NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD OTTOBRE 2016

ADHD Atten Deficit Hyperact Disord. 2016;1-7.

DO ADULT ATTENTION DEFICIT HYPERACTIVITY DISORDER QUALITY-OF-LIFE (AAQOL) SCALE AND THE SF-36 SCALE MEASURE THE SAME CONSTRUCT OF HEALTH-RELATED QUALITY OF LIFE?

Zare R, Jafari P, Ghanizadeh A.

It has never been investigated whether the assessment tools of Adult Attention Deficit Hyperactivity Disorder Quality-of-Life (AAQoL) scale and the SF-36 measure the same construct. The participants were 101 parents of children with ADHD and 243 parents of school children. The parents completed both the Persian version of the AAQoL and the SF-36 questionnaires. The present study revealed that the Persian version of both AAQoL and SF-36 for the assessment of HRQoL in parents of children with ADHD has convergent and discriminant validity and internal consistency. MultitraitΓÇômultimethod correlation matrix showed that the domains of two questionnaires were moderately correlated. Current results support that AAQoL and SF-36 in parents of children with ADHD measure the same HRQoL constructs. Hence, for assessing the HRQoL of parents of children with ADHD, one of the two questionnaires can be used regard to the objective of study. The Persian version of the AAQoL loaded on four domains which were in line with the original version. HRQoL of parents of children with ADHD is markedly less than the community sample of children

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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.

Anesthesia and Analgesia. 2016;123:303.

THE INCIDENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN PEDIATRIC PATIENTS AFTER GENERAL ANESTHESIA IN TAIWAN: A NATIONWIDE POPULATION-BASED STUDY.

Chu CC.

Background & Objectives: We aimed to investigate the association of early exposure to general anesthesia with attention-deficit/hyperactivity disorder (ADHD) in pediatric patients.

Materials & Methods: We used a database containing a nation-wide birth cohort from 1999–2002 in Taiwan and those had ever been exposed to general anesthesia for surgery or procedure before their second birthdays were identified. Children with any congenital neurodeficit were excluded. The birth cohort was followed up until the end of 2011. The study endpoint was the frequency and incidence rate of ADHD after anesthetic exposure.

Results: In the 1999Γê+2002 birth cohort, 1,089,355 neonates were borne. We identified 27,925 children receiving general anesthesia with endotracheal tube, laryngeal airway or mask ventilation (GA-tube/mask) and 1,631 cases had intravenous/intramuscular GA (GA-iv/im) before the age of 2. There were 2,160 (7.74%) children being diagnosed ADHD in GA-tube/ mask group, with an incidence rate of 10.01/1,000 person-years, whereas, 153 (9.38%) children in IV/IM GA group being diagnosed ADHD, with an incidence rate 12.29/1,000 person years. For the control group, 50,970 (5.68%) of 1,041,430 children had ADHD, with incidence rate /person-year 6.24/1,000. The adjusted hazard ratio of developing ADHD was 1.34 (95% CI: 1.28–1.40) for GA-tube/mask and 1.81 (95% CI: 1.55–2.12) for GA-iv/im exposure.

Conclusion: Exposure to general anesthesia before the age of 2 years was associated an increased hazard with the development of ADHD

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Appl Neuropsychol Child. 2016 Oct;5:264-72.

ATTENTION-DEFICIT HYPERACTIVITY DISORDER STATUS AND BASELINE NEUROCOGNITIVE PERFORMANCE IN HIGH SCHOOL ATHLETES.

Salinas CM, Dean P, LoGalbo A, et al.

Approximately 136,000 concussions occur annually in American high school sports. Neuropsychological data indicate that children with preexisting cognitive difficulties, such as attention-deficit hyperactivity disorder (ADHD), may have protracted recovery from concussion. ADHD, with an estimated prevalence of 11% in youth, may increase an athlete's vulnerability to sustaining sports-related traumatic brain injury (TBI). The preponderance of evidence focusing on TBI and ADHD has derived from motor vehicle accidents rather than sports-related incidents. Thus, it is paramount to explore how ADHD may relate to injury in the sports concussion context, as well as to assess how ADHD may affect baseline neurocognitive testing. Adolescent athletes with ADHD (n = 256) demonstrated significantly reduced Verbal Memory, Visual Motor, and Impulse Control index scores compared with their peers without ADHD (n = 256). Athletes with ADHD were nearly twice as likely to have sustained a prior concussion (ADHD, 14.1%; non-ADHD, 7.8%). Knowledge regarding the unique neurocognitive profile of athletes with ADHD may enhance clinical management decisions.

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Arq Neuro-Psiquiatr. 2016;74:701-07.

SLEEP DISORDER INVESTIGATION MIGHT BE CONSIDERED TO BE MANDATORY IN ATTENTION DEFICIT/HYPERACTIVITY DISORDER GUIDELINE.

Henriques Filho PSA.

Objective: To determine the prevalence of obstructive sleep apnea (OSA) in children with attention deficit/hyperactive disorder (ADHD) and compare amplitude and latency of the P300 potential among children with and without OSA.

Method: Sixty-one children with ADHD underwent oddball auditory attention tests for detection of P300 (ERPs) followed by an all-night polysomnography. The children were divided in two groups, those with and without OSA.

Results: Significant decreased amplitude of the P300 potential was observed in children with OSA when compared with children without OSA.
Conclusion: The study showed that sleep fragmentation as a result of OSA can exacerbate the attention disorder that characterizes ADHD, and highlights the importance of assessing the presence of OSA in the differential diagnosis of children with attention deficits

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Arq Neuro-Psiquiatr. 2016;74:785-90.
WORKING MEMORY AND LEFT MEDIAL TEMPORAL CORTICAL THICKNESS.
Pastura G, Kubo TTA, Regalla MA, et al.
Objective: To perform a pilot study to investigate the association between working memory and cortical thickness in a sample of attention deficit/hyperactivity disorder (ADHD) children.
Methods: Seventeen children aged 7-10 years diagnosed with ADHD and 16 healthy children underwent a magnetic resonance scan for cortical thickness measurements. Data was correlated with working memory performance using the Backwards Digit Span subtest of the Wechsler Intelligence Scale for Children.
Results: Working memory impairment, evidenced by lower scores on the Backwards Digit Span, was observed in patients with ADHD compared to healthy controls. There was a direct correlation between working memory and cortical thickness of the left medial temporal lobe (Spearman's correlation coefficient: 0.499; $p < 0.005$).
Conclusions: Our data suggests, for the first time, a correlation between working memory, evaluated by the Backwards Digit Span, and left medial temporal cortical thickness

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Biomedical Research (India). 2016;2016:S31-S37.
DEVELOPMENT OF ARDUINO BASED LOW COST NEURO-FEEDBACK APPLIED TO ADHD.
Abdulhay E, Abdelhay A, Kilani A, et al.
The main purpose of the presented paper is to implement a low-cost user-friendly neuro-feedback tool that can be used by children in underprivileged or developing countries in order to cope with Attention Deficit Hyperactivity Disorder (ADHD) via EEG signal analysis. First, the EEG is detected and analyzed with the help of an in-house designed and built system. The EEG signal spectrum is then divided into: Alpha, Beta, Theta and Gamma ranges. Second, the introduced work focuses on the analysis of power values related to Beta band of frequencies. Finally, the results of EEG analysis are exploited to switch on/off a game with the purpose of stimulation of child concentration

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BJOG Int J Obstet Gynaecol. 2016;123:2050-51.
RE: ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER IN CHILDREN BORN TO MOTHERS WITH THYROID DYSFUNCTION: A DANISH NATIONWIDE COHORT STUDY: MATERNAL HYPOTHYROIDISM AND RISK OF AUTISM.
Fluegge K.

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BJOG Int J Obstet Gynaecol. 2016;123:2051-52.
AUTHORS' REPLY RE: ATTENTION DEFICIT HYPERACTIVITY DISORDER AND AUTISM SPECTRUM DISORDER IN CHILDREN BORN TO MOTHERS WITH THYROID DYSFUNCTION: A DANISH NATIONWIDE COHORT STUDY.
Andersen SL, Laurberg P.

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BMC Psychiatry. 2016 Mar;16:65.

THE EFFECT OF A FAMILY-BASED MINDFULNESS INTERVENTION ON CHILDREN WITH ATTENTION DEFICIT AND HYPERACTIVITY SYMPTOMS AND THEIR PARENTS: DESIGN AND RATIONALE FOR A RANDOMIZED, CONTROLLED CLINICAL TRIAL (STUDY PROTOCOL).

Lo HH, Wong SY, Wong JY, et al.

BACKGROUND: About 4 % of children in Hong Kong have attention deficit hyperactivity disorder (ADHD). The parents of children with ADHD report higher levels of stress and show more negative parenting behavior. Medication and behavior training are evidence-based treatments, but both show significant limitations. In short, medical treatment is not suitable for preschool children and would suppress growth, whereas parents under stress may not be capable of consistently applying behavior management skills. Mindfulness training can improve attention and facilitate cognitive development and overall functioning. It has been widely adopted as a treatment option in health care, but its application in a family context is limited. In this context, a family-based mindfulness intervention (FBMI) has been developed to promote the attention and mental health of children with attention symptoms and to reduce the stress experienced by their parents. This article describes the design and conduct of the trial.

METHODS/DESIGN: A multicenter, 8-week, waitlist, randomized controlled trial of FBMI is currently being conducted in Hong Kong (from mid-2015 to mid-2016). Its effectiveness will be examined by comparing the participants who receive treatment to those in a waitlist control group. The study population consists of one hundred twenty children with ADHD, or with symptoms of inattention and hyperactivity, between 5 and 7 years of age and their parents. To be included in the study, the children are required to meet or exceed the borderline cutoff score of the Chinese version of the Strengths and Weaknesses of ADHD Symptoms and Normal Behaviors Rating Scale (SWAN-C). The primary outcome measures are the children's ADHD symptoms and behavior and the parents' stress. The secondary outcome measures include the children's overall behavioral problems and performance on the Attention Network Test, the parents' ADHD symptoms, the parents' mindful parenting scores, and heart rate variability of parents.

DISCUSSION: This study is probably the first randomized controlled trial of FBMI for young children and their caregivers. A rigorous design and multiple outcome measures are used to examine the effectiveness of FBMI. If the hypotheses are confirmed, FBMI may serve as an additional treatment option for children with ADHD.

TRIAL REGISTRATION: This study is registered with the Chinese Clinical Trial Registry (reference number: ChiCTR-IOR-15007292). Registered 28 October 2015

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BMJ Open. 2016 Feb;6:e009089.

ASSOCIATION OF SCREEN TIME WITH SELF-PERCEIVED ATTENTION PROBLEMS AND HYPERACTIVITY LEVELS IN FRENCH STUDENTS: A CROSS-SECTIONAL STUDY.

Montagni I, Guichard E, Kurth T.

OBJECTIVE: To investigate whether high levels of screen time exposure are associated with self-perceived levels of attention problems and hyperactivity in higher education students.

DESIGN: Cross-sectional study among participants of the i-Share cohort.

SETTING: French-speaking students of universities and higher education institutions.

PARTICIPANTS: 4816 graduate students who were at least 18 years old.

EXPOSURE: Screen time was assessed by self-report of the average time spent on five different screen activities on smartphone, television, computer and tablet and categorised into quartiles.

MAIN OUTCOME MEASURE: We used the Attention Deficit Hyperactivity Disorder Self-Report Scale (ASRS-v1.1) concerning students' behaviour over the past 6 months to measure self-perceived levels of attention problems and hyperactivity. Responses were summarised into a global score as well as scores for attention problems and hyperactivity.

RESULTS: The 4816 participants of this study had a mean age of 20.8 years and 75.5% were female. Multivariable ordinary regression models showed significant associations of screen time exposure with quintiles of the total score of self-perceived attention problems and hyperactivity levels as well as the individual domains. Compared to the lowest screen time exposure category, the ORs (95% CI) were 1.58

(1.37 to 1.82) for each increasing level of quintiles of the global score, 1.57 (1.36 to 1.81) for increasing quintiles of attention levels and 1.25 (1.09 to 1.44) for increasing quartiles of hyperactivity.
CONCLUSIONS: Results of this large cross-sectional study among French university and higher education students show dose-dependent associations between screen time and self-perceived levels of attention problems and hyperactivity. Further studies are warranted to evaluate whether interventions could positively influence these associations

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Brain Behav. 2016.

DOPAMINERGIC MODULATION OF DEFAULT MODE NETWORK BRAIN FUNCTIONAL CONNECTIVITY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Silberstein RB, Pipingas A, Farrow M, et al.

Introduction: Recent evidence suggests that attention deficit hyperactivity disorder (ADHD) is associated with a range of brain functional connectivity abnormalities, with one of the most prominent being reduced inhibition of the default mode network (DMN) while performing a cognitive task. In this study, we examine the effects of a methylphenidate dose on brain functional connectivity in boys diagnosed with ADHD while they performed a cognitive task.
Method: Brain functional connectivity was estimated using steady-state visual evoked potential partial coherence before and 90 min after the administration of a methylphenidate dose to 42 stimulant drug-naïve boys newly diagnosed with ADHD while they performed the A-X version of the continuous performance task (CPT A-X).
Results: Methylphenidate robustly reversed the transient functional connectivity increase in the A-X interval seen premedication to a postmedication decrease during this interval. In addition, methylphenidate-induced reductions in individual reaction time were correlated with corresponding reductions in functional connectivity.
Conclusion: These findings suggest that methylphenidate suppresses the increased functional connectivity observed in ADHD and that such suppression is associated with improved performance. Our findings support the suggestion that the increased functional connectivity we have observed in ADHD is associated with abnormal DMN activity. In addition, we comment on the significance of specific frequency channels mediating top-down communication within the cortex and the extent to which our findings are selectively sensitive to top-down intracortical communication

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Brain Imaging Behav. 2016;1-10.

DEFAULT MODE NETWORK ACTIVITY AND NEUROPSYCHOLOGICAL PROFILE IN MALE CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER AND CONDUCT DISORDER.

Uytun MC, Karakaya E, Oztop DB, et al.

It is known that patients with Attention Deficit and Hyperactivity disorder (ADHD) and Conduct disorder (CD) commonly shows greater symptom severity than those with ADHD alone and worse outcomes. This study researches whether Default mode network (DMN) is altered in adolescents with ADHD + CD, relative to ADHD alone and controls or not. Ten medication-na+»ve boys with ADHD + CD, ten medication-na+»ve boys with ADHD and 10-age-matched typically developing (TD) controls underwent functional magnetic resonance imaging (fMRI) scans in the resting state and neuropsychological tasks such as the Wisconsin Card Sorting Test (WCST), Stroop Test TBAG Form (STP), Auditory Verbal learning Test (AVLT), Visual Auditory Digit Span B (VADS B) were applied to all the subjects included. fMRI scans can be used only nine patients in each groups. The findings revealed group differences between cingulate cortex and primary mortor cortex; cingulate cortex and somatosensory association cortex; angular gyrus (AG) and dorsal posterior cingulate cortex, in these networks increased activity was observed in participants with ADHD + CD compared with the ADHD. We found that lower resting state (rs)-activity was observed between left AG and dorsal posterior cingulate cortex, whereas higher rs-activity connectivity were detected between right AG and somatosensory association cortex in ADHD relative to the ones with ADHD + CD. In neuropsyhcological tasks, ADHD + CD group showed poor performance in WISC-R, WCST, Stroop, AVLT

tasks compared to TDs. The ADHD + CD group displayed rs-functional abnormalities in DMN. Our results suggest that abnormalities in the intrinsic activity of resting state networks may contribute to the etiology of CD and poor prognosis of ADHD + CD

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Brain Imaging Behav. 2016;1-11.

THE INTERACTION BETWEEN 5-HTTLPR AND STRESS EXPOSURE INFLUENCES CONNECTIVITY OF THE EXECUTIVE CONTROL AND DEFAULT MODE BRAIN NETWORKS.

Van Der Meer D, Hartman CA, Pruim RHR, et al.

We recently reported that the serotonin transporter polymorphism 5-HTTLPR moderates the relation between stress exposure and attention-deficit/hyperactivity disorder (ADHD) severity. This gene-environment interaction (GxE) has been previously tied to the processing of emotional stimuli, which is increasingly recognized to be a key factor in ADHD-related impairment. The executive control and default mode brain networks play an important role in the regulation of emotion processing, and altered connectivity of these networks has also been associated with ADHD. We therefore investigated whether resting-state connectivity of either of these networks mediates the relation of 5-HTTLPR and stress exposure with ADHD severity. Resting-state functional magnetic resonance imaging, genetic, and stress exposure questionnaire data was available for 425 adolescents and young adults (average age 17.2 years). We found that 5-HTTLPR S-allele carriers showed a more negative relation between stress exposure and connectivity of the executive control network than L-allele homozygotes, specifically in the pre/postcentral gyrus, striatum, and frontal pole. In the default mode network, we found a positive association between the GxE and supramarginal gyrus connectivity. Connectivity of either network did not significantly mediate the effect of this GxE on ADHD. Opposite effects of stress exposure on connectivity in the executive and default mode networks may contribute to findings that stress exposure is associated with lowered cognitive control and heightened levels of rumination and worrying, for S-allele carriers but not L-allele homozygotes. When combined, these effects on connectivity of both networks may relate to the emotional problems seen in individuals with ADHD

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Br J Psychiatry. 2016;209:202-08.

IMMUNE SIGNATURES AND DISORDER-SPECIFIC PATTERNS IN A CROSS-DISORDER GENE EXPRESSION ANALYSIS.

De Jong S, Newhouse SJ, Patel H, et al .

Background Recent studies point to overlap between neuropsychiatric disorders in symptomatology and genetic aetiology.

Aims To systematically investigate genomics overlap between childhood and adult attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD) and major depressive disorder (MDD).

Method Analysis of whole-genome blood gene expression and genetic risk scores of 318 individuals. Participants included individuals affected with adult ADHD (n = 93), childhood ADHD (n = 17), MDD (n = 63), ASD (n = 51), childhood dual diagnosis of ADHD-ASD (n = 16) and healthy controls (n = 78).

Results Weighted gene co-expression analysis results reveal disorder-specific signatures for childhood ADHD and MDD, and also highlight two immune-related gene co-expression modules correlating inversely with MDD and adult ADHD disease status. We find no significant relationship between polygenic risk scores and gene expression signatures.

Conclusions Our results reveal disorder overlap and specificity at the genetic and gene expression level. They suggest new pathways contributing to distinct pathophysiology in psychiatric disorders and shed light on potential shared genomic risk factors. Declaration of interest G.B. acts a consultant in preclinical genomics for Eli Lilly

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Can J Psychiatry. 2015 Dec;60:556-63.

NONMEDICAL USE OF PRESCRIPTION MEDICATION AMONG ADOLESCENTS USING DRUGS IN QUEBEC.

Roy E, Nolin MA, Traore I, et al.

OBJECTIVE: To determine the prevalence and factors associated with nonmedical use of prescription medication (NMUPM) among adolescents who use drugs (ages 12 to 17 years) in Quebec.

METHOD: Secondary data analyses were carried out with data from a 6-month study, namely, the 2010-2011 Quebec Health Survey of High School Students-a large-scale survey that sought to gain a better understanding of the health and well-being of young Quebecers in high school. Bivariate and multivariate logistic regression analyses were conducted to study NMUPM among adolescents who use drugs, according to sociodemographic characteristics, peer characteristics, health indicators (anxiety, depression, or attention-deficit disorder [ADD] with or without hyperactivity), self-competency, family environment, and substance use (alcohol and drug use) factors.

RESULTS: Among adolescents who had used drugs in the previous 12 months, 5.4% (95% CI 4.9% to 6.0%) reported NMUPM. Based on multivariate analyses, having an ADD (adjusted odds ratio [AOR] 1.47; 95% CI 1.13 to 1.91), anxiety disorder (AOR 2.14; 95% CI 1.57 to 2.92), low self-esteem (AOR 1.62; 95% CI 1.26 to 2.08), low self-control (AOR 1.95; 95% CI 1.55 to 2.45), low parental supervision (AOR 1.43; 95% CI 1.11 to 1.83), regular alcohol use (AOR 1.72; 95% CI 1.36 to 2.16), and polysubstance use (AOR 4.09; 95% CI 3.06 to 5.48) were associated with increased odds of reporting NMUPM.

CONCLUSIONS: The observed prevalence of NMUPM was lower than expected. However, the associations noted with certain mental health disorders and regular or heavy use of other psychoactive substances are troubling. Clinical implications are discussed

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Can J Psychiatry. 2015 Oct;60:432-40.

LIFETIME PREVALENCE OF ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN YOUNG ADULTS: EXAMINING VARIATIONS IN THE SOCIOECONOMIC GRADIENT.

Yallop L, Brownell M, Chateau D, et al.

OBJECTIVE: It has only recently been accepted that attention-deficit hyperactivity disorder (ADHD) persists into adulthood. Accordingly, less is known about adult diagnostic and treatment prevalence. We aimed to determine the lifetime prevalence of ADHD diagnosis and psychostimulant prescriptions for young adults in the province of Manitoba and to explore how diagnosis differs according to sociodemographic characteristics and age at diagnosis; and to investigate whether a socioeconomic gradient exists within young adults with a lifetime ADHD diagnosis, as well as the variables that moderate the gradient.

METHODS: Using the Manitoba Population Health Research Data Repository, our cross-sectional analysis used 24 fiscal years of data (1984/85 to 2008/09) and included all adults aged 18 to 29 during 2007/08 to 2008/09 in Manitoba (n = 207 544) who had a lifetime diagnosis of ADHD (n = 14 762). Regression analyses tested for differences in rates by sex, region, age, age at diagnosis, and socioeconomic status.

RESULTS: Lifetime prevalence for ADHD diagnosis (7.11%) and psychostimulant prescriptions (3.09%) differed according to sex, region, and age. In contrast to previous Manitoban research on childhood ADHD, the socioeconomic gradient for ADHD diagnosis was not found in young adulthood. When region was accounted for, a small negative gradient in the urban population and a positive gradient in the rural population were evident. People from the highest income quintile were significantly less likely to be diagnosed before age 18, compared with other income quintiles.

CONCLUSIONS: Given the high lifetime prevalence of ADHD in Manitoban young adults and significant socioeconomic correlates for diagnosis, further investigation into the trajectory of this relatively unexplored population is recommended

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Can J Psychiatry. 2015 Oct;60:415-16.
THEMATIC ISSUE ON CHILD AND ADOLESCENT PSYCHIATRY.
Smith DH.

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Child Abuse Negl. 2016;62:1-9.
EFFECTS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ON CHILD ABUSE AND NEGLECT.
Sari Gokten E, Saday Duman N, Soylu N, et al.
It is known that children with mental and developmental problems are at risk of abuse and neglect. Attention-deficit/hyperactivity disorder is one of the most frequent neurodevelopmental disorders in children and adolescents. The purpose of this study is to examine whether children diagnosed with ADHD are under more risk in terms of child abuse and neglect compared to controls. In this case-control study, 104 children, who applied to Child and Adolescent Psychiatry Unit of Bursa Yuksek Ihtisas Training and Research Hospital between January and June 2015, were diagnosed with ADHD, and had no other psychiatric comorbidity except for disruptive behavior disorders, and 104 healthy children were compared. Abuse Assessment Questionnaire was applied to children after approval of the families was received. It was determined that the children diagnosed with ADHD were exposed to more physical (96.2%) and emotional abuse (87.5%) in a statistically significant way compared to controls (46.2%; 34.6%), they were exposed to physical and emotional neglect (5.8%) at a lower rate compared to healthy children (24.0%), and there was no difference between them and healthy children in terms of witnessing family violence (56.7%; 47.1%) and being exposed to sexual abuse (5.8%; 1.9%). The children diagnosed with ADHD were exposed to physical and emotional abuse at a higher rate; further studies should emphasize the role of parents in this topic and how parental education and treatment programs change the results

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Child Neuropsychol. 2016;1-18.
EQUIVALENCE OF MOTHER AND FATHER RATINGS OF ADHD IN CHILDREN.
Mayfield AR, Parke EM, Barchard KA, et al.
Obtaining data from multiple informants provides a more comprehensive diagnostic picture in the assessment of attention deficit hyperactivity disorder (ADHD). Differences in symptom ratings have been observed between parent- and teacher-report scales, though less information is available regarding differences between mothers and fathers. To address this gap, this study examines the rater agreement between mothers and fathers on the Diagnostic and Statistical Manual of Mental Disorders ΓÇô Fourth Edition (DSM-IV) ADHD Symptom Rating Scale (DSM-ADHD-SRS). The participants consisted of 337 children diagnosed with ADHD who underwent comprehensive neuropsychological assessment. Confirmatory factor analysis indicates that a three-factor model comprising inattention, hyperactivity, and impulsivity symptoms provides the best fit for both mothersΓÇÖ and fathersΓÇÖ ratings. Mothers provided higher mean ratings for the inattention scale. These results suggest that the factor structure for the DSM-ADHD-SRS is the same, regardless of parent gender. However, symptoms of inattention may vary depending upon which parent completes the ratings. This discrepancy could lead to differences in diagnostic impressions in clinical evaluations

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Cognitive Neuropsychiatry. 2016;1-19.
Neurological soft signs are associated with attentional dysfunction in children with attention deficit hyperactivity disorder.
Pitzianti M, D'Agati E, Casarelli L, et al.
Introduction: Inattention is one of the core symptoms of Attention Deficit Hyperactivity Disorder (ADHD). Most of patients with ADHD show motor impairment, consisting in the persistence of neurological soft signs

(NSS). Our aim was to evaluate attentional and motor functioning in an ADHD sample and healthy children (HC) and possible link between attentional dysfunction and motor impairment in ADHD.
Method: Twenty-seven drug-naive patients with ADHD and 23 HC were tested with a test battery, measuring different aspects of attention. Motor evaluation has provided three primary variables: overflow movements (OM), dysrhythmia and total speed of timed activities.
Results: Compared to HC, patients were impaired in a considerable number of attentional processes and showed a greater number of NSS. Significant correlations between disturbances of attention and motor abnormalities were observed in ADHD group.
Conclusion: Our findings suggest that attentional processes could be involved in the pathophysiology of the NSS and add scientific evidence to the predictive value of NSS as indicators of the severity of functional impairment in ADHD. Given the marked improvement or complete resolution of NSS following treatment with methylphenidate, we suggest that evaluation of NSS is useful to monitor the effectiveness of pharmacological treatment with MPH in ADHD

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Comput Med Imaging Graph. 2016;52:82-88.
NETWORK-BASED CLASSIFICATION OF ADHD PATIENTS USING DISCRIMINATIVE SUBNETWORK SELECTION AND GRAPH KERNEL PCA.
Du J, Wang L, Jie B, et al.
Background Attention Deficit Hyperactivity Disorder (ADHD) is one of the most prevalent behavioral disorders in childhood and adolescence. Recently, network-based diagnosis of ADHD has attracted great attentions due to the fact that ADHD disease is related to not only individual brain regions but also the connections among them, while existing methods are hard to discover disorder patterns related with several brain regions.
New method To overcome this drawback, a discriminative subnetwork selection method is proposed to directly mine those frequent and discriminative subnetworks from the whole brain networks of ADHD and normal control (NC) groups. Then, the graph kernel principal component (PCA) is applied to extract features from those discriminative subnetworks. Finally, support vector machine (SVM) is adopted for classification of ADHD and NC subjects.
Results We evaluate the performances of our proposed method using the ADHD200 dataset, which contains 118 ADHD patients and 98 normal controls. The experimental results show that our proposed method can achieve a very high accuracy of 94.91% for ADHD vs. NC classification. Moreover, our proposed method can also discover the discriminative subnetworks as well as the discriminative brain regions, which are helpful for enhancing our understanding of ADHD disease. Comparison with existing method(s) The accuracy of our proposed method is 9.20% higher than those of the state-of-the-art methods.
Conclusions A lot of experiments in ADHD200 dataset show that, our proposed method can improve the performance significantly comparing to the state-of-the-art methods

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Crim Behav Ment Health. 2016.
ATTENTION DEFICIT HYPERACTIVITY DISORDER SYMPTOMS, TYPE OF OFFENDING AND RECIDIVISM IN A PRISON POPULATION: THE ROLE OF SUBSTANCE DEPENDENCE.
Román-Ithier JC, González RA, Vélez-Pastrana MC, et al.
Background: It is unclear whether adult offenders with a history of attention deficit hyperactivity disorder (ADHD) are more likely to re-offend, and if so, in any specific offences.
Aim: This study aimed to examine correlates of childhood ADHD symptoms among prisoners.
Methods: A randomly selected sample of 1179 participants from the adult sentenced population of Puerto Rico (USA) reported their history of violent and non-violent offences, age of first arrest and re-offending. Participants completed retrospective measures of ADHD and a diagnostic interview for substance use disorders.

Results: Self-reported ADHD was associated with age of first arrest, a number of violent and non-violent offences and re-offending. The association with any non-violent offending was explained statistically by substance use disorders and other psychosocial covariates. ADHD was independently associated with being under 15years of age at first arrest and with re-offending.
Conclusions: Although some associations between ADHD and offending may be accounted for by co-morbidity with substance use disorders, early onset of offending and repeated violent offending appear to be directly related to ADHD. Criminal justice policies should, therefore, incorporate ADHD screening accompanied by appropriate rehabilitation programmes when such neurodevelopmental disorder is identified

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Disabil Health J. 2016 Oct;9:663-72.

ASSOCIATIONS BETWEEN NEURODEVELOPMENTAL DISORDERS AND FACTORS RELATED TO SCHOOL, HEALTH, AND SOCIAL INTERACTION IN SCHOOLCHILDREN: RESULTS FROM A SWEDISH POPULATION-BASED SURVEY.

Beckman L, Janson S, von Kobyletzki L.

Background: Children and adolescents with autism spectrum disorder (ASD) or attention-deficit/hyperactivity disorder (ADHD) are more likely to be surrounded by different risk factors. In order to work preventively with decreasing ADHD and ASD symptoms, there is a need of more knowledge concerning risk factors.
Objective: This study aimed to investigate school, health, lifestyle and social interactions association with autism spectrum disorder (ASD) and attention-deficit/hyperactivity disorder (ADHD) among schoolchildren aged 6–17 years.
Methods: Data for 18,416 children and adolescents aged 6–17 years in the county of Värmland, Sweden, from the school year 2012/2013 and 2013/2014 were obtained from the Student Health Database, which includes information on health examinations by school nurses and self-reported information of mental and physical health, social relations, physical activity, and school conditions.
Results: Of all participants, 2.4% reported only ADHD and 1.6% reported only ASD. The results confirmed that ADHD or ASD was significantly associated with worse school experiences, lower socioeconomic status, less physical activity, more substance use, weaker social network and more impairments than those without ADHD or ASD.
Conclusions: Knowledge of risk or protective factors during school years is needed to develop interventions to reduce symptoms of neurodevelopmental disorders in children and adolescents

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Early Intervent Psychiatry. 2016;10:191.

A SURVEY ON MENTAL HEALTH OF CHILDREN WHOSE PARENTS HAVE PSYCHIATRIC DISORDERS.

Park SM, Kim Y, Yang YH, et al.

This study aimed to understand mental health of children of psychiatric patients. Forty-eight children, age from 9 to 18, whose parents are registered in community mental health centres were recruited in Seoul. We administered age-matched protocol as 3 domains as following: 1) cognition: Korean version of Learning Disability Evaluation Scale (K-LDES), Comprehensive Attention Test (CAT) 2) emotion and behavior - parent report: Korean Children's' Behavior Checklist (KCBCL), Korean ADHD Rating Scale (K-ARS) 3) emotion and behavior - Self report: Beck Depression Inventory-II (BDI-II) or Children Depression Inventory-II (CDI-II), Youth Self Report (YSR). For demographic data, sex consists of 24 male (50.0%) there were 18 elementary school (37.5%), 21 middle school (47.4), and 4 (8.3%) high school students. For parent's psychiatric diagnosis, depression were 31(64.6%), and schizophrenia were 11 (22.9%), bipolar disorder 3 (6.3%) and so on. We defined high risk at mental health as those' scores were over cut-off levels at least in 2 of 3 domains. As a result, 12 (25%) children were classified as high risk. Children who have scores over cut-off level in one domain were also 20 (41.6%). For each test, 23.1% were met cut-off score for CAT attention task; 23.4% for K-ARS suggesting ADHD, 17.4% for BDI-II / 28.0% for CDI-II depression scale, 45.9% (problem behavior) / 25.0% (adaptation) for CBCL, and 22.2% (problem behavior) / 33.3% (adaptation) for

YSR. Our results suggest that children of psychiatric patients might be vulnerable to mental illness as well and need early prevention or intervention for mental health

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Early Intervent Psychiatry. 2016;10:34.

FAMILY STRUCTURE, BEHAVIOR AND SYMPTOMS IN YOUNG CHILDREN AT FAMILIAL RISK FOR SCHIZOPHRENIA.

Seidman L, Molokotos E, Brent B, et al.

Objective: To evaluate function in parents with schizophrenia, and behaviour in their offspring.

Methods: Using a family high-risk (FHR) design, we evaluated 20 non-psychotic, offspring of parents with psychotic disorders (HRP), contrasting them with 30 non-psychotic controls (CON) without any first-degree relatives with psychosis. The mean age of the child sample was 9 years (range 7-12).

Results: Preliminary analyses on the first half of the sample were revealing. Of the first 10 families, 70% of the ill parents were mothers, 20% were fathers, and 10% were siblings. In virtually all of these families, the mother was the primary caretaker, and in only two families was there a partner. Mothers were primarily from lower socio-economic status and often conveyed a sense of being overwhelmed economically and emotionally. More than half of the children met criteria for ADHD and/or oppositional defiant disorder. The children were significantly impaired on all dimensions of the BRIEF including the Executive Composite (P = .003). They were also significantly impaired on many dimensions of the CBCL including both Internalizing and Externalizing Problems. The HRP children did not show significant differences on scales of Magical Thinking or Psychotic-Like Experiences.

Conclusion: These results demonstrate that significant behavioural difficulties are present in pre-teen HRP children, especially in aspects of executive control of behaviour, and not in pre-psychotic experiences. Also striking was the sense of being overwhelmed in the parents. These preliminary results suggest interventions building social support for the parents to reduce stress and help build structure for their children

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Environ Int. 2016;94:649-60.

THE INFLUENCE OF MATERNAL DIETARY EXPOSURE TO DIOXINS AND PCBS DURING PREGNANCY ON ADHD SYMPTOMS AND COGNITIVE FUNCTIONS IN NORWEGIAN PRESCHOOL CHILDREN.

Caspersen IH, Aase H, Biele G, et al.

BACKGROUND: Polychlorinated dibenzo-p-dioxins/dibenzofurans (dioxins) and polychlorinated biphenyls (PCBs) are persistent organic pollutants (POPs) with potentially adverse impact on child neurodevelopment. Whether the potential detrimental effects of dioxins and PCBs on neurodevelopment are of specific or unspecific character is not clear.

OBJECTIVES: The purpose of the current study was to examine the influence of maternal dietary exposure to dioxins and PCBs on ADHD symptoms and cognitive functioning in preschoolers. We aimed to investigate a range of functions, in particular IQ, expressive language, and executive functions.

MATERIAL AND METHODS: This study includes n=1024 children enrolled in a longitudinal prospective study of ADHD (the ADHD Study), with participants recruited from The Norwegian Mother and Child Cohort Study (MoBa). Boys and girls aged 3.5years participated in extensive clinical assessments using well-validated tools; The Preschool Age Psychiatric Assessment interview (PAPA), Stanford-Binet 5th revision (SB-5), Child Development Inventory (CDI), and Behavior Rating Inventory of Executive Function, Preschool version (BRIEF-P). Maternal dietary exposure to dioxins and PCBs was estimated based on a validated food frequency questionnaire (FFQ) answered mid-pregnancy and a database of dioxin and PCB concentrations in Norwegian foods. Exposure to dioxins and dioxin-like PCBs (dl-compounds) was expressed in total toxic equivalents (TEQ), and PCB-153 was used as marker for non-dioxin-like PCBs (ndl-PCBs). Generalized linear and additive models adjusted for confounders were used to examine exposure-outcome associations.

RESULTS: Exposure to PCB-153 or dl-compound was not significantly associated with any of the outcome measures when analyses were performed for boys and girls together. After stratifying by sex, adjusted analyses indicated a small inverse association with language in girls. An increase in the exposure variables of 1 SD was associated with a reduction in language score of -0.2 [CI -0.4, -0.1] for PCB-153 and -0.2 [CI -

0.5, -0.1] for dl-compounds in girls. For boys, exposure to PCB-153 or dl-compounds was not associated with language skills. The difference between sex-specific associations was not statistically significant (p-value=0.13). No sex-specific effects were observed for ADHD-symptoms, IQ scores, or executive functions. **CONCLUSIONS**: We found no indications that variation in current low-level exposure to PCB-153 or dl-compounds in Norway is associated with variation ADHD-symptoms, verbal/non-verbal IQ, or executive functions including working memory in preschoolers. However, our findings indicated that maternal dietary exposure to PCB-153 or dl-compounds during pregnancy was significantly associated with poorer expressive language skills in preschool girls, although the sex-specific associations were not significantly different

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Eur Child Adolesc Psychiatry. 2016 Oct;25:1081-89.

EPIGENETIC REGULATION OF THE DRD4 GENE AND DIMENSIONS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN CHILDREN.

Dadds MR, Schollar-Root O, Lenroot R, et al.

Recent evidence suggests that epigenetic regulation of the DRD4 gene may characterise specific aspects of ADHD symptomology. We tested associations between ADHD symptoms and epigenetic changes to the DRD4 gene in DNA extracted from blood and saliva in N = 330 children referred for a variety of behavioural and emotional problems. ADHD was indexed using DSM diagnoses as well as mother, father, and teacher reports. Methylation levels were assayed for the island of 18 CpG sites in the DRD4 receptor gene. A nearby SNP, rs3758653, was also genotyped as it has previously been shown to influence methylation levels. There was high consistency of methylation levels across CpG sites and tissue sources, and higher methylation levels were associated with the major allele of SNP rs3758653. Higher methylation levels were associated with more severe ADHD independent of SNP status, tissue source, ethnicity, environmental adversity, and comorbid conduct problems. The association applied specifically to the cognitive/attentional, rather than hyperactivity problems that characterise ADHD. The results indicate that epigenetic regulation of the DRD4 gene in the form of increased methylation is associated with the cognitive/attentional deficits in ADHD

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Eur Child Adolesc Psychiatry. 2016;1-12.

CAN PSYCHIATRIC CHILDHOOD DISORDERS BE DUE TO INBORN ERRORS OF METABOLISM?

Simons A, Eyskens F, Glazemakers I, et al.

Many patients who visit a centre for hereditary metabolic diseases remarkably also suffer from a child psychiatric disorder. Those child psychiatric disorders may be the first sign or manifestation of an underlying metabolic disorder. Lack of knowledge of metabolic disorders in child psychiatry may lead to diagnoses being missed. Patients therefore are also at risk for not accessing efficacious treatment and proper counselling. To search the literature for the co-occurrence of child psychiatric disorders, such as ADHD, autism, psychosis, learning disorders and eating disorders and metabolic disorders. A search of the literature was conducted by performing a broad search on PubMed, using the terms "ADHD and metabolic disorders", "autism and metabolic disorders", "psychosis and metabolic disorders", "learning disorders and metabolic disorders", and "eating disorders and metabolic disorders". Based on inclusion criteria (concerning a clear psychiatric disorder and concerning a metabolic disorder) 4441 titles and 249 abstracts were screened and resulted in 71 relevant articles. This thorough literature search provides child and adolescent psychiatrists with an overview of metabolic disorders associated with child psychiatric symptoms, their main characteristics and recommendations for further investigations.

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Eur Child Adolesc Psychiatry. 2016 Mar;25:235-45.

PSYCHOTROPIC MEDICINE PRESCRIPTIONS IN ITALIAN YOUTHS: A MULTIREGIONAL STUDY.

Piovani D, Clavenna A, Cartabia M, et al.

The aim of the study was to evaluate the trend of paediatric psychotropic drug prescriptions in Italy. Data sources were regional, outpatient prescription databases. Seven Italian regions, covering 50 % of the Italian population, provided data from 2006 to 2011. Prevalence and incidence of prescriptions by age and gender were evaluated for psychotropic, antidepressant, antipsychotic, and attention-deficit/hyperactivity disorders (ADHD) medications. The hospital admission rate for psychiatric conditions was calculated, also at the local health unit (LHU) level. The presence of trends in prescription prevalence and incidence during the 6 year period was assessed. Finally, the correlation between prevalence, prescription, hospital admission rates, latitude, longitude, and average annual income at the LHU level was also investigated. In 2011, 8834 youths received at least one psychotropic drug prescription, with a prevalence of 1.76 per thousand (95 % CI 1.72-1.80). The incidence of new psychotropic drug users was 1.03 per thousand (1.00-1.06). The prevalence of antidepressants was 1.02 per thousand (0.99-1.04), while that of antipsychotics was 0.70 per thousand (0.68-0.72), and that of ADHD medications 0.19 per thousand (0.18-0.21). The psychotropic drug prevalence increased with increasing age. Males were more exposed to psychotropic drugs than females (AUC0-17 male/female = 1.23). Antipsychotics were the most prescribed psychotropic drugs in males, while antidepressants were in females. Between-region prevalence ranged from 1.56 to 2.17 per thousand. The overall prevalence of psychotropic drug from 2006 to 2011 was stable (chi(t)2 </= 0.001, p = 0.97). No correlation was found between prevalence and the variables investigated. Psychotropic drug prescription was very limited and stable. No geographical patterns were found

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Eur Child Adolesc Psychiatry. 2016;25:1121-32.

VALIDITY OF PROPOSED DSM-5 ADHD IMPULSIVITY SYMPTOMS IN CHILDREN.

Ünsel Bolat G, Ercan ES, Salum GA, et al.

The American Psychiatric Association (APA) working group on Attention-Deficit/Hyperactivity Disorder (ADHD) proposed the inclusion of four new impulsivity symptoms. However, they were not included in DSM-5 due to the lack of sufficient evidence. The aim of this study is to investigate the performance of the proposed four ADHD impulsivity symptoms with respect to: (a) ADHD factor structure; (b) performance in predicting clinical impairment; (c) specificity for ADHD diagnosis and (d) best symptomatic threshold to predict clinical impairment. The sample comprised 416 children (31 ADHD subjects according to both DSM-IV and proposed DSM-5, 20 ADHD subjects according to just one diagnostic system and 365 controls) from 12 schools. Diagnoses were derived using semi-structured interviews and ADHD rating scales. Results from confirmatory factor analysis indicate that addition of the four new impulsivity items provided a slightly better factor structure if compared to models including only 18 items. Regression analyses showed that only one of the new impulsivity symptoms (impatient) was part of the list of best predictors of impairment. None of the four new impulsivity items was specifically associated with ADHD diagnosis. The best cutoff point in the hyperactivity/impulsivity dimension for predicting impairment did not change significantly. Overall, our findings suggest that the determination on how to best capture impulsivity dimension as part of the ADHD construct needs more investigation and that there is not enough evidence to include these four assessed impulsivity symptoms as part of the ADHD criteria

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Eur Child Adolesc Psychiatry. 2016;1-12.

AN RCT INTO THE EFFECTS OF NEUROFEEDBACK ON NEUROCOGNITIVE FUNCTIONING COMPARED TO STIMULANT MEDICATION AND PHYSICAL ACTIVITY IN CHILDREN WITH ADHD.

Geladé K, Bink M, Janssen TWP, et al.

Neurofeedback (NFB) is a potential alternative treatment for children with ADHD that aims to optimize brain activity. Whereas most studies into NFB have investigated behavioral effects, less attention has been paid to the effects on neurocognitive functioning. The present randomized controlled trial (RCT) compared

neurocognitive effects of NFB to (1) optimally titrated methylphenidate (MPH) and (2) a semi-active control intervention, physical activity (PA), to control for non-specific effects. Using a multicentre three-way parallel group RCT design, children with ADHD, aged 7-13, were randomly allocated to NFB (n = 39), MPH (n = 36) or PA (n = 37) over a period of 10-12 weeks. NFB comprised theta/beta training at CZ. The PA intervention was matched in frequency and duration to NFB. MPH was titrated using a double-blind placebo controlled procedure to determine the optimal dose. Neurocognitive functioning was assessed using parameters derived from the auditory oddball-, stop-signal- and visual spatial working memory task. Data collection took place between September 2010 and March 2014. Intention-to-treat analyses showed improved attention for MPH compared to NFB and PA, as reflected by decreased response speed during the oddball task [$\eta p2 = 0.21$, $p < 0.001$], as well as improved inhibition, impulsivity and attention, as reflected by faster stop signal reaction times, lower commission and omission error rates during the stop-signal task (range $\eta p2 = 0.09$-0.18, p values <0.008). Working memory improved over time, irrespective of received treatment ($\eta p2 = 0.17$, $p < 0.001$). Overall, stimulant medication showed superior effects over NFB to improve neurocognitive functioning. Hence, the findings do not support theta/beta training applied as a stand-alone treatment in children with ADHD

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Eur Child Adolesc Psychiatry. 2016;25:1055-66.

EARLY DEVELOPMENT IN CHILDREN THAT ARE LATER DIAGNOSED WITH DISORDERS OF ATTENTION AND ACTIVITY: A LONGITUDINAL STUDY IN THE DANISH NATIONAL BIRTH COHORT.

Lemcke S, Parner ET, Bjerrum M, et al.

Not much is known about the early development in children that are later diagnosed with disorders of attention and activity (ADHD). Using prospective information collected from mothers in the Danish National Birth Cohort (DNBC), we investigated if developmental deviations in the first years of life are associated with later ADHD. In the DNBC 76,286 mothers were interviewed about their child's development and behaviour at age 6 and 18 months. At the end of follow-up, when the children were 8-14 years of age, 2034 were registered in Danish health registers with a clinical diagnosis of ADHD. The Hazard Ratio of ADHD was estimated using Cox regression model. At 6 months of age deviations in development showed associations with the child later being diagnosed with ADHD such as duration of breastfeeding, motor functioning, and incessant crying. At 18 months, many observations clearly associated with ADHD as for example the child not being able to fetch things on request [HR 3.0 (95 % CI 2.4; 3.7)], or the child being significantly more active than average [HR 2.0 (95 % CI 1.8; 2.2)]. An association to ADHD was shown, especially at 18 months, if the mother found it difficult to handle the child [HR 2.9 (95 % CI 2.4-3.5)]. However, it goes for all observations that the positive predictive values were low. Many children with ADHD showed signs of developmental deviations during the first years of their life. In general, however, ADHD cannot be identified solely on basis of the questions in DNBC

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Eur J Paediatr Neurol. 2016;20:925-37.

PREVALENCE OF SLEEP DISORDERS AND THEIR RELATIONSHIP WITH CORE SYMPTOMS OF INATTENTION AND HYPERACTIVITY IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Vélez-Galarraga R, Guillén-Grima F, Crespo-Eguílaz N, et al.

Objectives To determine the prevalence of sleep disorders in children with attention-deficit/hyperactivity disorder (ADHD) and in a control population. To examine the relationship between sleep disorders and symptoms of inattention, hyperactivity/impulsiveness and executive dysfunction.

Materials and methods We studied 126 children with ADHD and 1036 control children aged between 5 and 18 years old. Caregivers completed the Pediatric Sleep Questionnaire and the ADHD Rating Scale (ADHD-RS). Children with ADHD were subsequently assessed for executive function with the Conner's Continuous Performance Test (CPT) or with AULA Nesplora.

Results Children with ADHD slept less at night and were more likely to display sleep-related rhythmic movements. Children in the ADHD group who were under 12 years old and who had total ADHD-RS scores

over the 90th percentile had more difficulty falling asleep than other children; there was also a relationship between total ADHD-RS scores over the 90th percentile and certain parasomnias in the control population. There was a correlation between shorter duration of night-time sleep and omission errors in children who were 12 or older and who were under pharmacological treatment for ADHD. Bedtime resistance and difficulty falling sleep were more frequent in children with ADHD whose symptoms were not treated pharmacologically, than in children receiving treatment.
Interpretation Symptoms of inattention and hyperactivity are correlated with impaired sleep duration and quality; specifically, there is an association between ADHD symptoms and problems falling asleep and parasomnias, however, the current study does not address the nature and direction of causality. Children with ADHD and receiving methylphenidate had fewer sleep disorders, suggesting that, at least in some children, stimulant treatment is associated with improvement of some aspects of sleep. Shorter sleep duration in adolescents under pharmacological treatment for ADHD tended to result in more errors of omission, suggesting that it is important to promote good sleep habits in this population

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Frontiers in Neuroscience. 2016;10.
NEW INSIGHTS INTO CLINICAL CHARACTERISTICS OF GILLES DE LA TOURETTE SYNDROME: FINDINGS IN 1032 PATIENTS FROM A SINGLE GERMAN CENTER.
Sambrani T, Jakubovski E, M++ller-Vahl KR.
Background: Gilles de la Tourette syndrome (TS) is a complex neuropsychiatric disorder defined by the presence of motor and phonic tics, but often associated with psychiatric comorbidities. The main objective of this study was to explore the clinical presentation and comorbidities of TS.
Method: We analyzed clinical data obtained from a large sample (n = 1032; 529 children and 503 adults) of patients with tic disorders from one single German TS center assessed by one investigator. Data was collected with the help of an expert-reviewed semi-structured interview, designed to assess tic severity and certain comorbidities. Group comparisons were carried out via independent sample t-tests and chi-square tests.
Results: The main findings of the study are: (1) tic severity is associated with the presence of premonitory urges (PU), copro-, echo-, and paliphenomena and the number of comorbidities, but not age at tic onset; it is higher in patients with comorbid obsessive-compulsive disorder (OCD) than in patients with comorbid attention deficit/hyperactivity disorder (ADHD). (2) PU were found to be highly associated with "not just right experiences" and to emerge much earlier than previously thought alongside with the ability to suppress tics (PU in > 60% and suppressibility in > 75% at age 8-10 years). (3) Self-injurious behavior (SIB) is highly associated with complex motor tics and coprophenomena, but not with OCD/obsessive-compulsive behavior (OCB). While comorbid ADHD is associated with a lower ability to suppress tics, comorbid depression is associated with sleeping problems.
Discussion: Our results demonstrate that tic severity is not influenced by age at onset. From our data, it is suggested that PU represent a specific type of "not just right experience" that is not a prerequisite for tic suppression. Comorbid ADHD reduces patients' ability of successful tic suppression. Our data suggest that SIB belongs to the coprophenomena spectrum and hence should be conceptualized as a complex tic rather than a compulsion. Finally, this study strongly supports the hypothesis that TS+OCD is a more severe form of TS and that comorbid OCD/OCB, depression, and anxiety belong to the TS spectrum, while ADHD should be better conceptualized as a separate problem

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Genome Biology. 2016;17.
GNB5 MUTATION CAUSES A NOVEL NEUROPSYCHIATRIC DISORDER FEATURING ATTENTION DEFICIT HYPERACTIVITY DISORDER, SEVERELY IMPAIRED LANGUAGE DEVELOPMENT AND NORMAL COGNITION.
Shamseldin HE, Masuho I, Alenizi A, et al.
BACKGROUND: Neuropsychiatric disorders are common forms of disability in humans. Despite recent progress in deciphering the genetics of these disorders, their phenotypic complexity continues to be a major

challenge. Mendelian neuropsychiatric disorders are rare but their study has the potential to unravel novel mechanisms that are relevant to their complex counterparts.
RESULTS: In an extended consanguineous family, we identified a novel neuropsychiatric phenotype characterized by severe speech impairment, variable expressivity of attention deficit hyperactivity disorder (ADHD), and motor delay. We identified the disease locus through linkage analysis on 15q21.2, and exome sequencing revealed a novel missense variant in GNB5. GNB5 encodes an atypical β subunit of the heterotrimeric GTP-binding proteins (Gβ5). Gβ5 is enriched in the central nervous system where it forms constitutive complexes with members of the regulator of G protein signaling family of proteins to modulate neurotransmitter signaling that affects a number of neurobehavioral outcomes. Here, we show that the S81L mutant form of Gβ5 has significantly impaired activity in terminating responses that are elicited by dopamine.
CONCLUSIONS: We demonstrate that these deficits originate from the impaired expression of the mutant Gβ5 protein, resulting in the decreased ability to stabilize regulator of G protein signaling complexes. Our data suggest that this novel neuropsychiatric phenotype is the human equivalent of Gnb5 deficiency in mice, which manifest motor deficits and hyperactivity, and highlight a critical role of Gβ5 in normal behavior as well as language and motor development in humans

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Health Soc Work. 2016 Aug;41:164-72.
THE SUBJECTIVE EXPERIENCES OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER OF CHINESE FAMILIES IN HONG KONG: CO-CONSTRUCTION OF MEANINGS IN MULTIPLE FAMILY GROUPS.
Wan ESF, Ma JLC, Lai KYC, et al.
The subjective experiences of Chinese children in Hong Kong with attention-deficit/hyperactivity disorder (ADHD) are underexplored. This article reports the results of a qualitative study that aims to understand the subjective experiences of children with ADHD in Hong Kong, taken from among a clinical sample of Chinese families with children struggling with ADHD who have participated in cross-disciplinary research of multiple family groups (MFG). The participating children revealed the subjective experiences of their struggle with the disorder in response to their parents' concern at a 'press conference,' one of the MFG activities, which underscored the importance of developing a new social work model to meet the multiple psychosocial service needs of these families. The article concludes with the discussion of the implications for the new model

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Int J Qual Stud Health Well -being. 2016;11:30938.
A DISCURSIVE ANALYSIS CONCERNING INFORMATION ON "ADHD" PRESENTED TO PARENTS BY THE NATIONAL INSTITUTE OF MENTAL HEALTH (USA).
Erlandsson S, Lundin L, Punzi E.
A discourse analysis was performed based on an online document under the headline: "What is Attention Deficit Hyperactivity Disorder (ADHD, ADD)?" published by the National Institute of Mental Health (NIMH), USA. Three parts of the document were analysed: (1) The introductory part, as this sets the tone of the whole text. (2) Parts of the text that were specifically addressed to parents. (3) Etiology and pathology of "ADHD" with reference to a number of different symptoms and behaviors. Inattention and hyperactivity are presented in the document as a floating spectrum of symptoms caused by "ADHD." Other factors of importance for children's development, that is, early attachment, close relationships, previous experiences, culture, and contexts are ignored. Children who are perceived as inattentive and hyperactive are portrayed as having inherent difficulties with no reference to their emotions or efforts to communicate. The child is viewed as suffering from a lifelong disorder that might not be cured but controlled by a diagnosis and subsequent medication. Parents are advised to control their child's behavior and to strive for early diagnosis in order to receive treatment provided by experts. Those who are presented as experts rely on a biomedical model, and in the document, detailed descriptions of medication to correct the undesired behaviors are provided. The value of judgment in the assessment of different symptoms and behaviors that signifies "ADHD" is absent, rather taken-for-granted beliefs were identified throughout the document. A heterogeneous set of behaviors

is solely described as a disorder and hereafter it is stressed that the same behaviors are caused by the disorder. In this manner, cause and effects of "ADHD" are intertwined through circular argumentation

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Iran J Child Neurol. 2016;10:56-61.

COMPARISON OF RELATION BETWEEN ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN WITH AND WITHOUT SIMPLE FEBRILE SEIZURE ADMITTED IN ARAK CENTRAL IRAN.

Salehi B, Yousefichaijan P, Safi Arian S, et al.

Objective Febrile seizure is one of the most prevalent childhood convulsions with the most common age of onset at 14-18 mo old. Fever decreases the brain threshold for seizure. Attention Deficit Hyperactivity Disorder (ADHD) is also a neurologic-behavioral problem defined by attention deficit and hyperactivity according to DSM-IV criteria in which the child must have these signs in two different environments. There is controversy on the possible relation between febrile seizure and ADHD; while some studies approve a strong relation, some exclude any relation and some attribute ADHD to the side effects of other reasons.

Materials & Methods This descriptive-analytic study enrolled all children of 3-12 yr old with febrile seizure (according to Nelson Pediatrics Textbook diagnosed by the pediatrician in charge) referring to Amir Kabir Hospital, Arak, central Iran in 2010-2011. Overall, 103 of them with no corporeal or psychological disorder (like depression, anxiety, schizophrenia and other CNS maternal disease) were compared to 103 children of the same age and gender admitted due to disease other than febrile seizure utilizing DSM IV criteria for ADHD. Data were analyzed using SPSS version 18.

Results The hyperactivity disorder in the control and case group was 34.3% and 16.7%, respectively, denoted a significant relation between simple febrile seizure and hyperactivity.

Conclusion Hyperactivity has a significant relation with febrile seizure in male gender, making further investigation in these children prudent for early diagnosis and management

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Iran J Psychiatry. 2016;11:99-103.

COMPARISON OF CREATIVITY BETWEEN CHILDREN WITH AND WITHOUT ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CASE-CONTROL STUDY.

Aliabadi B, Davari-Ashtiani R, Khademi M, et al.

OBJECTIVE: The aim of this study was to compare creativity in children with and without attention deficit hyperactivity disorder.

METHOD: This was an analytic and descriptive study. Participants were 33 children aged 7-12 years selected from a child and adolescent psychiatric clinic at Imam Hossein hospital (Tehran, Iran), who were diagnosed with ADHD by a child and adolescent psychiatrist. They met the DSM-IV diagnostic criteria for ADHD and had no comorbidity according to K-SADS (Kiddi-Scadule for Affective disorders and Schizophrenia). They were requested not to take any medication. They took the Figural TTCT (Torrance Test of Creativity Thinking) and Raven Intelligence test after using medication. Thirty-three age and sex-matched children selected from the regional schools were recruited for the control group. They did not have any psychiatric disorders according to K-SADS. The Figural TTCT and Raven Intelligence test were conducted for the controls as well.

RESULTS: No statistically significant difference was found in the intelligence score and the mean±SD of the total score of creativity between children with ADHD (125.2 ± 42.6) and the control group (130.6 ± 47.5) (P value = 0.49). Children with ADHD had worse function in fluency and flexibility items and were not different in originality and elaboration items.

CONCLUSION: The creativity of children with ADHD is not different from that of the control group

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J Child Psychol Psychiatry. 2015 Dec;56:1314-15.

COMMENTARY: DOES HELPING MOTHERS WITH ADHD IN MULTIPLEX FAMILIES HELP CHILDREN? REFLECTIONS ON JANS ET AL. (2015).

Stein MA.

Reflecting on the accompanying article by Jans et al., we draw the following thoughts. Future research on multiplex ADHD families is needed to elucidate mechanisms, timing, and a sequencing of interventions, preferably in treatment naive participants. Furthermore, in addition to symptom measures, it is likely that multi-informant measures of functional impairments such as parenting and parent-child observations may help elucidate the complex mechanisms linking maternal and child ADHD, and eventually lead to more targeted, efficient, and feasible prevention and intervention strategies

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J Abnorm Child Psychol. 2016 Oct;44:1425-38.

ACADEMIC AND SOCIAL FUNCTIONING ASSOCIATED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: LATENT CLASS ANALYSES OF TRAJECTORIES FROM KINDERGARTEN TO FIFTH GRADE.

DuPaul GJ, Morgan PL, Farkas G, et al.

Children with attention-deficit/hyperactivity disorder (ADHD) are known to exhibit significantly lower academic and social functioning than other children. Yet the field currently lacks knowledge about specific impairment trajectories experienced by children with ADHD, which may constrain early screening and intervention effectiveness. Data were analyzed from a nationally representative U.S. cohort in the Early Childhood Longitudinal Study, Kindergarten Class of 1998–1999 (ECLS-K) for 590 children (72.7 % male) whose parents reported a formal diagnosis of ADHD. Children's math, reading, and interpersonal skills were assessed at 5 time points between kindergarten and fifth grade. Growth mixture model analyses indicated 4 latent trajectory classes for reading, 8 classes for math, and 4 classes for interpersonal skills. Membership in reading and math trajectory classes was strongly related; overlaps with interpersonal skills classes were weaker. Trajectory class membership was correlated with demographic characteristics and behavioral functioning. Children with ADHD display substantial heterogeneity in their reading, math, and interpersonal growth trajectories, with some groups of children especially likely to display relatively severe levels of academic and social impairment over time. Early screening and intervention to address impairment, particularly reading difficulties, among kindergarten students with ADHD is warranted

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Journal of Advanced Pharmaceutical Technology and Research. 2016;7:43-47.

COMPARISON OF RISPERIDONE AND ARIPIPRAZOLE IN THE TREATMENT OF PRESCHOOL CHILDREN WITH DISRUPTIVE BEHAVIOR DISORDER AND ATTENTION DEFICIT-HYPERACTIVITY DISORDER: A RANDOMIZED CLINICAL TRIAL.

Safavi P, Hasanpour-Dehkordi A, Amirahmadi M.

Although pharmacotherapy with atypical antipsychotics is common in child psychiatry, there has been little research on this issue. To compare the efficacy and safety of risperidone and aripiprazole in the treatment of preschool children with disruptive behavior disorders comorbid with attention deficit-hyperactivity disorder (ADHD). Randomized clinical trial conducted in a university-affiliated child psychiatry clinic in southwest Iran. Forty 3-6-year-old children, diagnosed with oppositional defiant disorder comorbid with ADHD, were randomized to an 8-week trial of treatment with risperidone or aripiprazole (20 patients in each group). Assessment was performed by Conners' rating scale-revised and clinical global impressions scale, before treatment, and at weeks 2, 4, and 8 of treatment. The data were analyzed by SPSS version 16. Mean scores between the two groups were compared by analysis of variance and independent and paired t-test. Mean scores of Conners rating scales were not different between two groups in any steps of evaluation. Both groups had significantly reduced scores in week 2 of treatment (P = 0.00), with no significant change in subsequent measurements. Rates of improvement, mean increase in weight (P = 0.894), and mean change in fasting blood sugar (P = 0.671) were not significantly different between two groups. Mean serum prolactin showed a significant increase in risperidone group (P = 0.00). Both risperidone and aripiprazole were equally

effective in reducing symptoms of ADHD and oppositional defiant disorder, and relatively safe, but high rates of side effects suggest the cautious use of these drugs in children

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J Allergy Clin Immunol. 2016;138:608-10.

CHILDHOOD ATOPIC DERMATITIS AND RISK OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER: A-ÁCOHORT STUDY.

Riis JL, Vestergaard C, Deleuran MS, et al.

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J Appl Dev Psychol. 2016 Sep;46:1-10.

PEER VICTIMIZATION LINKED TO NEGATIVE AFFECT IN CHILDREN WITH AND WITHOUT ADHD .

Fogleman ND, Walerius DM, Rosen PJ, et al.

Objective: Children with ADHD are more likely to experience peer victimization relative to unaffected peers. Affect appears to be an important factor in determining which children are likely to experience peer victimization, as peers typically prefer children who demonstrate less negative and more positive affect. In this study, we explored the association between child affect and peer victimization in children with and without ADHD.

Method: One hundred and four 8–12 year old children (59 ADHD, 45 non-ADHD) and their parents completed measures of peer victimization. Parents completed an Ecological Momentary Assessment protocol whereby they rated the child's affect three times daily for 28 days.

Results: Hierarchical linear regression analyses significantly supported the relation of negative affect to peer victimization in both child- and parent-report, with parent-report of peer victimization moderated by child ADHD diagnostic status.

Conclusion: Overall, this study suggested that negative affect plays an important role in peer victimization in children with and without ADHD

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J Atten Disord. 2016 Oct;20:889-902.

CAN THE ERROR-MONITORING SYSTEM DIFFERENTIATE ADHD FROM ADHD WITH READING DISABILITY? READING AND EXECUTIVE DYSFUNCTION AS REFLECTED IN ERROR MONITORING.

Horowitz-Kraus T.

Objectives: ADHD and reading disability (RD) are distinct disorders that often appear together. Individuals with both disorders are currently diagnosed based on questionnaires/behavioral performance. The present study aimed to determine whether ADHD alone differs from ADHD with RD in error monitoring, which is part of the executive system, as measured while reading.

Method: Event-related potentials were recorded during a lexical decision task performed by children with comorbid ADHD and RD and children with ADHD.

Results: Lower executive function and reading abilities were accompanied by decreased event-related potential components in participants with ADHD and RD, compared with participants with ADHD.

Conclusion: Results suggest that the error monitoring activation can be used as a possible biomarker to objectively differentiate ADHD with RD from ADHD alone

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J Atten Disord. 2016 Oct;20:825-35.

DISSOCIABLE RESPONSE INHIBITION IN CHILDREN WITH TOURETTE'S SYNDROME COMPARED WITH CHILDREN WITH ADHD.

Hovik KT, Plessen KJ, Skogli EW, et al.

Objective: This study investigates whether performance in a verbal response task (Color-Word Interference Test [CWIT]) and a motor response task (Conners' Continuous Performance Test [CCPT]) discriminates children with Tourette's Syndrome (TS), ADHD, and typically developing children (TDC).
Method: Nineteen children with TS, 79 with ADHD, and 50 with TDC participated (8-17 years).
Results: Children with TS committed significantly fewer errors in the verbal response task than those with ADHD. Moreover, children with TS but without ADHD performed better than TDC. Errors in motor task and speed of response did not distinguish between groups. A cautious tendency of response correlated positively with rates of tics in children with TS.
Conclusion: Children with TS were superior in inhibiting a prepotent verbal response; however, comorbidity with ADHD in those children negatively influenced performance. Results support the hypothesis that levels of inhibitory control distinguish children with TS, ADHD, and TDC

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J Atten Disord. 2016 Oct;20:836-44.

BEHAVIORAL AND EMOTIONAL PROBLEMS ASSOCIATED WITH CONVERGENCE INSUFFICIENCY IN CHILDREN: AN OPEN TRIAL.

Borsting E, Mitchell GL, Arnold LE, et al.

Objective: This study investigated behavioral and emotional characteristics of children with convergence insufficiency (CI), before and after treatment with office-based vergence accommodative therapy (OBVAT).
Method: Parents of 44 children ages 9 to 17 years with symptomatic CI completed the Conners 3 ADHD Index and the Child Behavior Checklist (CBCL) before and after OBVAT. Pre-treatment scores were compared with normative data and post-treatment scores were compared with baseline using the Wilcoxon sign rank test.
Results: Following OBVAT, CI children showed a significant mean improvement ($p < .0001$, effect size of 0.58) on the Conners 3 ADHD Index with the largest changes occurring in the 23 children who scored the highest at baseline. On the CBCL, anxious/depressed, somatic, and internalizing problems improved significantly ($p < .001$, effect sizes of -0.36, -1.15, and -0.67, respectively).
Conclusion: In an open trial, attention and internalizing problems improved significantly following treatment for CI

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J Atten Disord. 2016 Oct;20:879-88.

CONGRUENT VALIDITY OF THE STRENGTHS AND DIFFICULTIES QUESTIONNAIRE TO SCREEN FOR COMORBIDITIES IN CHILDREN WITH ADHD.

Bekker J, Bruck D, Sciberras E.

Objective: This study aimed to determine whether the Strengths and Difficulties Questionnaire (SDQ) is an effective screening tool for identifying comorbid mental health difficulties in children with ADHD.
Method: Parents of children with ADHD (5-13 years) completed the SDQ and the Anxiety Disorders Interview Schedule for DSM-IV–Parent Version (ADIS-C/P-IV). Data from both the measures were compared to determine congruent validity.
Results: Analyses revealed that significant relationships exist between the SDQ total score and the total number of comorbidities on the ADIS-C/P-IV. The SDQ emotional problem and conduct problem scales were significantly related to internalizing and externalizing comorbidities on the ADIS-C/P-IV, respectively.
Conclusion: While significant relationships were found between the SDQ and ADIS-C/P-IV across various domains, this relationship was stronger for externalizing comorbidities. Additional screening questions are

required to effectively screen for less common internalizing comorbidities in children with ADHD, for example, major depression and panic disorder

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J Child Adolesc Ment Health. 2016;28:1-19.

MANAGEMENT OF ADHD IN CHILDREN AND ADOLESCENTS: CLINICAL AUDIT IN A SOUTH AFRICAN SETTING.

Vrba K, Vogel W, De Vries PJ.

OBJECTIVES: Attention deficit hyperactivity disorder (ADHD) is common, yet under-recognised and undertreated, particularly in low socio-economic settings. Little is known about compliance to evidence-based guidelines in low- and middle-income countries, and no clinical audits have been published in Africa. We undertook to measure compliance in a South African setting using the National Institute for Clinical Excellence (NICE) guidelines for ADHD as the gold standard to compare compliance and socio-demographic characteristics between two treatment locations in Cape Town and to generate an audit checklist for standardising care.

METHODS: The study used a sample of 100 randomly selected cases of school-age patients diagnosed with ADHD, at the Division of Child & Adolescent Psychiatry, Red Cross War Memorial Children's Hospital and University of Cape Town, South Africa. Fifty cases each from a central and a peripheral clinic location were reviewed retrospectively using audit tools, including 17 audit standards derived from NICE guidelines. We defined compliance as "good" with ≥80%, "fair" with 50-79%, and "poor" with <50% adherence.

RESULTS: Compliance was low, with only four audit standards rated as "good". Physical monitoring was especially poor. The central group received more treatment options and relatively safer monitoring.

CONCLUSIONS: We recommend introducing structured protocols followed by re-auditing to improve service delivery, and present a checklist for use in future audit cycles

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J Child Adolesc Psychopharmacol. 2016;26:672-85.

THE GROUNDSKEEPER GAMING PLATFORM AS A DIAGNOSTIC TOOL FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: SENSITIVITY, SPECIFICITY, AND RELATION TO OTHER MEASURES.

Faraone SV, Newcorn JH, Antshel KM, et al.

Objective: The purpose of this study was to assess the relative accuracies of the Conners' Brief Rating Scale, Parent Version, the Conners' Continuous Performance Test II (CPT II), and a novel interactive game called "Groundskeeper" to discriminate child psychiatric patients with and without attention-deficit/hyperactivity disorder (ADHD).

Methods: We administered the three assessments to 113 clinically referred ADHD and non-ADHD patients who had been diagnosed with the Kiddie-Schedule of Affective Disorders and Schizophrenia- Present and Lifetime (K-SADS-PL), Version 19.

Results: As measured by the area under the curve (AUC) statistic from receiver operating characteristic (ROC) analysis, the diagnostic accuracy of Groundskeeper (0.79) was as high as the accuracy of the Conners' parent rating of inattention (0.76) and better than the CPT II percent correct (0.62). Combining the three tests produced an AUC of 0.87. Correlations among the three measures were small and, mostly, not significant.

Conclusions: Our finding of similar diagnostic accuracies between Groundskeeper and the Conners' inattention scale is especially remarkable given that the Conners' inattention scale shares method variance with the diagnostic process. Although our work is preliminary, it suggests that computer games may be useful in the diagnostic process. This provides an important direction for research, given the objectivity of such measures and the fact that computer games are well tolerated by youth

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J Child Adolesc Psychopharmacol. 2016;26:713-20.

NEUROCOGNITIVE CHANGES IN SELECTIVE SEROTONIN REUPTAKE INHIBITORS - TREATED ADOLESCENTS WITH DEPRESSION.

Shehab AAS, Brent D, Maalouf FT.

Objectives: Adolescents with major depressive disorder (MDD) were found to have deficits in executive function, attention, and memory. Despite the fact that some neurocognitive functions have been shown to be present in acute stage of the illness, but not in remission, longitudinal studies are lacking. The current study aimed to investigate the changes in neurocognitive functioning in adolescents with depression during an acute treatment course with selective serotonin reuptake inhibitor.

Methods: Twenty-four adolescents with current MDD and 24 healthy controls (HCs) were administered subtests of the Cambridge Neuropsychological Test Automated Battery as well as clinical scales at baseline and were retested at weeks 6 and 12. Those with MDD were started on fluoxetine after the baseline assessment.

Results: Despite considerable improvement in depressive symptoms in the MDD group, there was a persistent deficit in visual memory in the MDD group over time compared with HCs ($p = 0.001$). On a task of sustained attention and inhibition, HCs became better at detecting target sequences at week 12 while there were residual sustained attention deficits in MDD ($p = 0.01$). On an executive function (planning) task, while HCs learned the task and improved substantially in performance over 12 weeks, MDD performance did not significantly change ($p = 0.04$).

Conclusion: When treating depressed adolescents, clinicians need to also monitor cognitive symptoms as they appear to lag behind mood symptoms in improvement

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J Child Adolesc Psychopharmacol. 2016;26:662-71.

TELEPSYCHIATRISTS' MEDICATION TREATMENT STRATEGIES IN THE CHILDREN'S ATTENTION-DEFICIT/HYPERACTIVITY DISORDER TELEMENTAL HEALTH TREATMENT STUDY.

Rockhill CM, Tse YJ, Fesinmeyer MD, et al.

Objective: The purpose of this study was to examine the prescribing strategies that telepsychiatrists used to provide pharmacologic treatment in the Children's Attention-Deficit/Hyperactivity Disorder (ADHD) Telemental Health Treatment Study (CATTS).

Methods: CATTS was a randomized controlled trial that demonstrated the superiority of a telehealth service delivery model for the treatment of ADHD with combined pharmacotherapy and behavior training (n=111), compared with management in primary care augmented with a telepsychiatry consultation (n=112). A diagnosis of ADHD was established with the Computerized Diagnostic Interview Schedule for Children (CDISC), and comorbidity for oppositional defiant disorder (ODD) and anxiety disorders (AD) was established using the CDISC and the Child Behavior Checklist. Telepsychiatrists used the Texas Children's Medication Algorithm Project (TCMAP) for ADHD to guide pharmacotherapy and the treat-to-target model to encourage their assertive medication management to a predetermined goal of 50% reduction in ADHD-related symptoms. We assessed whether telepsychiatrists' decision making about making medication changes was associated with baseline ADHD symptom severity, comorbidity, and attainment of the treat-to-target goal.

Results: Telepsychiatrists showed high fidelity (91%) to their chosen algorithms in medication management. At the end of the trial, the CATTS intervention showed 46.0% attainment of the treat-to-target goal compared with 13.6% for the augmented primary care condition, and significantly greater attainment of the goal by comorbidity status for the ADHD with one and ADHD with two comorbidities groups. Telepsychiatrists' were more likely to decide to make medication adjustments for youth with higher baseline ADHD severity and the presence of disorders comorbid with ADHD. Multiple mixed methods regression analyses controlling for baseline ADHD severity and comorbidity status indicated that the telepsychiatrists also based their decision making session to session on attainment of the treat-to-target goal.

Conclusions: Telepsychiatry is an effective service delivery model for providing pharmacotherapy for ADHD, and the CATTS telepsychiatrists showed high fidelity to evidence-based protocols

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Journal of Clinical Epidemiology. 2016;76:65-75.

N-OF-1 TRIALS CAN BE AGGREGATED TO GENERATE GROUP MEAN TREATMENT EFFECTS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Punja S, Xu D, Schmid CH, et al.

Objectives To evaluate how data from n-of-1 trials may be used in systematic reviews and meta-analyses by examining the effects of amphetamine and methylphenidate for attention-deficit hyperactivity disorder (ADHD).

Study Design and Setting Electronic search of MEDLINE, EMBASE, and PsychINFO for English language articles published from 1950 to 2013. N-of-1 trials of pediatric participants with ADHD that assessed either amphetamine or methylphenidate vs. placebo were included. The primary outcome was improvement of core symptoms of ADHD, which was assessed by multiple rating scales. Studies with obtainable individual participant data were included in the meta-analysis. Weighted mean differences were computed using a random-effects model.

Results Nine studies were included in the amphetamine-placebo comparison and 10 in the methylphenidate-placebo comparison. Meta-analyses were consistently in favor of amphetamine in 10 of 11 ADHD symptom domains and methylphenidate in 7 of 12 symptom domains. A high degree of heterogeneity across participant treatment response was observed.

Conclusions Meta-analysis of n-of-1 trials suggests that amphetamine and methylphenidate are effective treatments for pediatric ADHD. Synthesizing n-of-1 trials enables assessment of individual responses to treatment as well as aggregate summaries across individuals and studies. It offers a promising general approach with applications across diverse treatments and disorders

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Journal of Clinical Oncology. 2016;34:3417-25.

BEHAVIORAL, SOCIAL, AND EMOTIONAL SYMPTOM COMORBIDITIES AND PROFILES IN ADOLESCENT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY.

Brinkman TM, Li C, Vannatta K, et al.

Purpose: In the general population, psychological symptoms frequently co-occur; however, profiles of symptom comorbidities have not been examined among adolescent survivors of childhood cancer.

Patients and Methods: Parents of 3,893 5-year survivors of childhood cancer who were treated between 1970 and 1999 and who were assessed in adolescence (age 12 to 17 years) completed the Behavior Problems Index. Age- and sex-standardized z scores were calculated for symptom domains by using the Childhood Cancer Survivor Study sibling cohort. Latent profile analysis identified profiles of comorbid symptoms, and multivariable multinomial logistic regression modeling examined associations between cancer treatment exposures and physical late effects and identified symptom profiles. Odds ratios (ORs) and 95% CIs for latent class membership were estimated and analyses were stratified by cranial radiation therapy (CRT; CRT or no CRT).

Results: Four symptoms profiles were identified: no significant symptoms (CRT, 63%; no CRT, 70%); elevated anxiety and/or depression, social withdrawal, and attention problems (internalizing; CRT, 31%; no CRT, 16%); elevated headstrong behavior and attention problems (externalizing; CRT, no observed; no CRT, 9%); and elevated internalizing and externalizing symptoms (global symptoms; CRT, 6%; no CRT, 5%). Treatment with ≥ 30 Gy CRT conferred greater risk of internalizing (OR, 1.7; 95% CI, 1.0 to 2.8) and global symptoms (OR, 3.2; 95% CI, 1.2 to 8.4). Among the no CRT group, corticosteroid treatment was associated with externalizing symptoms (OR, 1.9; 95% CI, 1.2 to 2.8) and ≥ 4.3 g/m(2) intravenous methotrexate exposure was associated with global symptoms (OR, 1.5; 95% CI, 0.9 to 2.4). Treatment late effects, including obesity, cancer-related pain, and sensory impairments, were significantly associated with increased risk of comorbid symptoms.

Conclusion: Behavioral, emotional, and social symptoms frequently co-occur in adolescent survivors of childhood cancer and are associated with treatment exposures and physical late effects. Assessment and consideration of symptom profiles are essential for directing appropriate mental health treatment for adolescent survivors

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J Clin Psychopharmacol. 2016.
ATOMOXETINE SUCCESSFULLY ADDRESSES DOUBLE-SPHINCTERIC INCONTINENCE IN A CHILD WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Naguy A.

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J Dev Behav Pediatr. 2016 Sep;37:541-47.
MANAGEMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER BY DEVELOPMENTAL-BEHAVIORAL PEDIATRICIANS: A DBPNET STUDY.
Harstad E, Blum N, Gahman A, et al.
Objective: To describe practice patterns for developmental-behavioral pediatricians (DBPs) practicing within Developmental-Behavioral Pediatrics Research Network (DBPNet) academic medical centers providing follow-up for children with attention-deficit/hyperactivity disorder (ADHD) and determine how well they adhere to American Academy of Pediatrics ADHD Clinical Practice Guidelines.
Methods: Seventy-eight DBPs at 12 academic medical centers participating in the DBPNet were asked to complete follow-up encounter surveys for patients with ADHD or autism spectrum disorder seen from 12/2011 through 6/2012. Data regarding patient characteristics, comorbid conditions, and medication management were obtained at the time of each visit.
Results: Fifty-seven DBPs completed 301 ADHD follow-up encounter surveys; 75.3% of patients were male with mean age 9.57 years (SD = 3.3). Race/ethnicity was primarily white/non-Hispanic with similar numbers on private insurance (41.5%) versus Medicaid (45.5%). DBPs identified comorbid learning disorders in 27.6% of children =6 years. Only 58.3% of children <6 years received counseling/behavioral therapy or had it recommended during the visit. DBPs primarily (90.6%) prescribed medications FDA-approved for ADHD treatment and growth was monitored for >98% of visits during which stimulants were prescribed. Parent- and teacher-completed rating scales were reviewed/completed during 43.9% and 37.8% of visits, respectively. There were no child or physician factors consistently associated with variation in practice patterns.
Conclusion: Developmental-behavioral pediatricians practicing within DBPNet medical centers adhere to the recommended medication prescribing practices for ADHD, including use of FDA-approved medications and monitoring growth. However, DBPs within DBPNet do not consistently review ADHD rating scales or recommend behavioral counseling for children <6 years of age as recommended

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J Invest Med. 2016;64:266.
PARENTAL PERCEPTIONS ABOUT EXERCISE AND ADHD.
Cohen SC, Taylor S, Rashedi R, et al.
Purpose of Study There is emerging evidence that exercise, including yoga, helps decrease ADHD symptoms in children, but we do not know which types of exercise parents perceive as the most beneficial and if parents are open to having their children participate in yoga. The purpose of this study is to survey parents about their perceptions regarding the effects of exercise on their children's ADHD symptoms, and evaluate parental receptiveness to yoga as a form of exercise for children with ADHD. Through this study we hope to learn which types of exercise children with ADHD are most likely to participate in, and look for trends in the types of exercise that parents perceive as the most beneficial for their children's ADHD symptoms.
Methods Used Parents of children 3-17 years of age with ADHD are being recruited to participate in this study, which involves completing an online survey, via REDCap (Research Electronic Data Capture), consisting of 18 questions with sub-questions to elicit parent responses regarding effects of different types of exercise on their children's ADHD symptoms. Study subjects are recruited from the UC Davis MIND Institute Subject Tracking System (STS) database which has 500 subjects with an ADHD willing to be contacted. Additional subjects are being recruited by fliers in pediatric waiting rooms, as well as online via the CHADD newsletter, UC Davis ADHD Facebook group, and MIND Institute website. The REDCap survey link on emails, fliers and web posts direct participants to the informed consent and survey through REDCap.

Survey data will be analyzed to estimate proportions, such as the proportion of children with ADHD reported to have improved behavioral responses after various types of exercise as well as the proportion of parents willing to consider yoga as an ADHD intervention. With a sample size of 150 to 200, proportions can be estimated with a margin of error of no greater than 0.08 to 0.07, which provides sufficient precision to characterize the responses elicited through the survey.
Summary of Results Preliminary study results will be analyzed and presented at the meeting.
Conclusions Preliminary study conclusions will be presented at the meeting

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J Invest Med. 2016;64:301.

EFFECTS OF RISPERIDONE USE IN PEDIATRIC POPULATION WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD).

Garcia AJ, Kim N, Chang J, et al.

Purpose of Study The use of antipsychotics in pediatric patients with ADHD has been a subject of debate. The objective of this study was to summarize the benefits and side effects of treatment with risperidone in pediatric patients with ADHD.
Methods Used A literature review was conducted utilizing PubMed and Google Scholar databases using the following search terms: ADHD, attention deficit, hyperactivity, children, pediatrics, risperidone, and antipsychotic. Studies that involved patients>18 years of age were excluded from our analysis. Only studies that reported the effectiveness as well as the side effects of risperidone were included in this review.
Summary of Results We found 5 studies that met our inclusion criteria. The studies were all prospective and included mostly school children. The average length of the risperidone treatment was 6 to 8 weeks with the exception of one study which provided 2 years of treatment. All but one study included ADHD patients who had aggressive behaviors or psychosis. The studies were mostly based on parental questionnaires and showed improvement of symptoms during the study period. Majority of studies reported side effects, such as weight gain, daytime drowsiness, and somnolence during treatment with risperidone. The monitoring of the side effects was limited to the duration of the study.
Conclusions The studies showed that risperidone improved the symptoms of ADHD patients with aggression or psychosis on a short-term basis. However, none of the studies conducted long term follow-up. Further studies are needed to evaluate the long-term benefits and side effects, such as adverse effect on the developing brain as well as long term metabolic side effects. (Table presented)

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J Neural Transm. 2016;1-10.

REGULATION OF EMOTION IN ADHD: CAN CHILDREN WITH ADHD OVERRIDE THE NATURAL TENDENCY TO APPROACH POSITIVE AND AVOID NEGATIVE PICTURES?

van Cauwenberge V, Sonuga-Barke EJS, Hoppenbrouwers K, et al.

Studies have demonstrated inefficient use of antecedent-focused emotion regulation strategies in children with ADHD attention-deficit/hyperactivity disorder (ADHD). In the current study we tested for the first time if ADHD is also associated with difficulties in response-focused strategies by measuring the ability to override action tendencies induced by emotional information. Performance data on a computer-based approach-avoidance paradigm of 28 children with ADHD and 38 typically developing children between 8 and 15 years of age were analyzed, by comparing a congruent condition in which they were instructed to approach positive and avoid negative pictures and an incongruent condition where they had to override these automatic reactions and approach negative and avoid positive pictures. Children also rated the valence and salience of the pictures. Children with ADHD and typically developing children rated the emotional valence of the pictures appropriately and similarly, while positive pictures were rated as more arousing by children with ADHD. Solid congruency effects were found indicating that the task measured response-focused emotion regulation; however groups did not differ in this respect. Our findings do not support a deficit in emotion

regulation in ADHD in terms of the ability to override natural tendencies to approach positive and avoid negative pictures

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J Neurodevelopmental Disord. 2015;7.

VISUAL SEARCH FOR FEATURE CONJUNCTIONS: AN FMRI STUDY COMPARING ALCOHOL-RELATED NEURODEVELOPMENTAL DISORDER (ARND) TO ADHD.

O'Conaill CR, Malisza KL, Buss JL, et al.

Background: Alcohol-related neurodevelopmental disorder (ARND) falls under the umbrella of fetal alcohol spectrum disorder (FASD). Diagnosis of ARND is difficult because individuals do not demonstrate the characteristic facial features associated with fetal alcohol syndrome (FAS). While attentional problems in ARND are similar to those found in attention-deficit/hyperactivity disorder (ADHD), the underlying impairment in attention pathways may be different.

Methods: Functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) was conducted at 3 T. Sixty-three children aged 10 to 14 years diagnosed with ARND, ADHD, and typically developing (TD) controls performed a single-feature and a feature-conjunction visual search task.

Results: Dorsal and ventral attention pathways were activated during both attention tasks in all groups. Significantly greater activation was observed in ARND subjects during a single-feature search as compared to TD and ADHD groups, suggesting ARND subjects require greater neural recruitment to perform this simple task. ARND subjects appear unable to effectively use the very efficient automatic perceptual 'pop-out' mechanism employed by TD and ADHD groups during presentation of the disjunction array. By comparison, activation was lower in ARND compared to TD and ADHD subjects during the more difficult conjunction search task as compared to the single-feature search. Analysis of DTI data using tract-based spatial statistics (TBSS) showed areas of significantly lower fractional anisotropy (FA) and higher mean diffusivity (MD) in the right inferior longitudinal fasciculus (ILF) in ARND compared to TD subjects. Damage to the white matter of the ILF may compromise the ventral attention pathway and may require subjects to use the dorsal attention pathway, which is associated with effortful top-down processing, for tasks that should be automatic. Decreased functional activity in the right temporoparietal junction (TPJ) of ARND subjects may be due to a reduction in the white matter tract's ability to efficiently convey information critical to performance of the attention tasks.

Conclusions: Limited activation patterns in ARND suggest problems in information processing along the ventral frontoparietal attention pathway. Poor integrity of the ILF, which connects the functional components of the ventral attention network, in ARND subjects may contribute to the attention deficits characteristic of the disorder

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J Psychopharmacol. 2016;30:976-82.

SARCOSINE TREATMENT FOR OPPOSITIONAL DEFIANT DISORDER SYMPTOMS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER CHILDREN.

Tzang RF, Chang YC, Tsai GE, et al.

Methylphenidate, a stimulant that activates dopaminergic and noradrenergic function, is an important agent in the treatment of attention deficit hyperactivity disorder (ADHD). Sarcosine, a glycine transporter-1 inhibitor, may also play a role in treating ADHD by modulating the glutamatergic neurotransmission system through activating N-methyl-D-aspartate type glutamate receptors. This study aimed to assess the efficacy of sarcosine in treating children with ADHD. We conducted a six-week, randomized, double-blind, placebo-controlled clinical trial. The primary outcome measures were those on the Inattention, Hyperactivity/impulsivity, and oppositional defiant disorder (ODD) subscales of the Swanson, Nolan, and Pelham, version IV scale. Efficacy and safety were measured bi-weekly. A total of 116 children with ADHD were enrolled. Among them, 48 (83%) of the 58 sarcosine recipients and 44 (76%) of the 58 placebo recipients returned for the first post-treatment visit. The missing data values were imputed by the last observation carry forward method. From a multiple linear regression analysis, using the generalized

estimating equation approach, and an intention to treat analysis, the efficacy of sarcosine marginally surpassed that of placebo at weeks 2, 4, and 6, with p-values=0.01, 0.026, and 0.012, respectively, although only for ODD symptoms. Treatment of ADHD by sarcosine (0.03 g/kg/day) was well tolerated. Sarcosine could possibly be a novel agent for managing ODD symptoms in the context of ADHD. However, future larger-scale studies are warranted to optimize its dosage

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J Safety Res. 2016 Sep;58:49-56.

INJURY RISKS IN SCHOOLCHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY OR AUTISM SPECTRUM DISORDER: RESULTS FROM TWO SCHOOL-BASED HEALTH SURVEYS OF 6- TO 17-YEAR-OLD CHILDREN IN SWEDEN.

Bonander C, Beckman L, Janson S, et al.

Introduction: Injuries are one of the leading causes of death and disability among children in Sweden and attention-deficit/hyperactivity disorder (ADHD) has previously been associated with an increased risk of injury in pediatric populations elsewhere in the world. Current evidence regarding the possible link between autism spectrum disorder (ASD) and injury risk appears limited, even though some potentially risk-increasing symptoms overlap. The purpose of this study was thus to study the association between both ADHD and ASD concerning the risk of injury among Swedish schoolchildren.

Methods: Two samples were used: a population-based register study containing data from 18,416 children ranging from the ages of 6-17years collected by school nurses during 2012/2014 (Survey A), and a national cross-sectional study of 3202 ninth-grade children (~15years old) collected from 92 schools in 2011 (Survey B). The data were analyzed using χ(2)-tests and log-binomial generalized linear models to obtain risk ratios (RR), comparing cases reportedly affected by ADHD or ASD to unaffected controls.

Results: After adjusting for confounders, ADHD was associated with a 65% increased risk of injury (RR 1.65 [95% CI: 1.32–2.05] in Survey A, and a 57% increased risk of injury (RR 1.57 [95% CI: 1.27–1.95]) in Survey B. ASD was not significantly associated with any differences in injury risk (RR 0.81 [95% CI: 0.57–1.14]).

Conclusions: The results indicate that there is an elevated injury risk among Swedish schoolchildren with ADHD but not for children with ASD. Future studies should focus on causal mechanisms mediating the association between ADHD and injuries in order to facilitate injury prevention strategies. Practical applications: Parents and teachers of schoolchildren with ADHD should be made aware of the elevated injury risks associated with the diagnosis. Safety experts and injury control professionals should consider the development of specialized prevention strategies in order to reduce these risks

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J Sleep Res. 2016;25:524-33.

CONCORDANCE OF ACTIGRAPHY WITH POLYSOMNOGRAPHY IN CHILDREN WITH AND WITHOUT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Waldon J, Begum E, Gendron M, et al.

This study sought to: (1) compare actigraphy-derived estimated sleep variables to the same variables based on the gold-standard of sleep assessment, polysomnography; (2) examine whether the correlations between the measures differ between children with attention-deficit/hyperactivity disorder and typically developing children; and (3) determine whether these correlations are altered when children with attention-deficit/hyperactivity disorder are treated with medication. Participants (24 attention-deficit/hyperactivity disorder; 24 typically developing), aged 6-12 years, completed a 1-week baseline assessment of typical sleep and daytime functioning. Following the baseline week, participants in the attention-deficit/hyperactivity disorder group completed a 4-week blinded randomized control trial of methylphenidate hydrochloride, including a 2-week placebo and 2-week methylphenidate hydrochloride treatment period. At the end of each observation (typically developing: baseline; attention-deficit/hyperactivity disorder: baseline, placebo and methylphenidate hydrochloride treatment), all participants were invited to a sleep research laboratory, where overnight polysomnography and actigraphy were recorded concurrently. Findings from intra-class correlations and Bland-Altman plots were consistent. Actigraphy was found to provide good estimates (e.g. intra-class correlations >0.61) of polysomnography results for sleep duration for all groups and conditions,

as well as for sleep-onset latency and sleep efficiency for the typically developing group and attention-deficit/hyperactivity disorder group while on medication, but not for the attention-deficit/hyperactivity disorder group during baseline or placebo. Based on the Bland-Altman plots, actigraphy tended to underestimate for sleep duration (8.6-18.5 min), sleep efficiency (5.6-9.3%) and sleep-onset latency, except for attention-deficit/hyperactivity disorder during placebo in which actigraphy overestimated (-2.1 to 6.3 min). The results of the current study highlight the importance of utilizing a multimodal approach to sleep assessment in children with attention-deficit/hyperactivity disorder

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J Am Acad Child Adolesc Psychiatry. 2016 Oct;55:886-95.

RELATIVE IMMATURITY IN CHILDHOOD AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS FROM CHILDHOOD TO EARLY ADULTHOOD: EXPLORING GENETIC AND ENVIRONMENTAL OVERLAP ACROSS DEVELOPMENT.

Brikell I, Kuja-Halkola R, Larsson JO, et al.

Objective: Attention-deficit/hyperactivity disorder (ADHD) has been linked to immaturity relative to peers in childhood, yet it is unclear how such immaturity is associated with ADHD across development. This longitudinal twin study examined the genetic and environmental contributions to the association between parents' perception of their child's immaturity relative to peers (RI) in childhood and ADHD symptoms across development.

Method: 1,302 twin pairs from the Swedish Twin Study of Child and Adolescent Development were followed prospectively from childhood to early adulthood. Parent ratings of RI were collected at 8 to 9 years and parent and self-ratings of ADHD symptoms were collected at 8 to 9, 13 to 14, 16 to 17, and 19 to 20 years using the Child Behavior Checklist Attention Problems scale. In addition, ADHD symptoms corresponding to DSM criteria were used for sensitivity analysis. Analyses were conducted using longitudinal structural equation modeling with multiple raters.

Results: RI-related etiologic factors, predominantly influenced by genes, explained 10-14% of the variance in ADHD symptoms from 8 to 9 up to 16 to 17 years. The influence of these RI-related factors on ADHD symptoms attenuated to 4% by 19 to 20 years of age. The remaining variance in ADHD symptoms was primarily explained by genetic factors independent of RI, which remained relatively stable across development, explaining 19% to 30% of the variance in ADHD symptoms from 13 to 14 up to 19 to 20 years.

Conclusion: The results show that RI is significantly associated with ADHD symptoms, particularly during childhood and adolescence, and that the association is primarily explained by a shared genetic liability. Nevertheless, the magnitude of associations across development was modest, highlighting that RI is merely one aspect contributing to the complex etiology of ADHD symptoms

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J Am Acad Child Adolesc Psychiatry. 2016 Oct;55:896-905.

A GENOME-WIDE ASSOCIATION META-ANALYSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS IN POPULATION-BASED PEDIATRIC COHORTS.

Middeldorp CM, Hammerschlag AR, Ouwens KG, et al.

Objective: The aims of this study were to elucidate the influence of common genetic variants on childhood attention-deficit/hyperactivity disorder (ADHD) symptoms, to identify genetic variants that explain its high heritability, and to investigate the genetic overlap of ADHD symptom scores with ADHD diagnosis.

Method: Within the EArly Genetics and Lifecourse Epidemiology (EAGLE) consortium, genome-wide single nucleotide polymorphisms (SNPs) and ADHD symptom scores were available for 17,666 children (< 13 years of age) from nine population-based cohorts. SNP-based heritability was estimated in data from the three largest cohorts. Meta-analysis based on genome-wide association (GWA) analyses with SNPs was followed by gene-based association tests, and the overlap in results with a meta-analysis in the Psychiatric Genomics Consortium (PGC) case-control ADHD study was investigated.

Results: SNP-based heritability ranged from 5% to 34%, indicating that variation in common genetic variants influences ADHD symptom scores. The meta-analysis did not detect genome-wide significant SNPs, but three genes, lying close to each other with SNPs in high linkage disequilibrium (LD), showed a gene-wide

significant association (p values between 1.46 × 10-6 and 2.66 × 10-6). One gene, WASL, is involved in neuronal development. Both SNP- and gene-based analyses indicated overlap with the PGC meta-analysis results with the genetic correlation estimated at 0.96.
Conclusion: The SNP-based heritability for ADHD symptom scores indicates a polygenic architecture, and genes involved in neurite outgrowth are possibly involved. Continuous and dichotomous measures of ADHD appear to assess a genetically common phenotype. A next step is to combine data from population-based and case-control cohorts in genetic association studies to increase sample size and to improve statistical power for identifying genetic variants

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J Am Acad Child Adolesc Psychiatry. 2016 Oct;55:839-40.
THE GENETICS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: FAILURE OR LEARNING PROCESS?
Cortese S.
Currently, genetics research findings do not have any direct application for the care of individual patients with ADHD, and the use of tests to inform about genetic risk would indeed pose important ethical problems. Rather, the hope is that uncovering the genetics architecture of ADHD will pave the way for innovative etiologically based treatments, in keeping with the move toward 'personalized medicine' that has already changed the practice in other disciplines of medicine. We need to move on to discovering additional relevant genes, elucidating how they interact with each other, and understanding the interplay between environmental factors and genes. Disentangling such interactions will likely contribute to addressing the missing heritability problem. Then, we need to understand how gene variants contribute to ADHD pathophysiology. Novel approaches such as pathway and network analyses will be instrumental for this. There is a long way to go. We have just begun.

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J Am Acad Child Adolesc Psychiatry. 2016 Oct;55:877-85.
AGE AND DRD4 GENOTYPE MODERATE ASSOCIATIONS BETWEEN STIMULANT TREATMENT HISTORY AND CORTEX STRUCTURE IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Schweren LJS, Hartman CA, Heslenfeld DJ, et al.
Objective: Attention-deficit/hyperactivity disorder (ADHD) has been associated with dopaminergic imbalance and subtle volume decreases in the brain. Stimulants acutely enhance dopaminergic neurotransmission. Long-term effects of prolonged manipulation of the dopaminergic system on brain structure remain poorly understood; they could be beneficial or unfavorable and could be moderated by common genetic variants and/or age.
Method: In a large observational ADHD cohort study (N = 316), the effects of cumulative stimulant treatment, genotype (for DAT1 haplotype and DRD4 variants), and treatment-by-genotype interactions on striatal, frontal, and hippocampal volumes and their interactions with age were evaluated.
Results: No main effects of treatment were found. Associations between treatment and bilateral frontal and left hippocampal volume depended on DRD4 genotype and age. At a younger age and lower treatment levels, but not at a younger age and higher treatment levels, carriers of the DRD4 7R allele showed decreased frontal cortex volumes. At an older age, carriers and non-carriers showed smaller frontal volumes irrespective of treatment history. Left hippocampal volume was similar to that in controls at average treatment levels and increased with treatment only in carriers of the DRD4 risk allele and at a younger age. No interaction effects were found in the striatum.
Conclusion: Carriers of the DRD4 risk allele at a younger age might be sensitive to cortical remodeling after stimulant treatment. The cross-sectional nature of this study warrants cautious interpretation of age effects. The present findings, although of small effect size, might ultimately contribute to optimal care for individuals with ADHD

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J Am Acad Child Adolesc Psychiatry. 2016 Oct;55:868-76.

ATOMOXETINE AND PARENT TRAINING FOR CHILDREN WITH AUTISM AND ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: A 24-WEEK EXTENSION STUDY.

Smith T, Aman MG, Arnold LE, et al.

Objective: The authors previously reported on a 2-by-2 randomized clinical trial of individual and combined treatment with atomoxetine (ATX) and parent training (PT) for attention-deficit/hyperactivity disorder (ADHD) symptoms and behavioral noncompliance in 128 5- to 14-year-old children with autism spectrum disorder. In the present report, they describe a 24-week extension of treatment responders and nonresponders.

Method: One-hundred seventeen participants from the acute trial (91%) entered the extension; 84 of these were in 2 subgroups: 'treatment responders' (n = 43) from all 4 groups in the acute trial, seen monthly for 24 weeks, and 'placebo nonresponders' (n = 41), treated with open-label ATX for 10 weeks. Participants originally assigned to PT continued PT during the extension; the remainder served as controls. Primary outcome measurements were the parent-rated Swanson, Nolan and Pelham ADHD scale and the Home Situations Questionnaire.

Results: Sixty percent (26 of 43) of treatment responders in the acute trial, including 68% of responders originally assigned to ATX, still met the response criteria at the end of the extension. The response rate of placebo nonresponders treated with 10-week open-label ATX was 37% (15 of 41), similar to the acute trial. Children receiving open-label ATX + PT were significantly more likely to be ADHD responders (53% versus 23%) and noncompliance responders (58% versus 14%) than those receiving open-label ATX alone.

Conclusion: Most ATX responders maintained their responses during the extension. PT combined with ATX in the open-label trial appeared to improve ADHD and noncompliance outcomes more than ATX alone

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J Am Acad Child Adolesc Psychiatry. 2016;55:800-08.

REDUCED DEFAULT MODE CONNECTIVITY IN ADOLESCENTS WITH CONDUCT DISORDER.

Broulidakis MJ, Fairchild G, Sully K, et al.

Objective Conduct disorder (CD) is characterized by impulsive, aggressive, and antisocial behaviors that might be related to deficits in empathy and moral reasoning. The brain's default mode network (DMN) has been implicated in self-referential cognitive processes of this kind.

Method This study examined connectivity between key nodes of the DMN in 29 adolescent boys with CD and 29 age- and sex-matched typically developing adolescent boys. The authors ensured that group differences in DMN connectivity were not explained by comorbidity with other disorders by systematically controlling for the effects of substance use disorders (SUDs), attention-deficit/hyperactivity disorder (ADHD) symptoms, psychopathic traits, and other common mental health problems.

Results Only after adjusting for co-occurring ADHD symptoms, the group with CD showed hypoconnectivity between core DMN regions compared with typically developing controls. ADHD symptoms were associated with DMN hyperconnectivity. There was no effect of psychopathic traits on DMN connectivity in the group with CD, and the key results were unchanged when controlling for SUDs and other common mental health problems.

Conclusion Future research should directly investigate the possibility that the aberrant DMN connectivity observed in the present study contributes to CD-related deficits in empathy and moral reasoning and examine self-referential cognitive processes in CD more generally

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J Am Acad Child Adolesc Psychiatry. 2016;55:469-78.

SEVERELY AGGRESSIVE CHILDREN RECEIVING STIMULANT MEDICATION VERSUS STIMULANT AND RISPERIDONE: 12-MONTH FOLLOW-UP OF THE TOSCA TRIAL.

Gadow KD, Brown NV, Arnold LE, et al.

Objective The objective of this study was to evaluate 52-week clinical outcomes of children with co-occurring attention-deficit/hyperactivity disorder (ADHD), disruptive behavior disorder, and serious physical aggression who participated in a prospective, longitudinal study that began with a controlled, 9-week clinical trial

comparing the relative efficacy of parent training + stimulant medication + placebo (Basic; n = 84) versus parent training + stimulant + risperidone (Augmented; n = 84).
Method Almost two-thirds (n = 108; 64%) of families in the 9-week study participated in week 52 follow-ups (Basic, n = 55; Augmented, n = 53) and were representative of the initial study sample. The assessment battery included caregiver and clinician ratings and laboratory tests.
Results Only 43% of participants in the Augmented group and 36% in the Basic group still adhered to their assigned regimen (not significant [NS]); 23% of those in the Augmented group and 11% in the Basic group were taking no medication (NS). Both randomized groups improved baseline to follow-up, but the 3 primary parent-reported behavioral outcomes showed no significant between-group differences. Exploratory analyses indicated that participants in the Augmented group (65%) were more likely (p = .02) to have a Clinical Global Impressions (CGI) severity score of 1 to 3 (i.e., normal to mildly ill) at follow-up than those in the Basic group (42%). Parents rated 45% of children as impaired often or very often from ADHD, noncompliant, or aggressive behavior. The Augmented group had elevated prolactin levels, and the Basic group had decreased weight over time. Findings were generally similar whether groups were defined by randomized assignment or follow-up treatment status.
Conclusion Both treatment strategies were associated with clinical improvement at follow-up, and primary behavioral outcomes did not differ significantly. Many children evidenced lingering mental health concerns, suggesting the need for additional research into more effective interventions.
Clinical trial registration information–Treatment of Severe Childhood Aggression (the TOSCA Study); http://clinicaltrials.gov/; NCT00796302

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J Am Acad Child Adolesc Psychiatry. 2016.
FUNCTIONAL ADULT OUTCOMES 16 YEARS AFTER CHILDHOOD DIAGNOSIS OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: MTA RESULTS.
Hechtman L, Swanson JM, Sibley MH, et al.
Objective: To compare educational, occupational, legal, emotional, substance use disorder, and sexual behavior outcomes in young adults with persistent and desistent attention-deficit/hyperactivity disorder (ADHD) symptoms and a local normative comparison group (LNCG) in the Multimodal Treatment Study of Children with ADHD (MTA).
Method: Data were collected 12, 14, and 16 years postbaseline (mean age 24.7 years at 16 years postbaseline) from 476 participants with ADHD diagnosed at age 7 to 9 years, and 241 age- and sex-matched classmates. Probands were subgrouped on persistence versus desistence of . DSM-5 symptom count. Orthogonal comparisons contrasted ADHD versus LNCG and symptom-persistent (50%) versus symptom-desistent (50%) subgroups. Functional outcomes were measured with standardized and demographic instruments.
Results: Three patterns of functional outcomes emerged. Post-secondary education, times fired/quit a job, current income, receiving public assistance, and risky sexual behavior showed the most common pattern: the LNCG group fared best, symptom-persistent ADHD group worst, and symptom-desistent ADHD group between, with the largest effect sizes between LNCG and symptom-persistent ADHD. In the second pattern, seen with emotional outcomes (emotional lability, neuroticism, anxiety disorder, mood disorder) and substance use outcomes, the LNCG and symptom-desistent ADHD group did not differ, but both fared better than the symptom-persistent ADHD group. In the third pattern, noted with jail time (rare), alcohol use disorder (common), and number of jobs held, group differences were not significant. The ADHD group had 10 deaths compared to one death in the LNCG.
Conclusion: Adult functioning after childhood ADHD varies by domain and is generally worse when ADHD symptoms persist. It is important to identify factors and interventions that promote better functional outcomes

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Korean J Pediatr. 2016;59:414-20.

BEHAVIORAL AND INTELLIGENCE OUTCOME IN 8- TO 16-YEAR-OLD BORN SMALL FOR GESTATIONAL AGE.

Yi KH, Yi YY, Hwang IT.

Purpose: We investigated behavioral problems, attention problems, and cognitive function in children and adolescents born small for gestational age (SGA).

Methods: Forty-six SGA children born at term and 46 appropriate for gestational age (AGA) children born at term were compared. Psychiatric symptoms were examined with reference to the Korean-Child Behavior Checklist, Korean-Youth Self Report, and Attention Deficit Hyperactivity Disorder Rating Scale (ADHD-RS). Cognitive function was estimated using the Wechsler Intelligence Scale. Sociodemographic data were recorded from interviews.

Results: SGA children had high scores on delinquent behavior, aggressive behavior, and the externalizing scale, and they also showed a propensity for anxiety and depression. The SGA group had a higher mean ADHD-RS score than the AGA group (10.52±8.10 vs.9.93±7.23), but the difference was not significant. The SGA group had a significantly lower verbal intelligence quotient (IQ) than the AGA group, but the mean scores of both groups were within normal limits.

Conclusion: This study indicates marked behavioral problems, such as delinquency, aggressiveness, and anxiety and depression, as well as low verbal IQ in the SGA group than in the AGA group. Even in cases in which these symptoms are not severe, early detection and proper treatment can help these children adapt to society

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Medicine (United Kingdom). 2016;44:683-86.

ADHD ACROSS THE LIFESPAN.

Asherson P.

Attention-deficit hyperactivity disorder (ADHD) is a common mental disorder with neurodevelopmental origins that typically starts in early childhood and follows a persistent trait-like course. It is characterized by inattention, impulsivity and hyperactivity that are persistent over time and lead to clinical and psychosocial impairments. Emotional instability is a common feature of ADHD that is sometimes the main presenting complaint. Neurodevelopmental and psychiatric co-morbidities are common. ADHD can be diagnosed and treated at all ages and persists into adulthood in around two-thirds of individuals. Many adults with ADHD were not diagnosed as children. In children with moderate impairment, psychological approaches, including parent training and cognitive behavioural therapy, are recommended as first-line treatment. Drug treatment should, however, be offered as a first line to children with ADHD with severe impairment, if psychological interventions have not been effective or if patients prefer medication. In adults, drug treatments are the recommended first-line treatments, with psycho-education and cognitive behavioural therapy as complementary approaches. Drug treatments are similar at all ages. Methylphenidate is the recommended first-line drug, followed by atomoxetine or dexamfetamine/lisdexamfetamine. Atomoxetine may be used as first line when there are concerns with potential drug abuse or diversion, or high levels of co-morbid anxiety

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Medicine. 2016;95.

LONGITUDINAL ASSOCIATION BETWEEN EARLY ATOPIC DERMATITIS AND SUBSEQUENT ATTENTION-DEFICIT OR AUTISTIC DISORDER A POPULATION-BASED CASE-CONTROL STUDY.

Lee CY, Chen MH, Jeng MJ, et al.

Atopic dermatitis (AD) is one of the common allergic diseases in children. The presence of allergic diseases was found to have association with the risk of developing attention-deficit hyperactivity disorder (ADHD) or autistic spectrum disorder (ASD) in children, but it is still inconclusive. This study was to investigate the longitudinal relationship between AD developed during toddlerhood and subsequent development of ADHD or ASD in later childhood. Toddlers born between 1998 and 2008 and diagnosed with AD at the age younger than 3 years and older than 1 month were retrieved from Taiwan's National Health Insurance Research Database. Ageand gender-matched toddlers with no lifetime AD were enrolled as the control group. All

enrolled toddlers were followed until 2011 to identify the development of ADHD or ASD. Multivariate Cox regression analysis was performed to analyze the hazard ratios (HRs). The risks associated with allergic comorbidities were analyzed. A total of 18,473 toddlers were enrolled into the AD group. The presence of AD significantly increased the risk of developing ADHD (HR=2.92, 95% confidence interval [CI]=2.48-3.45) or ASD (HR=8.90, 95% CI=4.98-15.92) when aged 3 years or older. Children from the AD group with 3 comorbidities together, namely, allergic rhinitis, allergic conjunctivitis, and asthma, had the greatest risk of developing ADHD and ASD (ADHD: HR=4.67, 95% CI= 3.81-5.43; ASD: HR=16.65, 95% CI=8.63-30.60). In conclusion, toddlers who suffer from AD at the age younger than 3 years are at a higher risk of developing ADHD and ASD during later childhood. Pediatricians taking care of toddlers with AD should have knowledge of this increased risk of developing ADHD and ASD later in life, especially when children have certain comorbidities such as allergic rhinitis, allergic conjunctivitis, and asthma

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Mental Health and Physical Activity. 2016;11:46-52.

DROPOUT FROM PHYSICAL ACTIVITY INTERVENTIONS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Vancampfort D, Firth J, Schuch FB, et al.

Physical activity (PA) interventions have shown promising in improving core symptoms of children and adolescents with ADHD, yet treatment dropout may pose a challenge to routine implementation in clinical practice. We conducted a meta-analysis to investigate the prevalence and predictors of treatment dropout from PA interventions in children and adolescents with ADHD. Electronic databases were searched from inception until 06/2016. Randomized control trials of PA interventions in children and adolescents with ADHD reporting dropout rates were included. A random effects meta-analysis and meta-regression analyses were performed. In 8 studies involving 9 PA intervention arms, 148 children or adolescents assigned to a PA intervention (mean age range = 8.2–15.8 years, 87.8% male) were included. The trim and fill adjusted treatment dropout rate was 17.5% (95%CI = 9.8%–29.4%). The prevalence of dropouts in exercisers was not significantly different from the dropouts in control conditions (odds ratio, OR = 1.12; 95%CI = 0.48–2.65; I2 = 0). Lower dropout was observed in sports interventions compared with structured aerobic exercise or yoga (p = 0.049). A higher proportion of male participants (β = 0.05; 95%CI = 0.001 to 0.10; p = 0.045, R2 = 1.0) appeared to moderate higher dropout rates from PA interventions. Our findings suggest that in order to maximize PA participation, and therefore health benefits, sports-related interventions should be offered in the multidisciplinary treatment of children and adolescents with ADHD. Our data also suggest that males with ADHD may be more likely to dropout. Dropout rates are comparable to control conditions, suggesting that PA interventions are feasible in adolescents with ADHD

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Mol Neurobiol. 2016;1-15.

AN EVALUATION ON THE EFFICACY AND SAFETY OF TREATMENTS FOR ATTENTION DEFICIT HYPERACTIVITY DISORDER IN CHILDREN AND ADOLESCENTS: A COMPARISON OF MULTIPLE TREATMENTS.

Li Y, Gao J, He S, et al.

Attention deficit hyperactivity disorder (ADHD) is one of the most common neurobehavioral disorders. We carried out this comparison of multiple treatments based on sufficient data in attempt to evaluate the efficacy and safety of ADHD medication for children and adolescents. PubMed, Embase and the Cochrane Database were used to search for relevant articles. Changes in the ADHD Rating Scale (ADHD-RS) scores and the ConnersΙ¯ÇÖ Parent Rating Scale-Revised (CPRS) scores were used as outcomes for efficacy. Withdrawals due to all-cause, adverse effects and lack of efficacy were defined as primary outcomes evaluating the safety of such medications. Both pair-wise and network meta-analyses were performed. Efficacy and safety of atomoxetine (ATX), bupropion (BUP), clonidine hydrochloride (CLON), guanfacine extended release (GXR), lisdexamfetamine dimesylate (LDX), and methylphenidate (MPH) were evaluated. LDX has the highest efficacy and a relatively lower rate of adverse effects compared to BUP, CLON and GXR. MPH has the lowest incidence rate of adverse effects and takes second place concerning ADHD-RS scores and third place

concerning CPRS scores. ATX has the lowest incidence rate of all-cause withdrawals. The efficacy of ATX seems, however, to be lower than CLON, GXR, LDX and MPH. Adversely, BUP has the highest incidence rate of withdrawals and the second highest probability of causing adverse effects as well as lack of efficacy; therefore it should not be recommended as a treatment for ADHD

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Mol Psychiatry. 2016;21:1434-40.

LINKAGE AND ASSOCIATION ANALYSIS OF ADHD ENDOPHENOTYPES IN EXTENDED AND MULTIGENERATIONAL PEDIGREES FROM A GENETIC ISOLATE.

Mastronardi CA, Pillai E, Pineda DA, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a heritable, chronic, neurodevelopmental disorder with serious long-term repercussions. Despite being one of the most common cognitive disorders, the clinical diagnosis of ADHD is based on subjective assessments of perceived behaviors. Endophenotypes (neurobiological markers that cosegregate and are associated with an illness) are thought to provide a more powerful and objective framework for revealing the underlying neurobiology than syndromic psychiatric classification. Here, we present the results of applying genetic linkage and association analyses to neuropsychological endophenotypes using microsatellite and single nucleotide polymorphisms. We found several new genetic regions linked and/or associated with these endophenotypes, and others previously associated to ADHD, for example, loci harbored in the LPHN3, FGF1, POLR2A, CHRNA4 and ANKFY1 genes. These findings, when compared with those linked and/or associated to ADHD, suggest that these endophenotypes lie on shared pathways. The genetic information provided by this study offers a novel and complementary method of assessing the genetic causes underpinning the susceptibility to behavioral conditions and may offer new insights on the neurobiology of the disorder

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Neuroimaging Clinics of North America. 2016;26:317-29.

THE ROLE OF THE PEDIATRIC CEREBELLUM IN MOTOR FUNCTIONS, COGNITION, AND BEHAVIOR: A CLINICAL PERSPECTIVE.

Salman MS, Tsai P.

This article discusses the contribution of the pediatric cerebellum to locomotion, ocular motor control, speech articulation, cognitive function, and behavior modulation. Hypotheses on cerebellar function are discussed. Clinical features in patients with cerebellar disorders are outlined. Cerebellar abnormalities in cognitive and behavioral disorders are detailed

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Neuropsychiatr Dis Treat. 2016;12:2635-47.

CHANGES IN BEHAVIOR AS SIDE EFFECTS IN METHYLPHENIDATE TREATMENT: REVIEW OF THE LITERATURE.

Konrad-Bindl DS, Gresser U, Richartz BM.

Background: Our review of the scientific literature focused on an analysis of studies describing instances of methylphenidate treatment leading (or not) to behavioral changes in the pediatric, adolescent, and adult populations.

Materials and methods: We conducted a literature search in PubMed, Medline, and Google using the keywords "methylphenidate", "behavioral changes", "adverse effects", and "side effects". A total of 44 studies were identified as reporting on the effects and adverse effects of methylphenidate administration, and were included in the analysis.

Results: Five studies specifically set out to study, record, and discuss changes in behavior. Eight studies did not set out to study behavioral effects, but record and discuss them. A total of 28 studies recorded behavioral effects, but failed to discuss these further. Three studies did not include behavioral effects.

Conclusion: This review records what data have been published in respect of changes in behavior in association with the use of methylphenidate. While there is some evidence to suggest that methylphenidate

causes changes in behavior, the majority of the studies reviewed paid little or no attention to this issue. Based on the available data, it is impossible to determine the point at which such behavioral effects occur. The frequency of occurrence of behavioral effects is also impossible to determine with certainty. Based on the available data, it is not possible to rule out whether behavioral effects may persist or not persist once treatment is discontinued. In conclusion, despite countless publications and extensive administration, especially to children, we have insufficient data to judge the long-term effects and risks of methylphenidate taking

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Neuropsychiatr Dis Treat. 2016;12:2521-26.

SCREENING FOR ATTENTION DEFICIT AND HYPERACTIVITY DISORDER, AUTISM SPECTRUM DISORDER, AND DEVELOPMENTAL DELAY IN TAIWANESE ABORIGINAL PRESCHOOL CHILDREN.

Chan HL, Liu WS, Hsieh YH, et al.

Objectives: This study aimed to estimate the percentages of attention deficit and hyperactivity disorder (ADHD) and autism spectrum disorder (ASD) in Taiwanese aboriginal preschool children. Child development level was compared between the two groups.

Methods: Teachers completed screening questionnaires for ADHD, ASD, and development level for 36- to 72-month-old children in kindergartens in Taiwan. The questionnaire results were compared between the aboriginal and nonaboriginal children. One child psychiatrist then interviewed the aboriginal preschool children to determine if they had ADHD and/or ASD.

Results: We collected 93 questionnaires from the aboriginal group and 60 from the nonaboriginal group. In the aboriginal group, 5.37% of the children were identified to have ADHD, while 1.08% were identified to have ASD. Significantly fewer aboriginal children had developmental delays for situation comprehension and personal-social development (P=0.012 and 0.002, respectively) than nonaboriginal children.

Conclusion: Aboriginal children in Taiwan had typical percentages of ADHD and ASD compared to those published in the literature. Aboriginal children showed relative strengths in situation comprehension and personal-social skills. Further studies are required to understand the learning styles of the aboriginal children and to develop effective screening and intervention strategies for ADHD and ASD

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Nord J Psychiatry. 2016;70:582-90.

PARENT-REPORTED SYMPTOMS, IMPAIRMENT, HELPFULNESS OF TREATMENT, AND UNMET SERVICE NEEDS IN A FOLLOW-UP OF OUTPATIENT CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Sollie H, Larsson B.

Background: Limited information exists regarding the associations between impairment, symptoms, helpfulness of treatments, and service needs after initial treatment of children with attention-deficit/hyperactivity disorder (ADHD).

Aims: The aims of this study were to examine persistence rates and associations between parent-reported symptoms, impairment, helpfulness of treatments, and service needs in a retrospective follow-up study of children with ADHD. Methods: Parents of 214 children with a mean age of 12.6 years (SD = 2.1) who were diagnosed with ADHD at five child and adolescent mental health clinics (CAMHS) completed questionnaires 1-10 years (mean = 3.7 years, SD = 2.2) after baseline assessment. The response rate was 43.4%. A community comparison group (n = 110) was recruited from the same area.

Results: Approximately two-thirds (60.3%) of the sample fulfilled the DSM-IV symptom criteria of ADHD at follow-up, 84.3% were functionally impaired, and most children (84.7%) were on medication. Inattentive and emotional symptoms were the strongest predictors of impairment across impairment areas. Perceived helpfulness of different treatments varied from 71.8-88.7%, and no significant difference was found between the ADHD sub-groups regarding reported helpfulness. 'Adjustment of the school situation' was the most frequent service need, and approximately half of the parents reported needs for care co-ordination. Children fulfilling the symptom criteria of the ADHD Combined sub-group were most impaired and had most service needs.

Conclusions: At follow-up, children were highly symptomatic and impaired, despite a high rate of persistent medication treatment. The findings underline the need for more tailored treatment and co-ordinated care over time

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Otolaryngology - Head and Neck Surgery (United States). 2016;155:256-57.
IMPACT OF ADENOTONSILLECTOMY ON CO-MORBID PEDIATRIC ADHD AND OSA.
Huon LK, Liu SYC, Wang PC.
Objectives: The purpose of this study is to determine the impact of adenotonsillectomy on patients with obstructive sleep apnea (OSA) and attention-deficit/hyperactivity disorder (ADHD), by comparing the changes in ADHD prescription between patients who did and did not undergo surgery.
Methods: A retrospective cross-sectional study was performed using Taiwan's National Health Insurance database (January to December 2012), where a group of OSA with ADHD subjects who underwent adenotonsillectomy (n = 325) was identified, along with a group of age- and gender-matched nonoperative subjects (n = 325). The outcome studied was changes in total prescription of methylphenidate (MPH) and atomoxetine (ATX) between the 2 groups as they were followed until the end of December 2013.
Results: The OSA/ADHD subjects who underwent adenotonsillectomy showed a significant decrease in person-days MPH and ATX prescriptions after adenotonsillectomy when compared with the nonoperative group (P < .01).
Conclusions: Our findings support a potential positive impact of adenotonsillectomy in decreasing stimulant prescriptions for ADHD patients with OSA. Co-morbid OSA and ADHD may be addressed by psychiatrists and otolaryngologists via a multidisciplinary approach

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Paediatr Child Health. 2016;26:464-67.
PRACTICAL GUIDE TO THE MANAGEMENT OF ADHD.
Fischer B, Herberholz N.

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Pediatr Ann. 2016;45:e367-e372.
SKILLS VERSUS PILLS: PSYCHOSOCIAL TREATMENTS FOR ADHD IN CHILDHOOD AND ADOLESCENCE.
Schoenfelder EN, Sasser T.
Although side effects and family concerns are common and long-term medication adherence is low, stimulant medications are a front-line treatment for attention-deficit/hyperactivity disorder (ADHD). Psychosocial treatments include classroom, family, and child-focused interventions that teach caregivers and teachers how to implement contingencies to shape behavior and provide children with skills to compensate for ADHD deficits. Such programs have a growing evidence-base and can be implemented alone or in conjunction with pharmacological treatments. The most efficacious psychosocial treatments for children with ADHD include Behavioral Parent Training, Behavioral Classroom Management, and Behavioral Peer Interventions, which all focus on contingency management by adults. Training interventions are increasingly used to teach organizational and interpersonal skills to children and adolescents. These treatments are found to improve functional outcomes associated with ADHD, including on-task behavior, compliance, academic performance, social relationships, and family functioning. Clinicians play an important role in educating families about psychosocial treatments for ADHD, increasing family motivation and engagement, and including these interventions in multimodal treatment plans for youth with ADHD across development

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Pediatr Nephrol. 2016;31:1786.

ATOMOXETINE AMELIORATES NOCTURNAL ENURESIS WITH SUBCLINICAL ADHD.

Ohtomo Y, Hara T, Endo A, et al.

a. Objectives Comorbid ADHD (attention-deficit/hyperactivity disorder) has been regarded important in refractory cases of NE (nocturnal enuresis). (Vande Walle J, Rittig S, Bauer S, Eggert P, Marschall-Kehrel D, Tekgul S (2012). Practical consensus guidelines for the management of enuresis. Eur J Pediatr 171(6):971-983.) b. Methods We treated 265 new patients with nocturnal enuresis at Juntendo University Nerima Hospital & Musashi-murayama Hospital (Tokyo, Japan) since May 2013 to October 2014, with ages of 6 - 14 (198 cases with MNE and 67 cases with NMNE). With the routine intervies and physical examinations at the patients' first visits, we had excluded the possibility of comobid ADHD and its related disorders. Patients with MNE were treated with or desmopressin and/or alarm and those with NMNE were treated with anti-cholinergics and/or alarm. At 12-weeks after the treatments, 52 with MNE and 13 with NMNE were classified as PR or NR. These 65 patients were reassessed whether they had cormobid ADHD, and 24 patients (15 with MNE and 9 with NMNE)met the diagnostic criteria. They were treated with atomoxetine (ATX) (1.8mg/kg/day) in addition to ongoing therapy for enuresis. c. Results After 8-weeks ATX therapy, the average wet nights per months were significantly decreased: 17.1 to 2.7 in MNE (P=0.0007) and 23.2 to 11.4 in NMNE (p=0.0117). Overall, ATX treatment was beneficial in 20 of 24 cases. d. Conclusions Our clinical experience support the use of atomoxetine may be one of the options for refractory NE with comorbid ADHD

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Pediatr Nephrol. 2016;31:1979.

CORRELATION BETWEEN ADHD AND GIGGLE INCONTINENCE.

Yousefichaijan P, Khosrobeigi A.

a. Objectives Attention Deficit Hyperactivity Disorder (ADHD) is the most common childhood neurological disorder which is more prevalent in some chronic diseases. The aim of this study was to investigate ADHD in girls with Giggle incontinence and compare it with healthy children.

b. Methods 150, 5-16-year-old girls with Giggle incontinence and 150 healthy girls without Giggle incontinence were included in this case - control study as case and control groups, respectively. Subjects were selected from girls who were referred to the pediatric clinic of Amirkabir Hospital of Arak, Iran. In the formof simple probability and based on inclusion and exclusion criteria. ADHD was diagnosed by Conner's Parent Rating Scale - 48 (CPRS-48) and DSM-IV criteria and was confirmed by psychologist consult.

c. Results Data were analyzed by Binomial test in SPSS18. ADHD inattentive type was observed in 34 cases with giggle incontinence and 3 controls (P=0.004). Moreover, in the case and control groups, 39 and 7 children were affected by ADHD hyperactive-impulsive type (p = 0.017), and 41 and 9 girls were affected by ADHD mixed type (p = 0.014), respectively. There were differences between prevalence of ADHD in the children with Giggle incontinence and the control group.

d. Conclusions However, due to the importance of relationships between different types of psychiatric disorders such as ADHD and Giggle incontinence and lack of enough evidence concerning the relationship between these two disorders, conducting further studies in this field is recommended

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Pediatr Pulmonol. 2016;51:464.

THE EFFECT OF COMORBID CYSTIC FIBROSIS AND ATTENTION DEFICIT/HYPERACTIVITY DISORDERS ON HOSPITALIZATIONS: A RETROSPECTIVE REVIEW.

Legare T, Spitzer NA, Livingston F.

Introduction: Cystic fibrosis (CF) is a common life-shortening autosomal recessive disorder that requires complex treatment. Treatment adherence is an important factor in determining the outcome of treatment and complications. Attention deficit/hyperactivity disorder (ADHD) is the most common pediatric psychiatric diagnosis that presents with inattention, hyperactivity, and concentration difficulties. There is a paucity of research on the effects of comorbid CF and ADHD diagnoses. It has been shown that the prevalence of

ADHD in the CF population mirrors that of the general population, but the effects of ADHD on CF treatment and outcomes has not been thoroughly investigated.
Methods: A retrospective chart review with two cohorts, comorbid ADHD/CF and CF-only patients were identified using ICD9 codes. Each patient that was identified to have ADHD/CF was age- and sex-matched to a CF-only patient based on their most recent pulmonary office visit. Each chart was then reviewed for forced expiratory volume in one second percent predicted (FEV-1%ile), body mass index (BMI) percentile, and hospitalizations for one year prior to the last pulmonary visit.
Results: A total of 46 patients were identified and were included for analysis in the ADHD/CF cohort. The primary outcome of mean total hospital admissions between the ADHD/CF cohort and the CF-only cohort were different, but not statistically significant (2.22 vs 1.834, p=.467). The difference between BMI percentile was also not statistically significant (48.634 vs 38.634, p=.135). The difference between the FEV-1%ile was statistically significant at 84.70% for the ADHD/CF group and 74.76% for the CF-only group (p=.042).
Conclusion: While the difference in total hospital admissions between the ADHD/CF cohort and the CF-only cohort did not reach statistical significance, the study was underpowered. There was a significant difference between the FEV-1% ile between the two groups, interestingly in favor of the comorbid ADHD/CF population. More research is needed to further elucidate the effects of a comorbid ADHD diagnosis on outcomes in the CF pediatric population. (Table Presented)

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Pediatr Pulmonol. 2016;51:470-71.
THE PREVALENCE OF ATTENTION DEFICIT/ HYPERACTIVITY DISORDER IN CYSTIC FIBROSIS PATIENTS: A RETROSPECTIVE REVIEW.
Spitzer NA, Legare T, Livingston F.
Introduction: Cystic fibrosis (CF) is a complex autosomal recessive disease that leads to chronic disorders in many systems in the body, mainly the lungs and gastrointestinal tract. The treatment for CF is very complex and can include a variety of therapies, all of which can take up to 3.5 hours per day, leading to a generally poor adherence rate. Attention deficit/hyperactivity disorder (ADHD) is the most common behavioral disorder in children and causes impairment in executive functioning leading to a variety of difficulties with daily tasks. There is a paucity of research on the effect that ADHD impairments have on CF treatment adherence. Our two-part study aims to illustrate the prevalence of ADHD in the pediatric CF population at Nemours Children's Hospital and then investigate the implications that comorbidity has on CF outcomes.
Methods: A data inquiry of all patients' charts with ICD9 code of 277. xx and those with ICD9 codes 277.xx and 314.0 was performed resulting in 1163 patients. 539 patients were excluded due to not meeting inclusion criteria. Charts were reviewed for biological sex, location of pulmonology clinic visit, and race.
Results: The prevalence of ADHD in the study CF population was 8.3%. The male to female ratio in CF-only cohort was almost 1:1. In the ADHD/CF cohort, 75% were male and 25% were female, which was statistically significant compared to the CF-only cohort.
Conclusions: The prevalence of ADHD in the CF population is comparable to the prevalence in the general population. Males were more likely to have an ADHD diagnosis as compared to females, which mirrors literature on the demographics of ADHD. Further research is warranted to explore whether or not an ADHD diagnosis will decrease treatment adherence leading to decreased lung function and increased disease exacerbations and hospitalizations. (Table Presented)

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Pediatrics. 2014;134:e935-e944.
ADHD, STIMULANT TREATMENT, AND GROWTH: A LONGITUDINAL STUDY.
Harstad EB, Weaver AL, Katusic SK, et al.
BACKGROUND AND OBJECTIVE: There is ongoing concern that stimulant medications may adversely affect growth. In a sample of attention-deficit/hyperactivity disorder (ADHD) cases and controls from a population-based birth cohort, we assessed growth and the association between stimulant treatment and growth.

METHODS: Subjects included childhood ADHD cases (N = 340) and controls (N = 680) from a 1976 to 1982 birth cohort (N = 5718). Height and stimulant treatment information were abstracted from medical records and obtained during a prospective, adult follow-up study. For each subject, a parametric penalized spline smoothing method modeled height over time, and the corresponding height velocity was calculated as the first derivative. Peak height velocity (PHV) age and magnitude were estimated from the velocity curves. Among stimulant-treated ADHD cases, we analyzed height Z scores at the beginning, at the end, and 24 months after the end of treatment.
RESULTS: Neither ADHD itself nor treatment with stimulants was associated with differences in magnitude of PHV or final adult height. Among boys treated with stimulants, there was a positive correlation between duration of stimulant usage before PHV and age at PHV (r = 0.21, P = .01). There was no significant correlation between duration of treatment and change in height Z scores (r = 20.08 for beginning vs end change, r = 0.01 for end vs 24 months later change). Among the 59 ADHD cases treated for ΓëÑ3 years, there was a clinically insignificant decrease in mean Z score from beginning (0.48) to end (0.33) of treatment (P = .06).
CONCLUSIONS: Our findings suggest that ADHD treatment with stimulant medication is not associated with differences in adult height or significant changes in growth

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Pediatrics. 2014;134:e1095-e1103.
ESZOPICLONE FOR INSOMNIA ASSOCIATED WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.
Sangal RB, Blumer JL, Lankford DA, et al.
OBJECTIVE: To evaluate efficacy and safety of eszopiclone compared with placebo in children and adolescents with insomnia associated with attention-deficit/hyperactivity disorder (ADHD).
METHODS: A 12-week, randomized, double-blind, placebo-controlled trial evaluated efficacy and safety of high- or low-dose eszopiclone (1 or 2 mg in children aged 6-11 years, 2 or 3 mg in children ages 12-17 years), given every evening, in 486 patients with ADHD-related insomnia. The primary efficacy variable was change in latency to persistent sleep from baseline to week 12, based on polysomnography. Key secondary measures were polysomnography-measured wake time after sleep onset, Clinical Global Impression Parent/Caregiver and Child scales, and the Conners' ADHD rating scales. The safety of eszopiclone was further studied over 1 year of open-label treatment in 55 patients who completed the double-blind study, and 249 patients with no previous eszopiclone exposure.
RESULTS: Neither low-dose nor high-dose eszopiclone significantly reduced latency to persistent sleep compared with placebo after 12 weeks of treatment. Secondary outcomes were considered nonsignificant based on the hierarchical statistical analysis plan. The most frequent treatment-emergent adverse events over 12 weeks with eszopiclone were headache, dysgeusia, and dizziness. The study results demonstrated that eszopiclone was well tolerated over 1 year of treatment, with 11.2% of patients discontinuing open-label treatment because of an adverse event.
CONCLUSIONS: Eszopiclone (up to 3 mg) failed to reduce latency to persistent sleep on polysomnography after 12 weeks in children aged 6 to 17 years with ADHD-related insomnia. Eszopiclone was well tolerated in the 1-year study

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Pediatrics. 2014;134:e992-e1000.
FUNCTIONAL STATUS IN CHILDREN WITH ADHD AT AGE 6-8: A CONTROLLED COMMUNITY STUDY.
Efron D, Sciberras E, Anderson V, et al.
OBJECTIVES: To examine the functional status (mental health, academic performance, peer problems) of a community-based sample of children who have attention-deficit/hyperactivity disorder (ADHD) and non-ADHD controls, and to investigate gender and subtype differences.
METHODS: Children aged 6 to 8 years were recruited through 43 Melbourne schools, using a 2-stage screening (parent and teacher Conners 3 ADHD index) and case confirmation (Diagnostic Interview Schedule for Children, Version IV; [DISC-IV]) procedure. Outcome measures were mental health disorders

(DISC-IV), academic performance (Wide Range Achievement Test 4), and peer problems (Strength and Difficulties Questionnaire). Unadjusted and adjusted linear and logistic regression were used to compare ADHD and non-ADHD controls.
RESULTS: A total of 179 children who have ADHD and 212 non-ADHD controls were recruited. Compared with controls, children who had ADHD had higher odds of externalizing (odds ratio [OR], 11.0; 95% confidence interval [CI], 5.6-21.6; P , .001) and internalizing (OR, 2.9; 95% CI, 1.2-7.2; P = .02) disorders; poorer reading (effect size, 20.66) and mathematics (effect size, 20.69) performance; and more peer problems (P , .001). Boys and girls who had ADHD were equally impaired. Only 17% of children in our ADHD group had been previously diagnosed. Previous diagnosis was higher in the Combined group and for boys.
CONCLUSIONS: In their second year of school, children who had ADHD performed worse than controls across all functional domains, yet only a minority had been formally diagnosed with ADHD. Findings highlight the need for earlier diagnosis and intervention

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Pharmacopsychiatry. 2016.

PHARMACOTHERAPY IN PSYCHIATRIC DISORDERS OF CHILDREN: CURRENT EVIDENCE AND TRENDS.

Kölch M, Plener PL.

Pharmacotherapeutic interventions are available for most psychiatric disorders in children. Evidence for these interventions varies, depending on the targeted disorders. For attention-deficit/hyperactivity disorder, a sound database on efficacy and safety of medication exists. For other common disorders or psychopathological phenomena like disruptive behavior, anxiety disorders, depressive disorders, or autism, data on efficacy and safety are much scarcer. This selective review aims to provide an overview about current psychopharmacological interventions in child and adolescent psychiatry. The literature indicates either a lower efficacy than other interventions or less beneficial effects compared to possible adverse events in these cases. Most guidelines recommend psychopharmacotherapy in children to be embedded in a psychosocial or therapeutic intervention plan. Decision for medication depends on the severity of symptoms, chronicity, and, most important, impairment of the child in academic performance, family relationships, and everyday life. The high rates of off-label use in the age group of children are often due to a lack of market authorization studies less indicative of low efficacy. As adverse events need to be monitored closely, pharmacotherapy should mainly be restricted to experienced mental health care providers

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PLoS ONE. 2016;11.

HIERARCHY AND PSYCHOMETRIC PROPERTIES OF ADHD SYMPTOMS IN SPANISH CHILDREN: AN APPLICATION OF THE GRADED RESPONSE MODEL.

Arias VB, Nuñez DE, Martínez-Molina A, et al.

The Diagnostic and Statistical Manual of Mental Disorders (DSM) diagnostic criteria assume that the 18 symptoms carry the same weight in an Attention Deficit with Hyperactivity Disorder (ADHD) diagnosis and bear the same discriminatory capacity. However, it is reasonable to think that symptoms may differ in terms of severity and even in the reliability with they represent the disorder. To test this hypothesis, the aim of this study was to calibrate in a sample of Spanish children (age 4-7; n = 784) a scale for assessing the symptoms of ADHD proposed by Diagnostic and Statistical Manual of Mental Disorders, IV-TR within the framework of Item Response Theory. Samejima's Graded Response Model was used as a method for estimating the item difficulty and discrimination parameters. The results showed that ADHD subscales (Attention Deficit and Hyperactivity / Impulsivity) had good psychometric properties and had also a good fit to the model. However, relevant differences between symptoms were observed at the level of severity, informativeness and reliability for the assessment of ADHD. This finding suggests that it would be useful to identify the symptoms that are more important than the others with regard to diagnosing ADHD

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Psychiatr Serv. 2016;67:964-69.

NATIONAL TRENDS IN ADHD DIAGNOSIS AND TREATMENT: COMPARISON OF YOUTH AND ADULT OFFICE-BASED VISITS.

Oehrlein EM, Burcu M, Safer DJ, et al.

Objectives: The study objective was to assess national trends in the diagnosis of attention-deficit hyperactivity disorder (ADHD) in outpatient visits by comparing adults and youths. Also examined were recent stimulant prescribing patterns for ADHD visits by youths and adults.

Methods: Databases from the 1999-2010 National Ambulatory Medical Care Survey and National Hospital Ambulatory Medical Care Surveywere used in this cross-sectional study to analyze outpatient visit data of youths (ages two to 17 years; unweighted N=112,404) and adults (ages 18-64; unweighted N=426,209). The 12-year trends in ADHD visitswere assessed as a proportion of youth and adult visits. The interaction of time period and age group was added to multivariable and weighted logistic regression models to assess whether trends in ADHD diagnosis differed by age group.

Results: As a percentage of total visits, those involving an ADHD diagnosis were more common among youths than adults. However, from 1999 through 2010, the percentage of total visits involving a diagnosis of ADHD increased proportionallymore among adult visits (from.3%, unweightedN=363 of 132,065, to .7%, unweighted N=1,015 of 154,764; adjusted odds ratio [AOR]=2.7, 95% confidence interval [CI]=2.1-3.7) than among youth visits (from 3.9%, unweighted N=2,033 of 36,263, to 5.2%, unweighted N=2,609 of 37,906; AOR=1.3, CI=1.1-1.6; p,.001). ADHD visits by adults compared with those by youths represented significantly greater proportions of females, Caucasians, patients with private insurance, and visits with a psychiatrist. Stimulant prescribing was common in ADHD visits regardless of age group (.70%).

Conclusions: As a percentage of total office-based visits, those at which ADHD was diagnosed increased more among adults than among youths from 1999 to 2010. Further research is warranted on the appropriateness, benefit-risk, and policy implications of stimulant use among adults with ADHD

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Psychiatry Clin Neurosci. 2016 Oct;70:442-47.

EXPLORATORY STUDY TO EVALUATE PLASMA VASOPRESSIN AND APELIN-13 LEVELS IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Bilgiç A, Toker A, Uysal S.

Aim: Vasopressin exerts robust influences on social communication and behavior in humans. Apelin is a relatively novel neuropeptide that could counteract vasopressin's actions and has been shown to be closely related with a broad range of physiological functions. Abnormalities in vasopressin and apelin have been detected in a variety of psychiatric disorders, but their relation to attention-deficit hyperactivity disorder (ADHD) is unknown. In the present study, we explored the plasma levels of vasopressin and apelin-13 in children with ADHD.

Methods: Thirty-four children with ADHD and 36 healthy controls were enrolled in this study. The severity of ADHD symptoms was assessed via Conners' Parent Rating Scale and Conners' Teacher Rating Scale. Plasma levels of vasopressin and apelin-13 were measured using commercial enzyme-linked immunosorbent assay kits.

Results: The mean plasma apelin-13 levels were significantly higher in male children with ADHD than in male control subjects; no significant difference was found between the groups for plasma apelin-13 levels in girls or in the entire subject cohort. Plasma vasopressin levels did not show any significant differences between groups. There were no significant correlations between plasma levels of these neuropeptides and scores for Conners' Parent Rating Scale and Conners' Teacher Rating Scale.

Conclusion: Our results suggest a sex-specific association between plasma apelin-13 levels and ADHD. Apelin-13 may play a role in the etiopathogenesis of ADHD either with a direct impact on the apelin receptor or via its opposing effect on the vasopressinergic system

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Psychiatr Invest. 2016;13:518-25.

BRAIN-DERIVED NEUROTROPHIC FACTOR GENE VAL66MET POLYMORPHISM IS A RISK FACTOR FOR ATTENTION-DEFICIT HYPERACTIVITY DISORDER IN A TURKISH SAMPLE.

Ozturk O, Basay BK, Buber A, et al.

Objective Attention-deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder that negatively affects different areas of life. We aimed to evaluate the associations between the Val66Met polymorphism of brain-derived neurotrophic factor (BDNF) and ADHD and to assess the effect of the BDNF polymorphism on the neurocognitive profile and clinical symptomatology in ADHD.

Methods Two hundred one ADHD cases and 99 typically developing subjects (TD) between the ages of 8 and 15 years were involved in the study. All subjects were evaluated using a complete neuropsychological battery, Child Behavior Checklist, the TeacherΓÇÖs Report Form (TRF) and the DSM-IV Disruptive Behavior Disorders Rating Scale-teacher and parent forms.

Results The GG genotype was significantly more frequent in the patients with ADHD than in the TD controls, and the GG genotype was also significantly more frequent in the ADHD-combined (ADHD-C) subtype patients than in the TDs. However, there were no significant associations of the BDNF polymorphism with the ADHD subtypes or neurocognitive profiles of the patients. The teacher-assessed hyperactivity and inattention symptom count and the total score were higher, and the appropriately behaving subtest score of the TRF was lower in the GG genotypes than in the GA and AA (i.e., the A-containing) genotypes.

Conclusion We found a positive association between the BDNF gene Val66Met polymorphism and ADHD, and this association was observed specifically in the ADHD-C subtype and not the ADHD-predominantly inattentive subtype. Our findings support that the Val66Met polymorphism of BDNF gene might be involved in the pathogenesis of ADHD. Furthermore Val66Met polymorphism of BDNF gene may be more closely associated with hyperactivity rather than inattention

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Psychiatry Res. 2016;246:326-31.

ADHD SYMPTOMS AND PAIN AMONG ADULTS IN ENGLAND.

Stickley A, Koyanagi A, Takahashi H, et al.

Prior research has produced conflicting findings on the association between attention-deficit/hyperactivity disorder (ADHD) and pain, while studies among community-dwelling adults are lacking. This study examined the association between ADHD symptoms and pain in the general adult population, and the extent to which this association is influenced by comorbid common mental disorders (CMDs). Data came from the 2007 Adult Psychiatric Morbidity Survey which included a representative sample of the English adult household population aged ≥16 years (N=7403). The Adult ADHD Self-Report Scale (ASRS) Screener was used to obtain information on ADHD symptoms, while pain was assessed by the degree to which it interfered with work activity in the previous month. The Clinical Interview Schedule Revised (CIS-R) was used to evaluate six categories of CMDs. In a binary logistic regression analysis adjusted for socio-demographic factors and physical health conditions, an ADHD symptom score ≥14 was strongly associated with extreme pain (odds ratio [OR]: 3.15, 95% confidence interval [CI]: 2.09-4.74). The OR was attenuated greatly after further adjustment for CMDs (OR: 1.64, 95% CI: 1.05-2.58) but remained statistically significant. Adults with ADHD symptoms have higher odds for experiencing pain. CMDs are influential in this association but do not fully explain it

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Psychol Assess. 2016 Oct;28:1290-302.

THE IMPACT OF FAILING TO IDENTIFY SUSPECT EFFORT IN PATIENTS UNDERGOING ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) ASSESSMENT.

Marshall PS, Hoelzle JB, Heyerdahl D, et al.

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Psychol Rep. 2016 Oct;119:365-73.

IMPACT OF THE DSM-V ATTENTION DEFICIT HYPERACTIVITY DISORDER CRITERIA FOR DIAGNOSING CHILDREN WITH HIGH IQ.

Thongseiratch T, Worachotekamjorn J.

This study compared the number of attention deficit hyperactivity disorder (ADHD) cases defined by Diagnostic and Statistical Manual (DSM)-IV versus DSM-V criterion in children who have learning or behavioral problems with high IQ. The medical records of children = 15 years of age who presented with learning or behavioral problems and underwent a Wechsler Intelligence Scale for Children (WISC)-III IQ test at the Pediatric Outpatient Clinic unit between 2010 and 2015 were reviewed. Information on DSM-IV and DSM-V criteria for ADHD were derived from computer-based medical records. Twenty-eight children who had learning or behavioral problems were identified to have a full-scale IQ = 120. Sixteen of these high-IQ children met the DSM-IV criteria diagnosis for ADHD. Applying the extension of the age-of-onset criterion from 7 to 12 years in DSM-V led to an increase of three cases, all of which were the inattentive type ADHD. Including the pervasive developmental disorder criterion led to an increase of one case. The total number of ADHD cases also increased from 16 to 20 in this group. The data supported the hypothesis that applying the extension of the age-of-onset ADHD criterion and enabling the diagnosis of children with pervasive developmental disorders will increase the number of ADHD diagnoses among children with high IQ

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Res Dev Disabil. 2016;59:428-36.

EMOTIONAL DYSREGULATION OF ADHD IN CHILDHOOD PREDICTS POOR EARLY-ADULTHOOD OUTCOMES: A PROSPECTIVE FOLLOW UP STUDY.

Qian Y, Chang W, He X, et al.

BACKGROUD: Emotional dysregulation (EDR) is commonly seen in individuals with attention deficit hyperactive disorder (ADHD). But few are known about the influence of EDR on early-adulthood outcomes.
AIMS: To detect the relationship between emotional dysregulation (EDR) in childhood and the outcomes in early-adulthood of participants with attention deficit hyperactive disorder (ADHD).
METHODS AND PROCEDURES: Han Chinese children who met DSM-IV ADHD criteria were followed up into early adulthood. The subjects were divided into two groups (with or without EDR) according to the emotion control subscale of Behavior Rating Scale of Executive Function in childhood. In the follow-up interview, their clinical outcomes were assessed by the Conner's Adult ADHD Diagnostic Interview and the Structured Clinical Interview for DSM-IV-TR Axis I and II Disorders. Information on after-school tutoring and suspension of schooling was also collected as indices of educational outcomes.
OUTCOMES AND RESULTS: We followed up 68 out of 90 individuals when they reached early adulthood. Data analysis showed that EDR predicted HI symptoms of ADHD both in childhood (OR=10.28, p<0.01) and in early-adulthood (OR=4.07, p=0.01). And EDR in childhood had trend to predicted adult ODD (X2=3.93, p=0.05). The suspension of schooling was also predicted by EDR (OR=9.31, p=0.04).
CONCLUSIONS AND IMPLICATIONS: This study illustrated that EDR of children with ADHD, independent of co-occurring ODD, predicted poor long-term clinical and educational outcome in early-adulthood

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Res Dev Disabil. 2016 Oct;57:1-10.

A RACKET-SPORT INTERVENTION IMPROVES BEHAVIORAL AND COGNITIVE PERFORMANCE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Pan CY, Chu CH, Tsai CL, et al.

The present study assessed the effects of a 12-week table tennis exercise on motor skills, social behaviors, and executive functions in children with attention deficit hyperactivity disorder (ADHD). In the first 12-week phase, 16 children (group I) received the intervention, whereas 16 children (group II) did not. A second 12-week phase immediately followed with the treatments reversed. Improvements were observed in executive functions in both groups after the intervention. After the first 12-week phase, some motor and behavioral functions improved in group I. After the second 12-week phase, similar improvements were noted for group

II, and the intervention effects achieved in the first phase were persisted in group I. The racket-sport intervention is valuable in promoting motor skills, social behaviors, and executive functions and should be included within the standard-of-care treatment for children with ADHD.

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Rev Colomb Psiquiatr. 2016;45:156-61.

ASSOCIATION BETWEEN THE CHARACTERISTICS OF COORDINATION DEVELOPMENT DISORDER AND SYMPTOMS OF ATTENTION DEFICIT DISORDER WITH HYPERACTIVITY IN CHILDREN IN THE CITY OF MANIZALES.

Salamanca Duque LM, Naranjo Aristizábal MM2, Castro Castro ÁL, et al.

INTRODUCTION: Developmental coordination disorder (DCD) in childhood is an important public health problem, which has important implications for different spheres of development: motor, cognitive, psychosocial and emotional. Therefore, the presence of comorbidity is common, along with other disorders in child development. This article presents a study that determines the association between DCD characteristics with attention deficit and hyperactivity disorder (ADHD) symptoms.

OBJECTIVE: To determine the association between DCD characteristics and ADHD symptoms in the city of Manizales, Colombia.

METHODS: Cross-sectional, descriptive and associative study, in a sample of 140 children aged 6-12, randomised in public and private institutions. A structured interview was conducted, along with the questionnaires MINIKID and Cuestionario para Trastorno del Desarrollo de la Coordinación (CTDC). A descriptive univariate analysis was performed on the the sociodemographic characteristics, as well as association tests with $\chi(2)$ test, and dependence level with φ coefficient.

RESULTS: A statistically significant association was found between the CTDC characteristics with ADHD symptoms (φ=.452; P=.001).

CONCLUSIONS: An association was found in the studied population between the CTDC characteristics and ADHD symptoms, indicating that children with difficulties in motor performance may also have attention difficulties and hyperactivity

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Sch Psychol Q. 2016 Sep;31:393-404.

WRITING ABILITIES LONGITUDINALLY PREDICT ACADEMIC OUTCOMES OF ADOLESCENTS WITH ADHD.

Molitor SJ, Langberg JM, Bourchtein E, et al .

Students with attention-deficit/hyperactivity disorder (ADHD) often experience a host of negative academic outcomes, and deficits in reading and mathematics abilities contribute to these academic impairments. Students with ADHD may also have difficulties with written expression, but there has been minimal research in this area and it is not clear whether written expression abilities uniquely contribute to the academic functioning of students with ADHD. The current study included a sample of 104 middle school students diagnosed with ADHD (Grades 6–8). Participants were followed longitudinally to evaluate whether written expression abilities at baseline predicted student grade point average (GPA) and parent ratings of academic impairment 18 months later, after controlling for reading ability and additional relevant covariates. Written expression abilities longitudinally predicted both academic outcomes above and beyond ADHD and oppositional defiant disorder symptoms, medication use, reading ability, and baseline values of GPA and parent-rated academic impairment. Follow-up analyses revealed that no single aspect of written expression was demonstrably more impactful on academic outcomes than the others, suggesting that writing as an entire process should be the focus of intervention

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Tijdschr Psychiatr. 2014;56:478-79.
EXPRESSED EMOTIONS OF MOTHERS AND BEHAVIORAL PROBLEMS IN CHILDREN WITH ADHD.
Richards J.

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Transl Psychiatry. 2016 Feb;6:e732.
USE OF MACHINE LEARNING FOR BEHAVIORAL DISTINCTION OF AUTISM AND ADHD.
Duda M, Ma R, Haber N, et al.
Although autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) continue to rise in prevalence, together affecting >10% of today's pediatric population, the methods of diagnosis remain subjective, cumbersome and time intensive. With gaps upward of a year between initial suspicion and diagnosis, valuable time where treatments and behavioral interventions could be applied is lost as these disorders remain undetected. Methods to quickly and accurately assess risk for these, and other, developmental disorders are necessary to streamline the process of diagnosis and provide families access to much-needed therapies sooner. Using forward feature selection, as well as undersampling and 10-fold cross-validation, we trained and tested six machine learning models on complete 65-item Social Responsiveness Scale score sheets from 2925 individuals with either ASD (n=2775) or ADHD (n=150). We found that five of the 65 behaviors measured by this screening tool were sufficient to distinguish ASD from ADHD with high accuracy (area under the curve=0.965). These results support the hypotheses that (1) machine learning can be used to discern between autism and ADHD with high accuracy and (2) this distinction can be made using a small number of commonly measured behaviors. Our findings show promise for use as an electronically administered, caregiver-directed resource for preliminary risk evaluation and/or pre-clinical screening and triage that could help to speed the diagnosis of these disorders

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World J Biol Psychiatry. 2016;1-9.
DAT1 METHYLATION IS ASSOCIATED WITH METHYLPHENIDATE RESPONSE ON OPPOSITIONAL AND HYPERACTIVE-IMPULSIVE SYMPTOMS IN CHILDREN AND ADOLESCENTS WITH ADHD.
Ding K, Yang J, Reynolds GP, et al.
OBJECTIVES: To examine the association of the DNA methylation of DAT1 and DRD4 gene with methylphenidate (MPH) response in attention deficit hyperactivity disorder (ADHD).
METHODS: One hundred and eleven DSM-IV defined ADHD Chinese Han children were recruited. Inattention, hyperactivity-impulsivity and oppositional symptoms were evaluated by the Swanson, Nolan and Pelham-IV-parent rating scale (SNAP-IV-P) at baseline and 6 weeks after MPH treatment. DNA methylation of CpG sites in the promoter sequences of DAT1 and DRD4 was examined for association with treatment response.
RESULTS: Greater improvement on the SNAP-IV-P total score and percentage change from baseline score were both significantly correlated with DAT1 methylation (rho =-0.222, P = .019 and rho = -0.203, P = .032, respectively). A secondary analysis demonstrated that the effect of DAT1 methylation on symptom response was primarily related to the percentage change in oppositional symptoms (rho = -0.242; P = .012), with a smaller significant effect on hyperactivity-impulsivity (rho = -0.192; P = .045). No significant correlation was found between the treatment effect on inattention and DAT1 methylation (rho = -0.101; P = .292). No significant correlation was observed between mean DRD4 methylation and measures of treatment outcome or baseline symptoms.
CONCLUSIONS: Our findings provide initial evidence for the involvement of the epigenetic alterations of DAT1 in modulating the response to MPH treatment in ADHD, primarily on oppositional and hyperactive-impulsive symptoms

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Z Kinder- Jugendpsychiatr Psychother. 2016;44:365-75.

BASIC NUMERICAL PROCESSING, CALCULATION, AND WORKING MEMORY IN CHILDREN WITH DYSCALCULIA AND/OR ADHD SYMPTOMS.

Kuhn JT, Ise E, Raddatz J, et al.

Objective: Defi cits in basic numerical skills, calculation, and working memory have been found in children with developmental dyscalculia (DD) as well as children with attention-defi cit/hyperactivity disorder (ADHD). This paper investigates cognitive profi les of children with DD and/or ADHD symptoms (AS) in a double dissociation design to obtain a better understanding of the comorbidity of DD and ADHD.

Method: Children with DD-only (N = 33), AS-only (N = 16), comorbid DD+AS (N = 20), and typically developing controls (TD, N = 40) were assessed on measures of basic numerical processing, calculation, working memory, processing speed, and neurocognitive measures of attention.

Results: Children with DD (DD, DD+AS) showed defi cits in all basic numerical skills, calculation, working memory, and sustained attention. Children with AS (AS, DD+AS) displayed more selective diffi culties in dot enumeration, subtraction, verbal working memory, and processing speed. Also, they generally performed more poorly in neurocognitive measures of attention, especially alertness. Children with DD+AS mostly showed an additive combination of the defi cits associated with DD-only and A Sonly, except for subtraction tasks, in which they were less impaired than expected. **Conclusions**: DD and AS appear to be related to largely distinct patterns of cognitive defi cits, which are present in combination in children with DD+AS

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Z Kinder- Jugendpsychiatr Psychother. 2016;44:351-61.

ATTENTION AND READING PERFORMANCE IN CHILDREN WITH ADHD, READING DISORDER AND THE COMBINED CONDITION.

Günther T, Peters K, Scharke W, et al.

Attention Deficit Hyperactivity Disorder (ADHD) and Dyslexia co-occur more often than expected by chance. Both disorders can have severe negative impact on children's development. The aim of the present study was to compare attention and reading performance in children with ADHD, dyslexia and the comorbid condition. Ninety-nine German children in 3rd and 4th grade with ADHD (n = 26), dyslexia (n = 22) and the comorbid condition (n = 24) compared to a healthy control group (n = 27) were assessed with a model oriented assessment battery for reading and attention. Additionally, comorbid problems were examined. Children with ADHD were characterized by difficulties in decoding and reading comprehension, while children with dyslexia showed impairments in their attentional performance. Psychometric data revealed that children with dyslexia showed both externalizing and internalizing symptoms, while children with the comorbid condition scored the highest on all psychopathological dimensions. The results suggest, that reading problems in children with ADHD might be an epiphenomenon of the task used dependent on time constraints inherent to the task. Impairments of attentional functions in children with dyslexia emphasize the importance of a sufficient diagnostic procedure for subclinical ADHD symptoms as possible comorbid disorder. Future studies should focus the impact of early treatment of attentional deficits on reading acquisition

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Zhongguo Zhong Xi Yi Jie He Za Zhi. 2015 Dec;35:1469-73.

ANALYSIS OF APPLYING CHINESE MEDICAL CLINICAL PATHWAY FOR TREATING ATTENTION-DEFICIT HYPERACTIVITY DISORDER.

Guo YQ, Han XM, Zhu XK, et al.

OBJECTIVE: To evaluate the application effect of Chinese medical clinical pathway for treating attention-deficit hyperactivity disorder (ADHD), and to provide evidence for further improving clinical pathways.

METHODS: Totally 270 ADHD children patients were recruited and treated at pediatrics clinics of 9 cooperative hospitals from December 2011 to December 2012. The treatment course for all was 3 months. Scores of attention deficit and hyperactivity rating scale, scores of behavior, Conners index of hyperactivity (CIH), and Chinese medical syndrome scores were compared between before and after treatment. The

efficacy difference in various sexes, ages, and disease courses were evaluated by judging standards for Chinese medical syndrome and ADHD.
RESULTS: Fifteen children patients who entered clinical pathway dropped out, and the rest 255 completed this trial. Compared with before treatment, total scores of attention deficit and hyperactivity rating scale, scores of attention deficit and hyperactivity rating scale, CIH, and Chinese medical syndrome scores obviously decreased (all $P < 0.01$). The total effective rate in disease efficacy was 87.8% (224/255 cases), and the total effective rate in Chinese medical syndrome curative effect was 87.5% (223/255 cases). The clinical curative effect was not influenced by age, gender, or course of disease when statistically analyzed from judging standards for Chinese medical syndrome or for disease efficacy.
CONCLUSION: Intervention by Chinese medical clinical pathway could improve ADHD patients' symptoms, and its efficacy was not influenced by sex, age, or course of disease

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COGNITIVE NEUROPSYCHIATRY, 2016
http://dx.doi.org/10.1080/13546805.2016.1235029

Routledge
Taylor & Francis Group

Neurological soft signs are associated with attentional dysfunction in children with attention deficit hyperactivity disorder

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ABSTRACT

Introduction: Inattention is one of the core symptoms of Attention Deficit Hyperactivity Disorder (ADHD). Most of patients with ADHD show motor impairment, consisting in the persistence of neurological soft signs (NSS). Our aim was to evaluate attentional and motor functioning in an ADHD sample and healthy children (HC) and possible link between attentional dysfunction and motor impairment in ADHD.

Method: Twenty-seven drug-naive patients with ADHD and 23 HC were tested with a test battery, measuring different aspects of attention. Motor evaluation has provided three primary variables: overflow movements (OM), dysrhythmia and total speed of timed activities.

Results: Compared to HC, patients were impaired in a considerable number of attentional processes and showed a greater number of NSS. Significant correlations between disturbances of attention and motor abnormalities were observed in ADHD group.

Conclusion: Our findings suggest that attentional processes could be involved in the pathophysiology of the NSS and add scientific evidence to the predictive value of NSS as indicators of the severity of functional impairment in ADHD. Given the marked improvement or complete resolution of NSS following treatment with methylphenidate, we suggest that evaluation of NSS is useful to monitor the effectiveness of pharmacological treatment with MPH in ADHD.

ARTICLE HISTORY
Received 6 November 2015
Accepted 6 September 2016

KEYWORDS
ADHD; attention and NSS

Introduction

Attention deficit hyperactivity disorder

Attention deficit hyperactivity disorder (ADHD), a neurodevelopmental disorder with a worldwide prevalence of 5.29% in childhood (Polanczyk, de Lima, Horta, Biederman, & Rohde, 2007), is characterised by developmentally inappropriate levels of inattentiveness,

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motor hyperactivity and impulsivity. Inattention is one of the core symptoms of ADHD. These children are easily distracted and experience problems in planning, organising and finishing assigned tasks (Curatolo, Paloscia, D'Agati, Moavero, & Pasini, 2009). Neuropsychological assessment revealed that children with ADHD experience difficulties in a variety of functions related to attention, including distractibility, selective and sustained attention in comparison to healthy children (HC) (Borger et al., 1999; Heaton et al., 2001; Lockwood, Marcotte, & Stern, 2001; Perugini, Harvey, Lovejoy, Sandstrom, & Webb, 2000).

Attentional functions

There is empirical evidence that attention represents a multidimensional construct, including several distinct functions, that may be selectively affected by brain dysfunction (Choen, 1993; Pashler, 1998; Posner & Boies, 1971; Posner & Rafal, 1987). Based on the multicomponent model of attention of Posner and colleagues (Posner & Boies, 1971; Posner & Rafal, 1987), Van Zomeren and Brouwer delineated a theoretical framework of attentional functions, including concepts of tonic and phasic alertness, vigilance/sustained attention, selective attention, divided attention and strategy/flexibility (Van Zomeren & Brouwer, 1994). Tonic alertness refers to a relatively stable level of attention which changes slowly according to diurnal physiological variations of the organism, while phasic alertness is the ability to enhance the activation level following a stimulus of high priority. Selective attention is defined as the ability to focus attention. Divided attention requires a simultaneous response to multiple tasks or multiple task demands. The ability to sustain attention enables a subject to direct attention to one or more sources of information over a relatively long and unbroken period of time. This multidimensional model also considers the distinction between aspects of selectivity and intensity made by Kahneman (1973) and the concept of a supervisory attentional control devised by Shallice (1982). Selective attention and divided attention are considered to be aspects of selectivity; instead, alertness and sustained attention are expressions of intensity of attention (Van Zomeren & Brouwer, 1994). Applying the multidimensional model of attention delineated by Van Zomeren and Brouwer, Tucha and colleagues found that children with ADHD suffer from a global deficit of attention, comprising impairments of vigilance, selective attention, focused attention, divided attention and shifting (Tucha et al., 2006a, 2006b, 2009).

Neurological soft signs

Motor ability of children with ADHD is often significantly poorer than it should be based on their age and level of intellectual functioning. Besides the core symptoms, they experience motor impairment and neurological soft signs (NSS) (D'Agati, Casarelli, Pitzianti, & Pasini, 2010; Pasini & D'Agati, 2009; Pasini, D'Agati, Pitzianti, Casarelli, & Curatolo, 2012). NSS are subtle motor, sensory and integrative abnormalities that cannot be related to impairment of a specific brain region and result in considerable sociopsychological dysfunction (Shafer, Shaffer, O'Connor, & Stokman, 1983). Although NSS are commonly observed in children with typical development and reflect the immaturity of the central nervous system, their persistence into later childhood and adolescence suggests

motor dysfunction and could be a "marker" of atypical neurodevelopment (Larson et al., 2007). NSS are mainly represented by overflow movements (OM) and dysrhythmia. OM are defined as co-movements of body parts not specifically needed to efficiently complete a motor task (Larson et al., 2007). There are a number of different forms of OM: associated movements, contralateral motor irradiation and mirror movements. Dysrhythmia is defined as an improper timing and/or rhythm of movement otherwise normal (Cole, Mostofsky, Larson, Denckla, & Mahone, 2008). OM seem to be related to a delay or defect of maturation into the intra-cortical and inter-cortical systems that support automatic inhibition (Mostofsky, Newschaffer, & Denckla, 2003), while dysrhythmia appears to be due to cerebellar dysfunction (Schmahmann, 2004). OM, impaired timing of motor responses and poor motor coordination seem to be the most prominent motor abnormalities in children with ADHD. These could reflect dysfunctions of frontal-striatal-cerebellar networks involved in motor control and white matter abnormalities in motor and pre-motor circuits (D'Agati et al., 2010; Pasini & D'Agati, 2009; Pasini et al., 2012).

Aim of study

The role of attentional processes in motor functioning has already been studied in typically developing school-aged children (Herzog & Durwen, 1992; Lazarus & Todor, 1992; Waber, Mann, & Merola, 1985), while it has not been studied in clinical groups. The aim of our study is to investigate the link between attentional processes and NSS in children with ADHD. In this study we have assessed several components of attention, as suggested by the multicomponent model of Van Zomeren and Brouwer (1994), and we have evaluated NSS by the Physical and Neurological Assessment of Subtle Signs (PANESS) (Denckla, 1985) in patients with ADHD compared with typically developing children. We also investigate the possible correlations between attentional and motor performances in our clinical group.

Methods and materials

Subjects

The study included 50 subjects divided into a clinical group and a control group: 27 patients with ADHD (23 boys, 4 girls) and 23 healthy controls (20 boys, 3 girls) aged 8–15 years with an IQ $\geq$ 85. The subjects of the clinical group were consecutive referrals of the Unit of Child Neurology and Psychiatry of "Tor Vergata" University of Rome, Italy. In accordance with the DSM-IV-TR criteria (APA, 2000), the diagnosis of ADHD was based on clinical assessment, observations of children and interviews with parents and children, which were carried out by an experienced child psychiatrist. Both the long version of the Conners' Parents Rating Scale-Revised (CPRS-R) (Nobile, Alberti, & Zuddas, 2007) and the Conners' Teachers Rating Scale-Revised (CTRS-R) (Nobile, Alberti, Zuddas, & Conners, 2007) were used to make the diagnosis of ADHD. To keep the sample of children with ADHD as homogenous as possible, only those who met the DSM-IV-TR criteria for ADHD/combined type were included in the study. The interview with the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997) was used to exclude

other psychiatric co-morbidities in the ADHD group. The HC were recruited in schools and selected from a pool of subjects who participated voluntarily in the study. None of them had a history of neurological or psychiatric disease or learning disability. Both the long version of the CPRS-R (Nobile, Alberti, & Zuddas, 2007) and the CTRS-R (Nobile, Alberti, Zuddas, & Conners, 2007) were used to exclude the diagnosis of ADHD in all healthy participants. The interview with the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime Version (K-SADS-PL) (Kaufman et al., 1997) was used to exclude other psychiatric disorders in the control group. All subjects included in the study had a normal IQ as measured with the Wechsler Intelligence Scale for Children-III (WISC-III) (Wechsler, 1991). At the time of the study, no participants were taking medication known to affect the central nervous system. Prior to the testing, every parent or legal guardian of the subjects included gave written informed consent. In Table 1 characteristics of children with ADHD and healthy controls are summarised.

Evaluation of attentional functioning

All participants were tested with four computerised tasks, measuring different aspects of attention. The tests of attention used were developed and validated for the assessment of attentional deficits in children and adults with cerebral lesions (Zimmermann & Fimm, 1993, 2002). Test procedures were presented on a computer screen. Instructions were given orally. Participants were instructed to perform the computerised tasks as quickly as possible but to maintain a high level of accuracy. In order to familiarise the participants with the tasks, a brief sequence of practice trials preceded each test. Tests were performed only after participants had completed the practice trials without errors. Participants were assessed individually in a quiet room and the examiner was present during the entire assessment.

In the *alertness task*, reaction time is examined under two conditions. The first condition represents a simple reaction time measurement, in which a cross appears on the

Table 1. Results of *Z*-Test and *t*-test for ADHD and control groups with regard to age, IQ and assessment using CPRS and CTRS.

	ADHD group	Control group	ADHD group vs control group				
	27 (23 boys and 4 girls)	23 (20 boys and 3 girls)					
Number of subjects	Mean ± SD	Mean ± SD	*Z*	*p*		*p*	*d*
Age (years)	10.11 ± 1.87	11.22 ± 2.57	−1.688	.091	−0.037	.971	0.49
TIQ	96.07 ± 10.12	98.96 ± 9.21	−0.997	.319	−0.817	.418	0.30
VIQ	96.81 ± 8.99	98.69 ± 8.36	−0.873	.383	−0.761	.450	0.22
PIQ	97.07 ± 9.05	97.60 ± 8.67	−1.078	.281	0.898	.374	0.05
CPRS-oppositional	62.00 ± 11.06	51.13 ± 5.64	−3.822	**.001***	4.260	**.001***	1.24
CPRS-inattention	75.00 ± 7.31	52.39 ± 5.28	−6.050	**.001***	12.339	**.001***	3.54
CPRS-hyperactivity	71.74 ± 8.71	53.52 ± 4.36	−6.059	**.001***	9.098	**.001***	2.64
CPRS-ADHD-index	75.00 ± 8.31	53.91 ± 4.22	−6.050	**.001***	11.008	**.001***	3.20
CTRS-oppositional	57.18 ± 6.89	50.30 ± 6.15	−3.242	**.001***	3.699	**.001***	1.05
CTRS-inattention	71.89 ± 6.71	53.35 ± 4.74	−5.872	**.001***	11.092	**.001***	3.19
CTRS-hyperactivity	69.92 ± 9.52	53.52 ± 4.42	−5.328	**.001***	7.568	**.001***	2.21
CTRS-ADHD-index	72.55 ± 7.15	53.73 ± 4.82	−5.962	**.001***	10.707	**.001***	3.09

Note: CPRS = Conners' Parents Rating Scale; CTRS = Conners' Teachers Rating Scale.
*Level of significance $p \leq .05$.

monitor at randomly varying intervals and to which the subject has to respond as quickly as possible by pressing a key. Intrinsic alertness is measured in this condition. In a second condition, reaction time is measured in response to a critical stimulus preceded by a cue stimulus presented as warning tone ("phasic arousal" or temporal orientation of attentional focus). Therefore, in the alertness task participants were asked to respond by pressing a button when a visual stimulus appeared on a computer screen. In the first 20 trials, the stimulus appeared on the screen without prior warning (tonic alertness task), while during the second 20 trials, a warning tone preceded the appearance of the stimulus (phasic alertness task). The time span between the warning tone and the appearance of the stimulus was random (Zimmermann & Fimm, 2012). Measures of tonic and phasic alertness are calculated on the basis of the reaction time of the participant. In addition, the variability of reaction time and number of omission errors are measured.

The *incompatibility task* tests the interference tendency in terms of stimulus-reaction incompatibility. For this test, arrows that are directed to the left or the right are presented on the left or right side of a fixation point. Depending on the direction of the arrow, the test person is requested to respond with the right or left hand irrespective of the side on which the arrow is presented. Therefore, in the incompatibility task, arrows pointing to the left or the right were presented briefly on the left or right side of a fixation point in the centre of the computer screen. The participants were requested to press a response button as quickly as possible on the side indicated by the direction of the arrow, independent of the position of the arrow. If the position of the arrow and its orientation accorded (e.g. arrow on the left side of the fixation point pointing to the left side), the trial was classified as a compatible trial while trials in which presentation and orientation were not in accordance (e.g. arrow on the left side of the fixation point pointing to the right side) were classified as incompatible trials. The sequence of trials was random, with about half of the trials compatible and half incompatible (Zimmermann & Fimm, 2012). Reaction time, variability of reaction time and number of commission errors are calculated, providing a measure of selective attention as the capacity to reject irrelevant information.

The *divided attention task* requires participants to process in parallel a visual and an auditory task presented by a computer. In the visual task, a series of matrices was presented in the centre of the computer screen. Each matrix, consisting of a regular array of 16 dots and crosses (4×4), was displayed for 2000 ms. The participant was asked to press the response button as quickly as possible whenever the crosses formed the corners of a square (visual target). In the acoustic task, the participant was requested to listen to a continuous sequence of alternating high and low sounds and to press the response button as quickly as possible when irregularities of the sequence occurred (acoustic target) (Zimmermann & Fimm, 2012). Reaction time for correct responses, variability of reaction time and number of omission errors (lack of response to target stimuli) and number of commission errors (responses to non-target stimuli) are calculated as a measure of divided attention.

In the *sustained attention task*, a sequence of stimuli is presented on the monitor. The stimuli vary in a range of feature dimensions: colour, shape, size and filling. A target stimulus occurs whenever it corresponds in one or the other of two predetermined stimulus dimensions with the preceding stimulus (e.g. the same shape but with different colour,

size and filling). Different levels of difficulty may be selected (e.g. reaction only to "shape" or reaction to "colour and shape"). In order to adapt the difficulty of the task to the performance level of the subjects, reaction only to "shape" was chosen (Zimmermann & Fimm, 2012). Reaction time for correct responses, variability of reaction time, number of omission errors (lack of response to target stimuli) and number of commission errors (responses to non-target stimuli) are calculated as a measure of sustained attention.

Assessment of NSS

For the assessment of NSS, the *PANESS* (Denckla, 1985) was applied. These evaluations were performed by a child neurologist who underwent training for the reliable application of the PANESS. The examiner was blind to the child's diagnostic status at the time of assessment and during scoring. The PANESS has been found to have adequate test-retest reliability (Holden, Tarnowski, & Prinz, 1982), inter-rater reliability, internal consistency (Vitiello, Ricciuti, Stoff, Behar, & Denckla, 1989) and sensitivity to age-related changes (Larson et al., 2007) in more current and diverse cohorts. The PANESS measures salient components of motor function, including lateral preference, gaits, balance, motor persistence, coordination, overflow, dysrhythmia and timed movements. Three primary outcome variables were obtained: (1) *total OM* included the total number of abnormal movements for age observed during stressed gaits (i.e. walking on heels, toes or sides of feet), tandem gaits (walking in tandem forward and backward, touching heels to toes) and during timed movements; (2) *total dysrhythmia* included total number of timed the motor examination trials in which the children failed to maintain a steady rhythm throughout the task; (3) *total speed of timed activities* of hands/feet included three repetitive movements and three sequenced movements which were performed bilaterally: toe tapping, alternating heel-toe tapping, repetitive hand patting, hand pronation/supination, repetitive finger tapping and finger sequencing.

Statistical analysis

For the statistical analysis, an alpha level of 0.05 was applied. All statistical analyses were carried out using the Statistical Package for Social Sciences SPSS software (version 17.0, Inc., Chicago, IL, USA). The Mann–Whitney-U test (Z-test) is used to compare differences between the clinical and control groups in regard to the variables collected for each subject enrolled for this study. Moreover, in order to consider the interaction effect of age, the second statistical analysis was conducted using t-test for independent samples. Effect sizes for differences between paired observations were computed. Cohen's d was used to calculate the effect size. Cohen's d is defined as the difference between two means divided by a standard deviation of the data. Following Cohen's (1988) guidelines for interpreting effect sizes, small effects ($d \geq 0.20$), medium effects ($d \geq 0.50$) and large effects ($d \geq 0.8$) were distinguished (Bezeau & Graves, 2001). The Kendall's rank correlation coefficient or Kendall's τ is used to find a correlation among multiple independent variables examined. The Kendall's τ is a non-parametric measure of the statistical dependence among various variables and it is indicative of the strength and direction of the association among various variables measured on at least an ordinal scale.

Results

Comparisons between ADHD group and control group

Age, IQ and Conners' Parents and Teachers Rating Scale

In our study patients and healthy controls did not differ in terms of age ($Z = -1.688$; $p = .091$) and IQ ($Z = -0.997$; $p = .319$). We found significant differences between the ADHD group and the control group with regard to the following ratings: Conners' Parents Rating Scale-Oppositional ($Z = -3.822$; $p < .001$), Conners' Parents Rating Scale-Inattention ($Z = -6.050$; $p < .001$), Conners' Parents Rating Scale-Hyperactivity ($Z = -6.059$; $p < .001$), Conners' Parents Rating Scale-ADHD-Index ($Z = -6.050$; $p < .001$), Conners' Teachers Rating Scale-Oppositional ($Z = -3.242$; $p < .001$), Conners' Teachers Rating Scale-Inattention ($Z = -5.872$; $p < .001$), Conners' Teachers Rating Scale-Hyperactivity ($Z = -5.328$; $p = .001$) and Conners' Teachers Rating Scale-ADHD-Index ($Z = -5.962$; $p < .001$). The *t*-test confirmed the significant differences between patients with ADHD and HC emerged through the *Z*-test. In Table 1 results of *Z*-test and *t*-test for independent samples are summarised.

Alertness

Comparison between the ADHD group and the control group using Mann–Whitney-U Test revealed no significant differences with regard to reaction time ($Z = -1.149$; $p = .251$) and number of omission errors ($Z = -0.870$; $p = .384$) in the tonic alertness task; however, we found a significant difference between the ADHD group and the control group with regard to variability of reaction time ($Z = -3.018$; $p = .003$). Moreover, the ADHD group did not differ from the control group in reaction time ($Z = -1.052$; $p = .293$) and number of omission errors ($Z = -1.217$; $p = .224$) in the phasic alertness task. A significant difference was found between groups in variability of reaction time ($Z = -2.765$; $p = .006$) of the phasic alertness task. The *t*-test confirmed the significant differences between patients with ADHD and HC emerged through the *Z*-test. In Table 2 results of *Z*-test and *t*-test for independent samples are summarised.

Selective attention

There was no significant difference between the ADHD group and the control group with regard to reaction time ($Z = -0.244$; $p = .823$) in the incompatibility task, but significant

Table 2. Results of *Z*-Test and *t*-test for ADHD and control groups with regard to alertness task.

	ADHD group Mean ± SD	Control group Mean ± SD		ADHD group vs control group				
				Z	*p*	*t*	*P*	*d*
Tonic alertness								
Reaction time in ms	342.33 ± 125.92	305.78	87.38	−1.149	.251	1.172	.247	0.96
Variability of reaction time in ms	104.37 ± 90.66	47.65	34.35	−3.018	**.003***	2.829	**.007***	0.83
Number of omission errors	0.11 ± 0.32	0.04	0.21	−0.870	.384	0.868	.390	1.39
Phasic alertness								
Reaction time in ms	306.85 ± 98.46	274.09	71.78	−1.052	.293	1.323	.192	1.04
Variability of reaction time in ms	82.11 ± 68.81	38.87	16.89	−2.765	**.006***	2.935	**.05***	0.86
Number of omission errors	0.15 ± 0.36	0.04	0.21	−1.217	.224	1.223	.227	1.39

*Level of significance $p \leq .05$.

differences in the variability of reaction time ($Z = -4.244$; $p < .001$) as well as the number of omission errors ($Z = -3.755$; $p < .001$) within the same task (see Table 3).

Divided attention

In the *auditory task* we found significant differences between the ADHD group and the control group with regard to reaction time ($Z = -2.735$; $p = .006$), variability of reaction time ($Z = -4.049$; $p < .001$) and number of omission errors ($Z = -6.159$; $p < .001$). Moreover, in the *visual task* we found significant differences between groups with regard to reaction time ($Z = -3.981$; $p < .001$), variability of reaction time ($Z = -4.458$; $p < .001$) and number of omission errors ($Z = -3.857$; $p < .001$). Finally, significant differences between patients with ADHD and HC were observed with regard to total number of commission errors ($Z = -3.705$; $p < .001$) (see Table 3).

Sustained attention

In the sustained attention task the ADHD group did not differ from the control group in reaction time ($Z = -0.710$; $p = .477$), but the patients with ADHD showed a significant higher variability of reaction time ($Z = -3.290$; $p < .001$), as well as increase number of both omission ($Z = -4.332$; $p < .001$) and commission errors ($Z = -4.622$; $p < .001$) when compared to the healthy controls (see Table 3).

Regarding to selective, divided and sustained attention tasks the *t*-test confirmed the significant differences between patients with ADHD and HC emerged through the *Z*-test. In Table 3 results of *Z*-test and *t*-test for independent samples are summarised.

Neurological soft signs

We found significant differences between the ADHD group and the control group with regard to total OM ($Z = -5.460$; $p < .001$), total dysrhythmia ($Z = -5.525$; $p < .001$) and

Table 3. Results of *Z*-Test and *t*-test for ADHD and control groups with regard to different attentional tasks.

	ADHD group Mean ± SD	Control group Mean ± SD	ADHD group vs control group				
			Z	*p*	*t*	*p*	*d*
Selective attention							
Reaction time in ms	531.96 ± 145.03	541.04 ± 119.62	−0.244	.823	−0.239	.812	0.07
Variability of reaction time in ms	156.11 ± 62.55	89.30 ± 30.72	−4.244	**.001***	4.661	**.001***	1.35
Number of omission errors	2.67 ± 4.01	0.17 ± 0.49	−3.744	**.001***	2.958	**.005***	0.87
Divided attention (auditory task)							
Reaction time in ms	879.85 ± 368.33	664.04 ± 117.68	−2.735	**.006***	2.692	**.010***	0.79
Variability of reaction time in ms	335.15 ± 274.97	133.35 ± 64.73	−4.049	**.001***	3.435	**.001***	1.01
Number of omission errors	13.07 ± 4.01	0.35 ± 0.49	−6.159	**.001***	15.107	**.001***	4.45
Divided attention (visual task)							
Reaction time in ms	1115.30 ± 179.87	881.30 ± 163.99	−3.981	**.001***	4.773	**.001***	1.36
Variability of reaction time in ms	437.81 ± 181.59	231.04 ± 98.72	−4.458	**.001***	4.877	**.001***	1.41
Number of omission errors	4.30 ± 2.73	1.52 ± 1.75	−3.857	**.001***	4.190	**.001***	1.21
Divided attention							
Number of commission errors	9.52 ± 11.45	2.39 ± 3.63	−3.705	**.001***	2.862	**.006***	0.84
Sustained attention							
Reaction time in ms	688.00 ± 181.86	701.78 ± 129.83	−0.710	.477	−0.303	.763	0.09
Variability of reaction time in ms	235.89 ± 93.55	150.91 ± 78.52	−3.290	**.001***	3.443	**.001***	0.98
Number of omission errors	22.44 ± 15.10	5.26 ± 6.32	−4.332	**.001***	5.084	**.001***	1.48
Number of commission errors	22.44 ± 15.10	4.35 ± 5.61	−4.622	**.001***	5.428	**.001***	1.59

*Level of significance $p \leq .05$.

total speed of timed activities ($Z = -3.583$; $p < .001$). The *t*-test confirmed the results obtained through the *Z*-test. In Table 4 results of *Z*-test and *t*-test for independent samples are summarised.

Correlations between attentional and motor performances within the clinical group

Regarding *alertness* the correlation analysis according to Kendall showed a significant correlation between the variability of reaction time in the tonic alertness task and total speed of timed activities ($\tau = -0.227$; $p = .05$). Regarding *selective attention* a significant correlation was found between number of omission errors and total dysrhythmia ($\tau = 0.247$; $p = .05$). Regarding *divided attention* significant correlations were observed between total dysrhythmia and number of omission errors in auditory tasks ($\tau = 0.268$; $p = .04$), variability of reaction time in the visual task ($\tau = 0.242$; $p = .05$) and the total number of commission errors ($\tau = 0.288$; $p = .02$). Furthermore, a significant association between the total number of commission errors and total OM, ($\tau = 0.399$; $p < .001$) was observed. Regarding *sustained attention* the correlation analysis according to Kendall revealed significant correlations between reaction time and total speed of timed activities ($\tau = 0.350$; $p < .001$), between number of omission errors and total OM ($\tau = 0.273$; $p = .03$), between number of omission errors and total speed of timed activities ($\tau = 0.260$; $p = .03$), between number of commission errors and total OM ($\tau = 0.273$; $p = .03$), between number of commission errors and total speed of timed activities ($\tau = 0.260$; $p = .03$). In Table 5 results of correlation analysis according to Kendall for ADHD group are summarised.

Discussion

ADHD is a childhood neurodevelopmental disorder, that may persist into adulthood, with deleterious effects on educational and vocational achievement and social adaptation at each developmental stage (Biederman et al., 1996; Weiss & Hechtman, 1993). Disturbances of attention are a core characteristic of children with ADHD (Borger et al., 1999; Heaton et al., 2001; Lockwood et al., 2001; Perugini et al., 2000). The aim of this study was to evaluate attentional function and NSS in a drug-naive sample of children with ADHD and HC and to elucidate a potential relationship between attentional and motor performances in ADHD. Attentional functioning was assessed according to the multidimensional perspective devised by Van Zomeren and Brouwer (1994). All participants

Table 4. Results of *Z*-Test and *t*-test for ADHD and control groups with regard to assessment using PANESS.

	ADHD group Mean ± SD	Control group Mean ± SD	ADHD group vs control group				
			Z	*p*	*t*	*p*	*d*
Total overflow movements							
Total dysrhythmia	6.63 2.44	1.74 ± 1.89	−5.460	**.001***	7.827	**.001***	2.24
Total speed of timed activities	6.52 2.17	1.78 ± 1.65	−5.525	**.001***	8.556	**.001***	2.46
	186.15 26.01	160.74 ± 14.39	−3.583	**.001***	4.169	**.001***	1.21

*Level of significance $p \leq .05$.

Table 5. Results of correlation analysis according to Kendall for ADHD group.

	Total overflow movements		Total dysrhythmia		Total speed of timed activities	
	τ	p	τ	p	τ	p
Tonic alertness						
Reaction time	0.058	.69	−0.009	.95	−0.135	.33
Variability of reaction time	−0.068	.32	−0.015	.46	−0.227	**.05***
Number of omission errors	−0.034	.84	−0.067	.70	0.202	.22
Phasic alertness						
Reaction time	0.133	.36	0.076	.60	0.029	.83
Variability of reaction time	0.083	.28	−0.009	.47	0.060	.33
Number of omission errors	0.084	.63	−0.047	.78	0.095	.56
Selective attention						
Reaction time	0.083	.28	−0.190	.09	−0.172	.10
Variability of reaction time	0.000	.50	−0.051	.36	−0.043	.36
Number of omission errors	−0.017	.46	0.247	**.05***	0.193	.09
Divided attention (auditory task)						
Reaction time	0.120	.20	0.087	.27	0.181	.09
Variability of reaction time	0.034	.41	0.094	.26	−0.026	.43
Number of omission errors	−0.017	.46	−0.268	**.04***	−0.059	.34
Divided attention (visual task)						
Reaction time	0.117	.21	−0.109	.22	0.052	.35
Variability of reaction time	0.190	.09	0.242	**.05***	−0.092	.25
Number of omission errors	0.100	.25	0.038	.40	0.063	.33
Divided attention						
Number of commission errors	0.399	**.001***	0.288	**.02***	−0.023	.43
Sustained attention						
Reaction time	0.160	.13	0.088	.27	0.350	**.001***
Variability of reaction time	0.144	.16	−0.045	.38	0.037	.39
Number of omission errors	0.273	**.03***	0.00	.50	0.260	**.03***
Number of commission errors	0.273	**.03***	0.00	.50	0.260	**.03***

*Level of significance $p \leq .05$.

were assessed with a computerised tests battery, which measure different aspects of attention, such as tonic and phasic alertness, selective attention, divided attention and sustained attention.

Attentional dysfunction in ADHD

The present study revealed that, compared to healthy sex- and age-matched children, patients with ADHD were seriously impaired in a considerable number of attentional processes, including alertness, selective attention, divided attention and sustained attention. Therefore, attentional dysfunction observed in these patients involves aspects of both selectivity and intensity of attention. Compared to healthy subjects, children with ADHD displayed an enhanced variability of reaction time in tasks of tonic and phasic alertness, selective attention and sustained attention. Moreover, children with ADHD showed an increased reaction time and an enhanced variability of reaction time in tasks of divided attention. These findings support previous studies showing an increase of reaction time and/or variability of reaction time in measures of alertness (Barkley, 1977; Cohen & Douglas, 1972; Oommen, Kapur, & Shanmugam, 1993; Van der Meere, Vreeling, & Sergeant, 1992), selective attention (Borger & Van der Meere, 2000; Tucha et al., 2006b; Van der Meere & Sergeant, 1998), divided attention (Tucha et al., 2006b) and sustained attention (Borger et al., 1999; Seidel & Joschko, 1990) and extend the results of our former study on attentional and executive functioning in ADHD. In the latter study children with

ADHD showed an impairment on measures of divided and selective attention, response inhibition and working memory compared to healthy peers. Moreover, the ADHD group displayed an increased variability of reaction time in sustained attention tasks compared to the control group (Pasini, Paloscia, Alessandrelli, Porfirio, & Curatolo, 2007). In our previous study, children with ADHD were markedly impaired in measures of alertness compared to typically developing children and this impairment appears to be due to low levels of arousal (Casagrande et al., 2012). The reaction time is considered a measure of attentional capacity and its variability is a measure of the fluctuation in a subject's efficiency in processing during the course of a continuous task (Van Zomeren & Brouwer, 1994). The reaction time and its variability may be affected by symptoms commonly observed in children with ADHD, including distractibility, deficient self-regulation of motivation and/or impaired perseverance (Barkley, 1998; Solanto, Wender, & Bartell, 1997). Evidence of increased variability of reaction time in ADHD led to the formulation of a mechanicistic hypothesis of default network interference. Sonuga-Barke and Castellanos (2007) postulated that deficient regulation of the default network by cognitive and attention networks underlies intrusions in their interplay that manifest as phasic lapses of attention or in impulsive behaviours (Sonuga-Barke & Castellanos, 2007). This hypothesis was supported by several studies that showed abnormalities involving the default network in subjects with ADHD (Cortese et al., 2012; Elton, Alcauter, & Gao, 2014). According to observations of Tucha and colleagues (2006b), the present study showed that in comparison with healthy peers, children with ADHD displayed a significant impairment of accuracy in all tests performed except alertness task. Indeed, a greater number of omission errors in selective attention task and a greater number of omission and commission errors in the divided and sustained attention task were observed in the ADHD group compared to the control group. Omission errors (lack of response to target stimuli) are considered as a measure of inattention; instead, commission errors (responses to non-target stimuli) are a measure of impulsivity (Matier-Sharma, Perachio, Newcorn, Sharma, & Halperin, 1995; Trommer, Hoeppner, Lorber, & Armstrong, 1988). Attentional processes are mediated by cerebral networks, including several cortical and subcortical brain regions. Alertness functions are supported by reticular formation, dorsolateral prefrontal cortex and inferior parietal cortex (Sturm et al., 1999). Selective attention is related to anterior cingulate gyrus, inferior frontal cortex (left hemisphere) and frontal-thalamic association connections to the reticular nucleus of thalamus (Cabeza & Nyberg, 2000). Divided attention is served by prefrontal cortex (left hemisphere) and anterior cingulate gyrus (Loose, Kaufmann, Auer, & Lange, 2003). Sustained attention is mediated by reticular and intralaminar thalamic nuclei and anterior cingulate gyrus (Cabeza & Nyberg, 2000). Based on our results, it may be hypothesised that all of these cerebral networks are involved in neurobiology of attentional dysfunction in ADHD. This hypothesis is confirmed by structural and functional neuroimaging studies. Indeed, the current body of structural imaging findings provides evidences for a global maturational delay based on reduced grey and white matter volumes and cortical thickness in children with ADHD relative to healthy peers (see review Chandan, 2012). The loci of the reported reductions are in multimodal association cortices such as frontal lobes and its sub-regions, motor and pre-motor cortices, cingulate gyrus, temporal lobes, cerebellum lobes and basal ganglia structures (caudate nucleus, globus pallidus, putamen and ventral striatum). Moreover, there is also evidence for altered maturational courses of selected cerebral regions such

as frontal cortical mantle and caudate nucleus in patients with ADHD relative to healthy controls (see review Chandan, 2012). Findings from functional imaging studies in children with ADHD point to multiple loci of abnormalities, including frontal-striatal-cerebellar networks, parietal-temporal networks, motor and pre-motor circuits and limbic-frontal networks. These brain networks are important for the integrity of executive, attentional, motor and motivational functioning (see review Chandan, 2012). Finally, an increasing number of studies suggests that structural and functional abnormalities in fronto-cortical and fronto-subcortical networks persist into adulthood, despite a relative symptomatic improvement in the adult form of the disorder (see review Cubillo, Halari, Smith, Eric Taylor, & Rubia, 2012).

Motor impairment in ADHD

According to our previous studies (D'Agati et al., 2010; Pasini & D'Agati, 2009; Pasini et al., 2012), the present study revealed that, in comparison to healthy sex- and age-matched children, patients with ADHD performed worse on the PANESS (Denckla, 1985), used to assess motor functioning. Indeed, the ADHD group showed multiple motor abnormalities as compared to the control group. These abnormalities included a greater number of OM, a greater dysrhythmia and a greater motor slowness. These findings are consistent with results of previous investigations, that emphasise the presence of motor dysfunction in children with ADHD. According to these studies, increased OM (Mostofsky et al., 2003; Uslu, Kapci, & Oztop, 2007), impaired timing of motor responses (Rubia et al., 1999), deficits in motor coordination (Watemberg, Waiserberg, Zuk, & Lerman-Sagie, 2007) and deficit in fine motor abilities (Pitcher, Piek, & Hay, 2003) were frequently observed in children with ADHD. Moreover, Meyer and Sagvolden found that children with ADHD performed worse on measure of manual dexterity, motor coordination, movement speed, accuracy and stability of movement in comparison to HC (Meyer & Sagvolden, 2006). OM likely reflects dysfunction within motor and pre-motor circuits that are important for the preparation and execution of motor responses (Cincotta et al., 2002). A functional neuroimaging study showed a smaller extent of activation in the contralateral primary motor cortex in patients with ADHD during performing a simple motor task. It may represent insufficient recruitment of neuronal activity necessary to mobilise transcallosal interhemispheric inhibition (Mostofsky et al., 2006). Dysfunctions in motor and pre-motor circuits, responsible for increased prevalence rate of OM in patients with ADHD, may be due to abnormalities in white matter tracts, including the corpus callosum, important for the effective transfer of transcallosal inhibition (D'Agati et al., 2010; Pasini & D'Agati, 2009). Dysrhythmia may reflect cerebellar dysfunction (Schmahmann, 2004) and slowness of timed activities may be due to functional deficits in frontal-striatal networks, cerebellum and basal ganglia structures (Pasini & D'Agati, 2009).

NSS and attentional dysfunction in ADHD

Given the increased prevalence of NSS in children with ADHD (Denckla & Rudel, 1978; Gillberg, 1998; Rasmussen & Gillberg, 2000; Uslu et al., 2007), it has been hypothesised that these "soft" signs may be indicative of an impaired integrity of attentional processes

and may provide important information about neurobiological bases of ADHD. Therefore, the goal of the present study was to analyse the relationship between attentional processes and motor functioning in the clinical population and particularly in a sample of children with ADHD. Using Kendall's correlation analysis we found significant correlations between disturbances of attentional functioning and motor abnormalities in children with ADHD. Based on our results, deficits of alertness (in terms of increased variability of reaction time) and sustained attention (in terms of an increase of reaction time and number of omission errors) interfere with speed timed activities. Dysfunctions of selective attention (in terms of increased number of omission errors) and divided attention (in terms of increased variability of reaction time in visual tasks and increased number of omission errors in auditory and visual tasks) correlate significantly with dysrhythmia. Impairment of sustained attention (in terms of increased number of omission errors) correlate significantly with OM. Given that selective attention and divided attention are expressions of selectivity and alertness and sustained attention are expressions of intensity of attention (Van Zomeren & Brouwer, 1994), the present study suggest that aspects of intensity are involved in the speed of movement and OM, while aspects of selectivity are involved in the dysrhythmia. Since reaction time, its variability and the number of omission errors are considered a measure of inattention, our findings suggest that there is a link between attentional processes and NSS in children with ADHD. Moreover, our results extend those of a previous study performed by Waber and colleagues in normal school-age children on the role of attentional processes in OM. In this study, in order to investigate the possible link between attentional processes and OM, the authors assessed OM in non-clinical school-aged children, to which were also given a task designed to measure attentiveness to task-relevant or -irrelevant cues. Children who produced high levels of OM were more responsive to task-irrelevant cues (maintained low levels of attention), whereas those produced low levels of OM were more responsive to task-relevant cues (maintained high levels of attention) (Waber et al., 1985). The relationship between reduced attention and increased OM was strengthened by subsequent findings of a reduction but not elimination of OM when participants were asked to inhibit it (Herzog & Durwen, 1992). Moreover, a study by Lazarus and Todor showed that children of all age groups reduced the magnitude of OM when receiving sensory feedback during the task (1992). The significance of mechanisms of attention on OM production is highlighted by a follow-up study performed by Lazarus on OM in young adults with post-acute traumatic left side brain injured. Over three days of training sessions, participants were asked to maintain a percentage of their MVC while involuntary EMG feedback was displayed. Following training, participants were able not only to reduce their overflow but also to maintain this reduction when tested a week later (Lazarus, 1992). Together, these findings that OM may be consciously suppressed emphasise the significance of the attention-OM relationship. In our study, an increased number of commission errors in divided and sustained attention tasks correlate significantly with OM. The commission errors are considered to be a measure of impulsivity, reflecting a general deficit of control in modulating behaviour in response to situational demands and may be affected by impairment of response inhibition (Barkley, 1994, 1997, 1998). This result extends the findings of Mostofsky and colleagues (2003), who observed significant association between OM and response inhibition in children with ADHD, but not in healthy controls, supporting the hypotheses that OM reflect immaturity of cortical systems involved in automatic

inhibition (2003). Finally, based on our data, impulsivity as indicated by an increased number of commission errors in divided and sustained attention interferes with movement speed and is involved in dysrhythmia.

Conclusions

The first strength of our study is the inclusion of a well-defined group of drug-naive children with ADHD, who were carefully screened for other comorbid psychiatric conditions. The second strength of this study is the inclusion of subjects with normal IQ. Indeed, lower IQ appears to be related to increased NSS in children with ADHD (Fellick, Thompsom, Sills, & Hart, 2001). The value of the present results is limited for several reasons. The first limitation of our study is the small sample size, constraining the interpretation of the presented findings. Future studies on a greater sample size will help to expand our knowledge about the role of higher order cognitive mechanisms such as attentional processes in motor functioning and to better understand the link between attentional dysfunction and NSS in clinical populations. The second limitation of this study is the inclusion only of children who met the DSM-IV-TR criteria for ADHD/combined type. So, it was possible to analyse a very homogeneous clinical sample, but it was not possible to study motor and attentional functioning according to the different clinical subtype. Further studies on other clinical subtypes will help to overcome this limitation and in particular future studies should differentiate the motor and attentional functioning according to different subtypes of ADHD. The third limitation of our study is the small number of females in both the clinical group and control group. Therefore, it was not possible to evaluate the effect of gender on motor and attentional performance. Future studies should differentiate the motor and attentional functioning according to the gender. In conclusion, our findings suggest that higher order cognitive mechanisms such as attentional processes could be involved in the pathophysiology of the NSS. Moreover, given the significant correlation between attention deficit and increased number of NSS, our findings add more scientific evidences to the predictive value of NSS as indicators of the severity of functional impairment in children with ADHD and suggest the necessity of including in treatment of patients suffering from ADHD therapeutic measures addressed to their motor development difficulties. It is interesting to note that OM may reflect immaturity and/or dysfunction of the motor/pre-motor circuits involved in motor response inhibition (Mostofsky, Cooper, Kates, Denckla, & Kaufmann, 2002). Deficits of automatic motor inhibition in patients with ADHD may be due to the volume reduction of these cerebral areas caused by the decrease in their white matter components (Ranta et al., 2009), suggesting a primarily axonal abnormality in patients with ADHD. The persistence of OM in patients with ADHD supports the hypothesis that the brain abnormalities in children suffering from this neuropsychiatric disorder have a developmental origin. Oligodendroglial abnormalities may be due to the dysfunction of a DA system (Sokolov, 2007). MPH treatment produces an increase in DA signalling through multiple actions, including blockade of the DA reuptake transporter, amplification of DA response duration, disinhibition of D2r and amplification of DA tone (Wilens, 2008). These effects could be important because D2r receptors are expressed in oligodendrocyte development and may also regulate the outgrowth of neuronal processes. Indeed, marked improvement or complete resolution of NSS following treatment with methylphenidate (MPH) was described in

patients with ADHD (MPH is the most frequently stimulant drug prescribed in the treatment of children with ADHD) (Lerer & Lerer, 1976). Therefore, we suggest that evaluation of NSS is useful to monitor the effectiveness of pharmacological treatment with MPH in children with ADHD. Finally, in order to evaluate whether the reduction of attentional problems produces a reduction of the NSS, future studies should assess motor and attentional functioning of patients with ADHD at baseline and after treatment. In the future fMRI studies could clarify the link between the attentional and motor dysfunction in patients with ADHD.

Disclosure Statement

No potential conflict of interest was reported by the authors.

References

American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorder*. Fourth Edition-Revised DSM-IV-TR.

Barkley, R. A. (1977). The effects of methylphenidate on various types of activity level and attention in hyperkinetic children. *Journal of Abnormal Child Psychology*, *5*, 351–369.

Barkley, R. A. (1994). Impaired delayed responding: A unified theory of attention deficit disorder. In D. K. Routh (Eds.), *Disruptive behaviour disorders in childhood* (pp. 11–57). New York, NY: Plenum Press.

Barkley, R. A. (1997). Behavioral inhibition, sustained attention, and executive functions: Constructing a unifying theory of ADHD. *Psychological Bulletin*, *121*, 65–94.

Barkley, R. A. (1998). *Attention deficit hyperactivity disorder: A handbook for diagnosis and treatment* (2nd ed.). New York, NY: Guilford.

Bezeau, S., & Graves, R. (2001). Statistical power and effect size of clinical neuropsychology research. *Journal of Clinical and Experimental Neuropsychology (Neuropsychology, Development and Cognition: Section A)*, *23*, 399–406.

Biederman, J., Faraone, S., Milberger, S., Curtis, S., Chen, L., Marrs, A., … Spencer, T. (1996). Predictors of persistence and remission of ADHD into adolescence: Results from a four-years prospective follow-up study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *35*, 343–351.

Borger, N., & Van der Meere, J. (2000). Motor control and state regulation in children with ADHD: A cardiac response study. *Biological Psychology*, *51*, 247–267.

Borger, N., Van der Meere, J., Ronner, A., Alberts, E., Geuze, R., & Bodge, H. (1999). Heart rate variability and sustained attention in ADHD children. *Journal of Abnormal Child Psychology*, *27*, 25–33.

Cabeza, R., & Nyberg, L. (2000). Imaging cognition II: An empirical review of 275 PET and fMRI studies. *Journal of Cognitive Neuroscience*, *12*, 1–47.

Casagrande, M., Martella, D., Ruggiero, M. C., Maccari, L., Paloscia, P., Rosa, C., & Pasini, A. (2012). Assessing attentional systems in children with attention deficit hyperactivity disorder. *Archives of Clinical Neuropsychology*, *27*, 30–44.

Chandan, J. V. (2012). Neurodevelopmental abnormalities in ADHD. *Current Topics Behavioral Neuroscience*, *9*, 49–66.

Choen, R. A. (1993). *The neuropsychology of attention*. New York, NY: Plenum Press.

Cincotta, M., Borgheresi, A., Boffi, P., Vigliano, P., Ragazzoni, A., Zaccara, G., & Ziemann, U. (2002). Bilateral motor cortex output with intended unimanual contraction in congenital mirror movements. *Neurology*, *58*, 1290–1293.

Cohen, J. (1988). *Statistical power analysis for the behavioral sciences* (2nd ed.). New Jersey: Lawrence Erlbaum Associates.

Cohen, N. J., & Douglas, V. I. (1972). Characteristics of the orienting response in hyperactive and normal children. *Psychophysiology*, *9*, 238–245.

Cole, W. R., Mostofsky, S. H., Larson, J. C., Denckla, M. B., & Mahone, E. M. (2008). Age-related changes in motor subtle signs among girls and boys with ADHD. *Neurology*, *71*, 1514–1520.

Cortese, S., Kelly, C., Chabernaud, C., Proal, E., Di Martino, A., Milham, M. P., & Castellanos, F. X. (2012). Towards systems neuro science of ADHD: A meta-analysis of 55 fMRI studies. *American Journal of Psychiatry*, *169*, 1038–1055.

Cubillo, A., Halari, R., Smith, A., Eric Taylor, E., & Rubia, K. (2012). A review of fronto-striatal and fronto-cortical brain abnormalities in children and adults with attention deficit hyperactivity disorder (ADHD) and new evidence for dysfunction in adults with ADHD during motivation and attention. *Cortex*, *48*(2), 194–215.

Curatolo, P., Paloscia, C., D'Agati, E., Moavero, R., & Pasini, A. (2009). The neurobiology of attention deficit/hyperactivity disorder. *European Journal of Paediatric Neurology*, *13*, 299–304.

D'Agati, E., Casarelli, L., Pitzianti, M., & Pasini, A. (2010). Overflow movements and White matter abnormalities in ADHD. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *34*, 441–445.

Denckla, M. B. (1985). Revised neurological examination for subtle signs. *Psychopharmacology Bulletin*, *21*, 773–800.

Denckla, M. B., & Rudel, R. G. (1978). Anomalies of motor development in hyperactive boys. *Annals of Neurology*, *3*, 231–233.

Elton, A., Alcauter, S., & Gao, W. (2014). Network connectivity abnormality profile supports a categorical-dimensional hybrid model of ADHD. *Human Brain Mapping*, *35*(9), 4531–4543.

Fellick, J. M., Thompsom, A. P., Sills, J., & Hart, C. A. (2001). Neurological soft signs in mainstream pupils. *Archives of Disease in Childhood*, *85*, 371–374.

Gillberg, C. (1998). Hyperactivity, inattention and motor control problems: Prevalence, comorbidity and background factors. *Folia Phoniatrica et Logopaedica*, *50*, 107–117.

Heaton, S. C., Reader, S. K., Preston, A. S., Fennell, E. B., Puyana, O. E., Gill, N., & Johnson, J. H. (2001). The test of everyday attention for children (TEA-Ch): Patterns of performance in children with ADHD and clinical controls. *Child Neuropsychology (Neuropsychology, Development and Cognition: Section C)*, *7*, 251–264.

Herzog, A. G., & Durwen, H. F. (1992). Mirror movements. In A. B. Joseph & R. R. Young (Eds.), *Movement disorders in neurology and neuropsychiatry* (pp. 704–712). Oxford: Blackwell scientific.

Holden, E. W., Tarnowski, K. J., & Prinz, R. J. (1982). Reliability of neurological soft signs in children: Reevaluation of the PANESS. *Journal of Abnormal Child Psychology*, *10*, 163–172.

Kahneman, D. (1973). *Attention and effort*. Englewood Cliffs, NJ: Prentice-Hall.

Kaufman, J., Birmaher, B., Brent, D., Rao, U., Flynn, Cynthia, Moreci, Paula, … Ryan, Neal (1997). Schedule for affective disorders and schizophrenia for school-age children-present lifetime version (K-SADS-PL): initial reliability and validity data. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*, 980–988.

Larson, J. C., Mostofsky, S. H., Goldberg, M. C., Cutting, L. E., Denckla, M. B., & Mahone, E. M. (2007). Effects of gender and age on motor exam in typically developing children. *Developmental Neuropsychology*, *32*, 543–562.

Lazarus, J. A. C. (1992). Associated movement in hemiplegia-the effects of exerted, limb usage and inhibitory training. *Archives of Physical Medicine and Rehabilitation*, *73*, 1044–1049.

Lazarus, J. A. C., & Todor, J. I. (1992). The role of attention in the regulation of associated movement in children. *Developmental Medicine & Child Neurology*, *33*, 32–39.

Lerer, R. J., & Lerer, M. P. (1976). The effects of methylphenidate on the soft neurological signs of hyperactive children. *Pediatrics*, *57*, 521–525.

Lockwood, K. A., Marcotte, A. C., & Stern, C. (2001). Differentiation of attention-deficit/hyperactivity disorder subtypes: Application of a neuropsychological model of attention. *Journal of Clinical and Experimental Neuropsychology (Neuropsychology, Development and Cognition: Section A)*, *23*, 317–330.

Loose, R., Kaufmann, C., Auer, D. P., & Lange, K. W. (2003). Human prefrontal and sensory cortical activity during divided attention tasks. *Human Brain Mapping*, *18*, 249–259.
Matier-Sharma, K., Perachio, N., Newcorn, J. H., Sharma, V., & Halperin, J. M. (1995). Differential diagnosis of ADHD: Are objective measures of attention, impulsivity, and activity level helpful? *Child Neuropsychology*, *1*, 118–127.
Meyer, A., & Sagvolden, T. (2006). Fine motor skills in South African children with symptoms of ADHD: Influence of subtype, gender, age and hand dominance. *Behavioral and Brain Functions*, *2*, 33.
Mostofsky, S. H., Cooper, K. L., Kates, W. R., Denckla, M. B., & Kaufmann, W. E. (2002). Smaller prefrontal and premotor volumes in boys with attention-deficit/hyperactivity disorder. *Biological Psychiatry*, *52*, 785–794.
Mostofsky, S. H., Newschaffer, C. J., & Denckla, M. B. (2003). Overflow movements predict impaired response inhibition in children with ADHD. *Perceptual and Motor Skills*, *97*, 1315–1331.
Mostofsky, S. H., Rimrodt, S. L., Schafer, J. G., Boyce, A., Goldberg, M. C., & Pekar, J. J. (2006). Atypical motor and sensory cortex activation in attention-deficit/hyperactivity disorder: A functional magnetic resonance imaging study of simple sequential finger tapping. *Biological Psychiatry*, *59*, 48–56.
Nobile, M., Alberti, B., & Zuddas, A. (2007). Conners CK. *Conners' Parents Rating Scales Revised*. Adattamento italiano, Giunti Organizzazioni Speciali, Firenze.
Nobile, M., Alberti, B., Zuddas, A., & Conners, C. K. (2007). *Conners' Teachers Rating Scales Revised*. Adattamento italiano, Giunti Organizzazioni Speciali, Firenze.
Oommen, A., Kapur, M., & Shanmugam, V. (1993). Attention, reaction time and visual-motor integration in hyperkinetic and conduct disordered children. *NIMHANS J*, *11*, 141–147.
Pashler, H. E. (1998). *The psychology of attention*. London: MIT Press.
Pasini, A., & D'Agati, E. (2009). Pathophysiology of NSS in ADHD. *The World Journal of Biological Psychiatry*, *10*(4), 495–502.
Pasini, A., D'Agati, E., Pitzianti, M., Casarelli, L., & Curatolo, P. (2012). Motor examination in children with attention-deficit/hyperactivity disorder and asperger syndrome. *Acta Paediatrica*, *101*, e15–e18.
Pasini, A., Paloscia, P., Alessandrelli, R., Porfirio, M. C., & CURATOLO, P. (2007). Attention and executive functions profile in drug naive ADHD subtypes. *Brain and Development*, *29*, 400–408.
Perugini, E. M., Harvey, E. A., Lovejoy, D. W., Sandstrom, K., & Webb, A. H. (2000). The predictive power of combined neuropsychological measures for attention-deficit/hyperactivity disorder in children. *Child Neuropsychology (Neuropsychology, Development and Cognition: Section C)*, *6*, 101–114.
Pitcher, T. M., Piek, J. P., & Hay, D. A. (2003). Fine and gross motor ability in males with ADHD. *Developmental Medicine and Child Neurology*, *45*, 525–535.
Polanczyk, G., de Lima, M. S., Horta, B. L., Biederman, J., & Rohde, L. A. (2007). The worldwide prevalence of ADHD: A systematic review and metaregression analysis. *American Journal of Psychiatry*, *164*(6), 942–948.
Posner, M. I., & Boies, S. J. (1971). Components of attention. *Psychological Review*, *78*, 391–408.
Posner, M. I., & Rafal, R. D. (1987). Cognitive theories of attention and the rehabilitation of attentional deficits. In M. J. Meier, A. L. Benton, & L. Diller (Eds.), *Neuropsychological rehabilitation* (pp. 182–201). New York, NY: Guilford Press.
Ranta, M. E., Crocetti, D., Clauss, J. A., Kraut, M. A., Mostofsky, S. H., & Kaufmann, W. E. (2009). Manual MRI parcellation of the frontal lobe. *Psychiatry Research: Neuroimaging*, *172*, 147–154.
Rasmussen, P., & Gillberg, C. (2000). Natural outcome of ADHD with developmental coordination disorder at age 22 years: A controlled, longitudinal, community-based study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *39*, 1424–1431.
Rubia, K., Overmeyer, S., Taylor, E., Brammer, M., Williams, S. C., Simmons, A., & Bullmore, E. T. (1999). Hypofrontality in attention deficit hyperactivity disorder during higher-order motor control: A study with functional MRI. *The American Journal of Psychiatry*, *156*, 891–896.

Schmahmann, J. D. (2004). Disorders of the cerebellum: Ataxia, dysmetria of thought, and the cerebellar cognitive affective syndrome. *The Journal of Neuropsychiatry and Clinical Neurosciences*, *16*(3), 367–378.

Seidel, W. T., & Joschko, M. (1990). Evidence of difficulties in sustained attention in children with ADDH. *Journal of Abnormal Child Psychology*, *18*, 217–229.

Shafer, S. Q., Shaffer, D., O'Connor, P. A., & Stokman, C. J. (1983). Hard thoughts on neurological soft signs. In M. Rutter (Ed.), *Developmental neuropsychiatry*, (pp. 133–143). New York: Guilford Press.

Shallice, T. (1982). Specific impairments of planning. In D. E. Broadbent & L. Weiskrantz (Eds.), *The neuropsychology of cognitive function* (pp. 199–209). London: The Royal Society.

Sokolov, B. P. (2007). Oligodendroglial abnormalities in schizophrenia, mood disorders and substance abuse. Comorbidity, shared traits, or molecular phenocopies? *The International Journal of Neuropsychopharmacology*, *10*, 547–555.

Solanto, M. V., Wender, E. H., & Bartell, S. S. (1997). Effects of methylphenidate and behavioral contingencies on sustained attention in attention-deficit hyperactivity disorder: A test of the reward dysfunction hypothesis. *Journal of Child and Adolescent Psychopharmacology*, *7*, 123–136.

Sonuga-Barke, E. J., & Castellanos, F. X. (2007). Spontaneous attentional fluctuations in impaired states and pathological conditions: A neurobiology hypothesis. *Neuroscience & Biobehavioral Reviews*, *31*, 977–986.

Sturm, W., De Simone, A., Krause, B. J., Specht, K., Hesselmann, V., Radermacher, I., … Willmes, K. (1999). Functional anatomy of intrinsic alertness: Evidence for a fronto-parietal-thalamic-brainstem network in the right hemisphere. *Neuropsychologia*, *37*, 797–805.

Trommer, B. L., Hoeppner, J. A., Lorber, R., & Armstrong, K. J. (1988). The go-no-go paradigm in attention deficit disorder. *Annals of Neurology*, *24*, 610–614.

Tucha, L., Tucha, O., Walitza, S., Sontag, T. A., Laufkotter, R., Linder, M., & Lange, K. (2009). Vigilance and sustained attention in children and adult with ADHD. *Journal of Attention Disorders*, *12*, 410–421.

Tucha, O., Prell, S., Mecklinger, L., Bormann-Kischkel, C., Kübber, S., Linder, M., … Lange, K. W. (2006a). Effects of methylphenidate on multiple components of attention in children with attention deficit hyperactivity disorder. *Psychopharmacology*, *185*, 315–326.

Tucha, O., Walitza, S., Mecklinger, L., Sontag, T. A., Kübber, S., Linder, M., & Lange, K. W. (2006b). Attentional functioning in children with ADHD-predominantly hyperactive-impulsive type and children with ADHD-combined type. *Journal of Neural Transmission*, *113*, 1943–1953.

Uslu, R., Kapci, E. G., & Oztop, D. (2007). Neurological soft signs in comorbid learning and attention deficit hyperactivity disorders. *Turkish Journal of Pediatrics*, *49*, 263–269.

Van der Meere, J., & Sergeant, J. A. (1998). Focussed attention in pervasively hyperactive children. *Journal of Abnormal Child Psychology*, *16*, 627–639.

Van der Meere, J., Vreeling, H. J., & Sergeant, J. (1992). A motor presenting study in hyperactive, learning disabled and control children. *Journal of Child Psychology and Psychiatry*, *35*, 1347–1354.

Van Zomeren, A. H., & Brouwer, W. H. (1994). *Clinical neuropsychology of attention*. New York, NY: Oxford University Press.

Vitiello, B., Ricciuti, A. J., Stoff, D. M., Behar, D., & Denckla, M. B. (1989). Reliability of subtle (soft) neurological signs in children. *Journal of the American Academy of Child & Adolescent Psychiatry*, *28*, 749–753.

Waber, D., Mann, M. B., & Merola, J. (1985). Motor overflow and attentional processes in normal school-age children. *Developmental Medicine and Child Neurology*, *27*, 491–497.

Watemberg, N., Waiserberg, N., Zuk, L., & Lerman-Sagie, T. (2007). Developmental coordination disorder in children with attention-deficit-hyperactivity disorder and physical therapy intervention. *Developmental Medicine and Child Neurology*, *49*, 920–925.

Wechsler, D. (1991). *Wechsler intelligence scale for children* (3rd ed.). San Antonio, TX: The Psychological Corporation.

Weiss, G., & Hechtman, L. (1993). *Hyperactive children grown up*. New York, NY: Guilford Press.

Wilens, T. E. (2008). Effects of methylphenidate on the catecholaminergic system in attention-deficit/hyperactivity disorder. *Journal of Clinical Psychopharmacology, 28*, S46–S53.
Zimmermann, P., & Fimm, B. (1993). *A computerized neuropsychological assessment of attention deficits (manual)*. Herzogenrath: PsyTest.
Zimmermann, P., & Fimm, B. (2002). A test battery for attentional performance. In M. Leclercq & P. Zimmermann (Eds.), *Applied neuropsychology of attention: Theory, diagnosis and rehabilitation* (pp. 110–151). New York, NY: Psychology Press.
Zimmermann, P., & Fimm, B. (2012). *Test of attentional performance (Version 2.3)*. Vera Fimm, Psychologische Testsysteme.

Eur Child Adolesc Psychiatry (2016) 25:235–245
DOI 10.1007/s00787-015-0726-0

ORIGINAL CONTRIBUTION

Psychotropic medicine prescriptions in Italian youths: a multiregional study

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Received: 16 December 2014 / Accepted: 18 May 2015 / Published online: 28 May 2015

Abstract The aim of the study was to evaluate the trend of paediatric psychotropic drug prescriptions in Italy. Data sources were regional, outpatient prescription databases. Seven Italian regions, covering 50 % of the Italian population, provided data from 2006 to 2011. Prevalence and incidence of prescriptions by age and gender were evaluated for psychotropic, antidepressant, antipsychotic, and attention-deficit/hyperactivity disorders (ADHD) medications. The hospital admission rate for psychiatric conditions was calculated, also at the local health unit (LHU) level. The presence of trends in prescription prevalence and incidence during the 6 year period was assessed. Finally, the correlation between prevalence, prescription, hospital admission rates, latitude, longitude, and average annual income at the LHU level was also investigated. In 2011, 8834 youths received at least one psychotropic drug prescription, with a prevalence of 1.76 ‰ (95 % CI 1.72–1.80). The incidence of new psychotropic drug users was 1.03 ‰ (1.00–1.06). The prevalence of antidepressants was 1.02 ‰ (0.99–1.04), while that of antipsychotics was 0.70 ‰ (0.68–0.72), and that of ADHD medications 0.19 ‰ (0.18–0.21). The psychotropic drug prevalence increased with increasing age. Males were more exposed to psychotropic drugs than females (AUC0–17 male/female = 1.23). Antipsychotics were the most prescribed psychotropic drugs in males, while antidepressants were in females. Between-region prevalence ranged from 1.56 to 2.17 ‰. The overall prevalence of psychotropic drug from 2006 to 2011 was stable ($\chi_t^2 \leq 0.001$, $p = 0.97$). No correlation was found between prevalence and the variables investigated. Psychotropic drug prescription was very limited and stable. No geographical patterns were found.

Keywords Psychotropic drugs · Pharmacoepidemiology · Child · Adolescent · Outpatients

Introduction

Paediatric psychopharmacology has developed rapidly over the last few decades. Large randomised clinical trials focused on the treatment of a spectrum of psychiatric illnesses—such as hyperactivity disorder (ADHD) [1], bipolar mania [2], behavioural problems associated with autism [3], and depressive [4] and anxiety disorders [5]—have been published, and the emphasis on pharmacological treatments has grown considerably.

As an increasing number of young patients began to receive psychotropic drugs, attention to the safety profile of such drugs in paediatric patients increased. In 2004, the US Food and Drug Administration (FDA) issued a safety warning—the so called "black box" warning—about the twofold higher risk of suicidal behaviour in adolescents receiving antidepressants [6]. Other important safety issues emerged, such as the increasing awareness of adverse metabolic effects of second-generation antipsychotic medicines [7], and the abusive potential of psychostimulants [8, 9]. Since then, paediatric psychopharmacology has become an increasingly relevant component of youths' healthcare, and

On behalf of the Italian Interregional Drug Utilisation Group.

The members of Italian Interregional Drug Utilisation Group are listed in Appendix.

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several drug utilisation studies have been performed with the aim to evaluate psychotropic drug use and prescribing.

Large variations were found in the psychotropic prevalence among youths worldwide [10–18]. Rates in Italy are lower (about 3 ‰) [10] than in Europe and in the USA (up to over 6 %) [11, 12]. The same general trend is noticeable in the different classes of psychotropic medications. For example, the prevalence of antidepressants ranges from over 2 % in the USA [12] and 1.7 % in Denmark [13] to 2.4 ‰ in Italy [10]. Concerning drugs used for ADHD the prevalence ranges from 2 to 4 % in the USA and Iceland, and from 1 to 2 % in Australia, Canada, Israel, and the Netherlands [14–18]. A similar trend was observed for antipsychotics: they are rarely prescribed in Italy (0.7 ‰) [10], while their prevalence is about 1 % in the US [12].

Large differences between countries are also present in terms of policy and resources for care and services for paediatric mental health. Only 1 in every 4 cases has access to services in high income countries [19], while in low and middle income countries the rate can be 20 times lower [20]. These factors, together with many others, contribute to the wide gap observed in treatments worldwide, where in some countries (especially in Europe) children are more likely to be pharmacologically undertreated with respect to their clinical needs, while in the USA, where such drugs are overprescribed, the opposite is true [21, 22]. There is also evidence that the chance of receiving an antidepressant may vary within the same country [23], where policy and organisation of services are expected to be more homogenous. In this context, it is essential to monitor psychotropic drug use in youths.

Data on paediatric psychotropic medication prescription and use in Italy are sparse and not updated [10, 24, 25]. In fact, the only two studies published in the last 5 years reported data of a single region or Local Health Unit [24, 25], and the only study representative of the Italian paediatric population reported 2004 data [10]. Data concerning the psychotropic drug prescription in the general population showed that there are differences in the amount of prescriptions filled at the regional level, and this could reflect differences in the prevalence of psychiatric disorders, and also in the access to psychiatric services [26]. Since a continuous monitoring and surveillance on paediatric psychotropic drug prescription is essential, we analysed the prescription of psychotropic drugs from 2006 to 2011. To assess for the first time differences among regions, we included seven Italian regions belonging to different geographical areas, providing a large—half of the paediatric population—and representative sample of the Italian child and adolescent population. Since there could be differences in the epidemiology of psychiatric disorders, we also collected the hospital admission rates at the regional level as a proxy of severe psychiatric illness in order to compare them to the prevalence of psychotropic drugs.

Methods

The Italian national health system

Italian healthcare is provided free or at a nominal charge through a network of 145 LHUs (Local Health Units). Every Italian resident is registered with a family (paediatric or general) practitioner. Children are assigned to a paediatrician until they are 6 years old; afterwards, the parents can choose to register a child with a general practitioner. A national formulary is available, in which medications are categorised into two classes: class A includes essential drugs reimbursed by the national health system (NHS), and class C contains drugs not covered by the NHS. Antidepressants, antipsychotics, and ADHD medications are reimbursed by the Italian NHS with the exception of oxitriptan and hypericum. Other psychotropic drugs such as anxiolytics, hypnotics and sedatives are not reimbursed by the NHS, and thus were excluded from this study.

Data source

Data sources were regional databases routinely updated for administrative and reimbursement reasons. The databases store all outpatient (i.e. outside the hospital) prescriptions reimbursed by the NHS.

In November 2013, Italian researchers who were part of the ENCePP® (European Network of Centres for Pharmacoepidemiology and Pharmacovigilance) network [27] were asked to participate in the study.

Seven of the eleven regions contacted participated in the study: Veneto, Lombardy, Friuli Venezia Giulia, Emilia Romagna, Abruzzo, Lazio and Puglia (69 LHUs). The centres involved have a long-standing experience in pharmacoepidemiological studies, and in the analysis of health administrative databases. Each researcher provided the prescription data concerning psychotropic drug prescriptions for the paediatric outpatient population (<18 years old) in his own region, through an agreement with the Regional Ministry of Health. For the Veneto region, data were provided for 15/22 LHUs (597,596 children and adolescents, 77 % of the regional population), which were those included in the CINECA consortium, a National Interuniversity Consortium constituted with the purpose of providing a friendly and efficient database that collects and monitors the general practitioners' prescriptions [10]. All regions provided data from 2006 to 2011.

For the Abruzzo region, data for years 2010–2011 were provided.

The study population in 2011 was composed of 5,019,564 youths less than 18 years of age living in the regions participating, representing 50.2 % of the Italian population of this age. The regions were representative of different geographic areas: North of Italy (Friuli Venezia Giulia, Lombardy, Emilia Romagna and Veneto, 71.2 % of the North population), Centre (Lazio, 49.9 %), and South (Puglia and Abruzzo, 36.5 %). The seven regions had different economic backgrounds. In particular, the mean annual income per resident in 2011 in Italy was 12,159 €, and ranged from 8,382€ (Puglia) to 15,502€ (Lombardy), source: Italian ministry of Economy and Financial Affairs. Aggregated, anonymous data were provided so ethical approval was not required.

Psychotropic drugs were defined according to the World Health Organization categories and comprised the following subgroups of the Anatomic Therapeutic Chemical (ATC) classification system: antipsychotics (N05A), antidepressants (N06A) and centrally acting sympathomimetics (ADHD medications, N06BA). Anticonvulsants (N03 subgroup) were excluded because in children they are mainly used to treat epilepsy, while anxiolytics, sedatives, and hypnotics were excluded because they are not reimbursed by the Italian NHS, and thus not retrieved in the database, as stated above.

Data concerning hospital admissions for psychiatric diagnoses were also collected at the regional level as a proxy of severe psychiatric illness in order to compare them to the prevalence of psychotropic drugs. To this purpose, the following ICD-9 (the International classification of diseases, 9th revision) codes were considered: 290–319.

Data analysis

For 2011, the following outcome measures were calculated by age and gender for the overall sample and for each region:

Prevalence of current users, defined as the number of individuals who received at least one psychotropic drug prescription per 1000 youths;
Incidence of new users, defined as the number of people who received a psychotropic drug prescription for the first time (did not receive it during the previous year) per 1000 youths;
Prescription rate, defined as the number of prescriptions per youth treated with at least one psychotropic drug in 1 year;
Hospital admission rate, defined as the number of resident youths admitted to hospital due to any psychiatric illness at least once in 1 year per 1000 youths.

For the 10 most prescribed psychotropic drugs in 2011, the prevalence was calculated for the following age strata: 0–5, 6–11, and 12–17 years old. Furthermore, the percentage of treated youths (number of children and adolescents who received at least one prescription of a certain drug, divided by the number of children that received any psychotropic drug prescription during 1 year) was calculated for each active substance.

For 2011, the main indicators (not stratified by age and gender) at the LHU level were retrieved. A choropleth map of prevalence at the LHU level was created using the software Arcmap version 10.1. The prevalence values were categorised into three classes calculated on the basis of the mean ± one standard deviation (SD).

The temporal utilisation trend of psychotropic drugs in youths in the period 2006–2011 was analysed. Prevalence, incidence, prescription, and hospital admission rates were calculated for all psychotropic drugs and for antipsychotics, antidepressants, and ADHD medications separately. The 5-year cumulative incidence of psychotropic medications was calculated for the 2007–2011 period.

The coefficient of variation (CV) was used to assess the variability in prevalence reported by LHUs among regions. The Welch's ANOVA and the Tukey post hoc tests were used to compare the prevalence reported by LHUs in the included regions. The Chi squared for linear trend (χ^2 trend) test was used to investigate the presence of a trend in the prevalence of psychotropic, antidepressant, antipsychotic and ADHD medications over the years in the whole population studied and in each region. The area under the prevalence–time curve (AUC) was calculated according to the linear trapezoidal rule for the intervals: 0–5, 6–11, 12–17 years in respect to gender. The Pearson test was used to investigate the correlation between prevalence and prescription, hospital admission rates, latitude, longitude and average annual income at the LHU level. A p value <0.05 was considered statistically significant. Statistical analysis was performed using SAS software, version 9.2 (SAS, Cary, NC, USA).

Results

Overall study population

During 2011, 8,834 youths received at least one psychotropic drug prescription. The prevalence was 1.76 ‰ (95 % CI 1.72–1.80), Table 1.

Antidepressants were prescribed to 5100 youths (1.02 ‰; 95 % CI 0.99–1.04), antipsychotics to 3512 youths (0.70 ‰; 95 % CI 0.68–0.72), and ADHD medications to 976 youths (0.19 ‰; 95 % CI 0.18–0.21). The mean number of prescriptions per treated youth was 4.4 for

Table 1 Number of youths 0–17 years old, number of Local Health Units (LHUs), average prevalence of prescription, prescription and hospital admission rate percentage by region, ordered by decreasing latitude from top to bottom (year 2011)

Regions	Population (*n*)	LHUs (*n*)	Prevalence				Prescr. rate	Hospital admission rate	
			(‰)	95 % CI	Range by LHUs	Male/female ratio		(‰)	95 % CI
FVG[a]	184,553	6	2.17	1.96–2.39	1.87–2.51	1.35	4.41	3.82	3.54–4.11
Veneto	597,596	15	1.57	1.47–1.67	1.07–2.25	1.36	4.46	3.40	3.25–3.55
Lombardy	1,688,543	15	1.56	1.50–1.62	1.09–2.78	1.26	4.33	1.12	1.07–1.17
E.Romagna	695,043	11	1.97	1.87–2.08	0.97–2.30	0.97	3.87	0.66	0.60–0.73
Abruzzo	205,774	4	1.88	1.69–2.06	1.39–2.68	1.50	5.36	0.89	0.77–1.02
Lazio	925,339	12	1.96	1.87–2.05	1.43–2.22	1.28	4.24	0.60	0.55–0.65
Puglia	722,716	6	1.78	1.68–1.87	1.54–2.11	1.53	5.33	1.75	1.65–1.85
Total	5,019,564	69	1.76	1.72–1.80	0.97–2.78	1.27	4.45	1.41	1.38–1.45

[a] Friuli Venezia Giulia

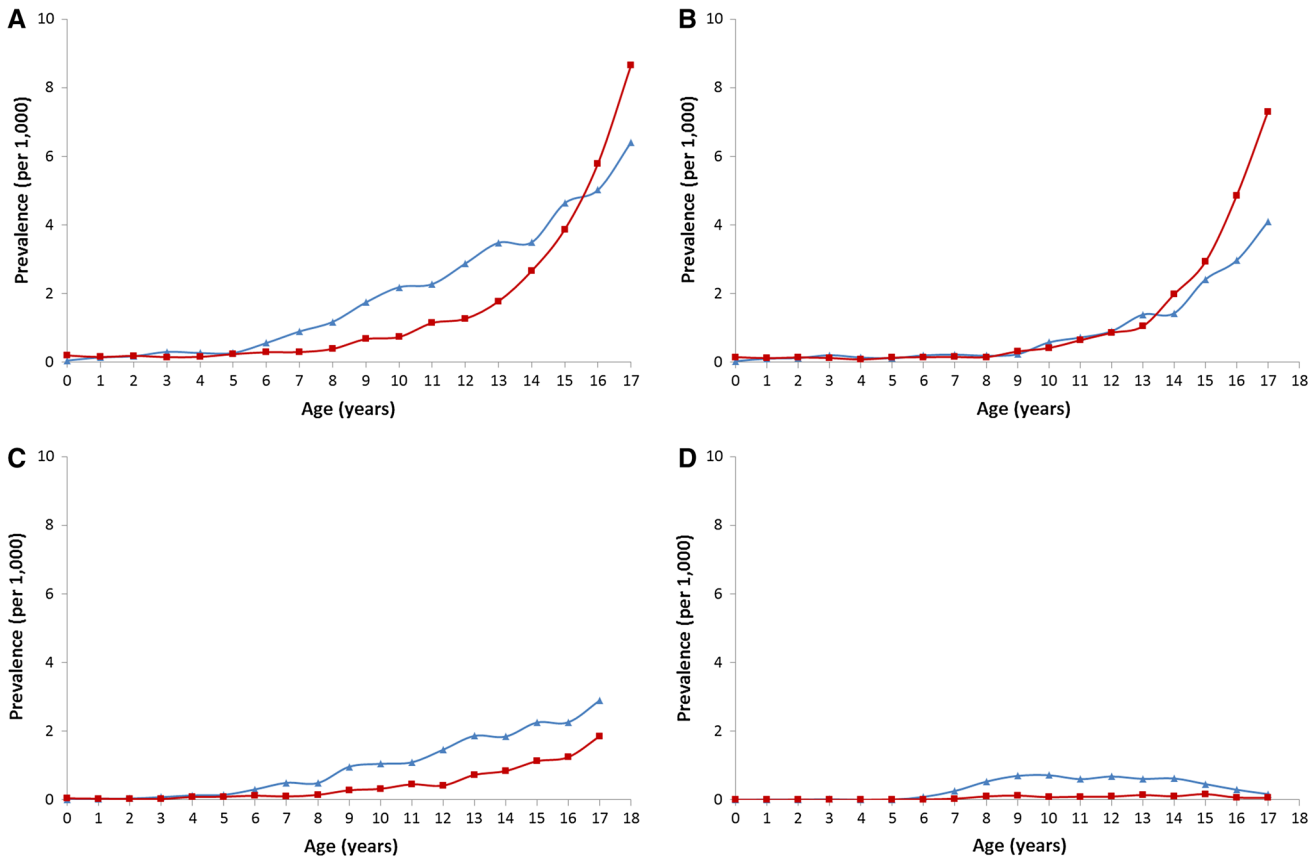

Fig. 1 Prevalence (per 1,000) by age and gender (male: *blue lined triangle*; female: *red lined square*) of overall psychotropic drugs (**a**), antidepressants (**b**), antipsychotics (**c**), and ADHD medications (**d**)

psychotropic drugs, and ranged from 3.2 for antidepressants to 6.0 for ADHD medications.

The psychotropic drug prevalence increased by increasing age following an exponential trend, both in males and females, with negligible exposure in the first year of life and a rate of 7.5 ‰ at 17 years old, Fig. 1. While antidepressants were the most prescribed psychotropic drug class in the overall population and in females($AUC_{N06A/all\ psychotropic\ drugs} = 0.76$), antipsychotics were the most prescribed psychotropic drugs in males ($AUC_{N05A/all\ psychotropic\ drugs} = 0.48$). The prevalence of psychotropic medications was similar for males and females up to 5 years old, higher

Table 2 The prevalence per 10,000 resident youths of the ten most prescribed psychotropic drugs in 2011 by age group

Drug							
0–5		6–11		12–17		0–17	
Trazodone	0.310	Risperidone	3.31	Sertraline	8.77	Risperidone	3.68
Risperidone	0.240	Methylphenidate	2.12	Risperidone	7.70	Sertraline	3.22
Escitalopram	0.181	Sertraline	1.01	Fluoxetine	3.37	Methylphenidate	1.27
Citalopram	0.158	Atomoxetine	0.63	*Paroxetine*	3.30	Fluoxetine	1.20
Sertraline	0.135	Periciazine	0.36	*Escitalopram*	2.26	*Paroxetine*	1.17
Venlafaxine	0.111	*Pimozide*	0.36	Aripiprazole	2.24	Amitriptyline	0.75
Duloxetine	0.100	*Amitriptyline*	0.34	*Citalopram*	1.78	*Escitalopram*	0.70
Paroxetine	0.082	*Aripiprazole*	0.23	Methylphenidate	1.57	Aripiprazole	0.69
Periciazine	0.053	*Haloperidol*	0.20	Olanzapine	1.17	*Citalopram*	0.57
Quetiapine	0.041	Chlorpromazine	0.18	Atomoxetine	0.66	*Olanzapine*	0.42

Drugs not approved for use in each age group are reported in italic, all values are ×10,000

in males in the 5–15 year range, and higher in females afterwards. Males were more exposed to psychotropic drugs than females ($AUC_{0–17}$ male/female = 1.23), particularly in the school age ($AUC_{6–11}$ male/female = 2.52). The disproportion was particularly evident for ADHD medications ($AUC_{0–17}$ male/female = 5.06) and antipsychotics ($AUC_{0–17}$ male/female = 2.16). Females were more exposed to antidepressants than males ($AUC_{0–17}$ male/female = 0.74). With antidepressants, the trend by gender and age was very similar that of psychotropic drugs, and began to increase in pre-adolescents, with females receiving more antidepressants than boys after 15 years of age (Fig. 1). The prevalence of antipsychotics began to increase in school-aged children, with males being more exposed than females at any age. For ADHD medications, the highest prevalence was in 9 year old children, particularly males, while the female prevalence was negligible at any age (Fig. 1).

The incidence of psychotropic drug prescriptions was 1.03 ‰ (95 % CI 1.00–1.06), with no significant differences between males and females ($AUC_{0–17}$ male/female = 1.02; 95 % CI 1.00–1.05). The incidence of antidepressants was 0.69 ‰ (95 % CI 0.67–0.72), while that of antipsychotics was 0.32 ‰ (95 % CI 0.31–0.34), and that of ADHD medications 0.08 ‰ (95 % CI 0.07–0.09). The 5-year cumulative incidence of psychotropic medications in the 2007–2011 period was 4.29 ‰, with a total of 26,142 incident cases.

The hospital admission rate was 1.41 ‰ (95 % CI 1.38–1.45). In 2011, a total of 20 different drugs were among the list of the ten most prescribed psychotropic drugs in the participating regions, Table 2. The most prescribed psychotropic drug was risperidone (20.6 % of children treated with psychotropic drugs), followed by sertraline (18.0 %), and methylphenidate (7.1 %).

Regional profile

During 2011, the prevalence of psychotropic drugs ranged from 1.56 ‰ (95 % CI 1.50–1.62) in the Lombardy region to 2.17 ‰ (95 % CI 1.96–2.39) in the Friuli Venezia Giulia region, Table 1. At the LHU level, the prevalence ranged from 0.97 to 2.78 ‰, Table 1 and Fig. 2. The CV of regional prevalence ranged from 0.13 in the Friuli Venezia Giulia region to 0.29 in the Abruzzo region. The number of prescriptions per youth ranged from 3.87 in Emilia Romagna to 5.36 in Abruzzo. The incidence rates were more homogenous and ranged from 0.86 ‰ (95 % CI 0.78–0.93) in the Veneto region to 1.27 ‰ (95 % CI 1.20–1.35) in the Lazio region. The hospital admission rates ranged from 0.60 ‰ in Lazio (95 % CI 0.55–0.65) to 3.83 ‰ (95 % CI 3.54–4.11) in Friuli Venezia Giulia.

Risperidone was the most prescribed psychotropic drug in five out of seven regions, Table 2. The only two active substances that were among the 10 most prescribed in all regions were risperidone and sertraline. In fact, risperidone, along with methylphenidate and paroxetine, were among the 10 most prescribed active substances in six out of seven regions.

The Welch's ANOVA analysis found a significant difference between regions in the prevalence by LHUs ($F = 3.16$, $p = 0.03$). The post hoc analysis found a significant difference between the prevalence of Friuli Venezia Giulia and Emilia Romagna regions (mean difference = 0.57 ‰; 95 % CI 0.01–1.12). There was no significant correlation between prevalence and prescription rates ($R_P = 0.05$; $p = 0.66$), latitude ($R_P = -0.10$; $p = 0.42$), longitude ($R_P = 0.17$; $p = 0.16$), average annual income ($R_P = 0.10$; $p = 0.42$) or hospital admission rates ($R_P = 0.21$; $p = 0.08$).

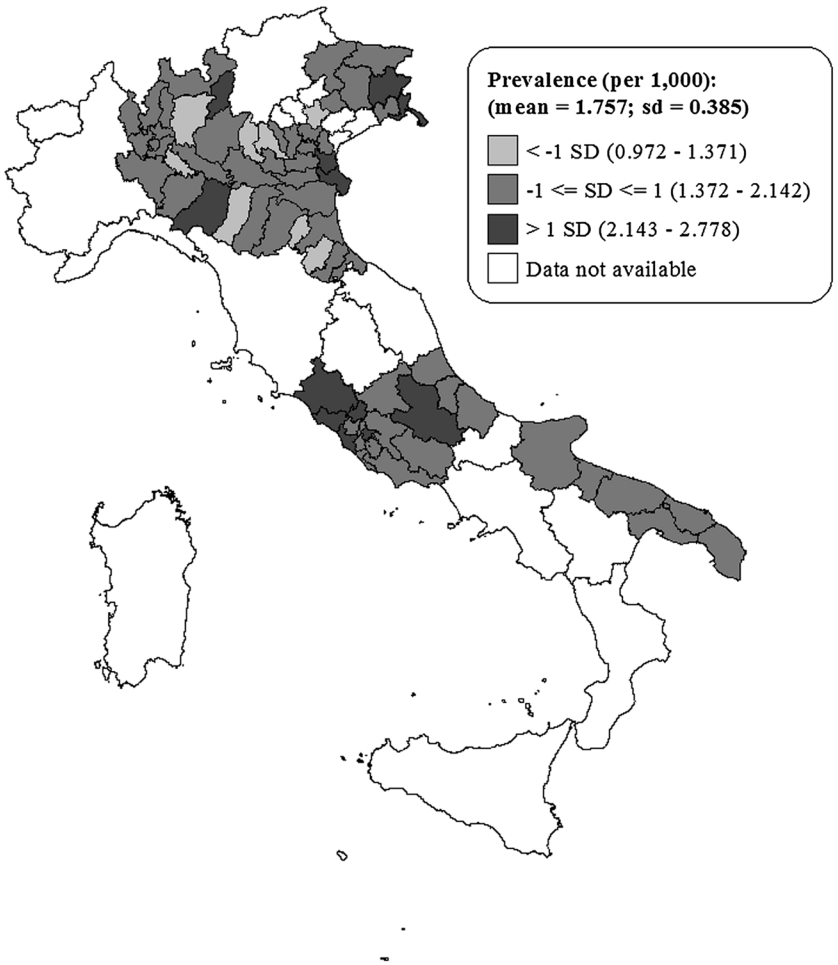

Fig. 2 Choropleth map of the participating regions and Local Health Units (LHUs). The values of prevalence were categorised into three classes calculated on the basis of the mean ± 1 SD

Temporal trend

The overall prevalence of psychotropic drug prescription from 2006 to 2011 was stable, and no significant trend was found ($\chi_t^2 = 0.001$; $p = 0.97$). There was a slight increase in antipsychotic prevalence ($\chi_t^2 = 32.4$; $p < 0.001$) from 0.60 to 0.69 ‰, and a decrease in antidepressants prevalence ($\chi_t^2 = 187$; $p < 0.001$) from 1.26 to 1.02 ‰. An increase was observed in ADHD medication prevalence ($\chi_t^2 = 1065$; $p < 0.001$), from 0.01 to 0.19 ‰, Table 3. The incidence of new psychotropic drug users decreased from 2006 to 2011 ($\chi_t^2 = 60{,}3$; $p < 0.001$) from 1.15 to 1.03 ‰. The same trends were observed in the incidence of new users considering each class of psychotropic drugs.

There was a significantly increasing trend in psychotropic drug prevalence in Friuli Venezia Giulia, from 1.68 to 2.17 ‰, and Veneto, from 1.30 to 1.57 ‰, (respectively $\chi_t^2 = 14.3$ and $\chi_t^2 = 31.6$; $p < 0.001$), while a slightly decreasing trend was present in Emilia Romagna ($\chi_t^2 = 5.27$ $p = 0.021$) with the prevalence shifting from 2.16 to 1.98 ‰. The prevalence observed in the other regions did not show significant trends.

The hospital admission rate decreased slightly ($\chi_t^2 = 5.30$ $p = 0.02$) from 1.49 in 2006 to 1.44 in 2011.

Discussion

This is the largest pharmacoepidemiological study evaluating psychotropic drug prescription in the Italian paediatric population, including multiple regions and covering half of the Italian population of this age.

Considering the 2011 data, the overall prevalence found was very low compared to those from epidemiological studies in most other countries [11, 12, 14, 15, 23, 28–41]. In particular, rates of prescribing of stimulants in Italy were much lower than that of other regions of the world. Stimulants were prescribed to 0.19/1000 children less than 18 years in Italy and to 42/1000 children in the USA who were commercially insured. Rates of prescribing of other medications in other countries to children (<18 years) are shown in Table 4.

Several reasons for the different prescription rates of psychotropic medications between countries have been

Table 3 Prevalence and incidence rate of psychotropic medicine prescriptions in youths <18 years, 2006 to 2011

	2006 $n = 4,569,190$	2007 $n = 4,641,857$	2008 $n = 4,688,005$	2009 $n = 4,752,154$	2010 $n = 4,991,496$	2011 $n = 5,019,564$
Antipsychotics						
Prevalence	0.60	0.62	0.65	0.65	0.65	0.69
Incidence	0.28	0.32	0.31	0.31	0.30	0.32
Antidepressants						
Prevalence	1.26	1.22	1.14	1.16	1.03	1.02
Incidence	0.92	0.89	0.81	0.84	0.72	0.70
ADHD medications						
Prevalence	0.01	0.04	0.11	0.14	0.16	0.19
Incidence	0.00	0.03	0.08	0.06	0.06	0.08
Any psychotropic						
Prevalence	1.74	1.74	1.76	1.81	1.70	1.75
Incidence	1.15	1.18	1.14	1.15	1.02	1.03

Values are expressed as rate per 1,000 children; (number of children)

Table 4 Prevalence rates (‰) of antidepressants (AD drugs), antipsychotics (AP drugs), and ADHD medications observed in ≤18 years old in western countries in the last 10 years

Country	AD drugs	AP drugs	ADHD drugs
USA (New England)	27–38 (2007–2010)[a]	7–26 (2007–2010)[a]	42–77 (2007–2010)[a]
UK	n.a.	0.77 (2005)	9.2 (2008)[b] 7.4 (2008)[c]
Germany	4.8 (2010)	3.2 (2012)	n.a.
The Netherlands	2.0 (2005)	6.8 (2005)	21 (2007)[d]
France	3 (2010)	3 (2010)	2 (2010)
Denmark	2.67 (2010)	2.05 (2010)	7.29 (2010)
Iceland	n.a.	n.a.	12.5 (2007)
Finland	5.93 (2005)	n.a.	1.2 (2007)
Sweden	n.a.	n.a.	2.5 (2007)
Norway	7.0 (2010)	n.a.	4.7 (2007)
Canada	15.4 (2007)	7.4 (2008)	21 (2007)
Italy	**1.02 (2011)**	**0.70 (2011)**	**0.19 (2011)**

Data concerning Italian children are reported in bold characters

[a] Prevalence for commercially insured patients (lower value) and medicaid-insured patients (higher value)

[b] 6–12 years old

[c] 13–17 years old

[d] 6–17 years old

proposed in the literature, the most common of which are differences in policy, regulation, and access to mental health services [21, 22]. Other important factors are cultural (i.e. perceived misuse of psychotropic medication in youths, possible adverse effects, etc.), but also include the role of non-pharmaceutical alternatives, and, ultimately, the uncertainty of indications (i.e. difficulty in deciding where to place cutoffs for the prescription of a drug) [22]. The observed, quite homogeneous and limited, prescription of psychotropic medications could be due to a generalised concern about psychotropic medications in children, at least in Italian parents [21]. For the same reasons, non-pharmacological treatments might be preferred in Italy, where drug therapy is reserved only to a small fraction of the children attending mental care services [24]. On the other hand, a study conducted in the Lombardy region showed that the majority of adolescents receiving antidepressant drugs were not followed by a child and adolescent psychiatrist, and this is clearly alarming [24].

A previous multiregional study that used a different database and sample population already analysed psychotropic drug prescriptions in Italian youths, in the 1998-2004 period [10]. By merging data from the two studies the prevalence of psychotropic medications was found to increase in 2001 and reach 3.08 ‰ in 2002 [10], then decrease to 1.76 ‰ in 2006, and afterwards remain quite stable. After the statement about the increased risk of suicidal in adolescents receiving SSRIs, the amount of psychotropic drugs relevantly decreased. The plateau trend observed in the years afterwards is different from what was observed in other countries, where psychotropic prevalence, especially antidepressants, started to climb again, this fact is discussed further later on [13, 15, 28, 34–39]. Even if we have no data to demonstrate this, we can speculate that the safety issue about SSRIs further increased the suspiciousness about paediatric psychotropic drug treatment and prevented the prevalence to reach the levels observed in the previous years like in other countries.

The analysis of prevalence by age and gender shows different utilisation patterns among males and females, which somewhat reflect the differences in terms of prevalence of mental diseases, with antipsychotics and ADHD medications prescribed more in males at all ages, and antidepressants prescribed more in adolescent females. Although the

amount of psychotropic drug prescriptions in Italian children is limited, a majority is represented essentially by antidepressant prescriptions for adolescent females.

Considering the single classes, there was a decreasing prevalence of antidepressants and a large increase in the prevalence of drugs used for ADHD. The reasons behind the large increase in ADHD medications are that the marketing authorization of methylphenidate and atomoxetine in Italy was granted in 2007. The prevalence in 2011, however, is still very low compared to other countries [14–18, 42]. The limited prescription of ADHD medications is partly due to the fact that in Italy the prescription requires strict diagnostic assessment and continuous monitoring [43, 44]. Drugs can be prescribed by child psychiatrists with expertise in ADHD treatment, after a standardised diagnostic process [43]. It is also possible that the prevalence of ADHD might be lower than in other countries. In fact, in recent studies the prevalence of ADHD ranged from 0.5 % [44], considering only those patients accessing child psychiatric services, to about 1 % (surveys) [45, 46]. Moreover, Italian youths with ADHD tend to be treated more frequently with non-pharmacological approaches, and, only in case of severe impairment, with a pharmacological treatment. A recent survey estimated that about 1 in 4 children with diagnosed ADHD receives drug therapy [43]. Furthermore, in Italy there are no external determinants that may increase pressure on drug prescription such as school, or insurance, like in other countries.

Despite their decreasing prevalence, antidepressants are still the most prescribed class of psychotropic medication, especially in adolescents. The negative trend observed could be partly explained by the fact that in Europe the warning concerning the higher risk of suicidal behaviour in adolescents treated with some SSRIs was issued in April 2005 [47], which was the beginning of our observation period. Nevertheless, the observed data are in contrast with what is shown in other European countries concerning antidepressant prescription in youth. In fact, for example, in Denmark there was a linear increase in the prevalence from 1996 to 2010 [27], and in UK [48] and Germany [23] there was a decrease only in the years around the 2002–2006 period (and was very marginal in Germany), after which prevalence rose again. The overall prevalence observed in this study is twofold lower than that in Denmark and UK in the same years, and about fivefold lower than the prevalence observed in Germany.

The most prescribed antidepressant was sertraline, which is approved for obsessive–compulsive disorder in children older than 6 years of age. The data are different from Germany, for example, where the most prescribed antidepressant in all age groups was fluoxetine [23].

In comparison with recent studies showing large increases in the use of antipsychotics in youths worldwide [27, 49–52], a modest increase in the study period was observed. Risperidone was the most prescribed antipsychotic, as well as the most prescribed psychotropic medication in the overall population and in school-aged children. In Italy, risperidone is approved for conduct disorder and is used mostly to treat autism-related symptoms, in particular aggressive behaviour.

Four out of the ten most prescribed psychotropic drugs were prescribed off-label by age: three SSRIs (paroxetine, escitalopram, and citalopram) and one antipsychotic (olanzapine). Besides these drugs, also pimozide and haloperidol are not approved in youths in Italy, amitriptyline is approved for adolescents older than 12 years of age, and aripiprazole for those older than 15. These drugs were, nevertheless, among the ten most prescribed in school-aged children. Similar results in terms of off-label use were observed in other international studies [53–55].

When looking at the geographical distribution of psychotropic drug prescriptions no clusters were identified. At the regional level, the most relevant difference was between Friuli Venezia Giulia and the rest of the regions, and, when comparing the distribution of prevalence at the LHU level by regions, only a tiny statistical difference was found. The prevalence of psychotropic drug prescriptions did not correlate with latitude or longitude, nor with annual income. On the contrary, a north–south trend and an inverse correlation between prevalence and annual income was found in studies evaluating the pattern of prescription of antibiotics and antiasthmatics [56, 57].

In particular, when comparing the regional distribution of overall prevalence of drug prescription observed in a previous study [58] with the prevalence of psychotropic medicines no correlation is found. This fact suggests that psychotropic prescribing pattern is different from that of other medicines prescribed in youths. It is likely that local differences in cultural factors, prescribing attitude, and environmental setting play a less important role in psychotropic drug prescription compared to other, more widely used, drug classes. These facts strengthen the hypothesis of a more homogeneous, or differently distributed, prescribing attitude concerning psychotropic drugs. Since in this study the diagnosis corresponding to each prescription was not available, we compared the psychotropic drug prevalence and hospital admission rates for psychiatric disorders at the regional level in order to investigate a possible correlation. The correlation was not found; hence, we could deduce that the regional differences observed in the epidemiology of severe psychiatric diseases alone may not explain the differences in drug prescriptions, but other factors may play a role.

Looking at the distribution of active substances by region, it was quite unexpected that only four active substances (risperidone, sertraline, methylphenidate, and paroxetine) are among the ten most prescribed in six out

of seven regions, and only risperidone and sertraline are among the most prescribed in all the regions. This geographic variability in the choice of psychotropic medicines is particularly evident for SSRIs and is probably due to prescriber attitude (e.g. medical specialty) and local variability in the marketing of different active substances. However, previous studies showed that in Italy about 3 out of 4 antidepressant prescriptions to children and adolescents are filled by general practitioners without the supervision of a child and adolescent psychiatrist [24, 25]. It is, therefore, likely that general practitioners prescribed adolescents the same active substances they usually prescribe to adults. It is striking that paroxetine, which is not approved for use in youths, is among the most prescribed active substances in six out of seven regions, while fluoxetine, which is approved for major depressive disorder in children older than 8 years of age, is not.

The major strength of this study is the fact that it is a large multiregional study, and that the regions included were representative of different socio-demographic and geographic settings, and covered about half of the Italian paediatric population. Some limitation must be considered, however. We were able to include only seven regions and not the overall paediatric Italian population; however, we included a representative sample of regions belonging to different geographic areas and with different socioeconomic backgrounds. It would be plausible to state that in our sample the South of Italy is a bit underrepresented; however, the two regions included almost 40 % of the overall South population.

Since we used drug prescription as a proxy of pharmacological treatment, it was not possible to assess if the drug was actually consumed by patients, and this is a limitation. However, this limitation does not influence the results of the study, since its aim was to monitor prescribing, and not consumption trends. Another possible limitation is the fact that only reimbursed prescriptions were included, excluding out-of-pocket dispensation and those filled by private practices. However, these phenomena are likely to be negligible for reimbursed drugs. Anxiolytics, sedatives, and hypnotics were not retrieved in the database used for this study, leading to an underestimate of the overall prevalence. However, this class of drugs should not account for a large proportion of psychotropic drugs in children, as shown in a recent Danish study [27]; the underestimate should therefore be marginal. Nevertheless, the prevalence of each single class of psychotropic drugs is lower in Italy than in other countries, as previously described. Information on the diagnosed diseases for which a drug was prescribed was not available, and precluded any evaluation of the appropriateness of prescribing. This is, however, an intrinsic limitation of most pharmacoepidemiological studies using prescription databases. Some data were not available concerning the Abruzzo region, as described in the methods section, leading to the exclusion of youths living in the Abruzzo region for the temporal trend analyses.

Conclusions

In this large pharmacoepidemiological study including about half of the Italian youth population, the prevalence of psychotropic drugs observed was substantially lower than in other countries and remained stable during the observation period. No significant clusters were found in the geographic distribution of psychotropic drug prescriptions, differently from what was observed for other classes of medicines, showing a quite uniform, limited prescription of psychotropic medications.

Acknowledgments We wish to thank the "Italian Interregional Drug Utilisation Group" for their helpful collaboration. We are grateful to Chiara Pandolfini for language editing.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical standards The manuscript does not contain clinical studies or individual patient data.

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References

1. The MTA Cooperative Group (1999) Multimodal treatment study of children with ADHD. A 14-month randomized clinical trial of treatment strategies for attention-deficit/hyperactivity disorder. Arch Gen Psychiatry 56:1073–1086
2. Tohen M, Kryzhanovskaya L, Carlson G et al (2007) Olanzapine versus placebo in the treatment of adolescents with bipolar mania. Am J Psychiatr 164:1547–1556
3. McCracken JT, McGough J, Shah B et al (2002) Research units on pediatric psychopharmacology autism network. Risperidone in children with autism and serious behavioral problems. N Engl J Med 347:314–321
4. March J, Silva S, Petrycki S et al (2004) Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: treatment for adolescents with depression study (TADS) randomized controlled trial. JAMA 292:807–820
5. Walkup JT, Albano AM, Piacentini J et al (2008) Cognitive behavioral therapy, sertraline, or a combination in childhood anxiety. N Engl J Med 359:2753–2766
6. Hammad TA, Laughren T, Racoosin J (2006) Suicidality in pediatric patients treated with antidepressant drugs. Arch Gen Psychiatry 63:332–339
7. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists (2004) North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 27:596–601
8. McCabe SE, Teter CJ, Boyd CJ, Guthrie SK (2004) Prevalence and correlates of illicit methylphenidate use among 8th, 10th, and 12th grade students in the United States, 2001. J Adolesc Health 35:501–504
9. Stoops WW, Glaser PE, Rush CR (2003) Reinforcing, subject-rated, and physiological effects of intranasal methylpheni- date in humans: a dose-response analysis. Drug Alcohol Depend 71:179–186
10. Clavenna A, Rossi E, Derosa M, Bonati M (2007) Use of psychotropic medications in Italian children and adolescents. Eur J Pediatr 166:339–347
11. Bonati M, Clavenna A (2005) The epidemiology of psychotropic drug use in children and adolescents. Int Rev Psychiatry 17:181–188
12. Zito JM, Safer DJ, de Jong-van den Berg LT et al (2008) A three-country comparison of psychotropic medication prevalence in youth. Child Adolescent Psychiatry Ment Health 2:26. doi:10.1186/1753-2000-2-26
13. Wijlaars LP, Nazareth I, Petersen I (2012) Trends in depression and antidepressant prescribing in children and adolescents: a cohort study in The health improvement network (THIN). PLoS One 7:e33181
14. Zoega H, Furu K, Halldorsson M et al (2011) Use of ADHD drugs in the Nordic countries: a population-based comparison study. Acta Psychiatr Scand 123:360–367
15. Mitchell B, Carleton B, Smith A et al (2008) Trends in psychostimulants and antidepressant use by children in 2 Canadian provinces. Can J Psychiatry 53:152–159
16. Preen DB, Calver J, Sanfilippo FM et al (2007) Patterns of psychostimulants prescribing to children with ADHD in Western Australia: variations in age, gender, medication type and dose prescribed. Aust N Z J Public Health 31:120–126
17. Vinker S, Vinker R, Elhayany A (2006) Prevalence of methylphenidate use among Israeli children:1998–2004. Clin Drug Invest 26:161–167
18. Zuvekas SH, Vitiello B (2012) Stimulant medication use in children: a 12 year perspective. Am J Psychiatry 169:160–166
19. Jensen PS, Goldman E, Offord D et al (2011) Overlooked and underserved: "action signs" for identifying children with unmet mental health needs. Pediatrics 128:970–979
20. Morris J, Belfer M, Daniels A et al (2011) Treated prevalence of and mental health services received by children and adolescents in 42 low-and- middle-income countries. J Child Psychol Psychiatry 52:1239–1246
21. Rapoport JL (2013) Pediatric psychopharmacology: too much or too little? World Psychiatry 12:118–123
22. Taylor E (2013) Pediatric psychopharmacology: too much and too little. World Psychiatry 12:124–125
23. Hoffmann F, Glaeske G, Bachmann CJ (2014) Trends in antidepressant prescriptions for children and adolescents in Germany from 2005 to 2012. Pharmacoepidemiol Drug Saf. doi:10.1002/pds.3649
24. Clavenna A, Cartabia M, Sequi M et al (2013) Burden of psychiatric disorders in the pediatric population. Eur Neuropsychopharmacol 23:98–106
25. Clavenna A, Andretta M, Pilati P et al (2011) Antidepressant and antipsychotic use in an Italian pediatric population. BMC Pediatr 11:40
26. L'uso dei farmaci in Italia, Rapporto Osmed 2011—Osservatorio nazionale sull'impiego dei medicinali—Italian Medicines Agency; available online at: http://www.agenziafarmaco.gov.it/sites/default/files/1_-_rapporto_osmed_2011.pdf
27. Blake KV, Devries CS, Arlett P et al (2012) Increasing scientific standards, independence and transparency in post-authorisation studies: the role of the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance. Pharmacoepidemiol Drug Saf 21:690–696
28. Steinhausen HC, Bisgaard C (2014) Nationwide time trends in dispensed prescriptions of psychotropic medication for children and adolescents in Denmark. Acta Psychiatr Scand 129:221–231
29. Rani F, Murray ML, Byrne PJ, Wong IC (2008) Epidemiologic features of antipsychotic prescribing to children and adolescents in primary care in the United Kingdom. Pediatrics 121:1002–1009
30. McCarthy S, Wilton L, Murray ML, Hodgkins P, Asherson P, Wong IC (2012) The epidemiology of pharmacologically treated attention deficit hyperactivity disorder (ADHD) in children, adolescents and adults in UK primary care. BMC Pediatr. 12:78. doi:10.1186/1471-2431-12-78
31. Weinstein SJ, House SA, Chang CH, Wasserman JR, Goodman DC, Morden NE (2014) small geographic area variations in prescription drug use. Pediatrics 134:563–570
32. Kovess V, Choppin S, Gao F, Pivette M, Husky M, Leray E (2015) Psychotropic medication use in French children and adolescents. J Child Adolesc Psychopharmacol. 25:168–175
33. Volkers AC, Heerdink ER, van Dijk L (2007) Antidepressant use and off-label prescribing in children and adolescents in Dutch general practice (2001–2005). Pharmacoepidemiol Drug Saf 16:1054–1062

34. Hodgkins P, Sasané R, Meijer WM (2011) Pharmacologic treatment of attention-deficit/hyperactivity disorder in children: incidence, prevalence, and treatment patterns in the Netherlands. Clin Ther 33:188–203
35. Kalverdijk LJ, Tobi H, van den Berg PB, Buiskool J, Wagenaar L, Minderaa RB, de Jong-van den Berg LT (2008) Use of antipsychotic drugs among Dutch youths between 1997 and 2005. Psychiatr Serv 59:554–560. doi:10.1176/appi.ps.59.5.554
36. Bachmann CJ, Lempp T, Glaeske G, Hoffmann F (2014) Antipsychotic prescription in children and adolescents: an analysis of data from a German statutory health insurance company from 2005 to 2012. Dtsch Arztebl Int. 111:25–34
37. Steffenak AK, Wilde-Larsson B, Nordström G, Skurtveit S, Hartz I (2012) Increase in psychotropic drug use between 2006 and 2010 among adolescents in Norway: a nationwide prescription database study. Clin Epidemiol 4:225–231
38. Meng X, D'Arcy C, Tempier R (2014) Long-term trend in pediatric antidepressant use, 1983–2007: a population-based study. Can J Psychiatry 59:89–97
39. Alessi-Severini S, Biscontri RG, Collins DM, Sareen J, Enns MW (2012) Ten years of antipsychotic prescribing to children: a Canadian population-based study. Can J Psychiatry 57:52–58
40. Brault MC, Lacourse É (2012) Prevalence of prescribed attention-deficit hyperactivity disorder medications and diagnosis among Canadian preschoolers and school-age children: 1994–2007. Can J Psychiatry 57:93–101
41. Foulon V, Svala A, Koskinen H, Chen TF, Saastamoinen LK, Bell JS (2010) Impact of regulatory safety warnings on the use of antidepressants among children and adolescents in Finland. J Child Adolesc Psychopharmacol 20:145–150
42. Thomas R, Sanders S, Doust J, Beller E, Glasziou P (2015) Prevalence of attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. Pediatrics 135:e994–e1001
43. Didoni A, Sequi M, Panei P, Bonati M (2011) Lombardy ADHD registry group one-year prospective follow-up of pharmacological treatment in children with attention-deficit/hyperactivity disorder. Eur J Clin Pharmacol 67:1061–1067
44. Bonati M, Reale L (2013) Reducing overdiagnosis and disease mongering in ADHD in Lombardy. BMJ 347:f7474
45. Donfrancesco R, Marano A, Calderoni D, Mugnaini D, Thomas F, Di Trani M, Innocenzi M, Vitiello B (2014) Prevalence of severe ADHD: an epidemiological study in the Italian regions of Tuscany and Latium. Epidemiol Psychiatr Sci. 15:1–9
46. Bianchini R, Postorino V, Grasso R, Santoro B, Migliore S, Burlò C, Tata C, Mazzone L (2013) Prevalence of ADHD in a sample of Italian students: a population-based study. Res Dev Disabil 34:2543–2550
47. European Medicines Agency (2005) European Medicines Agency finalises review of antidepressants in children and adolescents. Available online at: http://www.ema.europa.eu/docs/en_GB/document_library/Referrals_document/SSRI_31/WC500013082.pdf
48. Wijlaars LP, Nazareth I, Petersen I (2012) Trends in depression and antidepressant prescribing in children and adolescents: a cohort study in The Health Improvement Network (THIN). PLoS One 7:e33181
49. Olfson M, Blanco C, Liu SM et al (2012) National trends in the office-based treatment of children, adolescents, and adults with antipsychotics. Arch Gen Psychiatry 69:1247–1256
50. Hayes J, Prah P, Nazareth I et al (2011) Prescribing trends in bipolar disorder: cohort study in the United Kingdom THIN primary care database 1995–2009. PLoS One 6:e28725
51. Pringsheim T, Lam D, Patten SB (2011) The pharmacoepidemiology of antipsychotic medications for Canadian children and adolescents: 2005–2009. J Child Adolesc Psychopharmacol 21:537–543
52. Karanges EA, Stephenson CP, McGregor IS (2014) Longitudinal trends in the dispensing of psychotropic medications in Australia from 2009–2012: focus on children, adolescents and prescriber specialty. Aust N Z J Psychiatry 48:917–931
53. Dörks M, Langner I, Dittmann U, Timmer A, Garbe E (2013) Antidepressant drug use and off-label prescribing in children and adolescents in Germany: results from a large population-based cohort study. Eur Child Adolesc Psychiatry 22:511–518
54. Volkers AC, Heerdink ER, van Dijk L (2007) Antidepressant use and off-label prescribing in children and adolescents in Dutch general practice (2001–2005). Pharmacoepidemiol Drug Saf 16:1054–1062
55. Leslie DL, Rosenheck R (2012) Off-label use of antipsychotic medications in Medicaid. Am J Manag Care. 18:e109–e117
56. Piovani D, Clavenna A, Cartabia M, Bonati M (2014) Antibiotic and anti-asthmatic drug prescriptions in Italy: geographic patterns and socio-economic determinants at the district level. Eur J Clin Pharmacol 70:331–337
57. Piovani D, Clavenna A, Cartabia M, Bonati M (2012) The regional profile of antibiotic prescriptions in Italian outpatient children. Eur J Clin Pharmacol 68:997–1005
58. Piovani D, Clavenna A, Bonati M (2013) Interregional Italian Drug Utilisation Group. Drug use profile in outpatient children and adolescents in different Italian regions. BMC Pediatr 13:46

REGIONE DEL VENETO
AZIENDA UNITÀ LOCALE SOCIO SANITARIA N. 10
"VENETO ORIENTALE"

Erickson

Convegno - 25 novembre - San Donà di Piave

"Disturbi del neurosviluppo e comorbilità: profili clinici, neuropsicologici e terapia"

Auditorium L. Da Vinci, Piazza Indipendenza 13

San Donà di Piave (Ve)

9.00-9.30 Saluto delle autorità: Direttore Generale ULSS 10, Dr. C. Bramezza

Sindaco di San Donà A. Cereser

Direttore Servizi Sociali M. Filippi

9.30-10.15 E. Baioni: "ADHD: Sottotipi clinici ed evoluzione prognostica"

10.15-11.00 G. Stella: "La comorbilità nei disturbi del neurosviluppo: esiste davvero?"

11.00-11.15 Pausa

11.15-12.00 G.M. Marzocchi: "I bambini con ADHD hanno veramente un deficit delle Funzioni Esecutive?"

12.00-12.45 C. Vio: "Il problema della comorbilità tra ADHD e DSA: analisi delle relazioni tra i due disturbi"

Pranzo

14.00- 14.45 I. Mammarella: "Diagnosi Differenziale e comorbilità tra il disturbo di apprendimento non verbale e altri disturbi del neurosviluppo"

14.45-15.30 D. Maschietto: "ADHD verso Disturbi dirompenti del comportamento"

15.30-15.45 Pausa

15.45-16.30 P. Muratori: "Coping Power per prevenire le problematiche comportamentali nella scuola primaria"

16.30-17.15 T. Mattiuzzo e F. Guaran: "L' autoregolazione comportamentale e problem-solving sociale nell'ADHD: l'intervento clinico e psicoeducativo"

17.15-18.00 Discussione - ECM

E. Baioni: Servizio NPPS- ULSS 10 Veneto Orientale

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T. Mattiuzzo, Servizio NPPS- ULSS 10 Veneto Orientale

F. Guaran, Specializzata Neuropsicologia dello Sviluppo - Parma.

Segreteria Organizzativa

Dr.ssa Federica Novello: 3803713457

Dr.ssa Silvia Santon: 3463746127

Per iscrizioni scrivere a convegno.neurosviluppo@ulss10veneto.it

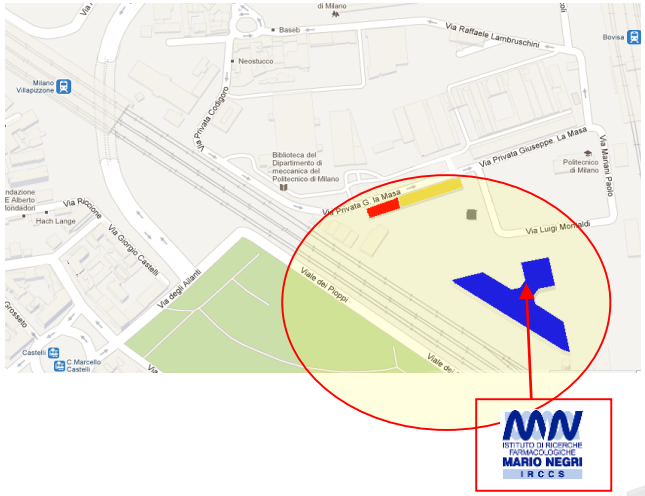
Indicando: Nome e Cognome, professione, numero di telefono, posta elettronica e se interessati ai crediti ECM

Con il patrocinio dell'

airipa

SPEAKERS

Marco Angriman
Neurologia e Neuroriabilitazione dell'Età Evolutiva, Azienda Sanitaria del Sudtirolo, Bolzano
Maurizio Bonati
Dipartimento Salute Pubblica, IRCCS Ist. "Mario Negri" di Milano
Serafino Corti
Dipartimento Disabili, Fondazione Ist. Ospedaliero di Sospiro (CR)
Antonella Costantino
SINPIA Presidente;
UONPIA, IRCCS "Ca' Granda" Osp. Maggiore Policlinico di Milano
Paolo Curatolo
UOC Neuropsichiatria Infantile - Policlinico Tor Vergata, Roma
Rocco Farruggia
Azienda USL RM A, U.O.S. Residenzialità Età Evolutiva, Roma
Antonella Gagliano
U.O.C di Neuropsichiatria Infantile dell'Azienda Policlinico "Gaetano Martino", Messina
Fulvio Guccione
Neuropsichiatria ASL di Novara
Ottaviano Martinelli
UOC di Neuropsichiatria dell'Infanzia e dell'Adolescenza, A.O. Provincia di Lecco
Gian Marco Marzocchi
Dipartimento di Psicologia, Università degli Studi di Milano-Bicocca, Milano
Dino Maschietto
Neuropsichiatria Infantile, ASL di San Donà di Piave (VE)
Luigi Mazzone
Neuropsichiatria Infantile, IRCCS Ospedale Pediatrico Bambino Gesù, Roma
Annarita Milone
Neuropsichiatria Infantile, IRCCS Fondazione Stella Maris, Calambrone PI
Massimo Molteni
IRCCS, Istituto Scientifico Eugenio Medea di Bosisio Parini
Annalisa Monti
Membro del Consiglio Direttivo SINPIA
Laura Reale
Dipartimento Salute Pubblica, IRCCS Istituto "Mario Negri" di Milano
Renata Rizzo
Neuropsichiatria Infantile, Dipartimento Scienze Mediche e Pediatriche, Università degli Studi di Catania
Monica Saccani
UONPIA, A.O. San Paolo, Università degli Studi di Milano
Renato Scifo
UOC di NPIA Ospedale Acireale, ASP Catania
Paolo Soli
Neuropsichiatria dell'Infanzia e della Adolescenza Regione Emilia Romagna, Bologna
Roberto Tombolato
Neuropsichiatria Infantile ULSS Vicenza
Alessandro Zuddas
Neuropsichiatria Infantile Università degli Studi di Cagliari



L'IRCCS – Istituto di Ricerche Farmacologiche Mario Negri si trova a Milano in zona Bovisa nelle vicinanze del Campus Politecnico (Ingegneria) e della Triennale Bovisa.
E' facilmente raggiungibile con il passante ferroviario, scendendo alle fermate di Bovisa (FNM) o Villapizzone (FS).
Se fermate a Bovisa ricordatevi di scendere le scale che si trovano sul lato destro della stazione.

Con il patrocinio della:

SINPIA
Società Italiana di Neuropsichiatria dell'Infanzia e dell'Adolescenza

Segreteria organizzativa:
Laboratorio per la Salute Materno Infantile
Dipartimento di Salute Pubblica
IRCCS - Istituto di Ricerche Farmacologiche Mario Negri
Via Giuseppe La Masa, 19. Milano
Tel. 02 39014511 – fax 02 3550924 - ADHD@marionegri.it

La partecipazione è gratuita e prevede l'assegnazione di 11,2 crediti ECM.
L'iscrizione è obbligatoria accedendo al link:

ADHDcongress.marionegri.it

ADHD
nei Servizi di Neuropsichiatria in Italia

La Comorbilità nell'ADHD

Milano, 14 dicembre 2016
10.00-18.00

15 dicembre 2016
9.00-18.00 - AULA A

IRCCS
Istituto di Ricerche Farmacologiche Mario Negri
Via G. La Masa 19 - 20156 Milano

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

Azienda Ospedaliera
SPEDALI CIVILI BRESCIA

RegioneLombardia

Il Progetto: "Condivisione dei percorsi diagnostico-terapeutici per l'ADHD in Lombardia" è stato in parte finanziato dalla Regione Lombardia con Decreto DG Welfare 2394 del 31 marzo 2016. Il progetto coinvolge 18 Centri di Riferimento per l'ADHD e il Laboratorio per la Salute Materno Infantile dell'IRCCS - Istituto di Ricerche Farmacologiche Mario Negri. Coordinatore del Progetto è la UONPIA degli Spedali Civili di Brescia.

PRESENTAZIONE

Il convegno si pone a conclusione di 6 anni di attività dei 18 Centri di riferimento per l'ADHD nell'ambito di uno specifico progetto regionale, in cui è stato definito in modo collegiale e valutato nella pratica il percorso per la diagnosi e il trattamento dell'ADHD del bambino e dell'adolescente in Regione Lombardia.

Il progetto ha consentito di delineare un percorso assistenziale condiviso, appropriato, aggiornato e attuabile nella pratica, di attuare attività formative mirate a supporto del percorso stesso, di introdurre strategie di monitoraggio e audit nonché di porre le basi per la riorganizzazione dei servizi e la strutturazione di un network coordinato di cura.

La prima giornata si pone come utile confronto tra il potenziale "modello lombardo" e quelli di altre regioni italiane in tema di modelli clinico-organizzativi specifici per l'ADHD.

La seconda giornata sarà invece dedicata all'approfondimento di uno dei temi più rilevanti sul piano clinico-organizzativo in neuropsichiatria dell'infanzia e dell'adolescenza. I tassi di comorbilità risultano infatti molto elevati sia per l'ADHD che per altri disturbi neuropsichici dell'età evolutiva, e richiedono riflessioni mirate. Le diverse comorbilità psichiatriche e mediche associate all'ADHD sono spesso correlate all'età e al livello di sviluppo, e possono influenzare la fenomenologia, la gravità, la prognosi e il trattamento dell'ADHD. Nonostante numerosi e approfonditi studi abbiano descritto le comorbilità più frequentemente associate all' ADHD, pochi sono stati condotti con adeguata metodologia e basandosi su un approccio multidimensionale, condiviso e multicentrico, valutando sia le componenti psicosociali che cliniche di un disturbo complesso come l'ADHD. In proposito anche il lavoro svolto nell'ambito del Progetto Regionale necessita di un appropriato approfondimento e sviluppo.

14 DECEMBER 2016

10.00 – 12.30

LA NEUROPSICHIATRIA INFANTILE: UNA EMERGENZA DIMENTICATA

Coordina:
…… ……..

Francesco Ciotti e Federico Marchetti

NE DISCUTONO
Antonella Costantino, Federica Zanetto, …

12.30 – 13.00

Il Progetto ADHD nella Regione Lombardia
Maurizio Bonati

14.00 – 18.00

ADHD NEI SERVIZI DI NEUROPSICHIATRIA IN ITALIA

Coordina:
Antonella Costantino

Piemonte	*Fulvio Guccione*
Veneto	*Roberto Tombolato*
Emilia Romagna	*Paolo Soli*
Toscana	*Annalisa Monti*
Lazio	*Rocco Farruggia*
Sardegna	*Alessandro Zuddas*
Sicilia	*Renato Scifo*

DISCUSSIONE

15 DECEMBER 2016

09.00 – 13.00

LA COMORBILITÀ NELL'ADHD

Coordinano e commentano:
Gian Marco Marzocchi, Dino Maschietto

Dal Registro della Regione Lombardia
Monica Saccani e Laura Reale

Disturbi ad alta Frequenza

- ✓ **Apprendimento** — *Antonella Gagliano*
- ✓ **Sonno** — *Marco Angriman*
- ✓ **Comportamento/Umore** — *Annarita Milone*

14.00 – 18.00

Coordinano e Commentano:
Serafino Corti, Ottaviano Martinelli

Disturbi a bassa Frequenza

- ✓ **TIC/Sindrome di Tourette** — *Renata Rizzo*
- ✓ **Autismo** — *Luigi Mazzone*
- ✓ **Epilessia** — *Paolo Curatolo*

La multidimensionalità della comorbilità nei disturbi psichiatrici dell'età evolutiva
Massimo Molteni

DISCUSSIONE

WebCenter

Questionario per la valutazione della Newsletter ADHD

Gent.mi lettori,

questo è un invito alla compilazione del questionario on-line sulla Newsletter ADHD.

Tale operazione Vi impegnerà per 2 minuti al massimo accedendo al seguente link:

http://www.adhd.marionegri.it/index.php/newsletter/valutazione-newsletter

Si confida nella Vs preziosa collaborazione.

Per ricevere la newsletter iscriversi al seguente indirizzo:
http://www.adhd.marionegri.it/index.php/newsletter/iscrizione-newsletter

Iniziativa nell'ambito del Progetto di Neuropsichiatria dell'Infanzia e dell'Adolescenza
(Delibera n. 406 - 2014 del 04/06/2014 Progetti NPI)
Il Progetto è realizzato con il contributo, parziale, della Regione Lombardia
(in attuazione della D.G. sanità n. 3798 del 08/05/2014 e n. 778 del 05/02/2015)
Capofila Progetto: UONPIA Azienda Ospedaliera "Spedali Civili di Brescia" "*Percorsi diagnostico-terapeutici per l'ADHD*".

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