental diagnosis. Multivariate results show that children with ADHD plus a physical and/or mental comorbidity were 24–63% more likely to be without a medical home compared to children with only ADHD. Having a medical home also had a bearing on several child health outcomes. Having a medical home was significantly associated with being less likely to have an unmet health need and having fewer missed school days; but also being less likely to have received needed mental health care ($P < .05$). Our results suggest that there are differences in parent's perceptions of receiving care among children with ADHD. Pediatric medical home projects and policies should acknowledge that children with ADHD often have comorbidities making their care more complex. These complexities should be addressed during practice transformation and setting reimbursement policies.

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Med Hypotheses. 2013.

UNDERSTANDING THE RELATIONSHIPS BETWEEN BREASTFEEDING, MALOCCLUSION, ADHD, SLEEP-DISORDERED BREATHING AND TRAUMATIC DENTAL INJURIES.

Sabuncuoglu O.

Attention-deficit/hyperactivity disorder (ADHD), one of the most common neuropsychiatric disorders that present at young age, may occasionally be associated with physical problems and disorders. Among them exists a group of oral-pharyngeal conditions with considerable clinical morbidity. Previous research that identified absence or short duration of breastfeeding in ADHD children has been reviewed. Essential nutritional factors in breast milk can affect brain development and regulate the manifestation of ADHD symptoms. Low ferritin levels caused by insufficient breastfeeding may contribute to ADHD susceptibility because of the role of iron in dopaminergic activity. Insufficient breast feeding and subsequently excessive bottle-feeding may lead to increased rates of non-nutritive sucking habits, such as pacifier use and thumb-sucking, all of which are associated with the risk of development of malocclusions. Malocclusion refers to an unacceptable deviation from the ideal relationship of the upper and lower teeth and necessitates orthodontic treatment. Sleep-disordered breathing in children may present with neurocognitive symptoms that resemble ADHD and abnormal craniofacial developments, as well as malocclusions, have been cited as part of the syndrome. Obesity, which is an outcome of insufficient breastfeeding, is a shared comorbidity of ADHD and sleep-disordered breathing. The risk of traumatic dental injury is higher in children with ADHD and presence of malocclusions further increases the likelihood of dental injuries. In this review, certain oral-pharyngeal conditions relating to ADHD have been reviewed and links among them have been highlighted in a tentative explanatory model. More research that will provide increased awareness and clinical implications is needed.

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Med Bambino. 2012;31:667.

PREVALENCE OF ADHD IN THE ITALIAN PAEDIATRIC POPULATION AND RATE OF EXPOSITION TO PHARMACOLOGICAL AND BEHAVIOURAL TREATMENT.

Maschietto D, Baioni E, Vio C, et al.

Objective-To assess the prevalence of ADHD in the Italian paediatric population and to evaluate the rate of exposition to pharmacological and behavioural treatment in children and adolescents.
Method-Observational post-marketing study, 4th phase. Assessment of the drugs prescribed to children and adolescents aged between 6-18 with ADHD in child psychiatry unit of San Dona di Piave.
Results-The population aged 6-18 years amount to 24,000 inhabitants. 2,503 (10.8%) were examined in 2007 for suspected developmental disorders and 286 (1.2%) were diagnosed positive for ADHD. 20 out of 286 (7.0%) patients had received the multimodal treatment and 186 the behavioural treatment alone. In 2010, the subjects suffering from ADHD were 263 (1.1%) on a population aged 6-18 of 24,650 individuals. 44 (16.7%) were in multimodal treatment and 153 received behavioural treatment.
Conclusions-The observed prevalence of ADHD corresponds to that expected on the basis of the data of previous epidemiological Italian surveys but considerably lower than the one reported in international literature. The rate of exposure to pharmacological treatment is similar to that of other European countries.

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Med Bambino. 2012;31:647-48.

ADHD FROM CHILDREN TO ADULTS.

Mencacci C.

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NeuroImage Clin. 2012;1:131-40.

RIGHT PREFRONTAL ACTIVATION AS A NEURO-FUNCTIONAL BIOMARKER FOR MONITORING ACUTE EFFECTS OF METHYLPHENIDATE IN ADHD CHILDREN: AN FNIRS STUDY.

Monden Y, Dan H, Nagashima M, et al.

An objective biomarker is a compelling need for the early diagnosis of attention deficit hyperactivity disorder (ADHD), as well as for themonitoring of pharmacological treatment effectiveness. The advent of fNIRS, which is relatively robust to the body movements of ADHD children, raised the possibility of introducing functional neuroimaging diagnosis in younger ADHD children. Using fNIRS, we monitored the oxy-hemoglobin signal changes of 16 ADHD children (6 to 13 years old) performing a go/no-go task before and 1.5 h after MPH or placebo administration, in a randomized, double-blind, placebo-controlled, crossover design. 16 age- and gender-matched normal controls without MPH administration were also monitored. Relative to control subjects, unmedicated ADHD children exhibited reduced activation in the right inferior frontal gyrus (IFG) and middle frontal gyrus (MFG) during go/no-go tasks. The reduced right IFG/MFG activation was acutely normalized after MPH administration, but not after placebo administration. The MPH-induced right IFG/MFG activation was significantly larger than the placebo-induced activation. Post-scan exclusion rate was 0% among 16 right-handed ADHD children with IQ>70. We revealed that the right IFG/MFG activation could serve as a neuro-functional biomarker for monitoring the acute effects of methylphenidate in ADHD children. fNIRS-based examinations were applicable to ADHD children as young as 6 years old, and thus would contribute to early clinical diagnosis and treatment of ADHD children.

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NeuroImage Clin. 2013;2:103-10.

IMAGING GENE AND ENVIRONMENTAL EFFECTS ON CEREBELLUM IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND TYPICAL DEVELOPMENT.

De Zeeuw P, Van Belle J, van Dijk S, et al.

This study investigates the effects of XKR4, a recently identified candidate gene for Attention-Deficit/Hyperactivity Disorder (ADHD), birth weight, and their interaction on brain volume in ADHD. XKR4 is

expressed in cerebellum and low birth weight has been associated both with changes in cerebellum and with ADHD, probably due to its relation with prenatal adversity. Anatomical MRI scans were acquired in 58 children with ADHD and 64 typically developing controls and processed to obtain volumes of cerebrum, cerebellum and gray and white matter in each structure. DNA was collected from saliva. Analyses including data on birth weight were conducted in a subset of 37 children with ADHD and 51 controls where these data were retrospectively collected using questionnaires. There was an interaction between genotype and birth weight for cerebellum gray matter volume (p =.020). The combination of homozygosity for the G-allele (the allele previously found to be overtransmitted in ADHD) and higher birth weight was associated with smaller volume. Furthermore, birth weight was positively associated with cerebellar white matter volume in controls, but not ADHD (interaction: p =.021). The interaction of genotype with birth weight affecting cerebellum gray matter is consistent with models that emphasize increased influence of genetic risk-factors in an otherwise favorable prenatal environment. The absence of an association between birth weight and cerebellum white matter volume in ADHD suggests that other genetic or environmental effects may be at play, unrelated to XKR4. These results underscore the importance of considering environmental effects in imaging genetics studies.

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Neuropsychiatr Enfance Adolesc. 2013.

DIAGNOSTIC, ASSESSMENT AND REMEDIATION OF THE ATTENTION DEFICIT AND HYPERACTIVITY DISORDER (ADHD): THE NEUROPSYCHOLOGIST'S POINT OF VIEW.

Catale C, Meulemans T.

Despite the advances made regarding both the characterization and classification of the disorder (e.g., DSM-IV), the diagnosis of the attention deficit and hyperactivity disorder (ADHD) in children remains very difficult. The principal aim of this paper is to present the interest of a integrative approach in the understanding, diagnosis and identification of difficulties in ADHD children. More particularly, it aims to underline the interest of the cognitive approach in the understanding of this disorder in the day-to-day life functioning, as well as the benefits of this approach when a specific remediation is planned.

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Neuropsychology. 2013 Jan;27:107-20.

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

Nikolas MA, Nigg JT.

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

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

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

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

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Neuropsychopharmacologia Hungarica. 2010;12:31-32.

ADULT ADHD-SYMPTOMS, AETIOLOGY, DIAGNOSIS AND TREATMENT.

Markhed M.

The condition now referred to as Attention-Deficit /Hyperactivity Disorder (ADHD) was scientificallydescribed already in 1902. Presently, according toDSM-IV, the core features of ADHD are differentexpressions of inattention and overactivity/impulsivtydivided into three subgroups; predominantly inattentive,predominantly hyperactive and combined.ADHD is a common disorder with childhood onsetwhich often persist in adulthood. ADHD is thusprobably one of the the most common and undiagnosedpsychiatric disorders of adult life.Prevalence and natural history data suggest thatabout 3-10% of children fulfill the diagnostic criteriaof ADHD, and that at least one to two thirds of themwill continue to manifest some form of ADHD symptomsas adults together with functional impairmentand/or suffering.Twin and family studies of ADHD have demonstrateda strong heritable component in children andadolescents. Several environmental risk factors havebeen suggested to contribute to the etiology of ADHD.Imaging studies of adults have revealed disturbancesin several cerebral structures such as theprefrontal cortex involved in executive funtioning.Dysfunction has also been revealed in the basalganglia and cerebellum.Diagnosing ADHD in adults is based on the DSMIVcriteria but the diagnostic procedure requires acomprehensive evaluation and the use of a multimodalapproach. Several diagnostic instruments areavailable and are often useful to support a diagnosisof adult ADHD. One of the most problematic issuesis connected to psychiatric comorbidity since adultsseeking evaluation of ADHD often fulfill the criteriaof other psychiatric disorders like antisocial- and borderline personality disorders, affective- and bipolardisorders as well as subanstance use disordersjust to mention a few.The treatment of ADHD with central stimulantshas a long history since it was observed in 1937that benzedrine had a calming effect on behaviorof children at a residential treatment center in USA.Accordingly, amphetamine became the first drugapproved for ADHD. Presently methylphenidate isregarded as first line treatment. In pharmacologicalstudies methylphenidate has shown to be effectiveand well tolerated among both children and adults.Atomoxetine, a norepinephrine-specific reuptakeinhibitor is approved for treatment of ADHD inchildren and adolescents. Scientific studies indicateatomoxetine to be an effective treatment option inadults as well.Since ADHD is often chronic disorder acrossthe lifespan, with varying levels of functioning andimpairment, it requires a flexibel and multimodaltreatment approach.Apart from pharmacological treatment, adultswith ADHD should also be offered psychoeducation,practical support in daily life when required, and insome instances psychotherapy.

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Neuropsychopharmacologia Hungarica. 2010;12:27.

BIPOLAR DISORDER OR ADHD? DIAGNOSTIC CONSIDERATIONS.

Isacsson G.

Co-morbid ADHD has been found in 25% of BDpatients.Furthermore, ADHD and Bipolar Disorder(BD) share several symptoms. In many patients, thecorrect diagnosis can therefore be difficult to establish.Depression is often superimposed on ADHD. ManyADHD symptoms may appear as BD symptoms:Affective instability and irritability might be interpretedas indicating manic or mixed affective episodes,the hyperactivity and impulsiveness in ADHD canmimic such manic symptoms as decreased need forsleep, talkativeness, increased activity and injudiciousbehaviour, while inattention can be interpreted asracing thoughts, loose associations and distractibility.In children, the manifestations of BD and ADHDcan be almost indistinguishable. Diagnostics musttherefore rely, besides the structured clinical investigation,on the time course, on the heredity and onnuances of symptoms requiring clinical experienceof both disorders to interpret correctly. Diagnosis exjuvantibus may be the ultimate method, not least toestablish co-morbid diagnoses.

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Neurosci Biobehav Rev. 2012;36:2248-56.

META-ANALYSIS OF FMRI STUDIES OF TIMING IN ATTENTION-DEFICIT HYPERACTIVITY DISORDER (ADHD).

Hart H, Radua J, Mataix-Cols D, et al.

Attention-deficit hyperactivity disorder (ADHD) is associated with deficits in timing functions with, however, inconclusive findings on the underlying neurofunctional deficits. We therefore conducted a meta-analysis of 11 functional magnetic resonance imaging (fMRI) studies of timing in ADHD, comprising 150 patients and 145 healthy controls. Peak coordinates were extracted from significant case-control activation differences as well as demographic, clinical, and methodological variables. In addition, metaregression analyses were used to explore medication effects. The most consistent deficits in ADHD patients relative to controls were reduced activation in typical areas of timing such as left inferior prefrontal cortex (IFC)/insula, cerebellum, and left inferior parietal lobe. The findings of left fronto-parieto-cerebellar deficits during timing functions contrast with well documented right fronto-striatal dysfunctions for inhibitory and attention functions, suggesting cognitive domain-specific neurofunctional deficits in ADHD. The meta-regression analysis showed that right dorsolateral prefrontal cortex (DLPFC) activation was reduced in medication-naive patients but normal in long-term stimulant medicated patients relative to controls, suggesting potential normalization effects on the function of this prefrontal region with long-term psychostimulant treatment.

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Nicotine Tob Res. 2013;15:149-57.

MATERNAL SMOKING DURING PREGNANCY AND ADHD: A COMPREHENSIVE CLINICAL AND NEUROCOGNITIVE CHARACTERIZATION.

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

Introduction: Evidence from epidemiological studies has consistently shown an association between maternal smoking during pregnancy (MSDP) and attention-deficit/hyperactivity disorder (ADHD). The objective of this study is to test the hypothesis that children with ADHD exposed to MSDP show a distinctive clinical and neurocognitive profile when compared with unexposed children.

Methods: Four hundred and thirty-six children diagnosed with ADHD were stratified by exposure to MSDP and compared with regard to severity of illness, comorbidity, IQ, and executive function as assessed by a battery ofneuropsychological tests. All comparisons were adjusted for socioeconomic status, ethnicity, mother 's age at child ' s birth, and maternal alcohol consumption during pregnancy.

Results: Exposed children had more severe behavioral problems with greater externalizing symptoms and more conduct and oppositional defiant disorder items, lower verbal IQ, and a sluggish cognitive profile on the Continuous Performance Test (CPT). Linear regression analyses revealed a dose-response relationship between the average number of cigarettes smoked per day during pregnancy and verbal IQ, CPT omission errors T score and several other clinical variables.

Conclusions: These results suggest that MSDP is associated with a more severe form of ADHD, characterized by more severe clinical manifestations and poorer neuropsychological performance. This phenotypic signature associated with MSDP may help to identify a morehomogenous subgroup of children with ADHD.

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Paediatr Child Health. 2013;23:1-4.

DEALING WITH ACUTELY DISRUPTIVE CHILDREN IN HOSPITAL.

Crabb A.

Disruptive children in a paediatric setting can be difficult to manage, can make treatment decisions more complex and put the young person, parents and staff at risk. Risks include delayed or incomplete treatment, and physical harm to the patient, parent or staff members. Anxiety generated around a young person acting in a disruptive way can further escalate the problem. Being aware of the systemic impact of disruptive behaviour is an important first step in managing it. Whilst there are legal frameworks to help manage the acutely disruptive patient, each case needs to be considered on its merits. The Mental Health Act is not always the most relevant legal framework and its implementation does not normally enable the responsible clinician to treat a physical illness. Maximizing use of play specialists and creating a suitable

environment can reduce the need for restraint and medication, which should be used with caution and only with adequate training.

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Pediatr Integr. 2012;16:691-99.

LEARNING DISORDERS.

Sans A, Boix C, Colome R, et al.

Learning disabilities (LD) occur in 5-15% of schoolaged population. School underachievement and disruptive behavior in classrooms may be frequent without an early recognition and adequate management. In our country, school drop off is an important issue that will determine the future of our scholars. In Spain, about 30% of students undergo school failure, a rate signifi cantly higher than other countries in Europe. The main purpose of this chapter is to review the different LD, that is, those diffi culties that may interfere with the scholar achievement in children with normal intellectual ability and instruction. Multidisciplinary intervention is essential, basically from neuroscience and education, and also from sociological and pediatrician sciences. The pediatrician, as a professional who assist children in school period, must be alert to the diffi culties related to learning. Healthcare includes, undoubtedly, a correct scholar performance.

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Pediatr Int. 2012;54:849-53.

KANA READING DISABILITY AND DAS-NAGLIERI COGNITIVE ASSESSMENT SYSTEM FINDINGS IN CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Nakashima N, Yamashita Y, Hirata R, et al.

Background: Epidemiological and clinical studies suggest that attention deficit hyperactivity disorder (ADHD) and reading disability co-occur more frequently than would be expected by chance. The purposes of this study were to (i) assess the frequency of Japanese syllabary (Kana) reading disability (RD) and (ii) measure the psychometric properties of the Das-Naglieri Cognitive Assessment System (DN-CAS) in a clinic-referred sample of Japanese children with ADHD.

Methods: Twenty children with ADHD aged 8-13 years were evaluated using both Kana reading tasks and the DN-CAS.

Results: Seven children (35%) showed excessive reading time in at least two of four Kana reading tasks and were diagnosed as ADHD plus RD. The children with ADHD plus RD took significantly longer to read a single mora, four-syllable words, and short sentences. There was no significant difference in the time it took the children with ADHD plus RD to read four-syllable non-words compared to the children with ADHD only. The children with ADHD plus RD had significantly lower simultaneous-processing scores in the DN-CAS compared to children with ADHD but not RD.

Conclusion: Children with ADHD should be given Kana reading tasks because RD is highly comorbid with ADHD. DN-CAS is a useful method for evaluating cognitive processing in children with ADHD with or without RD.

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Pediatr Int. 2012;54:838-43.

PREVALENCE OF ADHD SYMPTOMS IN PATIENTS WITH CONGENITAL HEART DISEASE.

Hansen E, Poole TA, Nguyen V, et al.

Objective: The presence of attention-deficit-hyperactivity disorder (ADHD) symptoms in children with congenital heart disease (CHD) was investigated.

Methods: Swanson, Nolan and Pelham teacher and parent rating scales, version 4 (SNAP-IV), commonly used for assessing symptoms of ADHD, were completed by parents and counselors of children who attended a CHD summer camp. Mean scores (n = 51) were compared with two comparison groups without

CHD: patients with ADHD (n = 75) and patients without ADHD (n = 41). Parent scores were also compared to previously published parent normative data.
Results: Patients with CHD were reported to have elevated SNAP-IV scores by parents and counselors (11.8%). Parent ratings of inattention were significantly greater in CHD subjects when compared to the comparison group without ADHD (P < 0.001), and similar to the ADHD-positive comparison group. Regarding parent ratings of hyperactivity and impulsivity, the CHD group was significantly lower than the ADHD-positive controls (P = 0.024) but greater than the ADHD-negative controls (P < 0.001).
Conclusion: ADHD symptoms are more prevalent in children with CHD. Parent ratings of inattention and hyperactivity symptoms in CHD patients are similar to ratings in children diagnosed with ADHD. There is a trend towards a greater prevalence of inattention symptoms in patients with cyanosis or single ventricle physiology.

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Personality and Individual Differences. 2012 Nov;53:874-79.
TEMPERAMENT AND COMMON DISRUPTIVE BEHAVIOR PROBLEMS IN PRESCHOOL.
Martel MM, Gremillion ML, Roberts B.
The study evaluated trait associations with common Disruptive Behavior Disorders (DBD), Oppositional Defiant Disorder (ODD) and Attention-Deficit/Hyperactivity Disorder (ADHD), during an understudied developmental period: preschool. Participants were 109 children ages 3–6 and their families. DBD symptoms were available via parent and teacher/caregiver report on the Disruptive Behavior Rating Scale. Traits were measured using observational coding paradigms, and parent and examiner report on the Child Behavior Questionnaire and the California Q-Sort. The DBD groups exhibited significantly higher negative affect, higher surgency, and lower effortful control. Negative affect was associated with most DBD symptom domains; surgency and reactive control were associated with hyperactivity-impulsivity; and effortful control was associated with ADHD and inattention. Interactive effects between effortful control and negative affect and curvilinear associations of reactive control with DBD symptoms were evident. Temperament trait associations with DBD during preschool are similar to those seen during middle childhood. Extreme levels of temperament traits are associated with DBD as early as preschool.

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PLoS ONE. 2012;7.
MEASUREMENT OF STIGMATIZATION TOWARDS ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.
Fuermaier ABM, Tucha L, Koerts J, et al.
Objectives: In general, assessment tools for stigma in mental disorders such as attention deficit hyperactivity disorder (ADHD) are lacking. Moreover, misbeliefs and misconceptions about ADHD are common, in particular with regard to the adult form of ADHD. The aim of the present study was to develop a questionnaire measuring stigma in adults with ADHD and to demonstrate its sensitivity.
Methods: A questionnaire initially containing 64 items associated with stigma in adults with ADHD was developed. A total number of 1261 respondents were included in the analyses. The psychometric properties were investigated on a sample of 1033 participants. The sensitivity of the questionnaire was explored on 228 participants consisting of teachers, physicians and control participants.
Results: Thirty-seven items were extracted due to exploratory factor analysis (EFA) and the internal consistency of items. Confirmatory factor analysis (CFA) revealed good psychometric properties of a 6-factor structure. Teachers and physicians differed significantly in their stigmatizing attitudes from control participants.
Conclusions: The present data shed light on various dimensions of stigma in adult ADHD. Reliability and Social Functioning, Malingering and Misuse of Medication, Ability to Take Responsibility, Norm-violating and Externalizing Behavior, Consequences of Diagnostic Disclosure and Etiology represent critical aspects associated with stigmatization.

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PLoS ONE. 2012;7.

LAMINAR THICKNESS ALTERATIONS IN THE FRONTO-PARIETAL CORTICAL MANTLE OF PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Hoekzema E, Carmona S, Ramos-Quiroga JA, et al.

Although Attention-Deficit/Hyperactivity Disorder (ADHD) was initially regarded as a disorder exclusive to childhood, nowadays its prevalence in adulthood is well established. The development of novel techniques for quantifying the thickness of the cerebral mantle allows the further exploration of the neuroanatomical profiles underlying the child and adult form of the disorder. To examine the cortical mantle in children and adults with ADHD, we applied a vertex-wise analysis of cortical thickness to anatomical brain MRI scans acquired from children with (n=43) and without ADHD (n=41), as well as a group of adult neurotypical individuals (n=31), adult patients with a history of stimulant treatment (n=31) and medication-naive adults with ADHD (n=24). We observed several clusters of reduced laminar cortical thickness in ADHD patients in comparison to neurotypical individuals. These differences were primarily located in the dorsal attention network, including the bilateral inferior and superior parietal cortex and a section of the frontal cortex (centered on the superior frontal and precentral gyrus bilaterally). Further laminar thickness deficits were observed in the bilateral orbitofrontal cortex and medial occipital cortex. The deficits in the cortical surface were especially pronounced in the child sample, while adult patients showed a more typical laminar thickness across the cerebral mantle. These findings show that the neuroanatomical profile of ADHD, especially the childhood form of the disorder, involves robust alterations in the cortical mantle, which are most prominent in brain regions subserving attentional processing.

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Psychiatr Genet. 2013.

ASSOCIATION OF THE CATECHOL-O-METHYLTRANSFERASE GENE AND ATTENTION DEFICIT HYPERACTIVITY DISORDER: RESULTS FROM AN EPIDEMIOLOGICAL STUDY OF ADOLESCENTS MEXICO CITY.

Martinez-Levy GA, Benjet C, Perez-Molina A, et al.

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Psychiatr Genet. 2013;23:38.

FAMILY-BASED ASSOCIATION STUDY OF TRYPTOPHAN HYDROXYLASE 2 AND SEROTONIN 1A RECEPTOR GENES IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Hsu CD, Tzang RF, Liou YJ, et al.

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Psychiatr Invest. 2012;9:384-90.

EFFECT OF METHYLPHENIDATE ON SLEEP PARAMETERS IN CHILDREN WITH ADHD.

Lee SH, Seox WS, Sung HM, et al.

Objective: The primary aim of this study was to investigate the acute impact of methylphenidate (MPH) on sleep parameters in attention-deficit/hyperactivity disorder (ADHD) children. The second aim was to investigate the different effects of intermediate- and longacting MPH on sleep parameters. The third aim was to test the different effects of dose and age on sleep parameters.

Methods: Ninety-three ADHD children were enrolled and randomized to two different MPH preparations. Baseline and daily sleep diaries were evaluated for four weeks after taking medication. Weekday and weekend bedtimes, wake-up times, sleep latencies and total sleep times were compared by weeks.

Results: After taking MPH, there was a significant delay in bedtimes and a significant reduction of total sleep time (TST) both on weekdays and at weekends. There was also a significant delay in wake-up time on weekdays. However, the difference was applied to younger age group children only. There was no difference in changes of TST between metadate-CD and OROS-MPH. There also was no difference in changes of TST with different doses of MPH.

Conclusion: MPH had negative impacts on sleep among young ADHD children, but different preparations and doses did not affect the result.

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Psychiatry Res. 2013.

STEEP TEMPORAL REWARD DISCOUNTING IN ADHD-COMBINED TYPE: ACTING UPON FEELINGS.

Scheres A, Tontsch C, Lee Thoeny A.

Children and adolescents (ages 6-17) with ADHD-C (n=25), ADHD-inattentive type (ADHD-I) (n=20) and matched difficulty waiting play a primary role in symptoms of ADHD, in particular impulsivity. Current theories suggest that relatively strong preferences for small immediate rewards as observed in ADHD-Combined type (ADHD-C) are the result of delay-related negative feelings. However, the measurement of difficulty waiting is typically limited to objective choices between small immediate and large delayed rewards. This study aimed at extending the measurement of difficulty waiting in ADHD-C with ratings about subjective feelings. Typically developing participants (n=37) performed temporal reward discounting tasks, and completed a Visual Analogue Scale of subjectively experienced ease/difficulty waiting. Although those with ADHD-C demonstrated relatively steep temporal reward discounting, as reported elsewhere (Scheres et al., 2010), there were no group differences for subjectively experienced ease/difficulty waiting. Additionally, correlations between subjective and objective measures of difficulty waiting were significantly higher in the ADHD-C group than in the control group. These findings suggest that (a) those with ADHD-C do not choose impulsively because they have more negative feelings about waiting than controls; and (b) choices in the ADHD-C group are more in accordance with, or driven by, their feelings than choices made by the participants in the control group.

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Psychiatry Research: Neuroimaging. 2012 Nov;204:161-67.

THALAMIC SHAPE AND CONNECTIVITY ABNORMALITIES IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Xia S, Li X, Kimball AE, et al.

Attention-deficit/hyperactivity disorder (ADHD) is characterized by widespread structural and functional abnormalities in the cortico-striato-thalmo-cortical (CSTC) loops that subserve attention and executive functions. In this study, we analyzed thalamic shape and its white matter connections using structural magnetic resonance imaging and diffusion (DTI) data acquired from children with ADHD (n = 19) and controls (n = 19). Shape morphology of the thalamus was assessed using shape-based analysis, while connectivity between the thalamus and other brain regions was determined using probabilistic diffusion tractography. Shape-based analysis indicated significant regional atrophy in the left thalamus in children with ADHD compared to controls. Group analyses of white matter connectivity measures showed significantly decreased mean fractional anisotropy (FA) and volume of the tracts between thalamus and striatum, hippocampus, and prefrontal lobe in children with ADHD compared to controls. The structural abnormalities within the thalamus and the reduced integrity of the white matter tracks between the thalamus and other brain regions, as shown from the results of this study, may be the anatomical bases of the impaired cognitive performances in the attention and executive function domains in ADHD.

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Res Dev Disabil. 2013;34:1036-43.

PARENTS PSYCHOPATHOLOGY OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Margari F, Craig F, Petruzzelli MG, et al.

Attention Deficit Hyperactivity Disorder (ADHD) is a disorder with extremely complex etiology, not yet well defined but certainly multi-factorial. This study investigated the possible etiopathogenetic role of ADHD symptoms and psychopathology disorders in parents of children with ADHD. We present a case-control study of parents of 50 children affected by ADHD and of 45 healthy children, matched to age and gender.

Parents of ADHD children reported higher levels of ADHD symptoms, depressive disorders and Depressive Personality Disorders than parents of healthy children. Mothers displayed greater presence of depression, while fathers showed problems concerning alcohol use. The occurrence of ADHD symptoms, psychopathology and personality disorders in parents highlights the importance to integrate the treatment programs in the ADHD children with the screening and treatment for psychopathological symptoms of the parents.

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Res Dev Disabil. 2013;34:1100-08.

INJURY-PRONENESS OF YOUTH WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER: A NATIONAL CLINICAL DATA ANALYSIS IN TAIWAN.

Tai YM, Gau SSF, Gau CS.

Limited literature documents injury-proneness of attention-deficit hyperactivity disorder in western population. However, only a few studies prospectively investigated the prediction of ADHD to injuries without considering other psychiatric and physical conditions and there is lack of such data in Asian population. To prospectively examine the prediction of ADHD to the risk of injury in a national sample of Taiwan, we conducted this study with samples including 1965 6-18-year-old youths with newly diagnosis of ADHD from 1999 to 2003, and 7860 sex-, age- and index day-matched non-ADHD controls from Taiwan's National Health Insurance Research Database (1997-2008). Relevant psychiatric and physical disorders, demographics, and medications were also included in the Cox proportional hazard models with injury as the outcome. Our results showed that ADHD cases had a roughly 2-fold and 5-fold higher risk of each injury, and overall injury than controls after considering all confounding factors, respectively. In addition to ADHD, use of anxiolytics, antidepressants, and antipsychotics, and comorbid physical illnesses also predicted the injury prospectively. Our findings strongly support that ADHD predicted injury risks and imply that physicians should take the risk of injury into consideration while prescribing medications other than stimulants to patients with ADHD, especially anxiolytics.

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Revista Brasileira de Psiquiatria. 2012;34:321-28.

IS THERE AN ASSOCIATION BETWEEN PERINATAL COMPLICATIONS AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-INATTENTIVE TYPE IN CHILDREN AND ADOLESCENTS?

Ketzer CR, Gallois C, Martinez AL, et al.

Objective: The objective of the present study is to investigate the association between attention-deficit/hyperactivity disorder (ADHD), predominantly inattentive type (ADHD-I) and prenatal, delivery and early postnatal complications (PDPC).

Method: In a case-control design, we assessed a sample of 124 children and adolescents with ADHD-I and 124 non-ADHD controls (6-17 years old) from both a non-referred (n=200) and a clinical sample (n = 48). Cases and controls, matched by gender and age, were systematically evaluated through structured diagnostic interviews. Prenatal, delivery and early postnatal complications (PDPC), as well as potential confounders were evaluated by direct interview with biological mothers.

Results: Conditional logistic regression analysis showed that children and adolescents whose mothers presented more PDPC had a significantly higher risk for ADHD-I (p=0.005; OR=1.25; CI 95%: 1.1-1.5).

Conclusions: In a case-control study, we expanded to ADHD-I previous findings suggesting the association between perinatal factors and broadly defined ADHD. Due to the preventable nature of some of these PDPC, our results have clear impact in public mental health policies.

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Social Psychiatry and Psychiatric Epidemiology. 2012 Dec;47:1885-90.

PREVALENCE, INCIDENCE, AND STIMULANT USE OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN TAIWAN, 1996–2005: A NATIONAL POPULATION-BASED STUDY.

Chien IC, Lin CH, Chou YJ, et al.

Purpose: We used National Health Insurance (NHI) database to examine the prevalence, incidence, and stimulant use of attention-deficit hyperactivity disorder (ADHD) diagnosis in Taiwan.

Methods: The National Health Research Institute provided a database of 10,00,000 random subjects for study. A population-based random sample of 372,642 patients aged younger than 18 was obtained as a dynamic cohort. Those study subjects who had at least one service claim from 1996 to 2005, with a principal diagnosis of ADHD, were identified.

Results: The cumulative prevalence of ADHD diagnosis increased from 0.06 to 1.64 % from 1996 to 2005. The annual incidence of ADHD diagnosis increased from 0.02 to 0.34 % from 1997 to 2005. The highest incidence rates of ADHD diagnosis for both males and females were in the 6- to 11-year age group. Higher incidence was detected in males (HR 3.76, 95 % CI 3.48–4.07), those who lived in northern region (HR 1.35, 95 % CI 1.07–1.71) and urban area (HR 1.53, 95 % CI 1.40–1.66). The percentage of stimulant use in children with ADHD diagnosis increased from 39.6 to 54.0 % from 1997 to 2005.

Conclusions: Our findings suggest increases in the prevalence and incidence rates of ADHD diagnosis in Taiwan, which was in line with those studies of Western countries. However, the prevalence of ADHD diagnosis in the NHI program was still much lower than in the community studies. The percentage of stimulant use in children with ADHD diagnosis also has an increasing trend, which warrants further study.

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Soc Sci Med. 2013;79:76-83.

"THEY SILENTLY LIVE IN TERROR..." WHY SLEEP PROBLEMS AND NIGHT-TIME RELATED QUALITY-OF-LIFE ARE MISSED IN CHILDREN WITH A FETAL ALCOHOL SPECTRUM DISORDER.

Ipsiroglu OS, McKellin WH, Carey N, et al.

Children and adolescents with a Fetal Alcohol Spectrum Disorder (FASD) are at high-risk for developing sleep problems (SPs) triggering daytime behavioral co-morbidities such as inattention, hyperactivity, and cognitive and emotional impairments. However, symptoms of sleep deprivation are solely associated with typical daytime diagnosis, such as attention deficit hyperactivity disorder (ADHD) and treated with psychotropic medications. To understand how and why SPs are missed, we conducted qualitative interviews (QIs) with six parents and seven health care professionals (HCPs), and performed comprehensive clinical sleep assessments (CCSAs) in 27 patients together with their caregivers referred to our clinic for unresolved SPs. We used narrative schema and therapeutic emplotment in conjunction with analyzes of medical records to appropriately diagnose SPs and develop treatment strategies. The research was conducted at British Columbia Children's Hospital in Vancouver (Canada) between 2008 and 2011. In the QIs, parents and HCPs exhibited awareness of the significance of SPs and the effects of an SP on the daytime behaviors of the child and the associated burdens on the parents. HCPs' systemic inattention to the sequelae of SPs and the affected family's wellbeing appears due to an insufficient understanding of the various factors that contribute to nighttime SPs and their daytime sequelae. In the CCSAs, we found that the diagnostic recognition of chronic SPs in children and adolescents was impaired by the exclusive focus on daytime presentations. Daytime behavioral and emotional problems were targets of pharmacological treatment rather than the underlying SP. Consequently, SPs were also targeted with medications, without investigating the underlying problem. Our study highlights deficits in the diagnostic recognition of chronic SPs among children with chronic neurodevelopmental disorders/disabilities and proposes a clinical practice strategy, based on therapeutic emplotment that incorporates patients and parents' contributions in recognizing SPs and related sequelae in designing appropriate treatment and care.

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TAF Prev Med Bull. 2012;11:741-48.

FAMILY FUNCTIONS AND LEVELS OF ANXIETY-DEPRESSIVE SYMPTOMS IN MOTHERS OF CHILDREN WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Karaman D, Durukan I, Kara K.

Aim: The aim of this study is to examine the family functions of children with attention-deficit hyperactivity disorder (ADHD) and depression-anxiety levels of their mothers.
Method: Forty-five mothers of children with ADHD aged 7-12 years old who were evaluated according to DSM-IV criteria were included in this study. The control group consisted of 44 mothers of healthy children. Sociodemographic data form, the Beck Depression Inventory (BDI), the State-Trait Anxiety Inventory (STAI) and the Family Assessment Device (FAD) were applied to the participants.
Results: It was revealed that the study group had depression (p<0.001), state (p=0.001) and trait anxiety levels (p=0.047), subtests of FAD in which roles (p=0.003), affective responsiveness (p= 0.008), affective involvement (p=0.023) and behavior control points (p=0.04) significantly higher than those of the control group.
Conclusion: The results suggest that parents of children with ADHD would be exposed to distress and might be vulnerable to depression and anxiety disorders compared to those of healthy controls. Moreover, ADHD negatively can affect the family's function. However, there is an actual cause and effect relationship requires further investigation.

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The Journal of Neuropsychiatry and Clinical Neurosciences. 2012;24:111-14.

CAN COMPUTERIZED COGNITIVE TESTS ASSIST IN THE CLINICAL DIAGNOSIS OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER?

Bloch Y, Fixman M, Maoz H, et al.

A group of 34 children and adolescents suspected of having attention-deficit hyperactivity disorder were referred for a computerized evaluation that included sustained attention, working memory, planning, and set-shifting. Although only sustained attention had reasonable specificity, all tests had questionable contribution to the diagnostic evaluation.

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Tijdschr Psychiatr. 2013;55:63-64.

ATOMOXETINE FOR ADHD SYMPTOMS IN CHILDREN WITH AUTISM SPECTRUM DISORDER.

Harfterkamp M.

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Zeitschrift für Neuropsychologie. 2012 Dec;23:205-13.

LONG-TERM EFFECTS OF A MULTIMODAL BEHAVIOURAL ADHD TRAINING: A FMRI STUDY.

Sotnikova A, Steinmann E, Wendisch V, et al.

Several studies have demonstrated that behavioural therapy oriented interventions exert a positive influence on the clinical course of the attention-deficit hyperactivity disorder (ADHD). However, the long-term effects of the behavioral treatment in ADHD, especially those on neuronal mechanisms underlying this disorder, have been studied insufficiently. Functional MRI (Go-NoGo paradigm) was carried out in 9 children with ADHD before and 1.5 years after a response cost and token-based training. In the follow-up, patients were still characterized by a significant increase in activation in the anterior cingulate and in the precentral gyrus compared with recordings done before the training. It seems likely that the behavioural training elicits stable neuronal changes in children with ADHD which correspond with an improvement of neuropsychological functioning and clinical symptoms.

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Learning and Individual Differences 22 (2012) 896–900

Contents lists available at SciVerse ScienceDirect

Learning and Individual Differences

journal homepage: www.elsevier.com/locate/lindif

Children with ADHD symptoms are less susceptible to gap-filling errors than typically developing children

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ARTICLE INFO

Article history:
Received 21 September 2011
Received in revised form 16 February 2012
Accepted 1 May 2012

Keywords:
False memories
Script
ADHD
Confidence ratings

ABSTRACT

Enhanced semantic processing is associated with increased false recognition of items consistent with studied material, suggesting that children with poor semantic skills could produce fewer false memories. We examined whether memory errors differed in children with Attention Deficit/Hyperactivity Disorder (ADHD) and controls. Children viewed 18 photographs for each of 4 scripts (e.g., eating at a restaurant). A recognition test followed which included old and new photographs, some of which presenting script consistent information and others depicting the cause (e.g., knocking over a glass of coke) of an effect actually viewed during encoding (wiping the table at the restaurant). Children with ADHD exhibited lower false recognition for script-consistent photographs and were more confident in their errors than controls.

1. Introduction

In recent years, the examination of developmental trends in spontaneous memory distortions (i.e., distortions that are not induced by provision of misleading information or social pressure) has motivated a large number of studies (for reviews: Brainerd, Reyna, & Zember, 2011; Brainerd, Reyna, & Ceci, 2008; Gallo, 2006). It has been shown that false memories increase with age when paradigms which involve the semantic processing of information are employed (e.g., Deese-Roediger-McDermott paradigm: Roediger & McDermott, 1995), revealing an important role of conceptual knowledge on the susceptibility to these memory errors. The result suggests that children with learning difficulties and poor semantic processing abilities could produce fewer false memories than typically developing children, with important implications for judging their eyewitness reliability in legal cases in which children with disabilities are required to testify; indeed, these cases are increasing in frequency. However, special populations of children with disabilities have only been studied in a handful of studies. For example, Brainerd and colleagues (Brainerd, Forrest, Karibian, & Reyna, 2006) found that children with learning disabilities compared to a control group were less prone to evince false memories induced with the Deese–Roediger–McDermott (DRM) task, which requires to memorize lists of semantically related words and results in high levels of false recognition for distracters that represent the theme of each of the studied lists. This result is likely due to their less efficient semantic processing abilities. Furthermore, Weekes, Hamilton, Oakhill, and Holliday (2008) showed that this false-memory effect was reduced in children with a specific reading comprehension disability.

While these studies provide convincing evidence that semantic processing may result in fewer false memories for children with learning disabilities, it is not clear whether other paradigms, involving different processes at the basis of illusory memories, may also differentiate typically developing children from children with certain disabilities. We thus decided to focus on two types of memory errors which have been found to influence recognition performance in a memory task which involves the presentation of materials organized in scripts, both in adults (Hannigan & Reinitz, 2001) and children (Lyons, Ghetti, & Cornoldi, 2010).

Early research on the organization of general event knowledge suggested that children as young as 3 years are able to temporally organize sequences of recurring events and report on them (Nelson & Gruendel, 1981). Children's event knowledge improves with age, and children's reports – in the form of scripts – about their familiar experiences become richer and with a greater amount of component actions as they grow older (e.g., Hudson & Shapiro, 1991). Although script knowledge facilitates recall and story comprehension (e.g., Brewer & Treyens, 1981), it also induces memory distortions when a person ought to make memory decisions about events that were not previously experienced but are consistent with a known script. In particular, if an individual is presented with images which are consistent with the script initially studied but that were nonetheless absent, s/he may incur in a *gap-filling error*, i.e., thinking that the image was part of the script when indeed it was not (Hannigan & Reinitz, 2001; Lyons et al., 2010). If the person is presented with an image that represents an effect of a possible, but not typical, action

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1041-6080/$ – see front matter © 2012 Elsevier Inc. All rights reserved.
doi:10.1016/j.lindif.2012.05.008

embedded in a script, then s/he may mistakenly recognize the inferred, but not presented, corresponding cause (*backward causal inference error*) (Hannigan & Reinitz, 2001; Lyons et al., 2010). In Hannigan and Reinitz' study (Experiment 2, 2001), gap-filling errors were reported by adults to be associated, at the subjective level, to a sense of familiarity with the encountered event, whereas the backward causal inference errors were associated to a vivid recollection. This is also supported by developmental evidence which suggests that the production of causal errors increases with increasing age, likely resulting from the influence of recollection, which is known to develop during childhood, whereas the production of gap-filling errors remains invariant, likely resulting from the process of familiarity, which is known to be stable from about age 7 (Ghetti & Angelini, 2008; Lyons et al., 2010).

The present study examines these phenomena in a special population of children, namely children with Attention Deficit/Hyperactivity Disorder (ADHD). This population is of particular interest, because an impaired semantic memory elaboration has been sometimes observed in this group (Cornoldi, Barbieri, Gaiani, & Zocchi, 1999; Shallice et al., 2002). Based on this research, we predict lower rates of gap-filling errors in children with ADHD compared to typically developing children.

Of interest, some studies indicate that episodic memory and autobiographical memory are particularly well-functioning in children with ADHD, given their levels of functioning in other cognitive domains (e.g., Skowronek, Leichtmann, & Pillemer, 2008). If this is the case, in this population, we should expect higher production of backward causal inference compared to gap-filling errors, given that the former errors are thought to largely depend on episodic recollection processes (Lyons et al., 2010). There is an additional reason why these errors should be more frequent in children with ADHD. The recollective nature of these errors makes their experience vivid and subjectively compelling (Lyons et al., 2010). Thus, they should be particularly difficult to inhibit. The main deficits of ADHD revolve around executive dysfunction (Pennington & Ozonoff, 1996; Willcutt, Doyle, Nigg, Faraone, & Pennington, 2005), including impulsivity and lack of attentional control, which can be assumed to influence the performance in a false memory paradigm. Executive dysfunction has been associated with the generation of memory errors (Barkley, 1996), and previous research showed that children with ADHD exhibited higher memory errors due to intrusions of irrelevant information (Cornoldi et al., 1999; Marzocchi, Lucangeli, De Meo, Fini, & Cornoldi, 2002). Thus, children with ADHD may encounter great difficulty at inhibiting backward causal inference errors.

However, we should consider one alternative hypothesis. Given the evidence of inhibitory difficulties in ADHD (e.g., Marzocchi et al., 2002), one could predict that children with ADHD will generate more errors overall thereby obscuring other errors such as gap-filling errors and backward causal inferences. Furthermore, if children with ADHD encounter particular difficulty at controlling and monitoring their cognitive processes, then they should be expected to manifest higher confidence in their errors, compared to control children, likely resulting from their impulsivity.

Thus, the general goal of this study was to investigate episodic false memories in children with ADHD symptoms. Due to study constraints and the lack of agreement in Italy for the diagnosis of ADHD, we adopted the same selection procedure adopted in previous studies (e.g. Cornoldi et al., 2001) based on teachers' ratings. To examine memory we used a recognition memory paradigm for material organized in scripts (adapted from Lyons et al., 2010). We decided to employ this type of material because of its ecological validity and its interesting appearance for children, especially for those who have problems keeping their attention on a particular task. The current paradigm, previously used with adults (Hannigan & Reinitz, 2001) and then adapted for typically developing children (Lyons et al., 2010) was further adapted. As in its original version, it allows for the investigation of memory accuracy and memory errors that may occur when a person sees pictorial images that represent the typical actions that compose a script, for example eating at a restaurant, and then remembers elements not presented, although consistent with the presented material. In the present study we administered four scripts: eating at a restaurant, going grocery shopping, getting up in the morning and attending a lesson in school. Embedded in the scripts were images of the effects of peculiar scenes whose causes were not presented. In the recognition phase some target photographs were presented with distracter images which could be either consistent with the script or causes whose effects had been previously presented. Participants had to perform a *yes/no* recognition test and tell their degree of confidence relative to their responses.

2. Method

2.1. Participants

Twenty-six children (23 males and 3 females) referred by teachers for ADHD symptoms (from now described as ADHD group) and 28 control children (13 males and15 females) participated in this study. The two groups were matched for age and educational level. Mean age was 9.5 years ($SD = .83$) for the ADHD group and 9.8 years ($SD = .75$) for the control group (age ranges were respectively 8–11 years and 8.5–11.2 years). Children in the control group were recruited from local schools. Nineteen children with ADHD symptoms were recruited from the same schools based on teachers' reports. Teachers' reports on ADHD symptoms were further supported by other convergent information collected on children on their behavior in out-of-school and family contexts. Seven children were recruited at the Unit for ADHD of San Donà di Piave, Italy on the basis of a diagnosis made by a clinical psychologist expert in ADHD. Children of the ADHD group did not receive any medication for ADHD symptoms. Both children with ADHD and control children were within the average for what concerns the cognitive level and did not present other serious psychological or social problems: these aspects were assessed through the specific items of the COM questionnaire (Marzocchi, Re, & Cornoldi, 2010) filled by the teachers and the clinicians (the Scale has been shown to have values of reliability and interjudge agreement between .49 and 1) or through a standardised intelligence test. Thus, all children had good intellectual abilities and those with low intellectual abilities were excluded from the study. The 19 children with ADHD symptoms were recruited from the schools on the basis of the cut-offs for ADHD validated for the *SDAI* scale (Marzocchi & Cornoldi, 2001): children had a mean score per item either above 1.5 in the attention subscale or above 1.3 in the Hyperactivity Subscale (or in both) of the *SDAI* ('Scala per i Disturbi di Attenzione/Iperattività per Insegnanti', *ADHD scale for teachers*; Marzocchi et al., 2010) (the group resulted to include 2 children of the Inattention subtype, 8 children of the Hyperactivity subtype and 9 children of the Combined subtype). The SDAI includes 18 items, each giving precise descriptions of one of the 18 symptoms of ADHD as indicated in the DSM-IV TR (APA, 2000). The scale has been validated and standardized for the Italian population (Marzocchi & Cornoldi, 2001) and has shown good reliability ($r = .81$) and inter-rater agreement ($r = .78$; Marzocchi & Cornoldi, 2001). The scale includes two subscales, one for Inattention (9 items), and one for Hyperactivity/Impulsivity (9 items). Teachers are required to observe closely the child's behavior for about 2 weeks, and report the frequency of symptomatic behaviors described in each item. Scores range from 0 (problematic behavior never present), to 1 (sometimes present), 2 (often present), and 3 (very often present). With the exception of the 7 children diagnosed at the ADHD Unit, both ADHD and control children were rated by the same teachers. The mean scores in the Inattention SDAI subscale were respectively 13 ($SD = 9.9$) and .26 ($SD = .73$) for the ADHD and the control group, while the mean scores for Hyperactivity Subscale were respectively 17 ($SD = 7.4$) and .47 ($SD = .77$).

2.2. Materials

2.2.1. Pictorial stimuli

A series of color photographs depicting one of four scripts was used. The scripts were: eating at a restaurant, attending a lesson at school, going grocery shopping and getting up in the morning. For each script, 24 photographs were created: 20 photographs depicted the typical sequence of actions in the script (16 were used in the presentation, the remaining 4 photographs were used as distracters in the recognition phase), 4 photographs depicted two sets of cause–effect scenes, in particular 2 negative sequences (e.g., effect: wiping the table at the restaurant; cause presented only at test: knocking over a glass of coke) and 2 positive sequences (e.g., wearing new shoes before going to school; cause: mum giving new shoes in a wrapped box). Pilot testing with younger children confirmed that the material was understandable even at the age of 5 years. Further, the study stimuli also included 10 photographs that were inconsistent with any of the script. They represented other children doing different actions such as playing in the yard, playing at the beach etc.

2.2.2. Recognition phase

A unique randomized sequence of 72 photographs was used for all participants. The test included, for each script: (a) 6 old script-consistent photographs, (b) 4 new script-consistent photographs, (c) 2 cause photographs whose effects had been presented during the encoding phase, (d) 2 control cause photographs (e.g., photographs of effects whose causes had not been seen at the encoding phase), (e) 2 old script-inconsistent photographs and (f) 2 new script-inconsistent photographs.

2.2.3. Confidence rating board (CRB; Ghetti, Qin, & Goodman, 2002)

Two photographs depicting respectively a child with a confident expression and the same child with a doubtful expression were positioned on the opposite sides of the board. Three dots were drawn between these photographs which represent the three degrees of confidence (very sure, somewhat sure, not sure at all). Children were instructed to point to the dot near the picture of the child with a confident facial expression when they were very sure (that they saw or that they did not see the photograph), the middle dot, when they were somewhat sure, and the dot near the doubtful facial expression when they were not at all sure.

2.3. Procedure

2.3.1. Encoding phase

All participants were tested individually in quiet rooms in their schools (with the exception of the 7 children who were tested at the clinical service for ADHD). They were told that they would view a series of photographs in logical order representing other children performing everyday actions. They were also told to pay close attention to every picture and to try to understand what the situation represented depicted. For each of the 4 scripts, participants studied 18 photographs in a logical sequence. Embedded in these photographs, there were 2 effect photographs (e.g., oranges on the floor of a grocery store) whose corresponding causes (e.g., a child removing an orange from the bottom of a stack) were not viewed. Each photograph was shown on the computer screen for 2 s followed by a 3-second interval during which a black slide was presented. Scripts were presented sequentially without interruptions among them. Script order was counterbalanced. Five script-inconsistent photographs were presented at the beginning and at the end of the encoding phase to reduce primacy and recency effects. Overall, the encoding phase lasted approximately 7 min.

2.3.2. Recognition phase

After a 15-minute filler task (during which participants performed a series of search tasks) participants were administered a self-paced *old/new* recognition task. The test included a sequence of 72 photographs (see the Materials section) presented in a randomized sequence. For each photograph, participants had to tell "yes" if they recognized the picture as seen during the encoding phase, and "no" if they thought the picture had not been seen in the encoding phase. Further, for each recognition answer, participants gave confidence ratings using the CRB. The overall duration of the task (including encoding, interval, and recognition test) was approximately 30 min.

3. Results

Given that – due to the typical characteristics of ADHD population – the group of children with ADHD symptoms included a higher number of males than did the control group, a preliminary analysis within the control group examined whether gender could affect the pattern of results. Such a comparison did not show any gender effect ($p > .6$) and therefore the subsequent analyses were conducted collapsing across genders.

To assess memory accuracy and memory errors, we measured the following dependent variables consistent with previous research (Lyons et al., 2010): (1) rate of "yes" responses to target photographs consistent with the script (i.e., hit consistent), (2) rate of "yes" responses to target photographs inconsistent with the script (i.e., hit inconsistent); (3) rate of "yes" responses to script-consistent distracters *minus* rate of "yes" responses to script inconsistent distracters (i.e., gap-filling errors); and (4) rate of "yes" responses to distracters representing the unseen cause of a seen effect *minus* rate of "yes" responses to distracters representing the unseen cause of an unseen effect (i.e., backward causal inference errors).

We conducted a 2 (group: ADHD vs. control) × 2 (item type: script consistent vs. inconsistent) mixed ANOVA with rates of "yes" responses to target images as the dependent measure. We found a main effect of item type, $F(1,52) = 24.8$, $p < .001$, $\eta_p^2 = .32$, such that in both groups of children, more target images inconsistent with the script were correctly recognized ($M = .93$, $SD = .20$) than were target images consistent with the script ($M = .77$, $SD = .16$). However, no significant main effect of group or interaction effect between group and item was found ($ps \geq .49$). In contrast, group differences emerged when we examined memory errors (see Table 1a). As evident in Table 1a, participants overall showed low levels of false alarms for script inconsistent and control cause distracters; and these levels were nearly identical in the two participant groups. We then conducted a 2 (group: ADHD vs. control) × 2 (error type: gap-filling vs. backward causal inference), and found that, in general, there was a difference in error type: $F(1,52) = 16.27$, $p < .001$, $\eta_p^2 = .24$, such that all participants produced a higher rate of gap-filling errors compared to backward causal inference errors. As the control group tended to produce more gap-filling errors than the ADHD group and the opposite was true for backward inference errors (see Table 1a), we computed a relative error score, computing the proportion of gap-filling errors with respect to the overall proportion of errors (backward + gap filling) and we found that the score was respectively .63 ($SD = .48$) for the ADHD group and .89 ($SD = .40$) for the controls, a difference which was significant, $t(48) = 2.06$, $p < .05$. Thus, children with ADHD symptoms exhibited a decreased propensity for gap-filling errors.

3.1. Confidence ratings

We first compared the two groups on their confidence judgments relative to the hit rates (both consistent and inconsistent) by performing a 2 (group: ADHD vs. control) × 2 (item type: script consistent vs. inconsistent) mixed ANOVA with confidence judgments associated with the hit consistent and inconsistent rates. We found a main effect of item type, $F(1,52) = 9.6$, $p < .01$, $\eta_p^2 = .16$, such that both groups of children reported higher confidence when they correctly endorsed script inconsistent photographs ($M = 1.89$, $SD = .19$)

Table 1
a. Mean proportions (and standard deviations) of the raw scores of false-alarm rates: "yes" responses to script-consistent distracters (i.e., False alarms Consistent), "yes" responses to script-inconsistent distracters (i.e., False alarms Inconsistent), "yes" responses to causal distracters (i.e., False alarms Causal) and "yes" responses to control causal distracters (i.e., False alarms Control causal), and corrected indices of gap-filling errors and backward causal inference errors in the group of children with ADHD symptoms and in the control group of children. *b*. Means of the raw scores of confidence ratings relative to both gap-filling errors and backward causal inference errors (scores went from 0 = unsure to 2 = very sure).

	ADHD group		Control group	
	M	*SD*	*M*	*SD*
a				
False alarms Consistent	.20	.16	.26	.23
False alarms Inconsistent	.00	.00	.009	.04
Gap-filling errors	.20	.16	.25	.24
False alarms Causal	.18	.26	.12	.15
False alarms Control causal	.05	.09	.05	.10
Backward causal inference errors	.13	.21	.07	.13
b				
Confidence relative to gap-filling errors	1.57	.39	1.15	.66
Confidence relative to backward causal inference errors	1.94	.16	1.63	.50

than the script consistent ones ($M = 1.82$, $SD = .23$). Further, we found a main effect of group, $F(1,52) = 6.4$, $p < .05$, $\eta_p^2 = .11$, which was qualified by an interaction with item type, $F(1,52) = 6.5$, $p < .05$, $\eta_p^2 = .11$: post-hoc comparisons showed that the group of children with ADHD associated higher confidence with the hit consistent rate ($M = 1.92$, $SD = .12$) compared to the control group ($M = 1.73$, $SD = .26$). This difference was not found for the hit inconsistent items.

As for memory errors (shown in Table 1b), confidence ratings associated with backward causal inference errors and gap-filling errors were entered in a 2 (group: ADHD vs. control) × 2 (error type: script consistent distracter vs. causal distracter) mixed ANOVA. A significant main effect of type of error was found, $F(1,18) = 6.9$, $p < .05$, $\eta_p^2 = .28$: all participants gave higher confidence ratings associated with backward causal inference errors than gap-filling errors (Table 1b). We also found a main effect of group, $F(1,18) = 6.3$, $p < .05$, $\eta_p^2 = .26$, with ADHD children reporting higher confidence ($M = 1.76$, $SD = .10$) than the control group ($M = 1.39$, $SD = .10$) when committing memory errors, regardless of the type of error.

4. Discussion

The main goal of this study was to examine memory for script-based material in children with ADHD symptoms, focusing on their tendency to form false memories. To our knowledge, performance in false-memory paradigms has never been examined in children with ADHD; yet given the high frequency of ADHD in the population and the frequency with which children with developmental disabilities provide allegations in forensic contexts (Bruck & Ceci, 1999), it is important to establish the extent to which their behavior matches normative developmental trends.

The first main result of the present study is that ADHD children do not produce a higher overall number of false memories than the control group. This result stands in apparent contradiction with the assumption that executive dysfunctions may promote memory errors and the observation that ADHD children may exhibit increased intrusion errors in memory tasks compared to matched controls (Cornoldi et al., 1999; West, Houghton, Douglas, & Whiting, 2002). However, in these studies, errors concerned intrusions of irrelevant, semantically unrelated, material. In contrast, in the present study false memories concerned plausible, semantically associated, materials. In our study we found that children with ADHD symptoms and control children do differ in regard to their performance in the production of false memories based upon the peculiar type of error: children with ADHD produce fewer gap-filling errors than their peers, but more backward causal inference errors. Gap-filling errors have been shown to be supported by the familiarity that the item at test shares with the target scripted material and thus reflect ease of access to script knowledge (Lyons et al., 2010). Our results show that children with ADHD may somewhat be protected from this false-memory effect because of a slower or less adept access to script knowledge. A poorer organization of script knowledge in semantic memory may also underlie this reduced propensity to gap-filling errors.

In contrast, backward causal inference errors likely emerge from a recollective state: When the individual is tested on the unseen cause of a seen effect they likely recollect inferring the cause, and misattribute this inference to direct experience of the photograph. If children with ADHD exhibit particularly good episodic recollection, they should have greater difficulty at differentiating such inferential mental state from a true memory, because both would be vividly recollected. Our results are consistent with this view. Of interest, these results also indicate that while script knowledge seems to be less readily accessible in children with ADHD, this difficulty does not extend to causal inferences: thus, to the extent that studied material depicts relatively unique or distinctive events, children with ADHD draw causal inferences readily and later recollect them. It may also be that backward causal inference errors have more direct implications in applied forensic contexts, given that erroneously inferring the cause of an experienced effect could have severe consequences on the reconstruction of the event itself.

The second main result of the present study concerns the differences in metacognitive judgments between the children with ADHD and controls. Despite the differences in type of false memories produced in the two groups, children with ADHD exhibited higher levels of confidence than controls across types of false memories (and, in part, in true memories as well). One of the hypotheses we set out to test was that children with ADHD compared to control participants would exhibit increased memory errors and confidence in these errors due to the documented impulsivity and reduced inhibition and control capacity in ADHD (Cornoldi et al., 1999; Marzocchi et al., 2002). While we found no evidence of such a tendency in memory performance, confidence judgments appeared to be generally inflated compared to control participants. This tendency cannot be interpreted as reflecting generally faulty metacognitive mechanisms; the high levels of memory performance observed suggest that monitoring and controlling mechanisms operated well enough not to interfere with memory performance. In addition, in some cases, high levels of confidence may be well justified given the high levels of memory discrimination. Nevertheless, it is possible that this over-confidence may be a reflection of a response style. Furthermore, we found that both groups of children attributed higher confidence to backward causal inference errors compared to gap-filling errors, thus, even children with ADHD maintain a certain ability to introspect on their memory states and discriminate between them.

Before concluding we acknowledge some limitations of the present study which should be overcome in future research. Specifically, ADHD is notoriously heterogeneous (Barkley, 1990); thus, future research should further differentiate children with ADHD into the specified subgroups of ADHD of clinical relevance to evaluate whether these findings would differ as a function of types and severity of ADHD symptoms (prevalence of inattention vs. hyperactivity). Furthermore, research should better understand the level of elaboration of scripts at which differences between ADHD children and controls emerged.

Nevertheless, the present study offers important theoretical and practical information on the nature of memory function in children with ADHD, with an emphasis on circumstances that can generate false-memory formation. The present results provide initial evidence that the nature of false-memory formation may differ in children with ADHD compared to control participants. While children with

ADHD appear to produce false memories based on associative encoding errors linking effects to their causes resulting in false recollection, in control children false memories seem to emerge from prompt access to script knowledge and processing of semantic gist of the situation.

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Research in Developmental Disabilities 34 (2013) 1036–1043

Contents lists available at SciVerse ScienceDirect

Research in Developmental Disabilities

Parents psychopathology of children with Attention Deficit Hyperactivity Disorder

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ARTICLE INFO

Article history:
Received 15 October 2012
Received in revised form 4 December 2012
Accepted 4 December 2012
Available online 3 January 2013

Keywords:
Cognitive functions
Parental psychopathology
ADHD
Mood and anxiety disorders
Psychiatric disorders

ABSTRACT

Attention Deficit Hyperactivity Disorder (ADHD) is a disorder with extremely complex etiology, not yet well defined but certainly multi-factorial. This study investigated the possible etiopathogenetic role of ADHD symptoms and psychopathology disorders in parents of children with ADHD. We present a case–control study of parents of 50 children affected by ADHD and of 45 healthy children, matched to age and gender. Parents of ADHD children reported higher levels of ADHD symptoms, depressive disorders and Depressive Personality Disorders than parents of healthy children. Mothers displayed greater presence of depression, while fathers showed problems concerning alcohol use. The occurrence of ADHD symptoms, psychopathology and personality disorders in parents highlights the importance to integrate the treatment programs in the ADHD children with the screening and treatment for psychopathological symptoms of the parents.

1. Introduction

Attention Deficit Hyperactivity Disorder (ADHD) is neurodevelopmental disorder with three core symptoms: inattention, hyperactivity and impulsivity. The ADHD etiology is multi-factorial whereby genetic factors are a predisposition to the disorder, but the activation of this susceptibility is modulated by acquired risk factors, both biological and environmental. Recent developments in the field of ADHD have led to a renewed interest in the link between parental psychopathology and child functioning. Indeed the family is an important aspect of the child's environment that has been linked to variability in comorbidity, academic performance and social difficulties for children with ADHD. In a review study, Johnston and Mash (2001) reported that the presence of ADHD in children is associated to varying degrees with disturbances in family and marital functioning, disrupted parent–child relationships, reduced parenting self-efficacy and increased levels of parenting stress and parental psychopathology, particularly when ADHD is comorbid with conduct problems. Children with ADHD often ignore parental requests, fight with siblings and peers and elicit negative reactions from teachers, in turn, the parents of children with ADHD tend to be more controlling, disapproving and rejecting of their children, they give more verbal direction, repeated commands, verbal reprimands and correction than parents of children without ADHD; they are also less rewarding and responsive than parents of children without ADHD (Johnston & Mash, 2001; Kim & Yoo, 2012; Mano & Uno, 2007). Thus, it is conceivable that parental psychopathology is likely to be linked to greater involvement in managing the problem. Parent diagnosed disorders and personality traits are rarely examined together but these might contribute differentially to child behavioral outcomes. Actually, parental mental illness influences directly and indirectly on the

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http://dx.doi.org/10.1016/j.ridd.2012.12.001

development of the child affected by ADHD (Bornovalova, Hicks, Iacono, & McGue, 2010; Loeber, Hipwell, Battista, Sembower, & Stouthamer-Loeber, 2009). Indeed, parents of children with ADHD are at risk of experiencing more mental disorders than parents of children with typical development (Humphreys, Mehta, & Lee, 2012; Johnston et al., 2001). For this reason, it is important to consider the relationship between parental psychopathology and parenting practices with respect to children's behavioral symptoms. A limited number of studies have reported that parent history of childhood ADHD is associated with child ADHD regardless of comorbid CD or ODD (Psychogiou, Daley, Thompson, & Sonuga-Barke, 2007). High levels of parental ADHD symptoms might also aggravate the negative parenting of children with ADHD and the arguing patterns of parent–child interactions (Ellis & Nigg, 2009; Harvey, Danforth, McKee, Ulaszek, & Friedman, 2003). Kashdan et al. showed that parental anxiety was also uniquely related to negative parenting practices with ADHD children. The authors suggested that parental anxiety might make parents particularly vulnerable to significant distress, with reciprocal interaction patterns between parents and children contributing to negative interpersonal styles (Kashdan et al., 2004). In a longitudinal study, Chronis et al. investigated the role of parent psychopathology and observed parent–child interactions, on the development of conduct problems in children with ADHD over early childhood. They detected that both maternal depression and parenting during early childhood (i.e. observed praise and positive affect) were unique predictors of the developmental course of conduct problems (Chronis, Gamble, Roberts, & Pelham, 2006; Chronis, Jones, & Raggi, 2006).

Although parent personality is thought to relate to the development of child psychopathology study of specific parent traits in relation to child ADHD and associated problems has been relatively neglected (Nigg & Hinshaw, 1998). We propose that parents' personalities might influence their parenting and children's developmental outcomes.

Moreover, greater severity of ADHD symptoms and the presence of comorbidity have been linked to the increase in family conflict, reduced family cohesion and in an authoritarian and punitive parenting style (Biederman et al., 2001; Buschgens et al., 2010). The relationship between parental psychopathology and ADHD symptoms in children is complex and appears to influence each other hence triggering a cycle of cause and effect that characterizes the entire family system. Hence further investigations are required into ADHD with a multidimensional approach that includes parental psychopathology and familial predisposition to ADHD into a dynamic system.

We hypothesized that parental psychopathology play a role in the development of ADHD. Thus, we investigated parental psychopathology in ADHD children to demonstrate a specific impairment in parental functioning and parenting practices. Moreover, we analyzed the differences between mother and father to detect specific psychopathological features in parents of ADHD children.

2. Methods

2.1. ADHD sample

We recruited the parents of 50 children (mean age = 8 years 4 months ± 3 years 8 months) affected by ADHD (45 males and 5 females). ADHD children, referred to the Child Neuropsychiatry Unit, Department of Neuroscience and Sensory Organs, University of Bari "Aldo Moro", were diagnosed according to the criteria of Diagnostic Statistic Manual of Mental Disorders IV Edition-Text Revised (DSM-IV-TR). The diagnosis of ADHD involved clinical observation and neuropsychological assessment including scales, structured and semi-structured interviews and questionnaires: Wechsler Intelligence Scale for Children (WISC-III) (Wechsler, 1991), Leiter International Performance Scale-Revised (Roid and Miller, 1997), Child Behavior Checklist (CBCL) (Achenbach, Howell, Quay, & Conners, 1991) for parents and Teacher Self Report (TSR) (Achenbach et al., 1990), Conners' Rating Scales-Revised (Conners et al., 1997), Clinical Global Impressions (CGI) (Guy, 2000); and Children's Global Assessment Scale (CGAS) (Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000).

2.2. Control group

The control group involved volunteer parents of 45 healthy children matched to age ($t = 1.25$; $p = 0.21$) and gender ($t = 2.04$; $p = 0.15$), that were recruited from regular primary and secondary schools and were fully informed about the research. Exclusionary criteria included a history of a seizure disorder, mental retardation, progressive neurological problems, traumatic brain injury, or any other serious medical condition. Children with non biological parents were not included in the study.

The study was approved by the local ethical committee "Azienda Ospedaliero-Universitaria Consorziale Policlinico di Bari"; all the parents who were interviewed provided a written consent.

2.3. Assessment

The assessment of the parents included clinical standardized interviews and scales, such as the Brown Attention Deficit Disorder Scales (BADDS), the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) and the Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II).

The Brown Attention-Deficit Disorder Scales for Adolescents and Adults (BADDS) (Brown, 2009) is used to assess Attention Deficit Disorder (ADD) symptoms in adults. These scales explore the executive cognitive functions associated with ADHD and consist of 40 items that assess five clusters of ADD-related executive function impairments: (1) organizing,

prioritizing and activating to work; (2) focusing, sustaining and shifting attention to tasks; (3) regulating alertness, sustaining effort and processing speed; (4) managing frustration and modulating emotions; (5) utilizing working memory and accessing recall, and (6) monitoring and self-regulating action (only for children ages 3–12 years). The final score allowed us to assess the presence or absence of ADD.

The Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) is an interview designed to assess psychopathology according to DSM-IV criteria for current and lifetime Axis I disorders. The SCID has generally demonstrated adequate inter-rater and testretest reliability for these diagnoses and validity for the Italian population (Zanarini & Frankenburg, 2001). The SCID-I is divided into six self-contained modules that can be administered in sequence: mood episodes; psychotic symptoms; psychotic disorders; mood disorders; substance use disorders, anxiety disorders, adjustment, and other disorders.

The Structured Clinical Interview for DSM-IV Axis II Disorders (SCID-II) (First, Spitzer, Gibbon, & Williams, 1996) is an interview designed to assess Personality Disorders according to DSM-IV (including Personality Disorder NOS) and the appendix categories Depressive Personality Disorder and Passive–Aggressive Personality Disorder. The SCID-II Personality Questionnaire is available as a screening tool to reduce the time it takes the clinician to administer the SCID-II. The examiner is required to investigate certain criteria based on the course of the interview, regardless of the answers given by the subject in the questionnaire during the interview, which is determined by the presence of several personality disorders. After the subject fills out the Personality Questionnaire (which usually takes 20 min), the clinician simply circles the numbers to the left of the SCID-II items that correspond to items answered 1 (absent), 2 (sub-threshold) or 3 (present). Adding the number of personality traits present we obtain a dimensional assessment for each personality disorders. For all personality disorders is indicated the categorical threshold according to DSM-IV criteria (the number of items necessary for diagnosis).

2.4. Data analysis

All demographic and clinical variables were subjected to statistical analysis. Descriptive analysis was conducted for socio-demographics featuring of the two samples. For the measurement of the clinical variables, the "Chi-square independence" (χ^2) was used, which allowed us to explore the relationship between two categorical variables (SCID-I, SCID-II and psychosocial difficulties). Where possible, odds ratio (OR) with 95% and confidence intervals (95% CI) were calculated. If OR is equal to 1, the risk factor does not affect the onset of the disease; if OR is greater than 1, the risk factor is, or may be implicated in the onset of the disease and if OR is less than 1 there is a negative association for which the risk factor is actually a defense against the disease. "Independent-samples" t-test was used to evaluate differences in continuous variables (BADDS) and effect size was calculated, which provided an indication of the magnitude of the difference between the groups. The most common effect size is eta squared, that can range from 0 to 1 and represents the proportion of variance in the dependent variable, which is explained by the independent variable. Then, a multivariate regression analysis with the global indicators of impairment in ADHD children with ADHD (CGAS and CGI) and psychopathological symptoms of parents (BADDS, SCID-I, SCID-II) was performed. The significance level was set at $p < 0.01$ for the differences between the groups (ADHD vs control), and at $p < 0.05$ for multivariate regression analysis. For statistical processing the data processing program SPSS version 20.0 was used.

3. Results

Eighty-three parents of ADHD children (49 mothers and 34 fathers) with a mean age of 39 ± 5.3 (range 23–50 years) and 76 parents of healthy children ADHD (41 mothers and 35 fathers) with a mean age of 38 ± 6.2 (range 25–54 years) were in agreement to participate in the study. The greater number of mothers in comparison to that of the fathers was a result of different circumstances: it was either a single parent household or in a two-parent household one parent refused to participate. All patients received a subtype diagnosis of ADHD, such as the inattentive subtype (9%), hyperactive subtype (6%) and combined type (85%). The socio-demographic and clinical characteristics are summarized in Tables 1 and 2.

Table 1
Socio-demographic characteristics of ADHD and control groups.

	ADHD	Control
N children	50	45
Age	8.44 ± 3.89	7.76 ± 3.54
Gender %		
Male	45 (90%)	37 (82%)
Female	5 (10%)	8 (18%)
Diagnoses %		
Inattentive	4 (9%)	–
Hyperactive	3 (6%)	–
Combination	43 (85%)	–
N parents	83	76
Mothers %	49 (59%)	37 (54%)
Fathers %	34 (41%)	8 (46%)
Parents age	39.5 ± 5.3	38.28 ± 6.2

ADHD, Attention-Deficit/Hyperactivity Disorder.

Table 2
Brown Attention-Deficit Disorder Scales for Adolescents and Adults Scales.

	Mean ± SD		F	p	r	95% confidence interval of the difference	
	ADHD	Control				Lower	Upper
[a]Organization	43.1 ± 7.4	39.16 ± 8.03	3.2	0.001*	0.09	1.59	6.45
[g]Mothers vs fathers	43.06 vs 43.25	7.63 vs 7.34	0.003	0.862	–	−3.62	3.04
[b]Focusing	46.6 ± 10.24	42.4 ± 11	2.56	0.011	0.06	.991	7.65
[g]Mothers vs fathers	46.49 vs 47.15	9.05 vs 11.8	3.74	0.057	–	−5.23	3.91
[c]Regulating	45.1 ± 10	34.4 ± 8.1	3.16	0.002*	0.09	1.95	8.42
[g]Mothers vs fathers	45.1 vs 45.12	9.74 vs 10.7	1.2	0.275	–	−4.52	4.49
[d]Modulating Emotions	48.6 ± 10.8	43.3 ± 13	3.16	0.007*	0.07	1.46	9.08
[g]Mothers vs fathers	48.24 vs 49.21	9.8 vs 12.2	1.73	0.192	–	−5.78	3.86
[e]Working memory	48.5 ± 11.3	43.7 ± 12	2.54	0.012	0.06	1.08	8.67
[g]Mothers vs fathers	49.84 vs 46.76	10.8 vs 11.9	1.16	0.284	–	−1.96	8.1
[f]ADHD tot	47.1 ± 9.7	41.8 ± 12	3.02	0.003*	0.08	1.83	8.76
[g]Mothers vs fathers	47.02 vs 47.29	8.7 vs 11.2	4.07	0.047	–	−4.635	4.088

r, effect size.
[a] Organizing, prioritizing and activating to work.
[b] Focusing, sustaining and shifting attention to tasks.
[c] Regulating alertness, sustaining effort and processing speed.
[d] Managing frustration and modulating emotions.
[e] Utilizing working memory and accessing recall.
[f] Total Attention-Deficit Disorder Scales.
[g] Parents of ADHD children.
* p value <0.01.

3.1. Parental psychopathology

BADDS: the parents of ADHD children reported an ADD total score significantly higher than the parents of healthy children (47.13 ± 9.7, $p = 0.003$; effect size = 0.08). Moreover, a significant difference was evident in the clusters of organizing, prioritizing and activating to work (43.18 ± 7.4; p value = 0.001; effect size = 0.09), regulating alertness, sustaining effort and processing speed (45.11 ± 7.4; p value = 0.002; effect size = 0.09) and managing frustration and modulating emotions (48.6 ± 10.8; p value = 0.007; effect size = 0.07). No significant difference between mothers and fathers of ADHD children was found (Table 4).

SCID-I: The analysis of clinical variables show that parents of ADHD children compared with the control groups showed a statistically significant presence of depressive disorder (37%; p value = 0.002; OR: 2.36) (Table 3). Considering the differences between parents of ADHD children, the mothers showed significantly higher rates of depressive disorder

Table 3
Rates of SCID-I and SCID-II diagnoses across group.

	ADHD	Control	χ^2	p	Odds ratio value	95% confidence interval	
	# (%) n = 83	# (%) n = 76				Lower	Upper
SCID-I							
Depression	31 (37.3%)	12 (15.8%)	16.2	0.002*	2.36	1.31	4.26
Anxiety disorder	24 (29%)	11 (14.5%)	13.3	0.028	2.01	1.05	3.79
Alcohol abuse	9 (10.8%)	1 (1.3%)	6.1	0.013	8.02	1.06	63.5
Alimentary disorder	2 (2.4%)	1 (1.3%)	0.25	0.560	–	0.169	19.05
Psychotic symptom	2 (2.4%)	0 (0%)	1.8	0.169	–	–	–
SCID-II							
Depressive	15 (18%)	1 (1.3%)	12.3	0.000*	13.73	1.85	101
Avoidant	10 (12%)	3 (4%)	3.4	0.063	3.05	0.87	10.6
Dependent	3 (4%)	0 (0%)	2.8	0.094	–	–	–
Passive–aggressive	27 (32.5%)	13 (17%)	5.01	0.025	2	1.06	3.4
Borderline	20 (24%)	8 (10.5)	5.03	0.025	2.28	1.07	4.88
Obsessive–compulsive	15 (18%)	13 (17%)	0.26	0.873	1.05	0.53	2.04
Schizoid	11 (13%)	7 (9.2%)	0.64	0.422	1.43	0.588	3.05
Paranoid	13 (16%)	6 (8%)	2.2	0.131	1.98	0.794	4.95
Antisocial	1 (1.2%)	1 (1.3%)	0.004	0.950	0.916	0.58	14.03
Schizotypal	2 (2.4%)	1 (1.3%)	0.25	0.613	0.169	0.169	19.07
Histrionic	4 (5%)	3 (3.9%)	0.07	0.789	1.22	0.276	5.27
Narcissistic	7 (8%)	8 (10.5%)	0.2	0.652	0.801	0.305	2.14

* p value <0.01.

Table 4
Difference between parents of children with ADHD to SCID-I and SCID-II.

	Mothers	Fathers	χ^2	p	OR value	95% confidence interval	
	# (%)	# (%)			e	Lower	Upper
SCID-I							
Depression	25 (51%)	6 (18%)	9.5	0.002*	2.89	1.33	6.28
Anxiety disorder	19 (39%)	5 (15%)	5.6	0.017	2.63	1.09	6.37
Alcohol abuse	1 (2%)	8 (35%)	9.5	0.002*	0.087	0.011	0.662
Alimentary disorder	2 (4%)	0	1.4	0.233	–	–	–
Psychotic symptom	1 (2%)	1 (3%)	0.06	0.793	0.694	0.045	10.71
SCID-II							
Depressive	10 (20.4%)	5 (14.7%)	0.44	0.507	1.38	0.521	3.69
Avoidant	8 (16.3%)	2 (6%)	2.06	0.151	2.776	0.628	12.272
Dependent	2 (4%)	1 (2.9%)	0.97	0.784	1.388	0.131	14.701
Passive–aggressive	19 (38%)	8 (23.5%)	2.1	0.145	1.648	0.818	3.321
Borderline	12 (24.4%)	8 (23.5%)	4.7	0.29	2.776	1.016	7.579
Obsessive–compulsive	11 (22.4%)	4 (11.8%)	1.5	0.213	1.908	0.663	5.494
Schizoid	6 (12.2%)	5 (14.7%)	0.1	7.45	0.833	0.276	2.51
Paranoid	6 (12.2%)	7 (20.6%)	1.05	0.304	0.595	0.219	1.615
Antisocial	0 (0%)	1 (2.9%)	1.4	0.227	–	–	–
Schizotypal	1 (2%)	1 (2.9%)	0.06	0.793	0.694	0.045	10.715
Histiornic	2 (4.1%)	2 (5.9%)	0.142	0.706	0.694	0.103	4.688
Narcissistic	3 (6.1%)	4 (11.8%)	0.83	0.363	0.52	0.124	2.178

* p value <0.01.

Table 5
Correlation analysis between severity of ADHD symptoms and psychopathological symptoms of parents.

	CGAS		CGI	
	r	p	r	p
ADD total	−0.269	0.015*	−0.209	0.047*
Organization	−0.109	0.195	−0.034	0.394
Focusing	−0.239	0.027*	−0.239	0.027*
Regulating	−0.129	0.153	−0.087	0.246
Modulating emotions	−0.238	0.028*	−0.063	0.308
Working memory	−0.253	0.021*	−0.218	0.041*
SCID-I	0.006	0.481	−0.029	360
SCID-II	−0.031	0.402	−0.132	0.111

r, Pearson's correlation; CGAS, Children's Global Assessment Scale; CGI, Clinical Global Impressions; ADD, Attention-Deficit Disorder Scales.
* p is significant to 0.05 level.

(51%; p value = 0.002, OR: 2.89) than fathers that showed significantly higher rates of alcohol abuse (35%, p value = 0.002; OR: 0.087) (Table 4).

SCID-II: results showed a statistically significant difference in the personality disorders of the parents of ADHD children compared to control group (Table 3). The personalities disorder more prevalent was the Depressive Personality Disorder (18%; p value = 0.000; OR: 13.73). No significant difference between mothers and fathers of ADHD children was found (Table 4).

We observed a negative relationship between general functioning of children and executive cognitive functions deficit of parents. As CGAS scores decrease, ADD total scores ($p = 0.015$), focusing scores ($p = 0.027$), modulating emotions scores ($p = 0.028$) and working memory scores ($p = 0.021$) increase. The results also highlight a negative correlation between ADHD symptom severity in children (CGI) and ADD total scores ($p = 0.047$), focusing scores ($p = 0.027$) and working memory scores ($p = 0.041$). These results indicated that the increase in executive cognitive functions deficit of parents, correspond with aggravation of ADHD symptoms and overall functioning of the child.

Unexpectedly no significant correlation was found between SCID-I and SCID-II with CGI and CGAS respectively (Table 5).

4. Discussion

ADHD is a disorder with an extremely complex etiology, not yet well defined but certainly multifactorial. Genetic factors interact with acquired factors, both biological and environmental, in the early phase of development leading to the onset of the disorder. This study investigated the possible etiopathogenetic role of parental psychopathology. Very little was found in literature on the question of the presence of ADHD symptoms in parents of children with ADHD. Some studies have revealed that parents of children with ADHD report a personal history of conduct problems and oppositional-defiant disorder (Chronis, Gamble, et al., 2006; Jensen, 2001). The Multimodal Treatment of Attention Deficit Hyperactivity Disorder (MTA)

study shows that a child with ADHD was associated with increased rates of maternal and paternal childhood ADHD, compared with the non-ADHD children (Epstein et al., 2000). Recent evidence suggests an increased presence of ADHD symptoms in the fathers (54%) compared to mothers (20%) (Chronis-Tuscano et al., 2009). On the contrary, previous studies have reported a higher percentage of ADHD symptoms in the mothers (21%) than the fathers (13%) (Faraone & Biederman, 1997). These contradictory results may be due to a different methodological approach and sampling. In the present study, we revealed a statistically significant level of ADHD symptoms in parents of ADHD children. In particular, we have encountered difficulties in ADD total score, organizing, prioritizing and activating to work; managing frustration and modulating emotions; and monitoring and self-regulating action. We did not find a significant difference between mothers and fathers. This finding has important implications for understanding of mechanisms that underlie the associations between parental psychopathology at the environmental level and ADHD in children in their development over time. The presence of executive cognitive functions deficit in parents lead to a lower management of the behavioral problems of ADHD children, aggravating the clinical picture and the general functioning of children.

Moreover, the occurrence of ADHD symptoms found in the sample, strongly suggests the genetic component of ADHD, supporting literature data. In fact, recently Wang et al. suggested that there may be a parent-of-origin effect for attention-deficit/hyperactivity disorder (ADHD) candidate genes. The authors identified several interesting genes or regions with parent-of-origin effects using GWA analysis of a large sample from the IMAGE project (Wang, Liu, Zhang, Aragam, & Pan, 2012). Some studies showed that parents of ADHD children reported higher levels of psychopathology and personality disorders than parents of children not suffering from any disorder (Chazan et al., 2011; Goldstein et al., 2007). Some authors report a high percentage of mood disorders and anxiety disorder in parents and siblings of children with ADHD compared with the controls (Biederman et al., 1995; Chronis, Jones, et al., 2006). Traditionally, research on the role of parental psychopathology in the development of behavioral problems of children has focused on mothers. However, more recent data suggests that the externalizing problems in children are equally associated with both maternal and paternal psychopathology, even though, there are various clinical patterns depending on whether the affected parent is the father or mother (Connell & Goodman, 2002). Maternal depression is closely associated with ADHD; on the contrary the substance abuse and alcohol, the use of aggressive behavior and ADHD symptoms are present more in the fathers than mothers (Vidair et al., 2011). In agreement with literature, data emerging from our study shows a higher rate of Axis-I disorders as mood disorders, in parents of ADHD children compared to the control parents. In particular, the mothers displayed greater presence of depression, while fathers showed problems concerning alcohol use. Further experimental investigations are needed to establish whether the presence of depressive disorders in mothers and alcohol abuse in fathers of children with ADHD may be connected to biological underpinnings of this disorder or impaired parenting in the management of their children. Nonetheless, teaching parenting skills may be important, as both parents disorders were significantly associated with children's clinical improvement and adherence to ADHD medication (Leslie, Aarons, Haine, & Hough, 2007). The link that we found between maternal and fathers symptoms and ADHD symptoms of children may be related to poor parenting (e.g., parental inconsistency, poor quality of attachment). This underlines the importance of addressing the clinical symptoms of parents.

In literature, few studies have described the role of personality disorders in parents of ADHD children. Chronis, Jones, et al. (2006) showed that the personality disorders as schizoid, schizotypal, paranoid, avoidant, dependent, and borderline personality mainly present in mothers. Our results show a higher presence of Depressive Personality in the parents of ADHD children compared to the parents of the healthy children. There was no significant difference between mothers and fathers of ADHD children. The Depressive Personality Disorders might influence the parenting style and parent–child interactions. However, it is not possible to determine whether the presence of depressive psychopathology in parents of children with ADHD is a real association or a consequence of the difficulties that parents have in the management of their children. The multivariate regression analysis indicated that the global indicators of impairment and the symptom severity in ADHD children are correlated with the psychopathological symptoms of parents. In particular we found a negative correlation with ADD total scores, attention skill, modulating emotions and working memory. These findings support the importance of the treatment of the parents' problems, in order to improve the overall functioning of the children with ADHD. In particular, in parents, the presence of executive cognitive functions deficit influence the parenting style and family relationships, aggravating ADHD symptom severity and the general functioning of children. The type of investigation used did not consent the determination the parents psychopathology onset. It is suggested that further research about the association of these factors needs to be done.

In conclusion, the results highlight the presence of ADHD symptoms, psychopathology and personality disorders in the parents of ADHD children. In fact, these results not only strengthens a genetic transmission of ADHD, but also it clarify the ways in which parental characteristics and child experiences interact to produce or alter the pathway of development of ADHD. The treatment programs for children may benefit from an integration with the treatment of the psychopathological symptoms of the parents. However, more research on this topic needs to be undertaken before the association between parental factors and child problems is more clearly understood.

Conflict of interest

We confirm that we have read the journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

None of the authors has any conflict of interest to disclose.
All co-authors have seen and approved the final version of the paper and accept responsibility for the data presented.
There is no financial or others conflict of interest that may be related to the authors.
All authors have seen and approved the final version of the paper and accept responsibility for the data presented.

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JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY
Volume 22, Number 6, 2012

Pp. 415–422
DOI: 10.1089/cap.2012.0003

Safety of Attention-Deficit/Hyperactivity Disorder Medications in Children: An Intensive Pharmacosurveillance Monitoring Study

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Abstract

Objective: Our intensive pharmacosurveillance monitoring program was performed to increase the number of adverse drug reactions (ADRs) recorded in the Italian spontaneous reporting database, and to systematically collect more thorough data about atomoxetine (ATX) and methylphenidate (MPH) safety in the pediatric setting.
Methods: From September 2007 to October 2010, 1841 youth were enrolled in the Italian Attention- Deficit/Hyperactivity Disorder Register, but we report here on the 76 children from the five Reference Prescription Centers in Campania, an Italian region where we administered our systematic adverse event checklist.
Results: Among our cohort, 68 children received a prescription of ATX and 8 received a prescription of MPH. Most children were male and between 10 and 13 years of age, had a diagnosis of attention-deficit/hyperactivity disorder-combined (ADHD-C) and had learning disability as the main comorbidity. Most ADRs reported to the Italian spontaneous reporting database occurred in patients from Campania. Twenty-five experienced at least 1 ADR for a total of 40 ADRs reported to the Italian drug agency. Most ADRs were common and not serious, and resolved completely. Weight loss was the most frequently reported ADR. Only two ADRs were unexpected and only one was uncommon. Sixteen ADRs resulted in permanent drug withdrawal. Based on the Naranjo algorithm, 25 ADRs were considered "probable" and 15 were considered "possible."
Conclusions: Although our data provide reassurance of the safety of ATX and MPH, several unexpected or uncommon ADRs (hepatomegaly, suicidal ideation, weight gain, or drug interactions) were identified by our intensive pharmacosurveillance monitoring program. Our results show that an intensive pharmacosurveillance monitoring program that involves pharmacovigilance centers and clinicians can improve the collection of information on drug safety in children.

Introduction

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) is a disorder of neuropsychiatric development of children and adolescents characterized by inattention and impulsivity/hyperactivity, according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV-TR) (American Psychiatric Association 2000). These symptoms are generally accompanied by depression, anxiety, oppositional defiant disorders (ODDs), and compulsive behaviors. Specifically, the DSM-IV-TR distinguishes three clinical types of ADHD: inattentive (ADHD-I), hyperactive (ADHD-H) and combined (ADHD-C).

The prevalence of ADHD is very heterogeneous and changes across countries. In fact, 7.8% of children and adolescents (4–17 years) living in the United States have ADHD (Centers for Disease Control and Prevention 2005), whereas in Italy, the prevalence of the syndrome is estimated at between 1% and 4% of children (5–12 years old) (Panei et al. 2004). The worldwide mean prevalence has recently been estimated to be 5% in children (Polanczy et al. 2007) and 3% among adults (Fayyad et al. 2007). In ~80% of children with ADHD, the symptomatic features continue into adolescence and in 30–65% even into adulthood (Vallejo et al. 2009).

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Treatment of ADHD is multimodal and includes medication management, behavioral interventions, and a combination of both approaches (Kaiser et al. 2008). Stimulant medications, such as methylphenidate (MPH), and nonstimulant medications, such as atomoxetine (ATX), are used for the pharmacological treatment of ADHD in children (National Institute for Health and Clinical Excellence 2006). A number of studies have demonstrated the efficacy of both drugs in patients with ADHD versus placebo (Cotton and Rothberg 1988; Klorman et al. 1990; Christman et al. 2004). Nevertheless, there is some concern about their long-term effectiveness (Jensen et al. 2007). Although relatively safe, both MPH and ATX have class-related warnings and contraindications and are associated with adverse effects that require consideration when prescribing (Wolraich et al. 2007). A number of trials involving ATX and MPH indicate that adverse effects are usually mild, and can be managed with medication withdrawal. These symptoms include neurological effects (headache, dizziness, insomnia, and seizures), psychiatric effects (mood/anxiety, tics, psychotic symptoms), and gastroenterological effects including poor appetite and overlapping with growth restriction (Graham et al. 2011). Nevertheless, such serious adverse effects as sudden cardiac death and suicidality require further investigation to allow a more precise understanding of these risks (Graham et al. 2011). Moreover, since their authorization, the use of ADHD drugs has given rise to ethical and legal issues (Foreman 2009).

Recent years have seen an exponential increase in ADHD diagnoses and in psychotropic drug prescriptions (Bonati and Clavenna 2005). A number of restrictive measures have been adopted to stop this trend. In 2007, following the reintroduction of MPH on the Italian market and the registration of ATX, the Italian drug agency (AIFA) introduced the ADHD National Register, an active tool with which to monitor the appropriateness of care, therapy efficacy, and adverse drug reactions (ADRs), and to prevent drug misuse. The ADHD National Register includes children enrolled by reference prescription centers. These centers, located throughout Italy, confirm the ADHD diagnosis and establish the pharmacological therapy. There are five reference prescription centers in the Campania Region, whereas the Regional Center of Pharmacosurveillance and Pharmacoepidemiology of the Second University of Naples is responsible for monitoring the risk/benefit ratio. Since its institution, one of the most important Regional Center objectives is to investigate drug safety in children. This aim is of paramount importance because children are not generally included in clinical trials and, therefore, drugs are prescribed based on data derived from trials performed with adults. Psychostimulants are an exception, because most of the subjects included in clinical trials are children; nevertheless, as clinical trials have time limits, these drugs are still under concern in terms of long-term tolerability. Despite the fact that in Italy spontaneous reporting of ADRs is mandatory, there is still a high frequency of under-reporting of ADRs in children. Therefore, as part of its postmarketing surveillance activities, the Regional Center of Pharmacosurveillance and Pharmacoepidemiology of the Second University of Naples started an intensive pharmacosurveillance monitoring program to increase the number of ADRs recorded in the Italian spontaneous reporting database, and to collect information on the safety profile of ATX and MPH in a Campania pediatric population with ADHD.

Methods

From September 2007 to October 2010, the Campania Center of Pharmacovigilance and Pharmacoepidemiology started an intensive pharmacosurveillance monitoring study of children with ADHD.

Patients

Children and adolescents, 6–17 years old, with a DSM-IV-TR diagnosis of ADHD, confirmed by the Campania reference prescription centers, were included in the study. Our intensive pharmacosurveillance monitoring study included the patients only if they were enrolled in the ADHD National Register and received a prescription for ATX or MPH from one of the five Campania Reference Centers for ADHD.

Study design

Starting from clinical and demographic data available from the ADHD National Register (gender, age, ADHD subtype, comorbidity, pharmacological treatment), we performed a descriptive analysis of the entire cohort of Italian children with ADHD.

A more detailed analysis concerning the drug safety assessment was performed for children and adolescents who met the abovementioned inclusion criteria. To this aim, we designed a detailed *ad hoc* form to further investigate the clinical status of patients and capture detailed information about any ADRs. According to the World Health Organization, an ADR is a "response to a medicine" that is noxious and unintended, and that occurs at doses normally used in humans (World Health Organization 2002). For each suspected ADR, the form collected data about: details of the suspect drug(s), that is, the name(s), start and stop dates, doses, and indications; details of the ADR, that is, signs and symptoms (according to MedDRA dictionary), start and stop dates, outcome, and any treatment provided; indication of the seriousness of the reaction (reactions that are fatal, life threatening, disabling or incapacitating, resulted in hospitalization or prolonged hospital stay, or are medically significant were considered serious); all concomitant medicines including those stopped in the past 3 months and those bought over the counter, together with dates, doses, route of administration, and indications; relevant laboratory tests; and medical history.

As required by the Italian Pharmacosurveillance System (D.lgs 219/2006), each suspected ADR was systematically reported to the AIFA and recorded in the Italian spontaneous reporting database. The Regional Center of Pharmacosurveillance and Pharmacoepidemiology evaluated causality using the Naranjo algorithm (Naranjo et al. 1981).

Follow-up

Subjects who met the inclusion criteria were monitored periodically by clinicians at the reference prescription center (1 week, 1 month, and every 3 months for the first year, and every 6 months thereafter).

Monitoring program

In the month before the study, the monitors, as specialists in clinical pharmacology, underwent an intensive course about the theoretical and practical aspects of the study. They were informed about the aims of the study and periodically visited each Campania reference prescription center. During each visit, monitors interviewed clinicians about enrolled subjects and filled out the *ad hoc* form.

Results

From September 2007 to October 2010, 1841 children and adolescents were listed in the Italian ADHD Register, of which 918

were treated with ATX (49.8%) and 924 were treated with MPH (50.2%) (Table 1). There was a preponderance of: males (88.6%), the 10–13-year-old age group (40.3%), the ADHD C subtype (84.2%), and learning disability as the main comorbidity (44.8%). Moreover, in Italy, 18% of subjects were treated with another drug in addition to ATX or MPH.

During our study, we enrolled 76 subjects which represents 4.1% of the entire cohort listed in the National Register. As shown in Table 1, the clinical and demographic characteristics of our study population were largely consistent with those of subjects listed in the National Register (86.8% in Campania were male; 34.2% were 10–13 years old, 64.5% had a diagnosis of ADHD-C, and 48.7% had a learning disability). The main differences were related to the prevalence of subjects diagnosed with hyperactive subtype (25% in Campania vs. 4.4% in Italy overall) and the prevalence of those with a behavioral disorder as comorbidity (22.4% vs. 6.6%). Moreover, although in Italy as a whole, patients were evenly distributed in the two treatment groups, almost the entirety (68 subjects) of our study population was treated with ATX (89.4%).

In addition to ATX or MPH, data obtained from the National Register showed that 18% of Campania subjects were additionally treated with another drug. Among subjects enrolled in the Campania Region, 12 (15.8%) received at least one concomitant medication: valproate (6), risperidone (5), ethosuximide (1), alprazolam (1), growth hormone (GH) (1), levothyroxine (1), phenobarbital (1 child), niaprazine (1), carbamazepine (1), and topiramate (1) (data not shown). We assessed if those on concomitant medications had more ADRs than did those on ATX or MPH alone.

TABLE 1. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF CHILDREN AND ADOLESCENTS OF THE CAMPANIA REGION RECORDED IN THE ADHD NATIONAL REGISTER ($N=76$) VERSUS THE TOTAL NUMBER RECORDED IN THE REGISTER ($N=1841$)

	Campania Region n (%)	*ADHD National Register* n (%)
Gender		
Female	10 (13.2)	209 (11.4)
Male	66 (86.8)	1632 (88.6)
Age, years		
6–7 years	22 (28.9)	353 (19.2)
8–9 years	20 (26.3)	491 (26.7)
10–13 years	26 (34.2)	743 (40.3)
14–17 years	8 (10.5)	254 (13.8)
ADHD subtype		
Combined	49 (64.5)	1550 (84.2)
Hyperactive	19 (25.0)	81 (4.4)
Inattentive	8 (10.5)	210 (11.4)
Comorbidity		
Learning disability	37 (48.7)	825 (44.8)
ODD	31 (40.7)	799 (43.4)
Anxiety disorder	8 (10.5)	295 (16.0)
Depression	2 (2.6)	123 (6.7)
Behavioral disorder	17 (22.4)	122 (6.6)
Pharmacological treatment		
ATX	68 (89.4)	918 (49.8)
MPH	8 (10.6)	924 (50.2)

ADHD, attention-deficit/hyperactivity disorder; ODD, oppositional defiant disorder; ATX, atomoxetine; MPH, methylphenidate.

TABLE 2. REASONS FOR DROPPING OUT OF ADHD NATIONAL REGISTER IN CAMPANIA REGION ($N=40$)

	ATX n (%)	*MPH* n (%)
Suspected ADR	10 (25)	1 (2.5)
Perceived lack of efficacy	4 (10)	—
Other	9 (22.5)	1 (2.5)
Improvement of clinical conditions	14 (35)	1 (2.5)
Total	37 (92.5)	3 (7.5)

ADHD, attention-deficit/hyperactivity disorder; ATX, atomoxetine; MPH, methylphenidate; ADR, adverse drug reaction.

At the time of analysis, among our study population the median follow-up period was 289 days (~9 months); 40 (52.6%) enrolled subjects stopped treatment and dropped out of the register. The reasons for dropping out were ADRs (27.5%); improvement of clinical condition (37.5%); perceived lack of efficacy (10%); and such other causes as patient decision, poor compliance, loss to follow up, or moving to another structure (25.0%) (Table 2).

TABLE 3. DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE CAMPANIA CHILDREN AND ADOLESCENTS WITH AND WITHOUT ADRS ($N=76$)

	Campania subjects with ADRs n (%)	*Campania subjects without ADRs* n (%)
Gender		
Female	3 (3.9)	7 (9.2)
Male	22 (28.9)	44 (57.9)
Age (years)		
Mean (SD)	9.5 (±3.4)	9.6 (±2.7)
Age groups		
6–7 years	9 (11.8)	13 (17.1)
8–9 years	5 (6.6)	15 (19.7)
10–13 years	7 (9.2)	19 (25.0)
14–17 years	4 (5.3)	4 (5.3)
ADHD subtype		
Combined	16 (21.1)	33 (43.4)
Hyperactive	7 (9.2)	12 (15.8)
Inattentive	2 (2.6)	6 (7.9)
Comorbidity		
Learning disability	13 (17.1)	24 (31.6)
ODD	11(14.5)	20 (26.3)
Anxiety disorder	2 (2.6)	6 (7.9)
Depression	1 (1.3)	1 (1.3)
Behavioral disorder	6 (7.9)	11(14.5)
Pharmacological treatment		
ATX	23 (30.3)	45 (59.2)
MPH	2 (2.6)	6 (7.9)
Total	25 (32.9)	51 (67.1)

ADR, adverse drug reaction; ADHD, attention-deficit/hyperactivity disorder; ATX, atomoxetine; MPH, methylphenidate; ODD, oppositional defiant disorder.

TABLE 4. ATX- OR MPH-INDUCED ADRS RECORDED IN THE ITALIAN SPONTANEOUS REPORTING DATABASE DURING THE STUDY PERIOD ($N=90$)

Italian regions	*ATX-induced ADRs* n (%)	*MPH-induced ADRs* n (%)
Campania[a]	32 (35.6)	2 (2.2)
Sicily	7 (7.8)	7 (7.8)
Lombardy	8 (8.9)	4 (4.4)
Lazio	4 (4.4)	3 (3.3)
Puglia	5 (5.6)	1 (1.1)
Emilia Romagna	5 (5.6)	—
Sardinia	2 (2.2)	1 (1.1)
Veneto	2 (2.2)	1 (1.1)
Piedmont	2 (2.2)	—
Liguria	1 (1.1)	—
Marche	1 (1.1)	—
Tuscany	1 (1.1)	—
Friuli Venezia Giulia	—	1 (1.1)
Total	70 (77.8)	20 (22.2)

[a]Two ADRs were experienced by two subjects who were not enrolled in the Register because of age limits.

ATX, atomoxetine; MPH, methylphenidate; ADR, adverse drug reaction.

TABLE 5. TYPE OF ATX- OR MPH-INDUCED ADRS IN CHILDREN AND ADOLESCENTS OF THE CAMPANIA REGION ($N=40$)

ADRs	*ATX-induced ADRs* n (%)	*MPH-induced ADRs* n (%)
Weight loss	8 (20.0)	1 (2.5)
Drug failure	6 (15.0)	—
Abdominal pain	4 (10.0	—
Hyperbilirubinemia	1 (2.5)	1 (2.5)
Hypertransaminasemia	1 (2.5)	1 (2.5)
Insomnia	2 (5.0)	—
Oppositive disease	2 (5.0)	—
Aggressiveness	1 (2.5)	—
Buccofacial dystonia	1 (2.5)	—
Depression	1 (2.5)	—
Gastralgia	1 (2.5)	—
Hepatomegaly	1 (2.5)	—
Hyperhidrosis	1 (2.5)	—
Impulsiveness	1 (2.5)	—
Loss of appetite	1 (2.5)	—
Somnolence	1 (2.5)	—
Suicidal ideation	1 (2.5)	—
Tachycardia	1 (2.5)	—
Vomiting	1 (2.5)	—
Weight gain	1 (2.5)	—
Total	37 (92.5)	3 (7.5)

ATX, atomoxetine; MPH, methylphenidate; ADR, adverse drug reaction.

Adverse effects

During the study period, 25 (32.9%) patients enrolled in Campania experienced at least one ADR. The demographic and clinical characteristics of these patients are shown in Table 3. Considering that 9 patients experienced more than one ADR several times, a total of 32 reports of suspected ADR (30 related to ATX and 2 to MPH) were recorded in the Italian spontaneous reporting database by the Campania Region. The rate of ADRs in the patient population was 40.5% (32/79).

As is shown in Table 4, Campania recorded the highest number of reports of ADRs (37.8%) in Italy (total = 90), followed by Sicily (15.6%), and Lombardy (13.3%). For all regions except Sicily, the majority of reports of ADRs were related to ATX.

Because each report may include more > 1 ADR, a total of 40 ADRs were filed in the Italian spontaneous reporting database by the Campania Region (1.6 adverse events per person on average). Namely, there were 27 reports of only one ADR, 5 of two ADRs and 1 of three ADRs (Table 5). Nineteen ADRs were classified "serious" (47.5%) and 21 as "not serious" (52.5%).

After an ADR, 16 subjects were recovering (38%), 6 were fully recovered (15%), 6 were unresolved (15%), and outcomes were not reported in 12 (30%) (data not shown). Moreover, 22 ADRs led to temporary or permanent drug withdrawal (55%), and 11 to dosage adjustment (27.5%). Information about drug discontinuation or dosage adjustment was not recoded in seven cases (17.5%) (data not shown). Based on causality assessed with the Naranjo algorithm, 25 cases (62.5%) were "probable" and 15 cases (37.5%) "possible."

Weight loss was the most common ADR (22.5%), followed by drug failure (15.0%), abdominal pain (10.0%), insomnia (5.0%), hypertransaminasemia (5.0%), hyperbilirubinemia (5.0%), and ODD (5.0%) (Table 5). Among the 19 serious ADRs, the most frequent were ODD exacerbation (10.5%), abdominal pain (10.5%), hyperbilirubinemia, and hypertransaminasemia (10.5%), followed by suicidal ideation (5.3%), drug failure (5.3%), depression (5.3%), impulsiveness (5.3%), vomiting (5.3%), loss of appetite (5.3%), tachycardia (5.3%), hyperidrosis (5.3%), weight gain (5.3%), weight loss (5.3%), and hepatomegaly (5.3%) (data not shown).

Of all reported ADR, only weight gain and dystonia were unexpected, as they were not listed in the suspected drugs' labeling; moreover, only suicide ideation was reported in a "box warning" of the ATX labeling because of its severity and rarity. Details about these cases are reported in Table 6.

ADRs were the cause of dropping out of the register in 11 (15%) enrolled subjects, among whom some experienced several ADRs simultaneously; therefore, a total of 16 ADRs resulting in dropping out were reported to AIFA (40%), 11 of which were serious (70.6%) (Table 7). Only two subjects having these ADRs (18.2%) were on a concomitant psychiatric medication. One was on ATX with valproate and ethosuximide and experienced weight loss and vomiting; the other one was on MPH with carbamazepine and topiramate and experienced somnolence. In both cases, ADRs were not serious.

In Italy ~8.4% of subjects dropped out of the ADHD National Register because of at least one ADR.

Discussion

To our knowledge, this is the first intensive pharmacosurveillance monitoring study that used not only the ADHD National Register data, but also the Italian spontaneous reporting database to investigate the tolerability of ADHD medications in a pediatric population. Other authors (Didoni et al. 2011), in a recent study, demonstrated the importance of the national register for monitoring the safety and efficacy of drug therapy. Nevertheless, data from registers generally lack full information; therefore, first we designed an *ad hoc* form to collect more thorough data about ATX and MPH safety and introduced expert monitors who closely collaborated with clinicians.

TABLE 6. UNLISTED, SERIOUS, UNCOMMON ADRs REPORTED IN THE CAMPANIA REGION

	Weight gain	*Dystonia*	*Suicidal ideation*
Patient			
Sex	Male	Male	Male
Age	8 years	13 years	10 years
Suspected drug information			
Name	ATX	a)ATX b) Risperidone	ATX
Dose	18 mg/day	a) 18 mg/day b) 0.5 mg/day	40 mg/day
Suspected ADR information			
Descriptions	Hyperidrosis and weight gain (10 kg)	Buccofacial dystonia	Suicidal ideation and worsening of ODD
Outcome	Clinical improvement	Resolved	Not reported
Treatment provided	Dosage reduction (from 35 mg to 18 mg) for 1 month. Drug withdrawal because there was not full resolution of symptoms.	Risperidone withdrawal	Dosage reduction (from 40 to 25 mg/day)
Seriousness	Clinically relevant	Not serious	Clinically relevant
Concomitant drugs	—	Valproate	—
Concomitant pathologies	—	Epilepsy	—
Causality assessment	Possible	Possible	Probable

ADR, adverse drug reaction; ATX, atomoxetine; ODD, oppositional defiant disorder.

Based on our findings, only 4% of subjects in the ADHD National Registry were enrolled from Campania. This can be explained by a distinctive local approach of preferring other therapies, such as behavioral therapy. Moreover, the limited number of reference prescription centers in Campania should be also taken in consideration. The distinct approach to ADHD in Campania is also confirmed by the different distribution of patients in the ATX and MPH groups. Whereas in the ADHD National Register a similar number of patients were treated with ATX or MPH, in Campania ~90% of enrolled patients received ATX and only ~10% received MPH.

Previous studies have shown that ATX and MPH have a similar efficacy (Cotton and Rothberg 1988; Klorman et al. 1990; Christman et al. 2004). On the contrary, other authors have reported that OROS MPH, a long-acting methylphenidate preparation (not marketed in Italy), had greater efficacy than ATX (Newcorn et al. 2008). Probably, the trend in MPH prescribing in Campania may reflect the fact that, as required by the AIFA-approved protocol, the first dose of MPH must be administered in a hospital and a number of Campania reference prescription centers lack a day hospital unit. The high percentage of patients treated with ATX in Campania gave us a unique opportunity to focus on the safety profile of this drug that still requires close monitoring because of its recent approval. In contrast, MPH was approved >50 years ago; therefore, its safety profile is well known and there was only a remote possibility of identifying rare or unexpected ADRs.

In addition to the pharmacological therapy, the demographic and clinical characteristics of Campania subjects were similar to those of other subjects enrolled in the National Register: Most of were male, between 10 and 13 years of age, had a diagnosis of ADHD-C, and had a learning disability as the main comorbidity. The prevalence of these characteristics in children and adolescents with ADHD varies across studies (Polanczyk et al. 2007; Skounti et al. 2007). However, it is generally agreed that male gender entails a greater risk of ADHD (Biederman et al. 2002). The prevalence in males may be related to under-identification and underdiagnosis of ADHD in females. Evidence suggests that females are more likely to have an adolescent inattentive disease, which is more easily overlooked than the disruptive component of ADHD that tends to affect males (Biederman et al. 2002).

In our study, valproate was the most frequently used add-on therapy, and it was administered to patients with epilepsy

TABLE 7. ADRs THAT RESULTED IN STUDY DISCONTINUATION

Age (years)	*Sex*	*ADRs*	*Severity*	*Concomitant psychiatric medication*
10	Male	Somnolence	Not serious	Topiramate, carbamazepine
6	Male	Weight loss	Serious	
14	Male	Hyperhidrosis and weight gain	Serious	
7	Male	Abdominal pain	Not serious	
6	Female	Tachycardia and abdominal pain	Serious	
6	Male	Abdominal pain, vomiting, loss of appetite	Serious	
6	Male	Hepatomegaly	Serious	
13	Male	Weight loss, vomiting	Not serious	Valproate, ethosuximide
6	Male	Weight loss	Not serious	
17	Male	Hyperbilirubinemia, hypertransaminasemia	Serious	

associated with ADHD. Parisi et al. (2010) recently reported a high frequency of association between epilepsy and ADHD, and suggested that there is bidirectional relationship between the two disorders.

Twenty-five (32.8%) patients from Campania reported at least one ATX- or MPH-induced ADR and five of these (20%) were on a concomitant psychiatric medication. Among all the ATX- or MPH-induced ADRs recorded in the Italian spontaneous reporting database, most occurred in patients from Campania, probably because of our intensive monitoring program.

In our study, the clinical and demographic characteristics were similar in subjects with and without ADRs. In most cases, ADRs were not serious and resolved after drug withdrawal. As expected, because of the unbalanced distribution of patients in the treatment groups, most ADRs were related to ATX treatment. The most common ADR was weight loss. In our study, we recorded this event in nine patients (eight on ATX, one on MPH1). In most cases, this symptom was mild-to-moderate and tended to subside over time. Only one case was clinically significant and led to discontinuation of therapy. We also found that weight loss was not related to days of therapy. Some patients experienced the most consistent weight loss after fewer days of therapy than other patients. This is in line with previous findings that both ATX and MPH may induce weight loss (Spencer et al. 2007; Faraone et al. 2008) especially during the initial months of treatment. Weight loss may be secondary to decreased appetite which in turn may be related to reported gastrointestinal symptoms such as nausea, vomiting, and/or upper abdominal pain. Alternatively, weight loss may occur consequent to loss of appetite probably resulting from temporary derangement of the central noradrenergic systems involved in hunger or satiety (Spencer et al. 2007).

All reported ADRs were expected, because they are listed in the summaries of product characteristics, except for a case of weight gain and a case of buccofacial dystonia, both related to ATX treatment. To our knowledge, ATX-induced weight gain has not been reported previously.

The one instance of weight gain was reported in an 8-year-old boy who gained 10 kg between the 6th and the 9th month of treatment with ATX 18 mg/day. He was not under treatment with other drugs. After exclusion of other possible causes such as increased food intake, the clinicians suspected that the weight gain was related to ATX. The Naranjo algorithm score was consistent with a possible causality link.

The case of dystonia was reported in a boy undergoing treatment with ATX 18 mg/day for 1 month. He had epilepsy and had been taking valproate for 3 months. Four days after he started cotreatment with risperidone 0.5 mg/day, he experienced buccofacial dystonia, which resolved after risperidone withdrawal. We believe this adverse reaction was related to an interaction between risperidone and ATX. Indeed, both ATX and risperidone are metabolized by the cytochrome P-450 2D6 isoform (CYP2D6) (Fang et al. 1999; Sauer et al. 2005). It is conceivable that ATX may have reduced the metabolism of risperidone and increased its plasma concentrations, thereby leading to dystonia. This possibility is substantiated by reports of extrapyramidal symptoms associated with ATX in combination with other drugs (Bond et al. 2007). Other possible explanations are that ATX induced an atypical effect, an increased level of ATX or its metabolites in the circulation because of the patient's poor metabolizer status or because of excess synaptic norepinephrine or dopamine (Bond et al. 2007). Although risperidone is not contraindicated in patients under treatment with ATX, clinicians should be aware of the possibility of a metabolic interaction with ATX that may lead to exacerbation of adverse extrapyramidal effects.

Another important ADR identified in this study was suicidal ideation. The patient experienced worsening of oppositional behavior and threatened to commit suicide 5 months after starting ATX 40 mg/day. He was not on concomitant medications. The clinician reduced the dose to 25 mg/day; the outcome was not reported. Suicidal ideation is a rare and extremely serious ATX adverse event that has been identified by spontaneous postmarketing alerts. Thus far, the risk of suicidal thoughts in ATX-treated children or adolescents has been described only in one short-term study (Donnelly et al. 2009). A small but significantly increased risk was also observed in a meta-analysis by Bangs et al. (2008b). As in our case, worsening of oppositional behavior could be a marker of distress that could lead to suicidal acts, but no causal link between the emergence of behavioral changes and suicidal impulses has been established (Graham et al. 2011).

During our analysis, two patients, 14 and 8 years old, experienced severe hepatic events. In the first case, the child showed hepatomegaly after 7 months of treatment with ATX. The drug was withdrawn and the clinical conditions improved. Subsequently, the child started a new treatment with MPH, but 2 months later he experienced severe hyperbilirubinemia and hypertransaminasemia. In the second case, hyperbilirubinemia and hypertransaminasemia arose in a child treated with ATX for 10 months. In both cases, the children were not on concomitant medications and, following discontinuation of therapy, liver enzymes levels returned to normal values.

Although the risk of ATX-induced hepatic events has not emerged from clinical trials, some cases of liver injury have been reported during postmarketing experience. Nevertheless, most of these cases contained possible confounding factors or had other explanations unrelated to ATX (Bangs et al. 2008a). Moreover, the probability of under-reporting and the lack of information about the usual prevalence of otherwise unexpected liver injuries, leave genuine uncertainty about the ATX hepatotoxic effect (Graham et al. 2011). The etiopathogenesis of this toxicity is unknown, but an idiosyncratic mechanism was hypothesized (Erdogan et al. 2011).

As with ATX, hepatotoxicity with MPH is a very rare event. A few cases are reported in the literature, but a definite causal relationship has not been established. For the first case described previously, pre-existent moderate liver damage following ATX can be inferred.

Based on the uncertainty about the possible liver toxicity of ADHD medications, our data add important information and may contribute to clarify the safety profile of these drugs.

Compared with in Italy overall, more patients enrolled in Campania dropped out of the ADHD National Register because of at least one ADR (8.4% and 15%, respectively). The most frequent ADRs leading to dropping out were abdominal pain (two serious, one not serious) and weight loss (one serious, two not serious). Among the patients who dropped out, four perceived lack of efficacy. In these four cases, lack of efficacy was not viewed as an ADR and the clinician did not report it to AIFA. According to Rowling and Thompson's ADR Classification (Rawlins and Thompson 1997), updated by Aronson (Aronson 2002), lack of efficacy, as drug failure, is an ADR-subtype and is one of the most frequently under-reported ADRs. Finally, although we did not evaluate treatment efficacy, ~80% of patients experienced improvement of their clinical conditions, and 24.5% of these discontinued pharmacological treatment for this reason.

The main strength of our study is that, unlike spontaneous reports in the United States Food and Drug Administration's (FDA's) Adverse Event Reporting (AER) system, the authors of this report knew the denominator of the sample and could calculate the AER rate. Our study population represents the entire cohort of Campania children and adolescents with a diagnosis of ADHD, and who take ATX or MPH.

During our study, we introduced monitors who periodically and systematically interviewed clinicians at reference prescription centers. This was an active method to enhance the identification of ADRs by clinicians and to solicit them to report ADRs. The high rate of adverse events in our study population confirms also that an *ad hoc* form, such as ours, could improve the gathering of data on ADRs, according to Greenhill et al. (2004).

Finally, all ADRs registered in our study population were promptly reported to AIFA, which exceeds the parameters of most of Italian Registries, which generally wait for spontaneous reporting.

Limitations

There are several limitations to this study. First, we did not have full access to the National ADHD Registry, but were limited in our adverse event elicitation to children and adolescents on ADHD medications in the Campania region. Our comparative analyses between subjects in Campania and in the national cohort are limited to diagnostic and clinical characteristics of the patients. For that reason, we could not calculate the relative risk of ADRs in the sample. Second, the resulting data set for the full analysis is small, and not representative of the national sample. Third, we cannot exclude uncontrolled biases that could have affected the reporting rate of ADRs.

Conclusions

Most ADRs from MPH and ATX were those commonly reported in the literature, were not serious, and resolved spontaneously. Nevertheless, several unexpected or uncommon ADRs were identified.

Moreover, our intensive pharmacosurveillance study shows that a close collaboration between the pharmacovigilance centers and clinicians is necessary for improving the effectiveness of the National Register and increasing the number of ADRs recorded in the Italian spontaneous reporting database.

As ADHD is a chronic disorder that typically requires pharmacological treatment for several years or more, further long-term systematic pharmacovigilance studies are needed to identify any rare and unexpected long-term and late-appearing ADRs associated with taking ATX or MPH.

Clinical Significance

Our study investigates a disease whose pharmacological therapy is still being studied for its long-term tolerability. Our active monitoring study allowed us to increase the number of ADRs recorded to the Italian spontaneous reporting database and to collect more thorough information on the safety profile of ADHD medications. Overall, our results provide reassurance of the safety of ATX and MPH in children and adolescents with ADHD. Although our results provide reassurance of the overall safety of ATX and MPH, some unexpected or uncommon ADRs, such as weight gain, hepatotoxicity, suicide ideation, and drug interactions require further investigation.

Disclosures

No competing financial interests exist.

Acknowledgments

The authors acknowledge the contributions of Giovanna Basilicata and Elena Guarino to the monitoring activities, and thank Jean Ann Gilder (Scientific Communication srl) for editing the text.

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DOTT.SSA EVA BENSO:
TRAINER COGNITIVO DELL'APPRENDIMENTO;

DOTT. GITTI FILIPPO:
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DOTT. ANDREA DI SOMMA:
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DOTT. VINCENZO DI MARO
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IL CORSO E' IN FASE DI ACCREDITAMENTO

INTRODUZIONE

IL CORSO SI COMPORRÀ DI TRE PARTI INTEGRABILI TRA LORO: FUNZIONI ESECUTIVE E ATTENZIONE; MODELLI DI SVILUPPO DEGLI APPRENDIMENTI; TESTISTICA E TRATTAMENTI.
LA PRIMA PARTE SARÀ CARATTERIZZATA DA PUNTUALI ARGOMENTAZIONI CHE PORTERANNO AD UN ESCURSUS ARGOMENTATO E CRITICO CHE VA DALLE FUNZIONI FRONTALI AL SISTEMA ATTENTIVO SUPERVISORE PER TERMINARE SULLE FUNZIONI ESECUTIVE/ATTENTIVE E SUL PROBLEMA QUASI INSOLUBILE DEI COSTRUTTI. SI PROSEGUIRÀ ILLUSTRANDO LE TAPPE DELLO SVILUPPO DELLE FUNZIONI DI BASE VALUTANDO ANCHE L'ETÀ MINIMA DI TESTABILITÀ. INFINE SI CONSIDERERÀ LA TEORIA GERARCHICA DELL'ATTENZIONE. NELLA SECONDA PARTE SI VALUTERANNO I MODELLI CHE INTEGRANO I SISTEMI CENTRALI E LO SVILUPPO DEGLI APPRENDIMENTI.
TALI MODELLI PERMETTERANNO:

1) DI INDAGARE PER I FUTURI APPRENDIMENTI GLI INDICI PREDITTIVI E I FATTORI DI RISCHIO, IN FUNZIONE DI STABILIRE PROTOCOLLI DI PREVENZIONE;
2) DI STUDIARE PROVE DI INDAGINE PIÙ MIRATE E TRATTAMENTI SPECIFICI NELLE DIVERSE PATOLOGIE DELL'ETÀ EVOLUTIVA.

DOPO LA PRESENTAZIONE E LA DISCUSSIONE DI ALCUNI CASI CLINICI, NELLA TERZA PARTE SI APPROFONDIRANNO, A LIVELLO DI LABORATORIO PRATICO, ALCUNE PROVE PSICOMETRICHE (A DISPOSIZIONE E/O REPERIBILI) E SI OSSERVERANNO DEI TRAINING SPECIFICI DI STIMOLAZIONE COGNITIVA ATTENTIVA DA APPLICARE IN MODO APPROPRIATO A DIVERSE PATOLOGIE.

7 MARZO 2013

15.00 - 16.00 INTRODUZIONE
D. ARISI - F. GITTI

16.00 - 17.00 IL SISTEMA ESECUTIVO ATTENTIVO
F. BENSO

17.00 - 17.15 COFFEE BREAK

17.15 - 19.00 FUNZIONI ESECUTIVE :INTRODUZIONE AI MODELLI
F. BENSO

8 MARZO 2013

9.00 - 10.45 SISTEMA ESECUTIVO, ATTENZIONE E MODULI : STRUMENTI DI MISURA
F. BENSO

10.45 - 11.00 COFFEE BREAK

11.00 - 12.45 ESECUZIONE DI ATTIVITÀ PRATICHE IN PICCOLO GRUPPO CON TUTOR SUGLI STRUMENTI DI MISURA
F. BENSO - F. MAZZOLI

12.45 - 13.15 DIBATTITO

13.15 - 14.30 LUNCH

14.30 - 16.30 TEORIA DEL TRATTAMENTO INTEGRATO
F. BENSO

16.30 - 16.45 COFFEE BREAK

16.45 - 18.00 ESECUZIONE DI ATTIVITÀ PRATICHE IN PICCOLO GRUPPO CON TUTOR SUL TRATTAMENTO INTEGRATO

18.00 - 18.30 DIBATTITO
F. BENSO - E. BENSO

9 MARZO 2013

9.00 - 10.30 TRATTAMENTI NEI DISTURBI DI ATTENZIONE
F. BENSO

10.30 - 11.00 POTENZIAMENTO ATTRAVERSO LO SPORT E LE ARTI
F. BENSO

11.00 - 11.15 COFEE BREAK

11.15 - 13.00 ESECUZIONE DI ATTIVITÀ PRATICHE IN PICCOLO GRUPPO CON TUTOR SUI TRATTAMENTI PER DSA E ADHD
E. BENSO - F. MAZZOLI

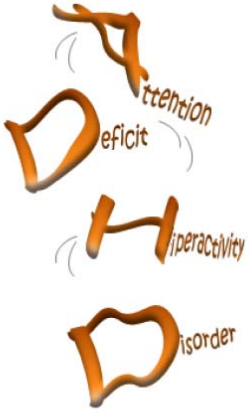
13.00 - 14.30 LUNCH

14.30 - 16.30 L'INTERAZIONE TRA IL SISTEMA ATTENTIVO SUPERVISORE E I SISTEMI SPECIFICI DEL LINGUAGGIO NELLA DETERMINAZIONE DELLA BALBUZIE E DELLA FLUIDITÀ VERBALE.
A. DI SOMMA - V. DI MARO

16.30 - 17.30 LABORATORIO PRATICO SUI DISTURBI DI APPRENDIMENTO E DELL'ATTENZIONE:
- ESECUZIONE DI ATTIVITÀ PRATICHE IN PICCOLO GRUPPO CON TUTOR -
E. BENSO - F. MAZZOLI

CHIUSURA DEI LAVORI.

ADHD: per una condivisione dei percorsi diagnostico-terapeutici



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Ore 9.00-18.00 - AULA A

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Il Progetto: "Condivisione di percorsi diagnostico-terapeutici per l'ADHD in Lombardia" è stato in parte finanziato dalla Regione Lombardia e coinvolge 18 Centri di Riferimento per l'ADHD e il Laboratorio per la Salute Materno Infantile dell'Istituto di Ricerche Farmacologiche "Mario Negri".
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"*Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia*".

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