NEWSLETTER

INDICE:

ISTITUTO DI RICERCHE FARMACOLOGICHE MARIO NEGRI IRCCS

BIBLIOGRAFIA ADHD DICEMBRE 2017

Advances in Cognitive Science. 2017;18:60-71.

FACIAL EMOTION RECOGNITION DEFICIT IN TWO GROUPS OF CHILDREN WITH ADHD- WITH AND WITHOUT CONDUCT DISORDER- COMPARED WITH NORMAL CHILDREN.

Nazari MA, Nasri S, Goodarzi I, et al.

Introduction: Children with attention deficit and hyperactivity disorder (ADHD) and conduct disorder (CD) have impaired interpersonal and social skills, highly due to deficiency in facial emotion processing. The aim of this study was to investigate facial emotion recognition between two groups of children with ADHD - with and without conduct disorder compared with normal children.

Method: Fifty-five male children with between the ages of 8 to 13 in Tabriz and Esfahan were selected by purposeful sampling method and assigned in the following three groups: 23 ADHD, 14 ADHD+CD and 18 children in normal control group. All participants performed facial emotion recognition task including unfamiliar faces which contain four basic emotions «anger, happiness, sadness, fear and neutral faces» for assessing ability to recognize facial emotion. The data was analyzed by MANOVA.

Results: Percent error analysis revealed that participants with ADHD and ADHD+CD have greater deficit in emotional face recognition when compared with control subjects. However, analysis of error response type showed that ADHD + CD children, often confused distress cues (sadness, fear) with neutral face on the one hand, and neutral face with anger on the other hand.

Conclusion: These findings would suggest that facial emotion recognition deficits in children with ADHD and ADHD+CD occur mostly due to ADHD symptoms such as attention deficit, emotion regulation and executive function deficit. Nevertheless, children with ADHD who have conduct symptoms perform in an exaggerated or reductionist manner in the processing of some facial expressions, which lead to perceptual distortion

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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.

Alcohol Clin Exp Res. 2017.

META-ANALYSES OF EXTERNALIZING DISORDERS: GENETICS OR PRENATAL ALCOHOL EXPOSURE?

Wetherill L, Foroud T, Goodlett C.

Background: Externalizing disorders are heritable precursors to alcohol dependence, common in children of alcoholics (COA), and in children with prenatal alcohol exposure (PAE). Pregnancies involving alcohol exposure sufficient to affect the fetus may involve women with genetic risk for alcohol dependence. We hypothesized that known PAE will increase the odds of having an externalizing disorder compared to COA.
Methods: The odds ratios of 3 externalizing disorders (attention-deficit hyperactivity disorder [ADHD], conduct disorder [CD], and oppositional defiant disorder [ODD]) were obtained for 2 domains: (i) PAE and (ii) COA, by estimating the logged odds ratio (LOR) for each study. Permutation tests were implemented to compare LORs for PAE versus COA studies within each disorder, including PAE versus an alcohol dependent (AD) mother and PAE versus an AD father.
Results: In PAE studies, the odds of ADHD and CD were elevated. Rates of all 3 disorders were elevated in COA studies. Permutation tests revealed that the mean LOR for ADHD was significantly higher in PAE studies compared to: COA ($p = 0.01$), AD mother ($p < 0.05$), and AD father ($p = 0.03$). No differences were found for ODD ($p = 0.09$) or CD ($p = 0.21$).
Conclusions: These results provide compelling evidence of an increased risk of ADHD in those with PAE beyond that due to parental alcohol dependence or a genetic liability, consistent with a unique etiology most likely due to direct alcohol exposure during prenatal development

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Am J Addict. 2017 Mar;26:99-111.

NEUROIMAGING THE NEURAL CORRELATES OF INCREASED RISK FOR SUBSTANCE USE DISORDERS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER-A SYSTEMATIC REVIEW.

Adisetiyo V, Gray KM.

BACKGROUND/OBJECTIVES: Children with attention-deficit/hyperactivity disorder (ADHD) are nearly three times more likely to develop substance use disorders (SUD) than their typically developing peers. Our objective was to review the existing neuroimaging research on high-risk ADHD (ie, ADHD with disruptive behavior disorders, familial SUD and/or early substance use), focusing on impulsivity as one possible mechanism underlying SUD risk.
METHODS: A PubMed literature search was conducted using combinations of the keywords "ADHD," "substance use," "substance use disorder," "SUD," "addiction," "dependence," "abuse," "risk," "brain" "MRI," "imaging" and "neuroimaging." Studies had to include cohorts that met diagnostic criteria for ADHD; studies of individuals with ADHD who all met criteria for SUD were excluded. Eight studies met the search criteria.
RESULTS: Individuals with high-risk ADHD have hyperactivation in the motivation-reward processing brain network during tasks of impulsive choice, emotion processing, and risky decision-making. During response inhibition tasks, they have hypoactivation in the inhibitory control brain network. However, studies focusing on this latter circuit found hypoactivation during inhibitory control tasks, decreased white matter microstructure coherence and reduced cortical thickness in ADHD independent of substance use history.
DISCUSSION/CONCLUSIONS: An exaggerated imbalance between the inhibitory control network and the motivation-reward processing network is theorized to distinguish individuals with high-risk ADHD. Preliminary findings suggest that an exaggerated aberrant reward processing network may be the driving neural correlate of increased SUD risk in ADHD.
SCIENTIFIC SIGNIFICANCE: Neural biomarkers of increased SUD risk in ADHD could help clinicians identify which patients may benefit most from SUD prevention. Thus, more neuroimaging research on this vulnerable population is needed.

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Anadolu Psikiyatr Derg. 2018;19:71-79.

SOCIAL COGNITION AND EMOTION REGULATION IN ADOLESCENTS WITH ADHD.

Åžan E, et al.

Objective: In our study, it's aimed to evaluate the emotion recognition and regulation skills of adolescents with attention deficit and hyperactivity disorder (ADHD) and to compare the results to healthy control cases.
Methods: To our study, 63 ADHD diagnosed and 32 control cases with similar sociodemographic characteristics to patient group aged 11-18 years were included. 'Schedule for Affective Disorders and Schizophrenia for School Age Children-Present and Lifetime Version' (K-SADS-PL) was applied to all cases in order to psychiatric evaluation. In all cases Child Behavior Checklist (CBCL), Turgay DSM-IV-Based Child and Adolescent Behavior Disorders Screening and Rating Scale (T-DSM-IV-S), Difficulties in Emotion Regulation Scale (DERS) and to evaluate social cognitive properties Faces Test, Reading the Mind in the Eyes Test (RMET), The Unexpected Outcomes Test (UOT) and Comprehension Test are applied.
Results: The scores of tests evaluating emotion recognition and regulation abilities in adolescents with ADHD were lower than control group.
Conclusion: The better understanding of the problems in emotion recognition and regulation abilities of the adolescents with ADHD may be helpful in determining the required interventions (social skill training etc.) in this respect

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Anadolu Psikiyatr Derg. 2018;19:80-86.

EVALUATION OF SERUM UROTENSIN-II LEVELS OF CHILDREN WITH ADHD AND AUTISM SPECTRUM DISORDER.

UÄŸur Ã, et al.

Objective: Urotensin-II (U-II) is one of the most vasoconstrictive substrates for the mammals. Lately, this substrate is thought to be responsible for developing of the neuropsychiatric disorders, by causing an abnormal brain blood-stream situation. Autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD) are frequently seen disorders in childhood and their etiologies are remain unclear. This study evaluated the serum urotensin-II levels of children with ASD and ADHD and compared with healthy subjects' urotensin-II levels.
Methods: Total of 179 children between age of 4-12, 60 of them diagnosed with ADHD and 60 of children with ASD, according to the DSM-5 criteria and both had no treatment for at least a month and 59 of healthy subjects whom they all admitted to the Ankara Pediatric Hematology-Oncology Training and Research Hospital were included. Schedule for Affective Disorders and Schizophrenia for School-Age Children, a semi-structured interview, was applied to all subjects. Venous samples of the participants were given after a-12 hours starvation. Serum U-II levels were analyzed by the use of ELISA kits. SPSS 16.0 was used for analysis and $p<0.05$ was accepted as significance level.
Results: U-II levels of children with ASD were found higher than that of ADHD and healthy groups. There was also a positive correlation between U-II levels and autism behavior checklist scores.
Discussion: Higher U-II levels and its levels' correlation with symptom severity of disorder are thought to be a responsible factor that could play a role in ASD etiology. Further studies with larger sample size could be useful to investigate the role of UII in the etiology and treatment research of ASD

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Anesth Analg. 2017 Dec;125:1988-98.

AGE AT EXPOSURE TO SURGERY AND ANESTHESIA IN CHILDREN AND ASSOCIATION WITH MENTAL DISORDER DIAGNOSIS.

Ing C, Sun M, Olfson M, et al.

BACKGROUND: Animals exposed to anesthetics during specific age periods of brain development experience neurotoxicity, with neurodevelopmental changes subsequently observed during adulthood. The corresponding vulnerable age in children, however, is unknown.
METHODS: An observational cohort study was performed using a longitudinal dataset constructed by linking individual-level Medicaid claims from Texas and New York from 1999 to 2010. This dataset was evaluated

to determine whether the timing of exposure to anesthesia </=5 years of age for a single common procedure (pyloromyotomy, inguinal hernia, circumcision outside the perinatal period, or tonsillectomy and/or adenoidectomy) is associated with increased subsequent risk of diagnoses for any mental disorder, or specifically developmental delay (DD) such as reading and language disorders, and attention deficit hyperactivity disorder (ADHD). Exposure to anesthesia and surgery was evaluated in 11 separate age at exposure categories: </=28 days old, >28 days and </=6 months, >6 months and </=1 year, and 6-month age intervals between >1 year old and </=5 years old. For each exposed child, 5 children matched on propensity score calculated using sociodemographic and clinical covariates were selected for comparison. Cox proportional hazards models were used to measure the hazard ratio of a mental disorder diagnosis associated with exposure to surgery and anesthesia.

RESULTS: A total of 38,493 children with a single exposure and 192,465 propensity score-matched children unexposed before 5 years of age were included in the analysis. Increased risk of mental disorder diagnosis was observed at all ages at exposure with an overall hazard ratio of 1.26 (95% confidence interval [CI], 1.22-1.30), which did not vary significantly with the timing of exposure. Analysis of DD and ADHD showed similar results, with elevated hazard ratios distributed evenly across all ages, and overall hazard ratios of 1.26 (95% CI, 1.20-1.32) for DD and 1.31 (95% CI, 1.25-1.37) for ADHD.

CONCLUSIONS: Children who undergo minor surgery requiring anesthesia under age 5 have a small but statistically significant increased risk of mental disorder diagnoses and DD and ADHD diagnoses, but the timing of the surgical procedure does not alter the elevated risks. Based on these findings, there is little support for the concept of delaying a minor procedure to reduce long-term neurodevelopmental risks of anesthesia in children. In evaluating the influence of age at exposure, the types of procedures included may need to be considered, as some procedures are associated with specific comorbid conditions and are only performed at certain ages

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Ann Transl Med. 2017;5.

ASSOCIATION BETWEEN CLINICAL PHENOTYPES AND NEURODEVELOPMENTAL OUTCOMES IN PEDIATRIC PATIENTS *WITH NEUROFIBROMATOSIS TYPE 1 AT SIRIRAJ HOSPITAL.*

Thamrongajariyakul C, Sathienkijkanchai A.

Background: Neurofibromatosis type 1 (NF1) is characterized by multiple cafÃ©-au-lait spots, skinfold freckling, cutaneous neurofibromas, and Lisch nodules. Additional signs and symptoms of NF1 include macrocephaly, skeletal abnormalities, hypertension, and learning disabilities. This study has objective to analyze the association between clinical phenotypes and neurodevelopmental outcomes in pediatric patients diagnosed with NF1 from 2005-2015 at Siriraj Hospital. The neurodevelopmental outcomes included intellectual disability (ID), developmental delay, epilepsy, attention deficit hyperactive disorder (ADHD), and learning disabilities (LD).

Methods: A retrospective chart review of all children clinically diagnosed with NF1 who were seen at Siriraj Hospital from 2005-2015 was performed. All children were 7-18 years old and underwent neurodevelopmental assessment by pediatricians or pediatric psychiatrists.

Results: Out of 256 patients with NF1, 70 (30%) patients were included in this study, including 38 males and 32 females. There were 6 (8.6%) patients with ID, 14 (20%) with ADHD, 14 (20%) with LD, and 4 (5.7%) with epilepsy. The associations were analyzed and found that patients with Lisch nodules had less common ID (5.1% vs. 27.3%; OR 0.143; 95% CI 0.024-0.833), patients with neurofibromas had less common ADHD (11.6% vs. 33.3%; OR 0.263; 95% CI 0.077-0.899), and patients with macrocephaly had more common LD (42.9% vs. 10.2%; OR 6.600; 95% CI 1.861-23.405).

Conclusions: In this hospital-based study of 70 patients with NF1, we found an association between macrocephaly and LD in patients with NF1. However, in patients with Lisch nodules and neurofibromas ID and ADHD were less commonly found, respectively. Given, this study is a hospital-based study and with limited number of patients, further study on a national scale are warranted to better elucidate the association of clinical phenotypes and neurodevelopmental outcomes in patients with NF1

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Brain Cogn. 2017.

FUNCTIONAL CONNECTIVITY OF THE VIGILANT-ATTENTION NETWORK IN CHILDREN AND ADOLESCENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Zepf FD, Bubenzer-Busch S, Runions KC, et al.

The ability to maintain attention to simple tasks (i.e., vigilant attention, VA) is often impaired in attention-deficit/hyperactivity disorder (ADHD), but the underlying pathophysiological mechanisms at the brain network level are not clear yet. We therefore investigated ADHD-related differences in resting-state functional connectivity within a meta-analytically defined brain network of 14 distinct regions subserving VA (comprising 91 connections in total), as well as the association of connectivity with markers of behavioural dysfunction in 17 children (age range: 9-14 years) with a diagnosis of ADHD and 21 age-matched neurotypical controls. Our analyses revealed selective, rather than global, differences in the intrinsic coupling between nodes of the VA-related brain network in children with ADHD, relative to controls. In particular, ADHD patients showed substantially diminished intrinsic coupling for 7 connections and increased coupling for 4 connections, with many differences involving connectivity with the anterior insula. Moreover, connectivity strength of several aberrant connections was found to be associated with core aspects of ADHD symptomatology, such as poor attention, difficulties with social functioning, and impaired cognitive control, attesting to the behavioural relevance of specific connectivity differences observed in the resting state

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Can J Public Health. 2017 Sep;108:e229-e239.

FLUORIDE EXPOSURE AND REPORTED LEARNING DISABILITY DIAGNOSIS AMONG CANADIAN CHILDREN: IMPLICATIONS FOR COMMUNITY WATER FLUORIDATION.

Barberio AM, Quinonez C, Hosein FS, et al.

OBJECTIVES: Recent studies have connected increased fluoride exposure with increased risk of neurodevelopmental-related outcomes, such as ADHD (attention deficit hyperactivity disorder) and lower IQ in children. Our primary objective was to examine the association between fluoride exposure and reported diagnosis of a learning disability among a population-based sample of Canadian children aged 3-12 years.

METHODS: We analyzed data from Cycles 2 and 3 of the Canadian Health Measures Survey. Four measures of fluoride exposure were available: 1) urinary fluoride (mumol/L), 2) creatinine-adjusted urinary fluoride (mumol/mmol), 3) specific gravity-adjusted urinary fluoride (mumol/L), and 4) fluoride concentration of tap water (mg/L) (Cycle 3 only). Diagnosis of a learning disability (yes/no) was based on parental- or self-report. Associations were examined using logistic regression (where possible), unadjusted and adjusted for covariates.

RESULTS: When Cycles 2 and 3 were examined separately, reported learning disability diagnosis was not significantly associated with any measure of fluoride exposure in unadjusted or adjusted models. When Cycles 2 and 3 were combined, a small but statistically significant effect was observed such that children with higher urinary fluoride had higher odds of having a reported learning disability in the adjusted model ($p = 0.03$). However, the association was not observed in models that used creatinine-adjusted urinary fluoride and specific gravity-adjusted urinary fluoride, which are believed to be more accurate measures due to their correction for urinary dilution.

CONCLUSION: Overall, there did not appear to be a robust association between fluoride exposure and parental- or self-reported diagnosis of a learning disability among Canadian children

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Can J Psychiatry. 2017;62:818-26.

TEMPORAL TRENDS IN THE PREVALENCE AND INCIDENCE OF DIAGNOSED ADHD IN CHILDREN AND YOUNG ADULTS BETWEEN 1999 AND 2012 IN CANADA: A DATA LINKAGE STUDY.

Vasiliadis H-M, Diallo FB, Rochette L, et al.

Objective: There is a need for the routine monitoring of treated attention-deficit hyperactivity disorder (ADHD) for timely policy making. The objective is to report and assess over a decade the prevalence and incidence of diagnosed ADHD in Canada.

Methods: Administrative linked patient data from the provinces of Manitoba, Ontario, Quebec, and Nova Scotia were obtained from the same sources as the Canadian Chronic Diseases Surveillance Systems to assess the prevalence and incidence of a primary physician diagnosis of ADHD (ICD-9 and ICD-10 codes: 314, F90.x) for consultations in outpatient and inpatient settings (Med-Echo in Quebec, the Canadian Institute of Health Information Discharge Abstract Database in the 3 other provinces, plus the Ontario Mental Health Reporting System). Dates of service, diagnosis, and physician specialty were retained. The estimates were presented in yearly brackets between 1999-2000 and 2011-2012 by age and sex groups.
Results: The prevalence of ADHD between 1999 and 2012 increased in all provinces and for all groups. The prevalence was approximately 3 times higher in boys than in girls, and the highest prevalence was observed in the 10- to 14-year age group. The incidence increased between 1999 and 2012 in Manitoba, Quebec, and Nova Scotia but remained stable in Ontario. Incident cases were more frequently diagnosed by general practitioners followed by either psychiatrists or paediatricians depending on the province.
Conclusion: The prevalence and incidence of diagnosed ADHD did not increase similarly across all provinces in Canada between 1999 and 2012. Over half of cases were diagnosed by a general practitioner

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Child Psychiatry Hum Dev. 2017 Dec;48:891-902.
ARE ANXIETY DISORDERS IN CHILDREN AND ADOLESCENTS LESS IMPAIRING THAN ADHD AND AUTISM SPECTRUM DISORDERS? ASSOCIATIONS WITH CHILD QUALITY OF LIFE AND PARENTAL STRESS AND PSYCHOPATHOLOGY.
Telman LGE, van Steensel FJA, Maric M, et al.
We compared clinically referred children with anxiety disorders (AD; n = 63) to children with autism spectrum disorder (ASD; n = 39), ADHD Combined (ADHD-C; n = 62), ADHD Predominantly Inattentive (ADHD-I; n = 64), and typically developing children (n = 42) on child quality of life (QOL), paternal and maternal psychopathology and parental stress. Diagnoses were based on DSM-IV-TR criteria. Multilevel analyses showed that QOL in AD was higher on school and social functioning, compared to respectively ADHD and ASD, and lower compared to normal controls on all five domains. Fathers reported their AD children higher QOL than mothers. Also, AD appeared to be associated with less parental stress and parental psychopathology than other child psychopathology. Therefore, parental factors may need to be considered more in treatment of children with ADHD/ASD than AD

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Child Psychiatry Hum Dev. 2017 Dec;48:960-66.
Tic severity and treatment in children: The effect of comorbid attention deficit hyperactivity disorder and obsessive compulsive behaviors.
Pringsheim T.
While attention deficit hyperactivity disorder (ADHD) and obsessive compulsive disorder have been shown to have major impacts on quality of life in individuals with Tourette syndrome, there is comparatively little data on how the presence of these comorbidities influence tic severity and treatment. 114 children (mean age 10.25 years) were extensively clinically phenotyped at a single specialty clinic. While there was no difference in Yale Global Tic Severity Scale (YGTSS) scores in children with versus without ADHD, children with obsessive compulsive behaviors had significantly higher YGTSS scores ($p = 0.008$). There was a significant correlation between YGTSS scores and age ($r = 0.344$, $p < 0.001$). Children with ADHD were more likely to be treated for their tics within the first two years of diagnosis (OR 3.51, $p = 0.009$). As tic severity does not appear to be greater in children with ADHD, this association may relate to greater overall psychosocial impairment in children with this comorbidity

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Child Psychiatry Hum Dev. 2017 Dec;48:870-80.

INFLUENCE OF DISRUPTIVE BEHAVIOR DISORDERS ON ACADEMIC PERFORMANCE AND SCHOOL FUNCTIONS OF YOUTHS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Liu CY, Huang WL, Kao WC, et al.

Childhood attention-deficit/hyperactivity disorder (ADHD) and comorbid oppositional defiant disorder/conduct disorder (ODD/CD) are associated with negative school outcomes. The study aimed to examine the impact of ADHD and ODD/CD on various school functions. 395 youths with ADHD (244 with ADHD + ODD/CD and 151 with ADHD only) and 156 controls received semi-structured psychiatric interviews. School functions were assessed and compared between each group with a multiple-level model. The results showed that youths with ADHD had poorer performance across different domains of school functioning. Youths with ADHD + ODD/CD had more behavioral problems but similar academic performance than those with ADHD only. The multiple linear regression models revealed that ADHD impaired academic performance while ODD/CD aggravated behavioral problems. Our findings imply that comorbid ODD/CD may specifically contribute to social difficulties in youths with ADHD. Measures of early detection and intervention for ODD/CD should be conducted to prevent adverse outcomes

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Clin Pediatr (Phila). 2018 Jan;57:46-51.

EDUCATION ON THE BRAIN: A PARTNERSHIP BETWEEN A PEDIATRIC PRIMARY CARE CENTER AND NEUROLOGY RESIDENCY.

Zwemer E, Bernson-Leung M, Rea C, et al.

The national shortage of pediatric neurologists is worsening, yet referral rates by pediatricians are high. Suboptimal training of pediatric residents in care of patients with neurologic disease may be a contributing factor. We formed a partnership between the Boston Children's Primary Care at Longwood clinic and Child Neurology Residency Training Program. The educational intervention included lectures, observed neurologic examinations, in-person and virtual triage, and an electronic medical record-based consult system. Residents in other primary care clinics served as the comparison group. Intervention-group residents reported significantly improved confidence in diagnosis of chronic/recurrent headache, attention deficit hyperactivity disorder (ADHD), and developmental delay; initial management of ADHD and developmental delay; and secondary management of ADHD, developmental delay, and concussion/traumatic brain injury. Comparison-group residents reported significantly improved confidence only in diagnosis of developmental delay. Our multipronged intervention is a promising approach to improving pediatric resident training in pediatric neurology and may be generalizable to subspecialty collaborations for other residency programs

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Clin Pediatr. 2018;57:52-56.

ONLINE INFORMATION-SEEKING BEHAVIORS OF PARENTS OF CHILDREN WITH ADHD.

Sage A, Carpenter D, Sayner R, et al.

This article describes (a) parent questions about ADHD (attention deficit/hyperactivity disorder), (b) parent Internet use to seek ADHD information, and (c) associations between type of Internet access and ADHD information-seeking. Seventy parents of children (ages 7-17 years) with ADHD completed questionnaires after their child's visit with their pediatrician. Bivariate relationships were assessed using chi-square statistics, Pearson correlation coefficients, or t tests. Parents identified an average of 8.9 questions about ADHD for their child's provider. Common questions were related to medication and long-term implications of ADHD. A majority of parents searched the Internet for general ADHD information (87%) and ADHD medication information (81%). White parents accessed the Internet significantly more via home computer, mobile phone, and tablet, and significantly less via public library than non-White parents. Parents who accessed the Internet via home computers and tablets were more likely to search the Internet for ADHD medication information than parents who did not

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Clin Psychol Rev. 2017 Dec;58:157-73.

USING TASK PERFORMANCE TO INFORM TREATMENT PLANNING FOR YOUTH WITH ADHD: A SYSTEMATIC REVIEW.

Molitor SJ, Langberg JM.

The role that neuropsychological task performance plays in the assessment of Attention-Deficit/Hyperactivity Disorder (ADHD) is currently ambiguous, and findings are mixed regarding whether tasks have validity for diagnosing the disorder. Irrespective of their validity for diagnosing ADHD, neuropsychological tasks could provide valuable information to mental health professionals if they can inform recommendations for treatment targets and modalities. Therefore, this review sought to synthesize the available evidence related to the use of neuropsychological task performance as a tool for informing treatment planning for youth with ADHD. Reviewed studies focused on examinations of associations between task performance and academic, social, and health outcomes, as well as response to treatment. Twenty-five relevant studies using samples of youth diagnosed with ADHD in clinical, community, and school settings were identified. Review of the evidence suggests that task performance may be useful in identifying individuals with ADHD at risk for academic impairment. However, the evidence is less compelling for identifying youth at risk for impaired social functioning or poor health outcomes. The review also found that task performance is likely useful for predicting response to treatment with methylphenidate. Across studies, evidence indicated that interpreting task performance in an integrated manner, such as a factor score or mean score, was more consistently useful for predicting outcomes of interest than interpreting performance from a single task. Implications for the use of tasks in ADHD assessments are discussed, and future directions are outlined for further examining the clinical utility of task performance

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Dev Psychobiol. 2017 Dec;59:984-96.

PRENATAL PROGRAMMING OF POSTNATAL PLASTICITY FOR EXTERNALIZING BEHAVIOR: TESTING AN INTEGRATED DEVELOPMENTAL MODEL OF GENETIC AND TEMPERAMENTAL SENSITIVITY TO THE ENVIRONMENT.

Tung I, Morgan JE, NoroÃ±a AN, et al.

Although both gene- and temperament-environment interactions contribute to the development of youth externalizing problems, it is unclear how these factors jointly affect environmental sensitivity over time. In a 7-year longitudinal study of 232 children (aged 5-10) with and without ADHD, we employed moderated mediation to test a developmentally sensitive mechanistic model of genetic and temperamental sensitivity to prenatal and postnatal environmental factors. Birth weight, a global measure of the prenatal environment, moderated predictions of child negative emotionality from a composite of dopaminergic polymorphisms (i.e., DRD4 and DAT1), such that birth weight inversely predicted negative emotionality only for children with genetic plasticity. Negative emotionality, in turn, predicted externalizing behavior 4-5 years later, beyond genetic and postnatal parenting effects. Finally, birth weight moderated the indirect effect of dopaminergic genotypes on externalizing problems through negative emotionality, partially supporting a prenatal programming model. We discuss theoretical and empirical implications for models of environmental sensitivity

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Dose-Resp. 2017;15.

ABNORMAL BRAIN CONNECTIVITY SPECTRUM DISORDERS FOLLOWING THIMEROSAL ADMINISTRATION: A PROSPECTIVE LONGITUDINAL CASE-CONTROL ASSESSMENT OF MEDICAL RECORDS IN THE VACCINE SAFETY DATALINK.

Geier DA, Kern JK, Homme KG, et al.

Background: Autism spectrum disorder (ASD), tic disorder (TD), and hyperkinetic syndrome of childhood (attention deficit disorder [ADD]/attention deficit hyperactivity disorder [ADHD]) are disorders recently defined as abnormal connectivity spectrum disorders (ACSDs) because they show a similar pattern of abnormal brain connectivity. This study examines whether these disorders are associated with exposure to thimerosal, a mercury (Hg)-based preservative.

Methods: A hypothesis testing case-control study evaluated the Vaccine Safety Datalink for the potential dose-dependent odds ratios (ORs) for diagnoses of ASD, TD, and ADD/ADHD compared to controls, following exposure to Hg from thimerosalcontaining Haemophilus influenzae type b vaccines administrated within the first 15 months of life. Febrile seizures, cerebral degeneration, and unspecified disorders of metabolism, which are not biologically plausibly linked to thimerosal, were examined as control outcomes.
Results: On a per 25 Î¼g Hg basis, cases diagnosed with ASD (OR = 1.493), TD (OR = 1.428), or ADD/ADHD (OR = 1.503) were significantly (P <.001) more likely than controls to have received increased Hg exposure. Similar relationships were observed when separated by gender. Cases diagnosed with control outcomes were no more likely than controls to have received increased Hg exposure.
Conclusion: The results suggest that Hg exposure from thimerosal is significantly associated with the ACSDs of ASD, TD, and ADD/ADHD

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East Mediterr Health J. 2017;23:589-93.

OUTCOMES OF CHILDREN WITH ATTENTION DEFICIT/HYPERACTIVITY DISORDER: GLOBAL FUNCTIONING AND SYMPTOMS PERSISTENCE.

Al AA, Hamadeh RR, Jahrami H, et al.

Many adolescents with ADHD show antisocial behaviour and low educational achievement. These issues have not been validated in the World Health Organization Eastern Mediterranean Region. The objective of this study was to assess the global functioning and behaviour of children with ADHD growing into adolescence 10 years after initial diagnosis. Parents were interviewed using a structured questionnaire, Conner's Short Version Test and the Children's Global Assessment Scale. Nearly half of our sample had low academic achievement and 36% had no friends. A quarter of the cases were smokers, one admitted abusing drugs and one had attempted suicide. One third of the sample continued to have ADHD symptoms. Adolescents with ADHD had similar school performance and peer relationships to those reported previously, but differences with regard to drug use, suicide and other impulsive behaviour. A follow-up study into adult life using a control group is recommended

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Environ Health Perspect. 2017 Aug;125:086001.

DEVELOPMENTAL PBDE EXPOSURE AND IQ/ADHD IN CHILDHOOD: A SYSTEMATIC REVIEW AND META-ANALYSIS.

Lam J, Lanphear BP, Bellinger D, et al.

BACKGROUND: In the United States, one in six children are affected by neurodevelopmental disorders, and polybrominated diphenyl ethers (PBDEs) in flame-retardant chemicals are measured ubiquitously in children.
OBJECTIVE: We conducted a systematic a systematic review regarding developmental exposure to PBDEs and intelligence or Attention Deficit/Hyperactivity Disorder (ADHD) and attention-related behavioral conditions in humans.
METHODS: We searched articles published up to 26 September 2016, and included original studies that quantified exposures to PBDEs incurred any time in proximity to conception or during in utero, perinatal, or childhood time periods. We evaluated the risk of bias of individual studies and the overall quality and strength of the evidence according to the Navigation Guide systematic review methodology. We established criteria in advance to identify studies that could be combined using random effects meta-analyses (DerSimonian-Laird method).
RESULTS: Fifteen studies met the inclusion criteria; 10 studies met the criteria for intelligence and nine for attention-related problems. We rated studies generally with "low" to "probably low" risk of bias and rated the overall body of evidence as "moderate" quality with "sufficient" evidence for an association between Intelligence Quotient (IQ) and PBDEs. Our meta-analysis of four studies estimated a 10-fold increase (in other words, times 10) in PBDE exposure associated with a decrement of 3.70 IQ points (95% confidence interval: 0.83, 6.56). We concluded the body of evidence was of "moderate" quality for ADHD with "limited" evidence for an association with PBDEs, based on the heterogeneity of association estimates reported by a

small number of studies and the fact that chance, bias, and confounding could not be ruled out with reasonable confidence.
CONCLUSION: We concluded there was sufficient evidence supporting an association between developmental PBDE exposure and reduced IQ. Preventing developmental exposure to PBDEs could help prevent loss of human intelligence. https://doi.org/10.1289/EHP1632

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Eur J Paediatr Neurol. 2017 May;21:593.
RESPONSE TO "SLEEP AND EXECUTIVE FUNCTIONS IN CHILDREN WITH ADHD".
Sanchez-Carpintero R.

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Eur Child Adolesc Psychiatry. 2017;1-9.
FINE MOTOR ABILITY AND PSYCHIATRIC DISORDERS IN YOUTH.
Mendes LST, Manfro GG, Gadelha A, et al.
Impaired fine motor ability has been linked to several domains of psychopathology. However, studies validating the specificity of this association among several categorical psychiatric disorders are still needed. The aim of this study was to assess differences in fine motor ability performance among four non-overlapping groups of psychiatric disorders and a group of typical developing comparisons (TDC). Our sample consisted of 2035 subjects aged 6-14-year-old. Diagnoses of psychiatric disorders were performed with the Development and Well-Being Assessment (DAWBA). Five non-overlapping groups without comorbidity were formed: phobic disorders (n = 101), distress disorders (n = 82), attention deficit hyperactivity disorder (ADHD) (n = 133), oppositional defiant disorder/conduct disorder (ODD/CD) (n = 52) and one group of typical developing comparisons (TDC) (n = 1667). Fine motor ability was evaluated by three tasks: sequential finger-thumb opposition, Oseretsky, and pronation/supination tests. Each task was assessed by total time to perform the movement and levels of accuracy, fluency, symmetry, precision, and coordination. We found that, when compared to TDC, the ADHD group performed more poorly in total fine motor ability (mean difference = âˆ’ 0.28; p = 0.014), time to complete the task (mean difference = 0.36; p < 0.001), accuracy (mean difference = âˆ’ 0.30; p = 0.005), fluency (mean difference = âˆ’ 0.26; p = 0.03), symmetry (mean difference âˆ’ 0.25; p = 0.04), precision (mean difference = âˆ’ 0.26; p = 0.026), and coordination (mean difference = âˆ’ 0.25; p = 0.042). The ADHD group also took more time to complete the task than the ODD/CD group (mean difference = 0.45; p = 0.037). No other significant between-group differences were found. Additional analyses showed those differences were statistically significant for all ADHD dimensions. Our results suggest that children with ADHD present impairments in all aspects of fine motor abilities compared to TDC, a difference not found in other psychiatric disorders

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Eur Child Adolesc Psychiatry. 2017;1-22.
WHAT IS THE LEVEL OF EVIDENCE FOR THE USE OF CURRENTLY AVAILABLE TECHNOLOGIES IN FACILITATING THE SELF-MANAGEMENT OF DIFFICULTIES ASSOCIATED WITH ADHD IN CHILDREN AND YOUNG PEOPLE? A SYSTEMATIC REVIEW.
Powell L, Parker J, Harpin V.
A number of technologies to help self-manage attention deficit hyperactivity disorder (ADHD) in children and young people (YP) have been developed. This review will assess the level of evidence for the use of such technologies. The review was undertaken in accordance with the general principles recommended in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis. 7545 studies were screened. Fourteen studies of technology that aim to self-manage difficulties associated with ADHD in children and YP were included. Primary outcome measures were measures that assessed difficulties related to ADHD. Databases searched were MEDLINE, Web of Science (Core collection), CINAHL, the Cochrane Library, ProQuest ASSIA, PsycINFO and Scopus. The methodological quality of the studies was assessed. This

review highlights the potential for the use of technology in paediatric ADHD management. However, it also demonstrates that current research lacks robustness; using small sample sizes, non-validated outcome measures and little psychoeducation component. Future research is required to investigate the value of technology in supporting children and YP with ADHD and a focus psychoeducation is needed

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Front Psychiatry. 2017;8.

DISRUPTED CONTROL-RELATED FUNCTIONAL BRAIN NETWORKS IN DRUG-NAIVE CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER.

Tao J, Jiang X, Wang X, et al.

Attention-deficit/hyperactivity disorder (ADHD) is a common neurodevelopmental disease featuring executive control deficits as a prominent neuropsychological trait. Executive functions are implicated in multiple sub-networks of the brain; however, few studies examine these sub-networks as a whole in ADHD. By combining resting-state functional MRI and graph-based approaches, we systematically investigated functional connectivity patterns among four control-related networks, including the frontoparietal network (FPN), cingulo-opercular network, cerebellar network, and default mode network (DMN), in 46 drug-naive children with ADHD and 31 age-, gender-, and intelligence quotient-matched healthy controls (HCs). Compared to the HCs, the ADHD children showed significantly decreased functional connectivity that primarily involved the DMN and FPN regions and cross-network long-range connections. Further graph-based network analysis revealed that the ADHD children had fewer connections, lower network efficiency, and more functional modules compared with the HCs. The ADHD-related alterations in functional connectivity but not topological organization were correlated with clinical symptoms of the ADHD children and differentiated the patients from the HCs with a good performance. Taken together, our findings suggest a less-integrated functional brain network in children with ADHD due to selective disruption of key long-range connections, with important implications for understanding the neural substrates of ADHD, particularly executive dysfunction

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Front Psychiatry. 2017;8.

EFFICACY AND TOLERABILITY OF DIFFERENT INTERVENTIONS IN CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Luan R, Mu Z, Yue F, et al.

Background: Our study is an analysis of multiple publications involving assessing the comparable efficacy and tolerability of six interventions, which are lisdexamfetamine dimesylate (LDX), atomoxetine (ATX), methylphenidate (MPH), clonidine hydrochloride (CLON), guanfacine extended release (GXR), and bupropion, for young patients (6-18 years old) suffering from attention deficit hyperactivity disorder (ADHD).
Methods: A conventional meta-analysis (MA) was performed to give direct comparisons and a network meta-analysis (NMA) was used to show the combination of direct and indirect evidence. Ranking preference for all the interventions under a certain outcome was given by the surface of cumulative ranking curve area (SUCRA).
Results: Overall, 15,025 participants from 73 studies were involved in our analysis. In the pairwise MA, LDX was associated with less withdrawal than ATX for lack of efficacy. MPH showed less effectiveness than LDX according to ADHD Rating Scale score. Based on the analysis of our NMA, significant results of efficacy that LDX is a competitive drug were observed when evaluating LDX in comparison with other drugs except for CLON. ATX and GXR presented higher rates of abdominal pain morbidity versus inactive treatment.
Conclusion: The stimulants LDX and MPH are still highly recommended because they are highly effective and are tolerated well by patients. Among the non-stimulants, CLON can be taken into consideration for its appreciable effectiveness and tolerability. ATX and GXR can be seen as moderate choices

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Hong Kong J Occup Ther. 2017;30:33-41.

THE EFFECTIVENESS OF MINDFULNESS-BASED INTERVENTION IN ATTENTION OF INDIVIDUALS WITH ADHD: A SYSTEMATIC REVIEW.

Lee CSC, Ma M-T, Ho H-Y, et al.

Background/Objective Mindfulness-based intervention has received more clinical interest and empirical support for individuals with ADHD especially to improve attention. However, no systematic review has been done to analyze and compare the effectiveness of mindfulness-based intervention on individuals with ADHD in different age groups. This review examined its effectiveness for individuals (children, adolescents and adults) with ADHD to improve attention.

Methods In 7 databases, totally of 152 studies were identified; 9 met the inclusion and exclusion criteria and were reviewed. Five of the studies recruited adults as the participants, two recruited adolescents as the participants, one recruited both adults and adolescents as the participants and one recruited children as the participants.

Results It was found that mindfulness-based intervention was comparatively more popularly used in adults with ADHD to improve attention, and the improvement was significant.

Conclusion It is still unclear whether mindfulness-based intervention is effective for children and adolescence with ADHD due to limited studies available and the limitations of the study design in the reviewed studies. Therefore, more research in the future is required to answer the question

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Indian J Psychiatry. 2016;58:S100.

CLINICAL PROFILE OF CHILDREN PRESENTING WITH SCHOOL REFUSAL: A RETROSPECTIVE ANALYSIS.

Sangoiajita B, Nachane N.

Introduction: School refusal is a serious problem seen in around 1-5% of all school going children. It can be defned as'child motivated refusal to attend or diffculties remaining in school for the entire day'. The child usually stays or returns home and doesn't attempt to conceal their non-attendance. It is generally associated with other behavioural and emotional problems, which if not addressed immediately, can have a negative impact on the mental health of the child in his crucial growing-up years.

Aims And Objectives: There is dearth of literature on school refusal in India The Aim was to study the clinical profiles, socio-demographic factors, and the diagnosis associated with school refusal. The type of family, parental conficts and birth complications were also studied.

Method: The study consisted of a retrospective analysis of children with school refusal attending the Child Guidance Clinic of a tertiary centre in Mumbai in the period of June 2013 to June2015. Children aged 5-16 d years were included in the study. A semi-structured proforma was useil to note the socio-demographic and birth details, and history of parental confict. The clinical diagnosis was made using DSM-IVTR.

Results And Conclusion: 45 children (27 males & 18 females) presented with school refusal. Depression was diagnosed in 49.2%, anxiety in 37.7%, ADHD in 22%, Mental Retardation in 20%, conversion disorder in 8.8% and unexplained physical symptoms found in 37.7%. 1child was diagnosed with schizophrenia and 3with OCD. Parental confict was present in 33.3% cases. Thus this study shows that children with school refusal should be screened for psychopathology so that early intervention can be instituted

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Indian J Psychiatry. 2016;58:S161.

CLINICAL STUDY OF IMPAIRMENT IN EXECUTIVE FUNCTIONS IN CHILDREN AND ADOLESCENTS WITH ADHD.

Kumar S, Arya A, Gupta PK, et al.

BACKGROUND: In recent past executive functions impairment have been implicated as a core defcit in ADHDindividual. Behavior rating scales are claimed to better assess the Executive Functions impairment in ADHD as they tell about impairment caused in real life situation. There is limited research on this area in India.

AIMS: To clinically assess the impairment in executive functions in children & adolescent with ADHD. And to compare the impairments (if any) in executive functions of ADHD with healthy controls.

METHOD: A total of 60 children and adolescents of 6-16 years, 30 ADHD and 30 normal controls were recruited from out-patient services of the department of psychiatry of a medical college in north India. Diagnosis was confrmed by DSM IV-TR. ADHD group is further divided on the basis of subtypes and presence or absence of comorbidities. Both the groups were assessed onMalin's Intelligence Scale for Indian Children (MISIC) and Brown Add scales for children and adolescents (BADDS). Data is statistically analyzed on SPSS.
RESULTS: Among the children with ADHD, 77.27% of children showed impairment in 4/6 domains of executive functions of BADDS. Among the adolescents with ADHD, 62.5% of adolescents showed impairment in 3/5 domains of executive functions of BADDS. The children and adolescent with ADHD did not show any signifcant difference in executive functions on the basis of subtype of ADHD and presence or absence of comorbidity. None of controls showed impairment in any domains of executive functions on BADSS. Both the study group and control group did not show any difference in IQ on the basis of MISIC.
CONCLUSION: Executive functions impairments are present in ADHD individuals. These impairments are core feature of ADHD and are not affected by subtypes of ADHD or either presence of absence of ADHD

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Indian J Psychiatry. 2016;58:S116-S118.

TO STUDY THE PREVALENCE OF ADULT ADHD AND ITS SIGNIFCANCE IN SUBSTANCE ABUSE PATIENTS.

Bhadoriya MS, Sidana R, Mushir U.

Introduction: Attention-defcit/hyperactivity disorder (ADHD) is a common childhood disorder, with an estimated worldwide incidence of 8%-12%, yet it is now known that ADHD often persists into adulthood. Studies have reported an association between a Specific genotype found in individuals with ADHD and the dopamine transporter. Other candidate genes that may be associated with ADHD have been identifed in the norepinephrine and serotonin systems. A familial pattern has been documented by case control studies indicating that children of adults with ADHD are themselves at increased risk for developing the disorder. Types Of Adult ADHD: According To the diagnostic and statistical manual of mental disorders, 4th edition, text revision (DSM-IV-TR), symptoms of ADHD begin in childhood (onset by age 7) and continue into adulthood. Three ADHD subtypes are recognized in the DSM-IV-TR: inattentive, hyperactive/impulsive, and combined type. ADHD not otherwise specifed is reserved for patients whose symptoms were not noted until or after age 7. To make a diagnosis of the predominantly inattentive subtype, atleast 6 of 9 symptoms of in attention must be present; to make a diagnosis of the predominantly hyperactive-impulsive subtype, 6 of 9 hyperactive impulsive symptoms must be present; for the combined subtype of ADHD to be diagnosed, criteria for both the preceding subtypes must be met.
Aims And Objectives: Primary Objectives To estimate the prevalence of Adult ADHD among Substance abuse patients. To compare the prevalence of Adult ADHD among Substance abuse cases and non-substance abuse controls.
Secondary Objectives: To compare the socio-demographic profile of patients with and without Adult ADHD among patients with substance abuse. To compare the co-morbid psychiatric illness in patients with and without Adult ADHD among patients with substance abuse. To compare the patterns of substance use and relapse in 6 months in patients with and without Adult ADHD among patients with substance abuse. Null Hypothesis Prevalence of ADHD symptoms do not differ with presence of the substance abuse. No signifcant difference in sociodemographic profile, clinical profile and comorbid psychiatric problems exists between presence and absence of ADHD in patients with Substance abuse
Materials And Methods: Study design: This was a prospective observational study. Study Venue: The study was conducted at Prerna De-addiction and Rehabilitation Centre at Tek Chand Sidana Memorial Psychiatric Hospital and De-addiction Centre, Sri Ganganagar, Rajasthan. Study duration: The study was conducted between June-2012 to June-2013. ^ Study population: Study population consisted of patients and those accompanying patients to the De-addiction centre. Sample size calculation: Sample Size was calculated using formula N= Z2 [P (1-P)]/d2, where d (width of confdence interval) was determine to be 5%, Z = 1.96 (5% precision), P (Prevalence) = 3.5 % (As in previous studies prevalence of adult ADHD was 2-5 %). Sample size was calculated to be 49 in each group. Finally study was conducted with a Sample size of 50 patients and 50 controls. STUDY GROUP Inclusion Criteria: a. Patients admitted in Prerna De-addicition& Rehabilitation Centre at Tek Chand Sidana Memorial Psychiatric Hospital & De-addiction Centre, Sri

Ganganagar (Raj.) b. Fulflling DSM IV-TR criteria for Substance use disorders (Substance Abuse or Substance Dependence) c. Males aged more than 18 years d. Willing to give written informed consent Exclusion Criteria: a. Patients with any substance induced disorders (eg. Intoxication, Withdrawal, induced sleep disorder, induced sexual disorder) without Substance Use Disorders. b. Patients having any co-morbid neurological problems other than seizures. c. Patients not willing to participate in the study. CONTROL GROUP: Inclusion Criteria: a. Subjects who are accompanying the patients to the De-addiction centre b. Males aged more than 18 years. c. Subjects do not use any psychoactive substance. d. Willing to give written informed consent Exclusion Criteria: a. Subjects with any history of any substance related disorder. b. Subjects having their frst degree relatives with substance related disorders. c. Subjects having any neurological problems. d. Subjects not willing to participate in the study. STUDY TOOLS a. Semi structured Performa for assessing Socio-demographic profile of the subjects and substance related behaviors and problems. b. Adult ADHD self report scale (ASRS VI.1) Study Procedure: Written informed consent was taken from the participant subjects. All sampled cases and controls were assessed using semi-structured questionnaire for socio-demographic profile and substance use. A detailed history, physical and mental status examination was done. The Adult ADHD Self Report Scale (ASRS-VI.1) was applied on both cases and controls. Subjects with four or more positive scoring in part-A have high chance of adult ADHD. It was confrmed by applying DSM-IV-TR criteria of adult ADHD. After discussing with a consultant psychiatrist the diagnosis of substance use disorders and comorbid psychiatric disorders made according to DSM IV-TR were recorded. All those fulflling DSM IV-TR criteria for substance use disorders viz., Substance abuse and substance dependence were termed patients with substance abuse in this study. Cases were assessed on frst day of admission and followed up every day till discharge. They were assessed for withdrawal symptoms, craving, aggressive behavior and impulsive behavior. The number of days taken for detoxification with an absence of signs of withdrawal was taken as duration for response to treatment. All patients with substance abuse (both Adult ADHD positive and negative) were followed for 6 months either during follow up or readmissions or through telephonic contact to know the recurrence of substance use behavior. Resuming the use of the substance after a period of atleast 3 weeks of abstinence was considered a relapse. Number of relapses during the six months including rehospitalization for relapse was recorded.

Results: The Results indicate that there was a signifcant difference in substance abuse and non-substance abuse subjects. It was identifed that subjects with substance abuse screened positive for ADHD had onset of substance abuse in early age, suffered from multiple substance abuse, and had delayed response to treatment in comparison to subject's diagnosed negative for ADHD. Lastly, substance abuse subjects had more mood fuctuations and lesser anxiety in those diagnosed positive for ADHD. There was a signifcant association of educational status in positive and negative ADHD substance abuse subjects (study group). Symptoms of ADHD were signifcantly associated with severity of addiction, onset of substance abuse, relapses, responding to therapy after treatment among substance abuse patients. Comorbid psychiatric illness among substance abuse patients was strongly associated with symptoms of ADHD. In non-substance abuse subjects (control group) the comorbid psychiatric illness such as depression was highly associated with symptoms of ADHD.

Conclusion: The prevalence of Adult ADHD in substance abuse was 22% and 4.0% in non-substance abuse subjects. Comorbidity of Psychiatric disorders and problems is signifcantly high in those with substance use disorder. Adult ADHD in substance abuse appears to increase the relapse rate and increase the chances of mood fuctuations even in absence of affective disorders. ADHD might also increase the risk of multiple substance abuse and delays the response to detoxifcation regimes. Above all interpretations and statistical confrmations sounded a concrete decision that Attention-Defcit/Hyperactive Disorder symptoms negatively infuence the substance abuse. Thus a routine screening for ADHD in substance abuse would better conceptualize the complex disorder. Thus research focusing on managing ADHD in substance use is the need of the day

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Indian J Psychiatry. 2016;58:S70.

A RETROSPECTIVE STUDY ON PSYCHIATRIC COMORBIDITIES AMONGST CHILDREN REFERRED TO TERTIARY CARE HOSPITAL FROM SCHOOL.

Dikshit RS.

Introduction: Education is one of the most important aspects of human resource development. Poor school performance not only Results in the child having a low self-esteem, but also causes signifcant stress to the parents and child. There are many reasons for children to under perform at school, such as, medical problems, below average intelligence, Specific learning disability, psychiatric disorders and even environmental causes

Material And Method: This is an observational cross sectional study.100 consecutive children referred to psychiatry department from Learning Disability clinic over a period of 6 months were studied. The students were referred to Learning Disability clinic from school.

Results: A signifcant number of children had Intellectual disability. These children had an eventful birth history and delayed developmental history. The most commonly seen psychiatric comorbidites were ADHD, ODD, conduct disorder, enuresis amongst others.

Conclusion: It is important to fnd the reason(s) for a child's poor school performance and come up with a treatment plan early so that the child can perform up to full potential. There is a need to have a structured multidisciplinary evaluation in such cases all over the country

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Indian J Psychiatry. 2016;58:S120.

A COMPULSION TO THROW AWAY PRESCRIBED TABLETS IN A CASE OF CHILDHOOD OCD WITH ATTENTION DEFCIT HYPERKINETIC DISORDER.

Chandran S, Kishor M, Navya ST, et al.

Obsessive-compulsive disorder (OCD) in children is one of the most complex and disabling disorders presenting to a hospital setting. It's symptomatology can mimic other psychiatric disorders, especially in children, making it confusing for the treatment team. It is often associated with co-morbidities like tics, depression and ADHD. The ADHD and OCD association still need to be established. We hereby report an instance of ADHD-OCD co-occurrence in a 16 year old boy, who presented with a 9 year history of restlessness, obsessions of contamination, symmetry, causing harm to others, setting fire, magical thoughts, with compulsions of washing, checking, ordering and arranging, counting and repeating, swallowing stones, mental rituals and self mutilating behaviour. The patient would pen his own rule book to ft his predilection for symmetry and though the patient recognized these repetitive rituals to be unwarranted and tried resisting most of them, there were multiple instances throughout his schooling where he would fnd himself in disciplinary trouble independent of these repetitive rituals. These instances were attributable to excessive activity which was disorganised and poorly regulated, an impaired attention Resulting in shifting to a new task without completion of the former one. The patient also had associated complex motor and vocal tics, and the Resulting distress had led to two suicidal attempts. His compulsion to throw away prescribed tablets was concerned with issues of contour, shape and texture. The interesting aspects of the phenomenology and management will be discussed

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Iran J Psychiatr Behav Sci. 2017;11.

EFFECT OF PARENT MANAGEMENT TRAINING ON ATTENTION, RESPONSE PREVENTION, IMPULSIVITY AND VIGILANCE OF BOYS WITH ATTENTION DEFICIENT/HYPERACTIVE DISORDER.

Shafiee-Kandjani AR, Noorazar G, Shahrokhi H, et al.

Background: Executive function of the brain consists of organizing, shifting attention, monitoring, self-regulating, inhibition and working memory, which are diversely affected in attention deficit/ hyperactivity disorder (ADHD). Parent management training (PMT) is a major intervention for ADHD with significant impact on clinical symptoms. However, little is known about its effect on cognitive aspects of ADHD.

Objectives: The aim of this study was to assess the effects of parent management training (PMT) on attention, response prevention, impulsivity, and vigilance of males with ADHD as well as their clinical symptoms.
Methods: In this clinical trial, 32 subjects were recruited from a child and adolescent psychiatric clinic in Tabriz, Iran. Participants (all males) were divided to 2 groups. One group received routine clinical care plus 8 sessions of PMT and the other group only received routine clinical care as a control group. Clinical symptoms were evaluated by Conner's rating scale and performance of children in terms of executive function was tested by the continuous performance test (CPT) and Go/ no Go test before and after the intervention. A follow-up measurement was performed at week 12. Using SPSS 17.0 statistics, chi-square and independent-sample t tests were used to compare sample means. A two-way repeated measures analysis of variance (time-treatment interaction) was also performed.
Results: Parent management training had a higher effect on hyperactivity (P = 0.032) and oppositional (P = 0.007) symptoms of children. Commission errors (reflecting impulsivity and response prevention), omission errors (reflecting inattention), and reaction time (reflecting vigilance) in Go/no Go test were not significantly different between the 2 groups. Omission errors in CPT and the reaction time significantly improved in PMT and routine clinical care (RCC) group (P = 0.032).
Conclusions: Parent management training may improve executive functions in children with ADHD in terms of reaction time and omission errors

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J Neurosci Methods. 2017 Feb;278:87-100.

LEARNING EFFECTIVE CONNECTIVITY FROM FMRI USING AUTOREGRESSIVE HIDDEN MARKOV MODEL WITH MISSING DATA.

Dang S, Chaudhury S, Lall B, et al.

BACKGROUND: Effective connectivity (EC) analysis of neuronal groups using fMRI delivers insights about functional-integration. However, fMRI signal has low-temporal resolution due to down-sampling and indirectly measures underlying neuronal activity.
NEW METHOD: The aim is to address above issues for more reliable EC estimates. This paper proposes use of autoregressive hidden Markov model with missing data (AR-HMM-md) in dynamically multi-linked (DML) framework for learning EC using multiple fMRI time series. In our recent work (Dang et al., 2016), we have shown how AR-HMM-md for modelling single fMRI time series outperforms the existing methods. AR-HMM-md models unobserved neuronal activity and lost data over time as variables and estimates their values by joint optimization given fMRI observation sequence.
RESULTS: The effectiveness in learning EC is shown using simulated experiments. Also the effects of sampling and noise are studied on EC. Moreover, classification-experiments are performed for Attention-Deficit/Hyperactivity Disorder subjects and age-matched controls for performance evaluation of real data. Using Bayesian model selection, we see that the proposed model converged to higher log-likelihood and demonstrated that group-classification can be performed with higher cross-validation accuracy of above 94% using distinctive network EC which characterizes patients vs.
CONTROLS: The full data EC obtained from DML-AR-HMM-md is more consistent with previous literature than the classical multivariate Granger causality method.
COMPARISON: The proposed architecture leads to reliable estimates of EC than the existing latent models.
CONCLUSIONS: This framework overcomes the disadvantage of low-temporal resolution and improves cross-validation accuracy significantly due to presence of missing data variables and autoregressive process

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J Affective Disord. 2017.

LIGHT UP ADHD: I. CORTICAL HEMODYNAMIC RESPONSES MEASURED BY FUNCTIONAL NEAR INFRARED SPECTROSCOPY (FNIRS).

Mauri M, Nobile M, Bellina M, et al.

Background: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by deficits in cognitive and emotional self-control. Optical technique acquisitions, such as near infrared spectroscopy (NIRS), seem to be very promising during developmental ages, as they are non- invasive techniques and less influenced by body movements than other neuroimaging methods. Recently, these new techniques are being widely used to measure neural correlates underlying neuropsychological deficits in children with ADHD.

Methods: In a short series of articles, we will review the results of functional NIRS (fNIRS) studies in children with ADHD. The present brief review will focus on the results of the fNIRS studies that investigate cortical activity during neuropsychological and/or emotional tasks. Results: According to the reviewed studies, children and adolescents with ADHD show peculiar cortical activation both during neurological and emotional tasks, and the majority of the reviewed studies revealed lower prefrontal cortex activation in patients compared to typically developmental controls.

Limitations: a consistent interpretation of these results is limited by the substantial methodological heterogeneity including patients' medication status and washout period, explored cerebral regions, neuropsychological tasks, number of channels and sampling temporal resolutions.

Conclusions: fNIRS seems to be a promising tool for investigating neural substrates of emotional dysregulation and executive function deficits in individuals with ADHD during developmental ages

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J Child Psychol Psychiatry. 2017 Dec;58:1290-300.

RESEARCH REVIEW: THE ROLE OF OBSTETRIC AND NEONATAL COMPLICATIONS IN CHILDHOOD ATTENTION DEFICIT AND HYPERACTIVITY DISORDER' A SYSTEMATIC REVIEW.

Serati M, Barkin JL, Orsenigo G, et al.

Background Attention deficit and hyperactivity disorder (ADHD) is a developmental disorder characterized by an inability to sustain attention, activity levels and impulse control, and, according to the latest studies, the prevalence is about 8% and in some countries less than 1%. Currently, it is well known that complications during the perinatal period have significant implications on child's physical and mental health. Purpose of the present paper is to review the literature about the association between perinatal complications and future risk of an ADHD diagnosis.

Methods A research in the main database sources has been conducted to obtain a systematic review on the perinatal risk factors of ADHD.

Results Among perinatal complications, available data indicate low birth weight (LBW) (Cohen's d effect size range: 0.31-1.64â€• small effect size) and preterm birth (PB) (range d: 0.41-0.68) as the most important factors associated with a future diagnosis of ADHD.

Conclusions PB and LBW children should be carefully monitored for an early diagnosis of ADHD limiting the impact of the disease in life span. A systematic review focusing on these risk factors have not been published until now, in the next future preventive strategies should be developed in order to minimize ADHD onset

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J Commun Disord. 2018;71:22-36.

YOUNG CHILDREN'S FAMILY HISTORY OF STUTTERING AND THEIR ARTICULATION, LANGUAGE AND ATTENTIONAL ABILITIES: AN EXPLORATORY STUDY.

Choi D, Conture EG, Tumanova V, et al.

Purpose The purpose of this study was to determine whether young children who do (CWS) and do not stutter (CWNS) with a positive versus negative family history of stuttering differ in articulation, language and attentional abilities and family histories of articulation, language and attention related disorders.

Method Participants were 25 young CWS and 50 young CWNS. All 75 participants' caregivers consistently reported a positive or negative family history of stuttering across three consecutive time points that were about 8 months apart for a total of approximately 16 months. Each participant's family history focused on the same, relatively limited number of generations (i.e., participants' parents & siblings). Children's family history of stuttering as well as articulation, language, and attention related disorders was obtained from one or two caregivers during an extensive interview. Children's speech and language abilities were measured using four standardized articulation and language tests and their attentional abilities were measured using caregiver reports of temperament.
Results Findings indicated that (1) most caregivers (81.5% or 75 out 92) were consistent in their reporting of positive or negative history of stuttering; (2) CWNS with a positive family history of stuttering, compared to those with a negative family history of stuttering, were more likely to have reported a positive family history of attention deficit/hyperactivity disorder (ADHD), and (3) CWNS with a positive family history of stuttering had lower language scores than those with a negative family history of stuttering. However, there were no such significant differences in family histories of ADHD and language scores for CWS with a positive versus negative family history of stuttering. In addition, although 24% of CWS versus 12% of CWNS's caregivers reported a positive family history of stuttering, inferential analyses indicated no significant differences between CWS and CWNS in relative proportions of family histories of stuttering.
Conclusion Finding that a relatively high proportion (i.e., 81.5%) of caregivers consistently reported a positive or negative family history of stuttering across three consecutive time points should provide some degree of assurance to those who collect such caregiver reports. Based on such consistent caregiver reports, linguistic as well as attentional vulnerabilities appear associated with a positive family history of stuttering, a finding that must await further empirical study for confirmation or refutation

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J Loss Trauma. 2017 Oct;22:540-63.
ADHD AND GRIEF: DIAGNOSIS AND DIFFERENTIATION AT ONE FEDERALLY QUALIFIED HEALTH CENTER.
Harris HW, Hess B, Polson EC, et al.
Family physicians provide medical care including diagnosis for children experiencing loss and grief. The cognitive impact of loss includes poor attention and concentration, suggestive of attention deficit hyperactivity disorder (ADHD). Our study examined this phenomenon in a community health center (CHC) utilizing physicians' surveys and a medical record audit of 378 children diagnosed with ADHD during a three-year period. Results identified ambiguous loss and trauma resulting from family instability, absent parent, domestic violence, abuse, and foster care, often unrecognized by physicians as producing grief accompanied by attention and concentration problems. Findings suggest exploration of repeated ambiguous losses in children with ADHD

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J Matern -Fetal Neonatal Med. 2017;1-4.
ASSOCIATION BETWEEN SMALL FOR GESTATIONAL AGE AND LOW BIRTH WEIGHT WITH ATTENTION DEFICIT AND IMPAIRED EXECUTIVE FUNCTIONS IN 3-6 YEARS OLD CHILDREN.
Shariat M, Gharaee J, Dalili H, et al.
BACKGROUND: Behavioral disorders and attention deficit hyperactivity disorder (ADHD) symptoms are frequently reported among children with history of small body size at birth and disproportionate intrauterine growth retardation. The current study aimed to investigate some factors like executive functions and attention deficit in children with history of Small for gestational age (SGA) and/or Low Birth Weight (LBW) at birth.
METHODS: A historical cohort study was done and 3-6 years old preschool children (with past history of SGA/LBW) from some kindergartens and health centers were selected. Control group was randomly selected among children with history of normal birth weight and appropriate for gestational age at birth. All children were interviewed by an expert psychologist. Variables related to their attention, development, and executive functions were assessed by ASQ, Conner's, and Wisconsin Card Sorting Test. Completed questionnaires

related Attention deficit and indexes of executive functions were evaluated between children in case groups and their counterparts in controls.
RESULTS: Based on inclusion criteria, 229 preschool children entered the study. With regard to size for gestational age, 124 cases were categorized in the SGA/LBW group and the rest were assigned in the appropriate for gestational age (AGA) group. In the case group, NPE and Percent Perseverative Errors (PPE) scores were significantly lower than normal birth weight group (p = .0001, p = .015). Scores related B item of Conner's was significantly different between cases and their controls (p = .039, p = .035).
CONCLUSIONS: Our results indicated that children with past history of some risks at birth may suffer from complications related attention and executive functions in their childhood. Recommendations for further research are strongly suggested

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J Neurosci Rural Pract. 2017;8:660-61.
CHROMOSOME 15 DUPLICATION AND ATTENTION-DEFICIT HYPERACTIVITY.
Gnanavel S.
Chromosome 15 duplication has been associated with a number of psychiatric illnesses including psychosis and autism. However, literature on association with attention-deficit hyperactivity disorder (ADHD) is scant. This case report describes a patient with chromosome 15 duplication diagnosed with ADHD in our neurodevelopmental clinic. The possible biological underpinnings are discussed along with possible challenges in diagnosis and management. The need for better understanding ADHD as a behavioral phenotype in such cases along with need for tailored management strategies is emphasized

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Rural Ment Health. 2017 Oct;41:306-09.
CHILD AND ADOLESCENT PSYCHIATRIC CONSULTATION IN MICRONESIA.
Ghiasuddin A.
Little is known about child mental health in Micronesia. The objective of this brief report is to describe some features of childhood attention-deficit hyperactivity disorder (ADHD) in 1 Micronesian state, Yap. A retrospective review of records from 2 site visits made in 2010 was conducted. During the visits, the author assessed the majority of the children on the island who had been identified as having 'special needs' by their primary care provider. The author's assessment included clinical interviews with the child, caregivers, and special education teachers, as well as review of medical records and school reports, when available. A total of 16 child cases were reviewed, 9 of whom carried a diagnosis of ADHD; 6 of these children were on clonidine, the only medication available for ADHD in Yap. Most children had multiple other diagnoses, usually a seizure disorder or some form of developmental delay. Behavior management strategies used by parents and teachers varied from child to child. Psychoeducation on ADHD and behavior management strategies (while respecting Micronesian culture and family structure) are potential areas to focus on during future site visits

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J Neurol Sci. 2018;385:7-11.
LACK OF AN ASSOCIATION BETWEEN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) AND AMYOTROPHIC LATERAL SCLEROSIS (ALS).
Ebel L, Petri S, Krauss JK, et al.
Background Lulé, Ludolph, and Ludolph (2008) hypothesized that there may be a pathophysiological link between attention-deficit/hyperactivity disorder (ADHD) and amyotrophic lateral sclerosis (ALS). They summarized common clinical features, specifically enhanced physical and psychological activity, which have been described typically for ADHD patients and also as common personality traits before disease onset in patients with ALS.

Methods We assessed the lifetime prevalence rate of ADHD in 104 patients with ALS using valid self-report instruments for ADHD symptoms in childhood (WURS-k) and adulthood (ADHD-SB). Results were compared with a population-based sample (n = 2069) and with patients with Parkinson's disease (PD, n = 52) using regression analyses and adjusting for sociodemographic differences. Physical activity was assessed by the 21-item exercise dependency scale (EDS-21).
Results ALS patients reported a lower prevalence of childhood ADHD compared to the general population. Both clinical groups reported significantly lower scores on the WURS-k scale and the attention deficit subscale of the ADHD-SB. The EDS-21 showed significantly longer exercise times in ALS and PD patients.
Conclusions We could not show that ADHD is more common in ALS patients. However, our results revealed shared personality traits in ALS and PD with lower rates of premorbid attention deficit symptoms and increased physical activity

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Konuralp Derg. 2017;9:31-36.

EVALUATION OF BLOOD PARAMETERS IN ATTENTION DEFICIENCY AND HYPERACTIVITY DISORDER.

Yildirmak ZY, et al.

Objective: Attention deficit hyperactivity disorder (ADHD) is a neuropsychiatric disorder that is common in the paediatric age group. Although some studies have been conducted on this purpose, the etiology has not been fully elucidated. We aimed to contribute on literature about the disease through investigating some blood parameters at pediatric ADHD patients.
Methods: The study included 91 children and 115 healthy children between the ages of 5 and 15 years. Serum iron, total iron binding capacity, ferritin, vitamin B12 level, folic acid level, free T4 and thyroid stimulating hormone levels were studied in whole group.
Results: The mean age of the patient group was 9.0 ± 2.5 years, the mean age of the control group was 9.7 ± 3.1 years, and there was no difference between them. Male sex ratio was higher in both groups. Significant changes were detected in MCV, RDW, neutrophil count, MPV, plateletcrit (PCT), platelet distribution width (PDW) results between control and experimental groups. Serum iron level was significantly lower in the control group comparing to the patient group. There was no statistical difference between the groups regarding ferritin values. When the results of vitamin B12, folic acid and thyroid function tests were evaluated, no statistically significant difference was found between the groups.
Conclusion: Further studies which involve larger population are essential to confirm the results that our findings to be find meaningful

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Med Lett Drugs Ther. 2017;59:183-84.

COTEMPLA XR-ODT - ANOTHER LONG- ACTING METHYLPHENIDATE FOR ADHD.

Anon.

The FDA has approved an extended-release orally disintegrating tablet formulation of methylphenidate (Cotempla XR-ODT - Neos Therapeutics) for oncedaily treatment of attention-defi cit/hyperactivity disorder (ADHD) in children 6-17 years old. Cotempla XR-ODT is the first extended-release orally disintegrating tablet formulation of methylphenidate to become available in the US

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Neuroimage Clin. 2017;14:112-21.

YOUNG ADOLESCENTS WITH AUTISM SHOW ABNORMAL JOINT ATTENTION NETWORK: A GAZE CONTINGENT FMRI STUDY.

Oberwelland E, Schilbach L, Barisic I, et al.

Behavioral research has revealed deficits in the development of joint attention (JA) as one of the earliest signs of autism. While the neural basis of JA has been studied predominantly in adults, we recently demonstrated a protracted development of the brain networks supporting JA in typically developing children

and adolescents. The present eye-tracking/fMRI study now extends these findings to adolescents with autism. Our results show that in adolescents with autism JA is subserved by abnormal activation patterns in brain areas related to social cognition abnormalities which are at the core of ASD including the STS and TPJ, despite behavioral maturation with no behavioral differences. Furthermore, in the autism group we observed increased neural activity in a network of social and emotional processing areas during interactions with their mother. Moreover, data indicated that less severely affected individuals with autism showed higher frontal activation associated with self-initiated interactions. Taken together, this study provides first-time data of JA in children/adolescents with autism incorporating the interactive character of JA, its reciprocity and motivational aspects. The observed functional differences in adolescents ASD suggest that persistent developmental differences in the neural processes underlying JA contribute to social interaction difficulties in ASD

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Neurology. 2017 Mar;88:1029-36.

MODERATORS AND PREDICTORS OF RESPONSE TO BEHAVIOR THERAPY FOR TICS IN TOURETTE SYNDROME.

Sukhodolsky DG, Woods DW, Piacentini J, et al.

OBJECTIVE: To examine moderators and predictors of response to behavior therapy for tics in children and adults with Tourette syndrome and chronic tic disorders.

METHODS: Data from 2 10-week, multisite studies (1 in children and 1 in adults; total n = 248) comparing comprehensive behavioral intervention for tics (CBIT) to psychoeducation and supportive therapy (PST) were combined for moderator analyses. Participants (177 male, 71 female) had a mean age of 21.5 +/- 13.9 years (range 9-69). Demographic and clinical characteristics, baseline tic-suppressing medication, and co-occurring psychiatric disorders were tested as potential moderators for CBIT vs PST or predictors of outcome regardless of treatment assignment. Main outcomes measures were the Yale Global Tic Severity Scale Total Tic score and the Clinical Global Impression-Improvement score assessed by masked evaluators.

RESULTS: The presence of tic medication significantly moderated response to CBIT vs PST (p = 0.01). Participants showed tic reduction after CBIT regardless of tic medication status, but only participants receiving tic medication showed reduction of tics after PST. Co-occurring psychiatric disorders, age, sex, family functioning, tic characteristics, and treatment expectancy did not moderate response. Across both treatments, greater tic severity (p = 0.005) and positive participant expectancy (p = 0.01) predicted greater tic improvement. Anxiety disorders (p = 0.042) and premonitory urge severity (p = 0.005) predicted lower tic reduction.

CONCLUSIONS: Presence of co-occurring attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, or anxiety disorders did not moderate response to CBIT. Although participants on tic medication showed improvement after CBIT, the difference between CBIT and PST was greater for participants who were not on tic-suppressing medication.

CLINICALTRIALSGOV IDENTIFIERS: The child and adult CBIT studies are listed on clinical trials.gov (NCT00218777 and NCT00231985, respectively). CLASSIFICATION OF EVIDENCE: This study provides Class I evidence that CBIT is effective in reducing tic severity across subgroups of patients with chronic tic disorders, although the difference between treatments was smaller for participants on tic-suppressing medications, suggesting reduced efficacy in this subgroup

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Neurosci Lett. 2018;665:176-81.

GENDER DIFFERENCES IN ANOMALOUS SUBCORTICAL MORPHOLOGY FOR CHILDREN WITH ADHD.

Wang Y, Xu Q, Li S, et al.

Although studies showed subtle reductions in brain volume in fronto-striatial regions in children with ADHD, there have been limited investigations of volume and lateralizaton in subcortical structures and a paucity of exploration of the influence of gender on these findings. This study aims to examine morphology of subcortical structures and their association with ADHD symptoms in boys and girls as compared to their typically-developing (TD) peers. One hundred and eighty five children aged 7-14 years with and without

ADHD were included from ADHD-200 Consortium. Results showed that compared to TD boys, boys with ADHD had reduced accumbens, amygdala and hippocampus volumes. There were no volumetric differences in any structure between ADHD and TD girls. Asymmetry analysis revealed right lateralization compressions within the thalamus in ADHD boys relative to TD boys. The findings suggest a gender dimorphic pattern of differences in subcortical structures in children with ADHD, and a possible neurobiological mechanism where boys with ADHD demonstrate increasing difficulties with hyperactivity/impulsivity

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Pediatrics. 2017 Dec;140.

PERINATAL OUTCOMES AFTER TREATMENT WITH ADHD MEDICATION DURING PREGNANCY.

Norby U, Winbladh B, Kallen K.

OBJECTIVES: To analyze perinatal outcomes after maternal use of attention-deficit/hyperactivity disorder (ADHD) medication during pregnancy.

METHODS: The study included singletons born between 2006 and 2014 in Sweden. Data on prescription drug use, pregnancies, deliveries, and the newborn infants' health were obtained from the Swedish Medical Birth Register, the Prescribed Drug Register, and the Swedish Neonatal Quality Register. We compared infants exposed to ADHD medication during pregnancy with infants whose mothers never used these drugs and infants whose mothers used ADHD medication before or after pregnancy. Analyses were performed with logistic regression.

RESULTS: Among 964 734 infants, 1591 (0.2%) were exposed to ADHD medication during pregnancy and 9475 (1.0%) had mothers treated before or after pregnancy. Exposure during pregnancy increased the risk for admission to a NICU compared with both no use and use before or after pregnancy (adjusted odds ratio [aOR], 1.5; 95% confidence interval [CI], 1.3-1.7; and aOR, 1.2; 95% CI, 1.1-1.4, respectively). Infants exposed during pregnancy had more often central nervous system-related disorders (aOR, 1.9; 95% CI, 1.1-3.1) and were more often moderately preterm (aOR, 1.3; 95% CI, 1.1-1.6) than nonexposed infants. There was no increased risk for congenital malformations or perinatal death.

CONCLUSIONS: Treatment with ADHD medication during pregnancy was associated with a higher risk for neonatal morbidity, especially central nervous system-related disorders such as seizures. Because of large differences in background characteristics between treated women and controls, it is uncertain to what extent this can be explained by the ADHD medication per se

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PLoS ONE. 2017;12.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER ASSOCIATED WITH KCHIP1 RS1541665 IN KV CHANNELS ACCESSORY PROTEINS.

Yuan F-F, Gu X, Huang X, et al.

Attention-deficit/hyperactivity disorder (ADHD) is an early onset childhood neurodevelop-mental disorder with high heritability. A number of genetic risk factors and environment factors have been implicated in the pathogenesis of ADHD. Genes encoding for subtypes of voltage-dependent K channels (Kv) and accessory proteins to these channels have been identified in genome-wide association studies (GWAS) of ADHD. We conducted a two-stage case-control study to investigate the associations between five key genes (KChIP4, KChIP1, DPP10, FHIT, and KCNC1) and the risk of developing ADHD. In the discovery stage comprising 256 cases and 372 controls, KChIP1 rs1541665 and FHIT rs3772475 were identified; they were further genotyped in the validation stage containing 328cases and 431 controls.KChIP1 rs1541665 showed significant association with a risk of ADHD at both stages, with CC vs TT odds ratio (OR) = 1.961, 95% confidence interval (CI) = 1.366-2.497, in combined analyses (P-FDR = 0.007). Moreover, we also found rs1541665 involvement in ADHD-I subtype (OR (95% CI) = 2.341(1.713, 3.282), and Hyperactive index score (P = 0.005) in combined samples.Intriguingly, gene-environmental interactions analysis consistently revealed the potential interactionsof rs1541665 collaboratingwith maternal stress pregnancy (Pmul = 0.021) and blood lead (Padd = 0.017) to modify ADHD risk. In conclusion, the current study provides evidence that genetic

variants of Kv accessory proteins may contribute to the susceptibility of ADHD.Further studies with different ethnicitiesare warranted to produce definitive conclusions

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Psicothema. 2017 Feb;29:91-95.

DETECTING DIFFERENTIAL ITEM FUNCTIONING IN BEHAVIORAL INDICATORS ACROSS PARALLEL FORMS.

Gomez-Benito J, Balluerka N, Gonzalez A, et al.

BACKGROUND: Despite the crucial importance of the notion of parallel forms within Classical Test Theory, the degree of parallelism between two forms of a test cannot be directly verified due to the unobservable nature of true scores. We intend to overcome some of the limitations of traditional approaches to analyzing parallelism by using the Differential Item Functioning framework.

METHOD: We change the focus on comparison from total test scores to each of the items developed during test construction. We analyze the performance of a single group of individuals on parallel items designed to measure the same behavioral criterion by several DIF techniques. The proposed approach is illustrated with a dataset of 527 participants that responded to the two parallel forms of the Attention Deficit-Hyperactivity Disorder Scale (Caterino, Gómez-Benito, Balluerka, Amador-Campos, & Stock, 2009).

RESULTS: 12 of the 18 items (66.6%) show probability values associated with the Mantel χ 2 statistic of less than .01. The standardization procedure shows that half of DIF items favoured Form A and the other half Form B.

CONCLUSIONS: The “differential functioning of behavioral indicators” (DFBI) can provide unique information on parallelism between pairs of items to complement traditional analysis of equivalence between parallel test forms based on total scores

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Psicothema. 2017 Feb;29:103-10.

CRITERION VALIDITY AND CLINICAL USEFULNESS OF ATTENTION DEFICIT HYPERACTIVITY DISORDER RATING SCALE IV IN ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD) AS A FUNCTION OF METHOD AND AGE.

Lopez-Villalobos JA, Andres-De LJ, Lopez-Sanchez MV, et al.

BACKGROUND: The aim of this research is to analyze Attention Deficit Hyperactivity Disorder Rating Scales IV (ADHD RS-IV) criteria validity and its clinical usefulness for the assessment of Attention Deficit Hyperactivity Disorder (ADHD) as a function of assessment method and age.

METHODOLOGY: A sample was obtained from an epidemiological study (n = 1095, 6-16 years). Clinical cases of ADHD (ADHD-CL) were selected by dimensional ADHD RS-IV and later by clinical interview (DSM-IV). ADHD-CL cases were compared with four categorical results of ADHD RS-IV provided by parents (CATPA), teachers (CATPR), either parents or teachers (CATPAOPR) and both parents and teachers (CATPA&PR). Criterion validity and clinical usefulness of the answer modalities to ADHD RS-IV were studied.

RESULTS: ADHD-CL rate was 6.9% in childhood, 6.2% in preadolescence and 6.9% in adolescence. Alternative methods to the clinical interview led to increased numbers of ADHD cases in all age groups analyzed, in the following sequence: CATPAOPR> CATPRO> CATPA> CATPA&PR> ADHD-CL. CATPA&PR was the procedure with the greatest validity, specificity and clinical usefulness in all three age groups, particularly in the childhood.

CONCLUSIONS: Isolated use of ADHD RS-IV leads to an increase in ADHD cases compared to clinical interview, and varies depending on the procedure used

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Psychiatry Res. 2017 Mar;249:70-77.

SITUATING VIOLENT IDEATIONS WITHIN THE LANDSCAPE OF MENTAL HEALTH: ASSOCIATIONS BETWEEN VIOLENT IDEATIONS AND DIMENSIONS OF MENTAL HEALTH.

Murray AL, Eisner M, Obsuth I, et al.

Violent ideations occur more frequently in individuals with mental health problems. They may be of interest in clinical contexts as possible indicators of dangerousness, as corollaries of mental health problems, as candidate treatment targets and as potentially playing a role in perpetuation or onset of symptoms. In spite of their relevance to mental health, some fundamental questions about their place within the broader landscape of mental health problems remain unanswered. To provide a basic characterisation of the relations between violent ideations and dimensions of mental health and provide a foundation for future research in this area we factor analysed a measure of violent ideations and an omnibus measure of mental health dimensions in a normative sample of 1306 youth (at age 17). Results supported a separate dimension of violent ideations with a small to moderate correlation with five other dimensions of mental health: internalising, prosociality, ADHD, indirect/proactive aggression, and physical/reactive aggression. Controlling for comorbidity among mental health dimensions, all but ADHD had unique relations with violent ideations. This suggests that violent ideations are potentially of broad relevance to mental health and related behaviours and there should be a greater research effort aimed at understanding their possible role in mental health

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Psychiatry Res. 2017 May;251:255-60.

MORTALITY IN INDIVIDUALS WITH DISRUPTIVE BEHAVIOR DISORDERS DIAGNOSED BY SPECIALIST SERVICES - A NATIONWIDE COHORT STUDY.

Scott JG, Giortz PM, Erskine HE, et al.

Disruptive behavior disorders (DBDs), inclusive of oppositional defiant disorder (ODD) and conduct disorder (CD), are associated with outcomes likely to increase risk of mortality. Using Danish National Registers, a total of 1.92 million individuals including 9495 individuals with DBDs diagnosed by specialist services were followed from their first birthday to 2013. Those with and without DBDs were compared using mortality rate ratios (MRRs) estimated using Poisson regression and adjusted for calendar period, age, sex, family history of psychiatric disorders, maternal age at time of birth, paternal age at time of birth, parental education status, and parental employment status. Over the course of follow up, which totalled 24.9 million person-years, 5580 cohort members died including 78 individuals with DBDs. The mortality rate per 10,000 person-years was 9.66 for individuals with DBDs compared to 2.22 for those with no diagnosis. This corresponded to a fully adjusted MRR of 2.57 (95% confidence interval 2.04-3.20). Comorbid substance use disorder and attention-deficit/hyperactivity disorder resulted in the highest MRR across all categories. These findings demonstrate the excess mortality associated with DBDs

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Psychiatry Res. 2017 Mar;249:244-51.

WHAT DO CHILDHOOD ATTENTION DEFICIT/HYPERACTIVITY SYMPTOMS IN DEPRESSED ADULTS TELL US ABOUT THE BIPOLAR SPECTRUM?

Purper-Ouakil D, Porfirio MC, Le SY, et al.

BACKGROUND: This study aims to establish if adult patients with major depressive disorder (MDD) and childhood Attention Deficit/Hyperactivity disorder (ADHD) symptoms would be more frequently within the bipolar spectrum than depressed patients without childhood ADHD.

METHODS: This study was carried out in outpatients recruited by psychiatrists in private practice, with 3963 participants being included in the final sample. Clinicians filled out questionnaires about current depressive symptoms in their patients, lifetime bipolar symptoms, global assessment of functioning and parental history of both major depression and bipolar disorder. Patients assessed current level of anxiety and depressive symptoms and antecedents of childhood ADHD symptoms.

RESULTS: Depressed adults with significant childhood ADHD symptoms had a specific pattern of their major depressive episode compared to depressed patients without such symptoms. Subjects with childhood ADHD

symptoms were more likely to report lifetime symptoms of mania/hypomania and to have a parent with type I or II bipolar disorder. The developmental trajectories of familial risk for lifetime bipolar symptoms showed that parental bipolar disorder influenced lifetime bipolar symptoms both through a direct pathway and an indirect pathway involving childhood ADHD symptoms. Childhood ADHD and number of depressive symptoms both made direct contributions to lifetime bipolar symptoms

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Psychiatry Res. 2017 Apr;262:55-62.

ABNORMAL FEAR CIRCUITRY IN ATTENTION DEFICIT HYPERACTIVITY DISORDER: A CONTROLLED MAGNETIC RESONANCE IMAGING STUDY.

Spencer AE, Marin MF, Milad MR, et al.

We examined whether non-traumatized subjects with Attention Deficit Hyperactivity Disorder (ADHD) have dysfunctional activation in brain structures mediating fear extinction, possibly explaining the statistical association between ADHD and other disorders characterized by aberrant fear processing such as PTSD. Medication naive, non-traumatized young adult subjects with (N=27) and without (N=20) ADHD underwent a 2-day fear conditioning and extinction protocol in a 3T functional magnetic resonance imaging (fMRI) scanner. Skin conductance response (SCR) was recorded as a measure of conditioned response. Compared to healthy controls, ADHD subjects had significantly greater insular cortex activation during early extinction, lesser dorsal anterior cingulate cortex (dACC) activation during late extinction, lesser ventromedial prefrontal cortex (vmPFC) activation during late extinction learning and extinction recall, and greater hippocampal activation during extinction recall. Hippocampal and vmPFC deficits were similar to those documented in PTSD subjects compared to traumatized controls without PTSD. Non-traumatized, medication naive adults with ADHD had abnormalities in fear circuits during extinction learning and extinction recall, and some findings were consistent with those previously documented in subjects with PTSD compared to traumatized controls without PTSD. These findings could explain the significant association between ADHD and PTSD as well as impaired emotion regulation in ADHD

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Psychol Med. 2017 May;47:1259-70.

DIAGNOSTIC UTILITY OF BRAIN ACTIVITY FLOW PATTERNS ANALYSIS IN ATTENTION DEFICIT HYPERACTIVITY DISORDER.

Biederman J, Hammerness P, Sadeh B, et al.

BACKGROUND: A previous small study suggested that Brain Network Activation (BNA), a novel ERP-based brain network analysis, may have diagnostic utility in attention deficit hyperactivity disorder (ADHD). In this study we examined the diagnostic capability of a new advanced version of the BNA methodology on a larger population of adults with and without ADHD.

METHOD: Subjects were unmedicated right-handed 18- to 55-year-old adults of both sexes with and without a DSM-IV diagnosis of ADHD. We collected EEG while the subjects were performing a response inhibition task (Go/NoGo) and then applied a spatio-temporal Brain Network Activation (BNA) analysis of the EEG data. This analysis produced a display of qualitative measures of brain states (BNA scores) providing information on cortical connectivity. This complex set of scores was then fed into a machine learning algorithm.

RESULTS: The BNA analysis of the EEG data recorded during the Go/NoGo task demonstrated a high discriminative capacity between ADHD patients and controls (AUC = 0.92, specificity = 0.95, sensitivity = 0.86 for the Go condition; AUC = 0.84, specificity = 0.91, sensitivity = 0.76 for the NoGo condition).

CONCLUSIONS: BNA methodology can help differentiate between ADHD and healthy controls based on functional brain connectivity. The data support the utility of the tool to augment clinical examinations by objective evaluation of electrophysiological changes associated with ADHD. Results also support a network-based approach to the study of ADHD

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Psychoneuroendocrinology. 2017 May;79:67-73.

IL-6 AND TNF-ALPHA IN UNMEDICATED ADULTS WITH ADHD: RELATIONSHIP TO CORTISOL AWAKENING RESPONSE.

Corominas-Roso M, Armario A, Palomar G, et al.

There is preliminary evidence that the immune system's cytokines may have impact on ADHD in children. Nevertheless, studies exploring the possible role of pro-inflammatory cytokines in adults with ADHD are lacking. This study aimed to assess differences in serum IL-6 and TNF-alpha between patients and controls and their possible relationship to resting cortisol. 108 adults with ADHD (DSM-IV), 44 inattentive and 64 combined, age ranging between 18 and 55 years, and 27 healthy controls were included. Major psychiatric disorders and organic comorbidities were excluded. Serum samples for IL-6 and TNF-alpha and salivary samples to assess cortisol awakening response were collected on the same day. Analysis of variance was applied to study differences in IL-6 and TNF-alpha between groups. Pearson correlations were used to study associations between IL-6, TNF-alpha, and CAR. There were no significant differences in serum IL-6 or TNF-alpha levels between patients and controls or between combined and inattentive patients. Negative associations between IL-6 (r=-0.386, p=0.020), TNF-alpha (r=-0.372, p=0.023) and cortisol awakening response were found in the inattentive subtype, whereas no association was seen in the combined subtype. A negative correlation between IL-6 and cortisol was also present in the control group (r=-0.44, 0.030). The peripheral pro-inflammatory markers, IL-6 and TNF-alpha, do not appear to be primarily involved in ADHD in adults, although the role of other inflammatory markers cannot be ruled out. The differences regarding the association between IL-6 and TNF-alpha and morning cortisol response suggest possible underlying neurobiological differences between the inattentive or combined patients that merit further studies

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Psychoneuroendocrinology. 2017 May;79:31-39.

ATTENTION-DEFICIT/HYPERACTIVITY DISORDER SYMPTOMS AND STRESS-RELATED BIOMARKERS.

Vogel SWN, Bijlenga D, Verduijn J, et al.

OBJECTIVE: The current study examined whether (a) Attention-Deficit/Hyperactivity Disorder (ADHD) symptoms were associated with dysregulation of stress-related mechanisms, and (b) whether ADHD symptoms interact with affective disorders in their association with dysregulated stress-related mechanisms.
METHODS: Data were obtained from 2307 subjects participating in the Netherlands Study of Depression and Anxiety. Stress-related mechanisms were reflected by the following biomarkers: (1) hypothalamic-pituitary-adrenal axis indicators (salivary cortisol awakening curve, evening cortisol, cortisol suppression after a 0.5mg dexamethasone suppression test (DST)); (2) autonomic nervous system measures (heart rate, pre-ejection period, respiratory sinus arrhythmia); (3) inflammatory markers (C-reactive protein, interleukin-6, tumor necrosis factor-alpha); (4) brain-derived neurotrophic factor. ADHD symptoms were measured using Conners' Adult ADHD Rating Scale and used both dichotomous (High ADHD symptoms (yes/no)) and continuous (Inattentive symptoms, Hyperactive/Impulsive symptoms, and the ADHD index).
RESULTS: Regression analyses showed associations between High ADHD symptoms, Inattentive symptoms, the ADHD index and a higher cortisol awakening curve, between Hyperactive/Impulsive symptoms and less cortisol suppression after DST, and between Inattentive symptoms and a longer pre-ejection period. However, the associations with the cortisol awakening curve disappeared after adjustment for depressive and anxiety disorders. No associations were observed between ADHD symptoms and inflammatory markers or BDNF. ADHD symptoms did not interact with affective disorders in dysregulation of stress-related mechanisms.
CONCLUSION: Some associations were observed between ADHD symptoms, the HPA-axis, and the pre-ejection period, but these were mostly driven by depressive and anxiety disorders. This study found no evidence that ADHD symptomatology was associated with dysregulations in inflammatory markers and BDNF. Consequently, ADHD symptoms did not confer an added risk to the disturbances of stress-related mechanisms in an - already at-risk - population with affective disorders

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Public Health Rep. 2017 Nov;132:654-59.

MEDICAID PRIOR AUTHORIZATION POLICIES FOR MEDICATION TREATMENT OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER IN YOUNG CHILDREN, UNITED STATES, 2015.

Hulkower RL, Kelley M, Cloud LK, et al.

OBJECTIVES: In 2011, the American Academy of Pediatrics updated its guidelines for the diagnosis and treatment of children with attention-deficit/hyperactivity disorder (ADHD) to recommend that clinicians refer parents of preschoolers (aged 4-5) for training in behavior therapy and subsequently treat with medication if behavior therapy fails to sufficiently improve functioning. Data available from just before the release of the guidelines suggest that fewer than half of preschoolers with ADHD received behavior therapy and about half received medication. About half of those who received medication also received behavior therapy. Prior authorization policies for ADHD medication may guide physicians toward recommended behavior therapy. Characterizing existing prior authorization policies is an important step toward evaluating the impact of these policies on treatment patterns. We inventoried existing prior authorization policies and characterized policy components to inform future evaluation efforts.

METHODS: A 50-state legal assessment characterized ADHD prior authorization policies in state Medicaid programs. We designed a database to capture data on policy characteristics and authorization criteria, including data on age restrictions and fail-first behavior therapy requirements.

RESULTS: In 2015, 27 states had Medicaid policies that prevented approval of pediatric ADHD medication payment without additional provider involvement. Seven states required that prescribers indicate whether nonmedication treatments were considered before Medicaid payment for ADHD medication could be approved.

CONCLUSION: Medicaid policies on ADHD medication treatment are diverse; some policies are tied to the diagnosis and treatment guidelines of the American Academy of Pediatrics. Evaluations are needed to determine if certain policy interventions guide families toward the use of behavior therapy as the first-line ADHD treatment for young children

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Qual Life Res. 2017 Jun;26:1405-15.

PREDICTING PARENT HEALTH-RELATED QUALITY OF LIFE: EVALUATING CONCEPTUAL MODELS.

Defenderfer EK, Rybak TM, Davies WH, et al.

PURPOSE: Parents of children with chronic illnesses are at risk for poor health-related quality of life (HRQoL), with numerous identified risk factors, but the most informative statistical model considering their combined impact is unclear. The authors conceptualized risk for poor HRQoL using a summed model, comprehensive multivariate model, and latent profile analysis (LPA).

METHODS: Community parents completed an online survey, providing information about demographics, child's chronic illness, family functioning, and parent and child HRQoL. Parents reported that their children had a variety of chronic conditions (e.g., asthma, headaches, attention deficit/hyperactivity disorder, neurofibromatosis).

RESULTS: The summed model did not account for a significant proportion of variance in parent HRQoL. The comprehensive multivariate model (R (2) = 0.614) and LPA (R (2) = 0.305) both significantly predicted parent HRQoL. The LPA identified two risk profiles for lower HRQoL: parents who reported milder illnesses, but poorer family functioning; and parents who reported greater disease severity, but better family functioning.

CONCLUSIONS: Comprehensive multivariate models or LPAs best conceptualize patterns of risk for poor parental HRQoL in the community; though the findings in the current community sample may not extend to parents recruited from specialty clinics whose children may have more severe chronic illnesses. Parents of children with mild chronic conditions are still at risk for poor HRQoL, warranting attention from health care providers

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Res Dev Disabil. 2017 Nov;70:11-21.

COORDINATION DIFFICULTIES IN PRESCHOOL-AGED CHILDREN ARE ASSOCIATED WITH MATERNAL PARENTING STRESS: A COMMUNITY-BASED CROSS-SECTIONAL STUDY.

Takahashi M, Adachi M, Takayanagi N, et al.

Background: Although coordination difficulties are sometimes observed even in children in the general population, no empirical studies have examined the impact of these difficulties on parenting stress. Aims: The aim of this study was to elucidate the relationship between coordination difficulties and parenting stress in a community-based sample of preschool-aged children and their mothers.
Methods: The study included 1691 families. Mothers with 4- or 5-year-old children completed questionnaires about parenting stress and children's coordination difficulties, as well as traits associated with attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorder (ASD).
Results: The results of hierarchical multiple regression analyses showed that coordination difficulties, and ADHD and ASD traits were each independent predictors of parenting stress. Among the significant predictive factors, impaired general coordination, as well as hyperactivity-impulsivity, showed a strong impact on parenting stress. In addition, a gender difference was observed in the manner in which coordination difficulties influenced parenting stress.
Conclusions: Coordination difficulties in preschool-aged children in the general population increased maternal parenting stress (as did ADHD and ASD traits). This highlights the need to provide support for mothers who have children with coordination difficulties, even when there is no clinical diagnosis

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Res Dev Disabil. 2018;72:166-78.

ASSESSING WORKING MEMORY IN CHILDREN WITH ADHD: MINOR ADMINISTRATION AND SCORING CHANGES MAY IMPROVE DIGIT SPAN BACKWARD'S CONSTRUCT VALIDITY.

Wells EL, Kofler MJ, Soto EF, et al.

Background Pediatric ADHD is associated with impairments in working memory, but these deficits often go undetected when using clinic-based tests such as digit span backward. Aims The current study pilot-tested minor administration/scoring modifications to improve digit span backward's construct and predictive validities in a well-characterized sample of children with ADHD.
Methods and procedures WISC-IV digit span was modified to administer all trials (i.e., ignore discontinue rule) and count digits rather than trials correct. Traditional and modified scores were compared to a battery of criterion working memory (construct validity) and academic achievement tests (predictive validity) for 34 children with ADHD ages 8-13 (M = 10.41; 11 girls).
Outcomes and results Traditional digit span backward scores failed to predict working memory or KTEA-2 achievement (all ns). Alternate administration/scoring of digit span backward significantly improved its associations with working memory reordering (r = .58), working memory dual-processing (r = .53), working memory updating (r = .28), and KTEA-2 achievement (r = .49).
Conclusions and implications Consistent with prior work, these findings urge caution when interpreting digit span performance. Minor test modifications may address test validity concerns, and should be considered in future test revisions. Digit span backward becomes a valid measure of working memory at exactly the point that testing is traditionally discontinued

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Semin Pediatr Neurol. 2017.

ATTENTION DEFICIT HYPERACTIVITY DISORDER AND ASSOCIATED COGNITIVE DYSFUNCTION IN PEDIATRIC EPILEPSY.

Vidaurre J, Twanow JDE.

Attention deficit hyperactivity disorder (ADHD) is the most common neuropsychiatric comorbidity associated with childhood epilepsy, affecting about a third of children with epilepsy. In contrast, ADHD in the general population occurs in 4%-12% of school-aged children. The cause of this association remains unclear. It is likely that common mechanisms underlie the vulnerability for both executive deficits and epileptogenesis.

There are characteristics unique to children with ADHD and epilepsy. The inattentive type of ADHD is more prevalent than the combined presentation in children with epilepsy, while the combined type is more common in the general population. Interestingly, there is an equal sex distribution of ADHD in patients with epilepsy, while in the general population, ADHD is 3-7 times more prevalent in boys. Specific features of ADHD seen in different epilepsy syndromes are frequently associated with executive deficits. Early screening of ADHD symptoms in children with epilepsy is essential, as timely interventions can improve academic and social function and outcomes. The mainstays of therapy include behavioral interventions and pharmacotherapy, with evidence demonstrating that stimulants are both safe and effective in children with ADHD and an epilepsy diagnosis

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Tehran Uni Med J. 2017;75:600-08.

THE EFFECTS OF VITAMIN D SUPPLEMENTATION ON THE ANTIOXIDANT SERUM LEVEL IN 6-13 YEARS OLD CHILDREN WITH ADHD.

Fasihi F, Alavi-Naeini A, Najafi M, et al.

Background: The causes of Attention-deficit/hyperactivity disorder (ADHD) (the most common psychological disorder is still unknown. The main symptoms include impulsivity, hyperactivity and attention deficit. Some studies have shown the relationship between ADHD and oxidative stress, and yet some researches have shown the effects on vitamin D on the antioxidants level. This research intends to identify the effect of vitamin D supplementation on the antioxidant serum level in 6-13 years old children with ADHD.

Methods: This double blind clinical trial was conducted in Isfahan city, the center of Iran, from October 2015 to February 2016. The sample included 35 subjects of both groups that were randomly selected among 6-13 years old children with ADHD diagnosed by pediatric psychologist. The intervention group consumed 1000 IU of vitamin D3 daily for three months, and the control group used placebo for the same period of time. Their stature and weight were recorded by digital instruments without the shoes with the least clothes. The next step was to train the food record of the students to the parents so that 3 food records were taken during the study. 25-hydroxyvitamin D3 (25(OH)D3), TAC (Total antioxidant capacity), MDA (Malondialdehyde), CAT (Catalase) and GSH (Glutathione) of the participants of both groups were measured before and after the intervention.

Results: In this Study, both groups were adjusted in terms of their age, gender and BMI. The mean score of the variables of leisure time and sport showed no significant difference in the both groups. Comparing the average TAC and MDA between the two groups before intervention didn't show a significant difference (P1TAC=0.06) (P1MDA=0.32), but after the intervention, the vitamin D intake group showed the increase in TAC and decrease in MDA (P2TAC=0.001) (P2 MDA=0.01). Moreover, CAT and GSH showed no significant difference in the two groups before and after intervention.

Conclusion: Vitamin D supplementation for 3 months led to the improvement of antioxidant capacity by the increase of TAC and decrease of MDA, but the CAT and GSH showed no significant change in the mentioned period of time

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Transl Psychiatry. 2017 Jan;7:e1014.

MEDICAL HISTORY OF DISCORDANT TWINS AND ENVIRONMENTAL ETIOLOGIES OF AUTISM.

Willfors C, Carlsson T, Anderlid BM, et al.

The environmental contributions to autism spectrum disorder (ASD) and their informative content for diagnosing the condition are still largely unknown. The objective of this study was to investigate associations between early medical events and ASD, as well as autistic traits, in twins, to test the hypothesis of a cumulative environmental effect on ASD risk. A total of 80 monozygotic (MZ) twin pairs (including a rare sample of 13 twin pairs discordant for clinical ASD) and 46 dizygotic (DZ) twin pairs with varying autistic traits, were examined for intra-pair differences in early medical events (for example, obstetric and neonatal factors, first year infections). First, differences in early medical events were investigated using multisource medical records in pairs qualitatively discordant for ASD. The significant intra-pair differences identified were

then tested in relation to autistic traits in the remaining sample of 100 pairs, applying generalized estimating equations analyses. Significant association of the intra-pair differences in the MZ pairs were found for the cumulative load of early medical events and clinical ASD (Z=-2.85, P=0.004) and autistic traits (beta=78.18, P=0.002), as well as infant dysregulation (feeding, sleeping abnormalities, excessive crying and worriedness), when controlling for intelligence quotient and attention deficit hyperactivity disorder comorbidity. The cumulative load of early medical events in general, and infant dysregulation in particular, may index children at risk of ASD owing to non-shared environmental contributions. In clinical practice, these findings may facilitate screening and early detection of ASD

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Transl Psychiatry. 2017 Jan;7:e999.

GLUTAMATERGIC AND GABAERGIC GENE SETS IN ATTENTION-DEFICIT/HYPERACTIVITY DISORDER: ASSOCIATION TO OVERLAPPING TRAITS IN ADHD AND AUTISM.

Naaijen J, Bralten J, Poelmans G, et al.

Attention-deficit/hyperactivity disorder (ADHD) and autism spectrum disorders (ASD) often co-occur. Both are highly heritable; however, it has been difficult to discover genetic risk variants. Glutamate and GABA are main excitatory and inhibitory neurotransmitters in the brain; their balance is essential for proper brain development and functioning. In this study we investigated the role of glutamate and GABA genetics in ADHD severity, autism symptom severity and inhibitory performance, based on gene set analysis, an approach to investigate multiple genetic variants simultaneously. Common variants within glutamatergic and GABAergic genes were investigated using the MAGMA software in an ADHD case-only sample (n=931), in which we assessed ASD symptoms and response inhibition on a Stop task. Gene set analysis for ADHD symptom severity, divided into inattention and hyperactivity/impulsivity symptoms, autism symptom severity and inhibition were performed using principal component regression analyses. Subsequently, gene-wide association analyses were performed. The glutamate gene set showed an association with severity of hyperactivity/impulsivity (P=0.009), which was robust to correcting for genome-wide association levels. The GABA gene set showed nominally significant association with inhibition (P=0.04), but this did not survive correction for multiple comparisons. None of single gene or single variant associations was significant on their own. By analyzing multiple genetic variants within candidate gene sets together, we were able to find genetic associations supporting the involvement of excitatory and inhibitory neurotransmitter systems in ADHD and ASD symptom severity in ADHD

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Turk J Pediatr. 2016;58:259-2665.

MENTAL HEALTH PROBLEMS IN CHILDREN WITH UNCOMPLICATED EPILEPSY; RELATION WITH PARENTAL ANXIETY.

Gokgoz-Durmaz F, Cihan FG, Uzun M, et al.

Mental health problems and parental anxiety in children with epilepsy were investigated. Parents of 83 children with epilepsy and 172 healthy children were asked to complete Strengths and Difficulties Questionnaire for their children and State-Trait Anxiety Inventory for themselves. In those with epilepsy, 39.8% (n: 33) were girls, 60.2% (n: 50) were boys and their mean age was 9.34 +/- 3.99 years. Control group was more successful in school ($p < 0.001$). Emotional problems score in children with epilepsy was higher than control group ($p < 0.001$). Case group's behavior problems and attention deficit hyperactivity scores were higher ($p < 0.001$, $p=0.009$ respectively). Prosocial behavior scores of the control group were significantly higher ($p=0.004$). State ($p=0.001$) and trait ($p=0.001$) anxiety levels of parents of children with epilepsy were higher. Children with epilepsy have more neuro-behavioral problems; and their parents have greater anxiety levels. Physicians should be in contact with children with epilepsy for the psychological health of the family besides seizure control

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Turk J Pediatr. 2016;58:271-81.

GENDER DIFFERENCES IN DEFENSE MECHANISMS, WAYS OF COPING WITH STRESS AND SENSE OF IDENTITY IN ADOLESCENT SUICIDE ATTEMPTS.

Foto-Ozdemir D, Akdemir D, Cuhadaroglu-Cetin F.

The main aim of this study was to investigate the gender differences in defense mechanisms, ways of coping with stress and identity formation in relation to adolescent suicidal behavior. This study involved 64 adolescents between 12-17 years of age, who were admitted to the emergency service with a suicide attempt. They were evaluated with a semi-structured clinical interview (K-SADS), Ways of Coping Inventory (WCI), Defense Mechanisms Inventory (DMI) and Sense of Identity Assessment Form (SIAF). 60.9% (n = 39) of the adolescents were female, and 39.1% (n=25) were male. There were no statistically significant differences between the girls and the boys with respect to the clinical characteristics of the suicide attempt and the rate of psychiatric disorders. Of the 64 adolescents with suicide attempt, 47 (73.4%) had at least one, and 26 (40.6%) had more than one psychiatric disorder according to K-SADS. Disruptive behavior disorders were more frequent in males, whereas depression was more frequent in girls. The data indicated the importance of identity confusion, major depression and ADHD in adolescents with suicide attempt in both genders. 43.6% (n=17) of the girls and 36% (n=9) of the boys obtained scores higher than the cut-off point of SIAF indicating identity confusion. Professional help seeking and NSSI behaviors before the suicide attempt were more common in adolescents with identity confusion. While there were differences between genders with respect to the defense mechanisms used, no significant difference was found in terms of ways of coping. Evaluation of DMI scores revealed that the turning against object subscale score was significantly higher in boys compared to girls. While evaluating the adolescents at risk, their defense mechanisms, way of coping and sense of identity, as well as their psychiatric diagnosis should be assessed in detail in order to identify the suicidal thoughts and prevent possible suicide attempts

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Special Section on "Transational and Neuroscience Studies in Affective Disorders"

Light up ADHD: I. Cortical hemodynamic responses measured by functional Near Infrared Spectroscopy (fNIRS)

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ABSTRACT

Background: Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by deficits in cognitive and emotional self-control. Optical technique acquisitions, such as near infrared spectroscopy (NIRS), seem to be very promising during developmental ages, as they are non- invasive techniques and less influenced by body movements than other neuroimaging methods. Recently, these new techniques are being widely used to measure neural correlates underlying neuropsychological deficits in children with ADHD.
Methods: In a short series of articles, we will review the results of functional NIRS (fNIRS) studies in children with ADHD. The present brief review will focus on the results of the fNIRS studies that investigate cortical activity during neuropsychological and/or emotional tasks.
Results: According to the reviewed studies, children and adolescents with ADHD show peculiar cortical activation both during neurological and emotional tasks, and the majority of the reviewed studies revealed lower prefrontal cortex activation in patients compared to typically developmental controls.
Limitations: a consistent interpretation of these results is limited by the substantial methodological heterogeneity including patients' medication status and washout period, explored cerebral regions, neuropsychological tasks, number of channels and sampling temporal resolutions.
Conclusions: fNIRS seems to be a promising tool for investigating neural substrates of emotional dysregulation and executive function deficits in individuals with ADHD during developmental ages.

Main body

Attention deficit hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by a lack of self-regulating behavior, cognition and emotional responses. ADHD's core symptoms include difficulty paying attention, excessive motor activity and high levels of impulsivity (American Psychiatric Association, 2013). ADHD's difficulties are often ascribed to deficits in executive functions (EFs) (Barkley, 1997). EFs refer to neuropsychological processes that enable individuals to maintain physical, cognitive and emotional self-control as well as to achieve their goals. Moreover, children with ADHD often experience social difficulties and emotional dysregulation, which is defined as lacking the ability to modify an emotional state to promote adaptive behaviors (Thompson, 1994).

The evidence in the literature shows functional and anatomical alterations, especially in the prefrontal cortex (PFC) (Kobel et al., 2008; Shaw et al., 2007). Despite this, there are very few functional magnetic resonance imaging (fMRI) studies investigating the neural correlates of ADHD symptoms in developmental-aged populations, mostly because of the difficulties children with ADHD children meet when undergoing an fMRI. Optical techniques, such as near infrared spectroscopy (NIRS), are employed to obtain hemodynamic information about the brain metabolism and have several clear advantages for studying children with developmental disorders such as ADHD (Scholkmann et al., 2014). NIRS is silent, requires few body fixities and the acquisition environment is not intrusive, so it is very usable with hyperactive children. Using light at specific wavelengths, NIRS allows researchers to probe oxygenated and deoxygenated hemoglobin (Oxy-Hb and Deoxy-Hb) and measure their concentration changes over time. The measures of these changes are valuable clinical indications, as they are closely related to functional brain activation. Furthermore, NIRS has a good temporal resolution (up to 0.1 s) in spatial resolutions of centimeter order (Scholkmann et al., 2014).

The present brief review summarizes the results of functional NIRS (fNIRS) studies published between January 2000 and December 2016 that investigate cerebral activity in children and adolescents with

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Table 1
Selection of studies investigating cortical activation with functional near infrared spectroscopy in patients with diagnosis of Attention Deficit Hyperactivity Disorder compared with typically developmental controls.

Study	Samples and Tasks	fNIRS Measures	Analysis	Main Findings
Inoue et al., 2012	SAMPLE: 20 ADHD, 14 males, mean age 9,58 y, all drug naïve. 20 TDC, 14 males, mean age 9,75 y. (age range 6–14 y). TASK: Go/NoGo software "MOGRAZ".	MEASURES: Oxy- and Deoxy-Hb from 16 CHs, sampling rate 3 Hz (0.3 s of temporal resolution). AREAS: PFC (frontal pole, orbitofrontal cortex, ventromedial- and ventrolateral-prefrontal cortices). The line of four light sources was set on the Fp1–Fp2 line; the center of the probe was positioned on Fpz (International 10–20 System).	Preliminary: Baseline correction by linear fitting based on the mean of the two baselines data (10 s before and 10 s after the task). All the time points of Oxy-Hb and Deoxy-Hb changes averaged and divided into four regions: left lateral, left medial, right medial, and right lateral. Mixed ANOVA design (Group x Condition x Area). Post hoc with t tests. Correlations between the mean Oxy-Hb or Deoxy-Hb changes and all demographic and behavioral parameters.	Oxy-Hb: significantly larger Oxy-Hb concentration changes during NoGo-condition vs Go-condition, in TDC. No significant difference in ADHD. Oxy-Hb changes during NoGo-condition were significantly lower in ADHD than in TDC. Deoxy-Hb: significantly smaller Deoxy-Hb concentration changes during NoGo-condition vs Go-condition, across the groups. No significant results for Area and for correlations with demographic or behavioral parameters.
Nakashima et al., 2014	SAMPLE: 19 ADHD, all males, mean age 8.2 ± 1.0 y, 15 medicated with MPH, 1 ATX, 1 ATX + MPH, 1 ATX + MPH + Aripiprazolo, 1 drug naïve. 14 TDC, all males, mean age 8.2 ± 1.6 y. TASK: Multi-Source Interference.	MEASURES: Oxy-Hb from 46 CHs, 0.1 s of temporal resolution. AREAS: Fronto-parietal regions. The lowest probe line was set along the Fp1-Fp2 line and the middle probe at the Fpz (International 10–20 System).	Preliminary: Baseline correction by linear fitting based on the mean of the two baselines data (10 s before and 10 s after the task). T tests between TDC mean Oxy-Hb changes during pre-task and task periods to detect "effective" channels. T tests between TDC and ADHD mean Oxy-Hb changes during task. For significant differences, correlations between mean Oxy-Hb concentration and clinical variables.	CH 2 and CH 6 were effective: Oxy-Hb decreased during task compared to pre-task. No effective channels in ADHD. Oxy-Hb means were different between the groups (ADHD < TDC) only for one (CH6) of the two effective channels, which covered left dorso lateral PFC. Oxy-Hb changes in CH6 did not correlate with ADHD severity or clinical data.
Negoro et al., 2010	SAMPLE: 20 ADHD, 18 males, mean age 9.55 ± 1.93 y, all drug naïve. 20 TDC, 17 males, mean 9.35 ± 2.13 y. (age range 6–13 y). TASK: Stroop Color-Word.	MEASURES: Oxy-Hb from 24 CHs, 0.1 s of temporal resolution. AREAS: Frontal regions. The lowest probe line was set along the Fp1-Fp2 line (International 10–20 System).	Preliminary: Baseline correction by linear fitting based on the mean of the two baselines data (10 s before and 25 s after the task). T tests between TDC and ADHD grand average waveforms of Oxy-Hb concentration changes.	The grand average waveform of Oxy-Hb concentration changes in TDC increased during task period, not in ADHD. From task to post task period: Oxy-Hb mean significantly differed between groups (ADHD < TDC) in CHs 18, 21, 22 (inferior PFC and inferior lateral PFC).
Xiao et al., 2012	SAMPLE: 16 ADHD, all males, mean age 9.75 ± 1.18 y, no information about medication. 16 TDC, all males, mean age 9.69 ± 1.74 y. (age range 8–14 y). TASK: Go/NoGo and Stroop Color-Word.	MEASURES: Oxy-Hb from 16 CHs, sampling rate 5 Hz (0,2 s of temporal resolution). AREAS: PFC.	Preliminary: Baseline correction by subtraction of the mean value of baseline (5 s before the task) to each time point during both baseline and task periods. One-way ANOVAs for Oxy-Hb mean value between hemispheres (Oxy-Hb mean changes during each task minus baseline). T tests between groups.	NoGo: Lower Oxy-Hb concentration in right PFC in ADHD than in TDC. Stroop: Higher Oxy-Hb concentration in right PFC in ADHD than in TDC.
Yasumura et al., 2014	SAMPLE: 10 ADHD, 8 males, mean age 11.18 ± 2.23 y, no information about medication.	MEASURES: Oxy-Hb from 16 CHs, 0.65 s of temporal resolution. AREAS: PFC. The lowest left and lowest right	Preliminary: Measures of each channel converted in z scores. Recordings more than 2 standard deviations away from the mean were excluded. Mixed ANOVAs design (Condition x Group x Hemisphere) of Oxy-Hb mean	Stroop Color-Word/Pseudo-word: no significant differences in Oxy-Hb between groups and hemispheres. Reverse Stroop: significantly lower Oxy-Hb changes in right hemisphere in ADHD than in TDC.

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Table 1 (*continued*)

Study	Samples and Tasks	fNIRS Measures	Analysis	Main Findings
			concentration during the last 20 s of each task. Post hoc analysis with Tukey HSD.	
	15 TDC, 6 males, mean age 9.56 ± 1.51 y. TASK: Stroop Color-Word/Pseudo-word and Reverse Stroop.	corners were located around F7 and F8, respectively; the center of the probe matrix was placed on Fpz (International 10–20 System).	For channels showing significant differences, correlations between signal and clinical variables regarding ADHD (SNAP questionnaire; Bussing et al., 2008).	Post-hoc indicated that Oxy-Hb at CH 4 was significantly lower in ADHD than in TDC. Negative correlations between CH 4 signal and SNAP inattention score in all groups.
Yasumura et al., 2015	SAMPLE: 22 ADHD, 15 males, mean age 10,25 ± 2.0 y, no information about medication. 37 TDC, 19 males, mean age 10,83 ± 1,66 y. TASK: Dimensional Change Card Sort.	MEASURES: Oxy-Hb from 16 CHs, 0.66 s of temporal resolution. AREAS: PFC. The lowest left and lowest right corners were located around F7 and F8, respectively; the center of the probe matrix was placed on Fpz (International 10–20 System).	Preliminary: Measures of each channel were converted in z score. Recordings more than 2 standard deviations away from the mean were excluded. T tests between groups for Oxy-Hb mean concentration during task. For channels showing significant differences, correlations between signal and clinical variables regarding ADHD symptoms (SNAP questionnaire; Bussing et al., 2008).	Oxy-Hb concentration significantly lower in ADHD than in TDC in CHs 1, 2 (right inferior frontal gyrus), 13. Negative correlations between CH 1 signal and two of the SNAP subscales (inattention and hyperactivity/impulsivity).
Arai et al., 2016	SAMPLE: 30 ADHD, all males, mean age 9.5 ± 1.6 y, all medicated with MPH (washout period before task: 24 h). 35 TDC, all males, mean age, 9.0 ± 1.6 y. (age range 7–13 y). TASK: Spatial Working Memory "CANTAB".	MEASURES: Oxy-Hb from 16 CHs, 0.65 s of temporal resolution. AREAS: PFC. The lowest left and lowest right corners were located around F7 and F8, respectively; the center of the probe matrix was placed on Fpz (International 10–20 System).	Preliminary: Oxy-Hb integration value within 30 s from the start of the Spatial Working Memory. Correlations between age and Oxy-Hb in each group. Regression slopes for ADHD and TDC were compered. T test between the mean integration value of Oxy-Hb of older ADHD and TDC (≥ 10 y old)[a].	Positive correlations between age and Oxy-Hb integration value in bilateral lateral PFC and frontal pole CHs in TDC. No correlation for ADHD. Slopes comparison revealed significant differences in CHs 10 and 11 (frontal pole) but not in bilateral lateral PFC. Older children: significantly higher Oxy-Hb mean integration value in TDC than in ADHD in CH 10.
Schecklmann et al., 2010	SAMPLE: 19 ADHD, 17 males, mean age 11.6 ± 1.5 y, 11 medicated with MPH (washout period before task: 24 h). 19 TDC, 15 males, mean age 11.6 ± 1.4 y. TASK: Visual and Spatial Working Memory with emotional faces stimuli.	MEASURES: Oxy-Hb from 52 CHs. AREAS: ventro-lateral prefrontal cortex (Brodmann Areas 44, 45), dorso-lateral prefrontal cortex (Brodmann Areas 9, 10, 46) and posterior superior frontal cortex (Brodmann Areas 6, 8).	Preliminary: Brain activation defined as increases of Oxy-Hb concentration after the stimulus compared with before stimulus values. Mixed ANOVA designs to detect activation in ROIs [Group x Condition (Visual or Spatial Working Memory or Control condition) x Hemisphere].	No task related activation. Significant effects of Condition and Hemisphere in all ROIs. No Group effect, so Oxy-Hb concentrations for ADHD with and without MPH medication were analyzed separately: ADHD without MPH > TDC > ADHD with MPH, with significant difference between ADHD with and without MPH. Posterior Superior Frontal Cortex: higher Oxy-Hb concentration in left hemisphere. dorso-lateral and ventro-lateral PFC: higher Oxy-Hb concentration in right hemisphere. Higher Oxy-Hb concentration for Visual and Spatial Working Memory compared with Control condition no

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Table 1 (*continued*)

Study	Samples and Tasks	fNIRS Measures	Analysis	Main Findings
				differences between Visual and Spatial Working Memory.
Tsujimoto et al., 2013	SAMPLE: 16 ADHD, all males, mean age 10.9 ± 2.0 y, all medicated, mostly with MPH, (for only 9, washout period before task: 24 h). 10 TDC, all males, mean age 10.1 ± 1.8 y. TASK: Visuo-Spatial Working Memory.	MEASURES: Oxy-Hb from 16 CHs, 0.67 s of temporal resolution. AREAS: lateral PFC. The lowest left and lowest right corners were located around F7 and F8, respectively; the center of the probe matrix was placed on Fpz (International 10–20 System).	Preliminary: Baseline correction by linear fitting based on the mean of the two baselines data (first 4 s and least 4 s of the interval between trials). Activation defined as the 4 s period beginning 4 s after the cue onset. Measures of each channel were converted in z score. Three regions identified: right, left and middle PFC. Two-way, mixed ANOVA design (Region x Group). For each region, correlations between error rate and changes in Oxy-Hb concentration.	Significant main effect of Group (ADHD > TDC). No main effect of Region. Right and middle PFC, but not the left PFC showed differences between groups. In ADHD group, positive correlations between error rate and Oxy-Hb changes in the right and middle PFC. No correlations for TDC.
Weber et al., 2005	SAMPLE: 11 ADHD, all males, mean age 10.4 ± 1.2 y, all drug naïve. 9 TDC, all males, mean age 11.3 ± 1.3 y. TASK: Trail Making Test	MEASURES: Oxy-Hb, Deoxy-Hb, Cyt, TOI (= OxyHb * 100 / OxyHB +DeoxyHb) CBV from 2 CHs, sampling rate 2 Hz (0.5 s of temporal resolution). AREAS: gyrus frontalis superior and middle gyrus frontalis, parts of dorsolateral PFC. The 2 CHs cover the areas between Fp1 and F3 and between Fp2 and F4 (International 10–20 System).	Preliminary: Oxy-Hb, Deoxy-Hb and Cyt changes and percentage of TOI calculated for each task, baseline and break period. CBV was calculated as total Hb. Wilcoxon test for intragroup changes and the Mann-Whitney test for intergroup differences, including the Monte-Carlo procedure. Short-attention task: Oxy-Hb Deoxy-Hb CBV, Cyt and TOI changes between the first baseline and the first task. Extended-attention task: Oxy-Hb, Deoxy-Hb, CBV, Cyt, TOI changes between the 4-task and the previous baseline or respective break.	Short-attention task: no hemodynamic changes in TDC. In ADHD, Oxy-Hb increased in right PFC and CBV increased bilaterally. TOI increased in left PFC. No significant Deoxy-Hb and Cyt changes. No intergroup differences. Extended-attention task: Oxy-Hb and CBV increased bilaterally in both groups. Deoxy-Hb increased in left PFC in TDC. TOI increased bilaterally in ADHD. No significant Cyt changes. Groups significantly differed for Deoxy-Hb increase in left PFC (TDC > ADHD). Intergroup differences in changes in TOI nearly significant in right PFC and significant in left PFC (ADHD > TDC).
Ichikawa et al., 2014	SAMPLE: 13 ADHD, all males, mean age 10,0 ± 1.25 y, 7 medicated with MPH, 1 ATX, 5 drug naïve. (age range 8–12) TASK: Passive viewing of happy and angry faces	MEASURES: Oxy-Hb and Deoxy-Hb from 24 CHs, 0.1 s temporal resolution. AREAS: Temporal cortex. The probes were centered at T5 and T6 (International 10–20 System).	Preliminary: Measures of each channel converted in z score, calculated separately for Oxy-Hb, Deoxy-Hb, and Total-Hb and for happy and angry face conditions. Z scores were averaged within left and right temporal areas.	Oxy-Hb: during angry-face condition, different concentrations between groups (TDC > ADHD), no difference during happy-face condition. Deoxy-Hb: main effect of area (no post hoc reported). ADHD: Oxy-Hb increased and Deoxy-Hb decreased in right hemisphere for happy face condition. No hemodynamic response for angry face condition. TDC: Oxy-Hb increased and Deoxy-Hb decreased in right hemisphere for both happy and angry face conditions.

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Table 1 (*continued*)

Study	Samples and Tasks	fNIRS Measures	Analysis	Main Findings
			Mixed ANOVAs for Oxy- and Deoxy-Hb concentrations (Group x Condition x Area and Condition x Area). Post hoc with t tests. Two-tailed one-sample t-test between baseline (averaged z scores) and task period (5–15 s after the face stimulus onset) in both temporal areas.	

ADHD = Attention Deficit Hyperactivity Disorder patients; TDC = Typically Developmental Controls; y = years; CH = Channel; Hz = Hertz; PFC = Prefrontal Cortex; Fp = Fronto Parietal; Fpz = Fronto Parietal zero; s = seconds; ANOVA = Analysis of variance; Oxy-Hb = Oxygenated Hemoglobin, Deoxy-Hb = Deoxygenated Hemoglobin; MPH = Methylphenidate, ATX = Atomoxetine; F = frontal; SNAP = Swanson, Nolan and Pelham; ROI = Region of interest; Cyt = cytochrome oxidase aa3; TOI = tissue oxygenation index; CBV = cerebral blood volume; T = temporal.

[a] Previous studies (Klingber et al., 2002; Kwon et al., 2002; Schweinsburg et al., 2005) report TDC children until around 10-years-old did not exhibit enough PFC activation

ADHD compared to typically developing (TD) children. The bibliographic research was conducted on PubMed and Google Scholar using "fNIRS and ADHD" and "NIRS and ADHD" as search criteria. We arbitrarily excluded all studies that used fNIRS to explicitly investigate pharmacological treatments' effects on hemodynamic responses, because this will be the focus of a following brief review.

The eleven studies that meet our inclusion criteria are summarized in Table 1. As this review is focused on the differences between ADHD and TD children, we do not report data regarding other clinical groups (Xiao et al., 2012; Yasumura et al., 2014).

All but one of the included studies investigate differences in cortical activation during neuropsychological tasks, which may involve different EFs. It is possible to cluster the studies focused on investigating inhibition and flexibility (Go/NoGo or Stroop tasks) (Inoue et al., 2012; Nakashima et al., 2014; Negoro et al., 2010; Xiao et al., 2012; Yasumura et al., 2014, 2015), memory (Visuo-spatial Working Memory tasks and Memory Span) (Arai et al., 2016; Schecklmann et al., 2010; Tsujimoto et al., 2013) and attention (Trail Making Test) (Weber et al., 2005).

Indeed, only Ichikawa and colleagues (2014) used NIRS to investigate hemodynamic responses in bilateral temporal areas in passive viewings of emotional faces in children with ADHD and TD.

Although the literature is in a very early stage and needs more work, some preliminary suggestions can be drawn from the reviewed studies. Most of the studies found lower activation in ADHD prefrontal cortex, suggested by the lower concentrations of Oxy-Hb compared to that in TD children during several neuropsychological tasks evaluating inhibition, flexibility and memory (Arai et al., 2016; Inoue at al, 2012; Nakashima et al., 2014; Negoro et al., 2010; Yasumura et al., 2014, 2015). Xiao and colleagues (2012) found the same lower activation, with lower concentrations of Oxy-Hb in ADHD children compared to TD children during a Go/NoGo task. Quite interestingly, they found higher concentrations of Oxy-Hb in children with ADHD during a Stroop task, thus suggesting that a Stroop task could involve different aspects of selective attention and impulse inhibition following different developmental courses.

Other studies reported mixed results. In Weber et al.'s study (2005) both children with ADHD and TD had increased Oxy-Hb concentrations during attention task, but TD children had an additional increase in Deoxy-Hb concentrations. The authors hypothesized that these findings were a sign of mismatched oxygen consumption under cognitive demands: increased Oxy-Hb without a change in Deoxy-Hb could be a failure in oxygen consumption, confirming the assumption of a frontal hypo-metabolism especially during an extended attention-driven task.

Tsujimoto and colleagues (2013) found that children with ADHD performed worse with visuo-spatial working memory at behavioral levels but had higher activations of Oxy-Hb prefrontal cortex concentrations compared to TD children. The authors suggest that this higher activation could be due to a compensatory activation with inefficient processing in the PFC.

Schecklemann and colleagues (2010) did not find between-group differences in cortical activation during visual and spatial working memory tasks. However, when they divided participants into two groups — drug-naïve ADHD and ADHD with methylphenidate (MPH) chronic intake — they found a significant difference between these ADHD subgroups, even though a possible acute effect of MPH on cortical activation was excluded because the medicated group underwent fNIRS after a 24-h washout.

The only study to explore cortical activation during facial expression viewings (Ichikawa et al., 2014) found that children with ADHD had cerebral activations comparable to the controls during the recognition of positive expressions (with increased Oxy-Hb and decreased Deoxy-Hb concentrations), but not in processing negative expressions.

One of the major limitations for a consistent interpretation of these results was the heterogeneity of patients' medication status and washout period across the reviewed papers. The possibility that the

presence or absence of medication affects the cortical response of children with ADHD could not be ruled out. A meta-analysis of structural MRI studies suggested differences in brain structure between drug-naïve and previously treated ADHD patients (Frodl and Skokauskas, 2012). Only 3 out of 11 studies recruited drug-naïve patients (Inoue et al., 2012; Negoro et al., 2010; Weber et al., 2005). Two studies reported that their ADHD groups were all composed of medicated children. Arai and colleagues (2016) stated that all their ADHD patients were medicated with MPH and underwent fNIRS after a 24-h washout; Tsujimoto and colleagues (2016) reported that their sample was "mostly medicated" with MPH, and that only 9 out of 16 children had a 24-h washout. Three studies (Ichikawa et al., 2014; Nakashima et al., 2014; Schecklmann et al., 2010) had mixed samples of children — drug-naïve and children medicated with MPH, atomoxetine or aripiprazole. Schecklmann and colleagues (2010) reported having a 24-h washout period. Ichikawa and colleagues (2014) and Nakashima and colleagues (2014) did not report any information regarding washout periods. Lastly, Yasumura and colleagues (2014, 2015) and Xiao and colleagues (2012) did not report any information about medications. It is worth noting that, although the acute effect of MPH was excluded in most of the studies with a washout period, the chronic MPH intake might have caused persistent neurobiological changes (Pliszka et al., 2005), which eventually led researchers to report mixed findings.

With respect to the explored cerebral regions, most of the selected studies investigated the activity of either prefrontal or lateral prefrontal cortices. Some studies took into account different cortical areas such as the frontoparietal (Nakashima et al., 2014), ventrolateral (Schecklmann et al., 2010) and temporal regions (Ichikawa et al., 2014). Xiao and colleagues (2012) and Shecklmann and colleagues (2010) did not report the examined cortical areas with reference to the International 10–20 system (Jasper, 1958). Moreover, the reviewed papers investigated differences in cortical activation during different neuropsychological task — assessing inhibition, flexibility, memory, attention. Mixed results could be due to heterogeneity involving both the cortical areas selected and the task performed by the patients during the fNIRS acquisition.

Lastly, the authors reported both a broad range of number of channels - from a minimum of 2 (Weber et al., 2005) to a maximum of 52 (Schecklmann et al., 2010) — and of sampling temporal resolutions — from a minimum of 0.1 s (Ichikawa et al., 2014; Nakashima et al., 2014; Negoro et al., 2010) to a maximum of 0.67 s (Tsujimoto et al., 2013). Shecklmann and colleagues (2010) did not report sampling temporal resolutions.

Although at this early stage of the literature, a consistent interpretation of the results presented here is limited by the methodological aspects stated above, the present review of the fNIRS studies suggests peculiar cortical activations both during neuropsychological and emotional tasks in children and adolescents with ADHD. The majority of the considered studies found lower activations in prefrontal cortices of children with ADHD compared to their TD peers during tasks assessing cognitive inhibition and flexibility, working memory and memory span and measuring attention abilities. Furthermore, temporal cortex reactivity to facial emotional stimuli was lower in ADHD children than in neurotypical control groups.

In conclusion, fNIRS seems to be a promising tool for investigating neural substrates of both executive function deficits and emotional processing difficulties in developmental-aged individuals with ADHD.

Further methodological efforts are urgently needed to improve the replicability and reliability of the fNIRS findings based on protocols investigating the same neuropsychological functions in well-defined cortical areas and with comparable time and/or spatial resolutions.

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Contributors

Maddalena Mauri, Maria Nobile and Monica Bellina wrote the first version of the manuscript, Alessandro Crippa and Paolo Brambilla contributed on the discussion of the results. All the authors agreed on the final version of the review.

Ethical statement

The authors declare that no human or animal experimentation was conducted for this work.

Conflict of interest

All the authors declare no conflict of interest.

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Research Review: The role of obstetric and neonatal complications in childhood attention deficit and hyperactivity disorder – a systematic review

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Background: Attention deficit and hyperactivity disorder (ADHD) is a developmental disorder characterized by an inability to sustain attention, activity levels and impulse control, and, according to the latest studies, the prevalence is about 8% and in some countries less than 1%. Currently, it is well-known that complications during the perinatal period have significant implications on child's physical and mental health. Purpose of the present paper is to review the literature about the association between perinatal complications and future risk of an ADHD diagnosis. **Methods:** A research in the main database sources has been conducted to obtain a systematic review on the perinatal risk factors of ADHD. **Results:** Among perinatal complications, available data indicate low birth weight (LBW) (Cohen's *d* effect size range: 0.31–1.64-small effect size) and preterm birth (PB) (range *d*: 0.41–0.68) as the most important factors associated with a future diagnosis of ADHD. **Conclusions:** PB and LBW children should be carefully monitored for an early diagnosis of ADHD limiting the impact of the disease in life span. A systematic review focusing on these risk factors have not been published until now, in the next future preventive strategies should be developed in order to minimize ADHD onset. **Keywords:** Attention deficit and hyperactivity disorder; perinatal; complications; child development; review.

Introduction

Maternal well-being during pregnancy, both physical and mental, has become a focus of interest in the last decade (Herrman, 2015). Currently, it is well known that perinatal complications and neonatal environment (as well as genetic/epigenetic factors) affect child's physical and mental health development (Allen, Lewinsohn & Seeley, 1998; Appleton et al., 2016; Johnson, 2007; Johnson & Marlow, 2014). Attention deficit and hyperactivity disorder (ADHD) prevalence varies across different studies between 1% and 8% (Polanczyk, Salum, Sugaya, Caye & Rohde, 2015; Štuhec, Locatelli & Švab, 2015; Štuhec, Švab & Locatelli, 2015) and it is caused by gene and environment interplay as reported by most studies (Biederman & Faraone, 2005; Fitzgerald, Bellgrove & Gill, 2007; Montiel-Nava, Peña & Montiel-Barbero, 2003). No gender differences have been found in the prevalence of ADHD combined type, including both inattentive and hyperactive-impulsive symptoms, whereas girls with ADHD show the predominantly inattentive type two times more frequently than boys (Levy, Hay, Bennett & McStephen, 2005; Staller & Faraone, 2006). In contrast, male ADHD patients present mainly hyperactivity and impulsivity (Biederman & Faraone, 2004). It is well-known that ADHD has a strong genetic loading as shown by several studies reporting increased ADHD rates and co-morbid psychiatric symptoms in ADHD children's parents in comparison with healthy controls (Okan Ibiloglu et al., 2016). Genetic ADHD background has been only partially explored: recent pathway analyses demonstrated that different mechanisms are involved in the pathogenesis of ADHD including neurotransmitter release dysregulation, and abnormalities in neurite outgrowth and axon guidance (Mooney, McWeeney, Faraone, Hinney & Hebebrand, 2016). As well as genetics, it is well-known that some environmental habits, such as smoking during pregnancy, alcohol consumption and lead exposure all increase the risk of ADHD onset (Jaspers et al., 2013; Koshy, Delpisheh & Brabin, 2011; Melchior et al., 2015; Pineda et al., 2007). Moreover, maternal psychological factors (e.g. depression, anxiety), maternal physical illnesses (e.g. diabetes), body mass index, vitamin levels have been studied as risk factors for ADHD (Pugh et al., 2016). In relation to mother well-being, a recent US study with a cohort of healthy 1–3-day-old infants underlined and supported the importance of perinatal variables in neurobehavioural child development. In this study, higher mother pregnancy weight gain and birthweight percentiles have been associated with greater probability of abnormal neurobehaviour in children, whereas, longer gestations and higher 5-min APGAR scores (a quick test based on a total score of 1–10, the higher the score, the better the baby is doing after birth) were found to be associated with better behavioural outcomes. In addition, maternal alcohol use during pregnancy and foetal

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distress have been associated to a lower likelihood of having a physiological neurobehaviour development in offspring (Appleton et al., 2016).

Perinatal complications can contribute to ADHD onset during childhood and complicate the disorder with a higher psychiatric comorbidity rate (Bhutta, Cleves, Casey, Cradock & Anand, 2002; Geller et al., 2008; Johnco et al., 2016; Nijmeijer et al., 2010; Pringsheim, Sandor, Lang, Shah & O'Connor, 2009). The 2011–2012 National Survey of Children's Health estimated the prevalence of parent-reported mental health problems in offspring to be 22.9% among children born prematurely, 28.7% among very-low-birth-weight (<1,500 g) and 18.9% among moderately low-birth-weight (1,500–2,499 g) children, compared with 15.5% in the general child population (AOR: 1.49; CI: 1.29–1.73)(Singh, Kenney, Ghandour, Kogan & Lu, 2013). Finally, a recent meta-analysis underlined the significant burden of ADHD on the family unit, impacting parents' emotional health (Klassen, Miller & Fine, 2004) and child's quality of life (Lee et al., 2016).

Methods

In order to provide an update overview, a search in main databases (Pubmed, ISIWEB of Knowledge, PsycINFO) was performed. Suitable articles were sourced from a comprehensive literature search and from references identified through other studies. The keywords were 'ADHD' matched with 'pregnancy', 'delivery', 'perinatal complications', 'obstetric complications', 'preterm birth', 'low birth weight', 'bleeding', 'asphyxia', 'small for gestational age', 'abnormal foetal presentation', 'Apgar'. Exclusion criteria were: animal studies, studies with a different diagnosis (e.g. bipolar disorder), adult ADHD, physiology studies, researches about ADHD comorbidity (e.g. diabetes, smoking) or aimed to investigate generic attention problems. Only articles in English were included. Obstetric complications (OCs) were defined as those reported in Lewis-Murray rating scale with particular attention to labour, birth weight, preterm birth, asphyxia, Apgar score (Lewis & Murray, 1987). Of note, studies considering maternal non-obstetric complications (e.g. smoking, obesity or alcohol abuse during pregnancy) were not taken into consideration.

The authors of this review searched and independently selected the included articles. The aim of the present systematic review is to synthesize the literature related to obstetric and neonatal complications and the risk of developing ADHD from birth up until 12 years of age (Ben Amor et al., 2005; Henriksen, Wu, Secher, Obel & Juhl, 2015; Zappitelli, Pinto & Grizenko, 2001).

The review covers findings from 1987, when the first article on obstetric complications and ADHD appeared, to 2016 and the last search was conducted on December 2016, even though most of the included articles have been produced in the last 10 years.

Results

Several perinatal complications have been associated with the subsequent onset of child ADHD. Table 1 summarizes methods and quality of included studies and Table 2 the effect sizes/ *p*-values where available. After applying the inclusion and exclusion criteria, a total of 40 papers were included in the review (Figure 1).

ADHD and labour

Perinatal pitocin exposure was associated with a subsequent ADHD diagnosis in a first study by Kurth and Haussmann (2011) ($p < .001$). A population based case-control study by Ketzer, Gallois, Martinez, Rohde and Schmitz (2012) reported that children and adolescents, whose mothers presented more perinatal complications, including complicated labour, had a significant higher risk for ADHD-Inattentive subtype (ADHD-IA) (OR = 1.25; 1.1–1.5). A retrospective study found that a history of cord prolapse was significantly associated with a higher risk of ADHD in females than in the control group (Silva, Colvin, Hagemann & Bower, 2014). A large Danish population-based study by Henriksen et al. (2015) reported no association between oxytocin-induced labour and ADHD in the offspring. The Millennium cohort study, a nationally representative UK cohort of children, found no association between emergency delivery and ADHD (OR: 1.28; CI: 0.61–2.66)(Curran, Cryan et al., 2016). In contrast, a subsequent large cohort study by the same research group reported the association between emergency caesarean delivery and ADHD (HR: 1.16; CI: 1.12–1.20) (Curran, Khashan et al., 2016).

ADHD and birth weight

In 1987 a follow-up of 57 very low birth weight children (VLBW, <1,500 g) found that at 5 years 18 (31%) of them had ADHD (Astbury, Orgill & Bajuk, 1987). In line with this study, in a sample of VLBW children 23% met ADHD clinical criteria compared with 6% of matched peers at 12 years ($p < .0001$) (Botting, Powls, Cooke & Marlow, 1997). As a result of the National Survey of Children's Health, Singh et al. (2013) found that VLBW children had 1.7 times (CI: 1.13–2.47) higher risk of ADHD. Similarly, a retrospective investigation showed as VLBW increased the risk of a future diagnosis of ADHD (OR: 2; 1.3–2.8)(Boulet, Schieve & Boyle, 2011). In a prospective study VLBW and very preterm (VP, <32 weeks) children were at higher risk for ADHD-IA but not for hyperactive-impulsive subtype (Jaekel, Wolke, & Bartmann, 2013). A prospective cohort study, The Bavarian Longitudinal Study, reported that the combination of VP birth and VLBW was significantly associated with a higher risk of ADHD-IA and ADHD combined type (ADHD-C) (Breeman, Jaekel, Baumann, Bartmann & Wolke, 2016). Finally, a recent National Survey of Children's Health reported the association between ADHD with preterm birth combined with VLBW (RR: 1.6; CI: 1.2–2.3)(Schieve et al., 2016).

In a cohort of extremely low birthweight children (ELBW, <1,000 g) 16% had subsequently developed ADHD compared with 6.9% of controls ($p = .04$) (Szatmari, Saigal, Rosenbaum, Campbell & King,

Table 1 Evaluation of methods and quality of included studies

Authors	Type of study	Sample size (patients/controls)	Source of cases	Quality
Astbury et al. (1987)	Prospective five-year follow-up	23/34	Scheduled follow-up visits at 1 –2–5 years	+
Ben Amor et al. (2005)	Intrafamily study design	50/50	Clinical evaluation	0
Botting et al. (1997)	Study cohort	136/148	Parent and child questionnaires	++
Boulet et al. (2011)	Retrospective	677	National Health Interview Survey Sample Child Core Questionnaire	+
Breeman et al. (2016)	Prospective cohort study	260/229	Parent reports, expert behaviour observations, clinical ADHD diagnosis	++
Breslau et al. (1996)	Case–control study	473/350	Diagnostic Interview Schedule for Children-Parent Version Teacher's rating behaviour problems	+++
Chu et al. (2012)	Case–control study	195/212	Child psychiatrists assessments with ADHD ratings scale and Clinical Global Impression Severity	+
Class et al. (2014)	Population cohort	619,712	Inpatient and outpatient assessments	+
Curran, Cryan et al. (2016)	Millenium cohort study	18,827	Strengths and Difficulties Questionnaire	++
Curran, Khashan et al. (2016)	Study cohort	1,772,548	International Classification of Diagnosis and prescription ADHD medication	++
El Marroun et al. (2012)	Large population based prospective cohort study	5,145	Child Behaviour Checklist	++
Getahun et al. (2013)	Nested case control study	13,613/68,065	Medical reports	++
Gustafsson, and Källén (2011)	Population based study	237/31,775	Medical reports	++
Hack et al. (2009)	Study population	219/176	Parent reports Child symptom inventory	+
Hanć et al. (2016)	Case control study	132/146	Medical records	+
Heinonen et al. (2010)	Longitudinal regional birth cohort study	828	Parent rated behavioural symptoms score	+++
Henriksen et al. (2015)	Population based study	546,146	Combination of ICD-10 diagnosis of hyperkinetic disorder and information on dispensed ADHD medication	+
Hultman et al. 2007)	Prospective Swedish Twin Study	1480	14-item checklist (parental rating)	++
Jaekel et al. (2013)	Prospective whole population sample	281/286	Child observations and assessments Parents' interview	+++
Ketzer et al. (2012)	Case–control study	124/124	Schedule for Affective Disorders and Schizophrenia for School-Age Children, Epidemiological Version Clinical evaluations	+
Kurth, and Haussmann (2011)	Case–control	172	Medical records Community mental rate reports	0
Langley et al. (2007)	Retrospective study	356	Research diagnostic interview assessments Parents' reports	0
Lehn et al. (2007)	Longitudinal survey study	95	Mothers' clinical interview Postinterview questionnaires to mothers and twin	+
Li et al. (2011)	Nationwide population-based cohort study	980,902	ADHD diagnosis registers from hospital discharge and medicinal product	++
Lindström et al. (2011)	Register study national cohort	7,506	Multigeneration register and patient discharge register	+

(continued)

Table 1 (continued)

Authors	Type of study	Sample size (patients/controls)	Source of cases	Quality
Martel et al. (2007)	Longitudinal study	823	Child Behaviour Checklist and teacher report form	++
Mick et al. (2002)	Case–control family study	252/231	Structured diagnostic/clinical interviews, cognitive assessments	+
Murray et al. (2016)	Cross-cohort study	6,849 (UK) and 3,509 (Brazil)	Strengths and difficult questionnaire Well-being assessments	++
O'Callaghan, and Harvey (1997)	Prospective study	125	Teacher and parent ADHD questionnaire	+
Perna, and Cooper (2012)	Case–control	14/38	Neuropsychological evaluation	+
Pineda et al. (2007)	Cohort study	200/286	Child mother questionnaire, Diagnostic Interview for Children and Adolescents, Behaviour Assessment System for Children	+
Sasaluxnanon, and Kaewpornsawan (2005)	Retrospective, hospital-based, case–control study	122/119	Child Behaviour Checklist and Conners Teacher Rating Scale, mother self report questionnaire	+
Schieve et al. (2016)	Periodic random digit-dial health survey of US nonhospitalized children	74,565	Parents' report	+
Silva et al. (2014)	Population based, record linkage case–control study	12,991/30,071	Medical records	++
Singh et al. (2013)	National Survey of Children's Health, cross-sectional	85,535	Parents' report telephone survey	+
Stein et al. (2006)	National Health Interview Survey	7,817	Health professional and parents report	+
Szatmari et al. (1990)	Regional cohort study	184/209	Interviewer administered questionnaire and diagnostic check list	++
Treyvaud et al. (2013)	Cohort study	177/65	Infant-Toddler-Social-Emotional Assessment-Strengths and Difficulties Questionnaire-Developmental and Well-Being Assessment	++
Tsai et al. (2014)	Nationwide cohort, 10-year retrospective follow-up study	728	Medical records	+
Van Lieshout et al. (2015)	Prospective longitudinal population based cohort	84/90	Mini International Neuropsychiatric Interview	++

Each + corresponds to one of these criteria:
1. Sample size >500
2. Controlled study (presence of a healthy control group)
3. Prospective design (direct evaluation of obstetric complications and subsequent diagnosis of ADHD)
0: none of the above criteria.
These criteria were extrapolated by Quality Assessment Tool for Quantitative Studies-Effective Public Health Practice Project.

1990). O'Callaghan and Harvey failed to find an association between ADHD and perinatal adversities in ELBW children (O'Callaghan & Harvey, 1997). Hack et al. (2009) reported that ADHD is more prevalent among ELBW children compared to offspring with normal weight (OR: 4.2; CI: 1.9–9.1). Tsai et al. (2014) found in a large nationwide database, with a 10-year retrospective follow-up, that mechanical ventilation for ≧15 days increased the risk for ADHD in ELBW infants even without significant neonatal brain damage (AHR: 1.95; CI: 1.02–3.76). Van Lieshout, Boyle, Saigal, Morrison and Schmidt (2015), in a prospective, longitudinal, population-based cohort, found that the combination of ELBW and small size for gestational age (SGA) was a risk factor for the subsequent development of ADHD-IA (AOR: 4.98; CI: 0.72–34.69).

In a first study, low birth weight (LBW) was associated with ADHD, particularly in children living

Table 2 Main predictors and effect sizes of included studies

Main predictors of ADHD diagnosis	*N*	Effect sizes (*r*/*d*) (*p*-value)	Studies
VLBW	284	.39/.84 ($p < .001$)	Botting et al. (1997)
VLBW	87,578	.19/.38 ($p < .05$)	Boulet et al. (2011)
VP and VLBW for ADHD-IA	489	.27/.56 ($p = .001$)	Breeman et al. (2016)
VP and VLBW for ADHD-C		.2/.4 ($p = .010$)	
LBW	473/350	N.A.	Breslau et al. (1996)
Birth weight	407	.33/.7 ($p = .011$)	Chu et al. (2012)
Gestational age (weeks)		.31/.65 ($p = .005$)	
Birth weight <2,500 g	3,619,712	.23/.47 (p = N.A.)	Class et al. (2014)
ELBW	394	.37/.79 ($p < .001$)	Hack et al. (2009)
SGA	828	.33/.71 ($p = .002$)	Heinonen et al. (2010)
GA <32 weeks	546,146	.10/.19 (p = N.A.)	Henriksen et al. (2015)
Birth weight ≤ 2,879 g		.07/.13 (p = N.A.)	
Oxytocin-induced labor		NS .013/.027 (p = N.A.)	
Decreasing birth weight	2,960	.63/1.64 ($p = .026$)	Hultman et al. (2007)
VP and VLBW for ADHD-IA (at 8 years)	567	.15/.29 ($p = .02$)	Jaekel et al. (2013)
Birth Weight (in relation to inattentive and hyperactive-impulsive symptom severity)	356	NS .03/.06 ($p = .40$)	Langley et al. (2007)
Difference in birth weight in discordant twins for ADHD	190	.33/.71 ($p = .031$)	Lehn et al. (2007)
Extreme preterm birth (≤28 weeks)	1,180,616	.2/.41 (p = N.A.)	Lindström et al. (2011)
LBW	823	.16/.32 ($p < .01$)	Martel et al. (2007)
Birth weight <2,500 g	483	.3/.62 ($p = .04$)	Mick et al. (2002)
LBW	6,849	.22/.46 ($p = .029$)	Murray et al. (2016)
PB		.23/.47 ($p = .009$)	
SGA	3,509	.14/.29 ($p = .043$)	
ELBW	125	N.A.	O'Callaghan, and Harvey (1997)
LBW	241	.33/.71 ($p = .03$)	Sasaluxnanon, and Kaewpornsawan (2005)
VLBW plus PB	74,565	.13/.25 (p = N.A.)	Schieve et al. (2016)
PB	95,677	.11/.21 (p = N.A.)	Singh et al. (2013)
VLBW		.14/.28 (p = N.A.)	
LBW	7,817	.16/.31 (p = N.A.)	Stein et al. (2006)
ELBW	84	.42/.93 ($p = .03$)	Szatmari et al. (1990)
ELBW and SGA for ADHD-IA	174	.4/.89 (p = N.A.)	Van Lieshout et al. (2015)
Perinatal Pitocin exposure	172	.31/.66 ($p < .001$)	Kurth, and Haussmann (2011)
Apgar scores <4	980,902	.15/.31 ($p < .001$)	Li et al. (2011)
Perinatal cyanotic episode	52	.29/.61 ($p = .05$)	Perna, and Cooper (2012)
Neonatal seizures	486	.43/.95 ($p = .016$)	Pineda et al. (2007)
Cord Prolapse (females)	43,060	.28/.57 (p = N.A.)	Silva et al. (2014)
VP (<30 weeks)	242	NS .36/.76 ($p = .06$)	Treyvaud et al. (2013)
Mechanical ventilation >15 days	728	.18/.37 ($p < .05$)	Tsai et al. (2014)
Emergency delivery	18,827	NS .07/.14 (p = N.A.)	Curran, Cryan et al. (2016)
Elective CS	1,722,548	N.A.	Curran, Khashan et al. (2016)
Perinatal complications	100	NS .1/.21 ($p = .99$)	Ben Amor et al. (2005)
Preterm birth <35 weeks	5,145	.32/.68 ($p < .05$)	El Marroun et al. (2012)
IHC	308,634	.13/.26 (p = N.A.)	Getahun et al. (2013)
Apgar score <7	32,012	.21/.43 (p = N.A.)	Gustafsson, and Källén (2011)
VP		.30/.61 (p = N.A.)	
Low Apgar score	278	.17/.35 (p = N.A.)	Hanć et al. (2016)
Perinatal complications for ADHD-IA	248	.06/.12 ($p = .005$)	Ketzer et al. (2012)

ADHD-C, Attention Deficit Hyperactive Disorder Combined Type; ADHD-IA, Attention Deficit Hyperactive Disorder Inattentive Type; *d*, Cohen's effect size; ELBW, Extremely low birth weight (<1,000 g); EPB, Extremely preterm birth (24–32 weeks); GA, Gestational age; IHC, In Utero Exposure to Ischaemic-Hypoxic Conditions; LBW, Low birth weight (<2,500 g); NA, not available; NS, not significant; PB, preterm birth (<37 weeks); *r*, Pearson's *r* effect size; SGA, Small for gestional age <2 standard deviations; VP, Very preterm birth (<32 weeks); VLBW, Very low birth weight (<1,500 g).
APGAR scores: quick test based on a total score of 1–10, the higher the score, the better the baby is doing after birth, performed on a baby at 1 and 5 min after birth.

in urban areas than in sub-urban ones (Breslau et al., 1996). Mick, Biederman, Prince, Fischer and Faraone (2002) reported that ADHD patients were three times more likely to have been born with a LBW than controls (OR: 3.1; CI: 1.03–9.3). In a retrospective, hospital chart-based study, by Sasaluxnanon and Kaewpornsawan (2005) the number of ADHD cases who had presented a birth weight below 2,500 g was 3.6 times greater with respect to subjects with normal birth weight ($p = .03$). An intrafamily design study, comparing children diagnosed with ADHD and their unaffected siblings, did not find

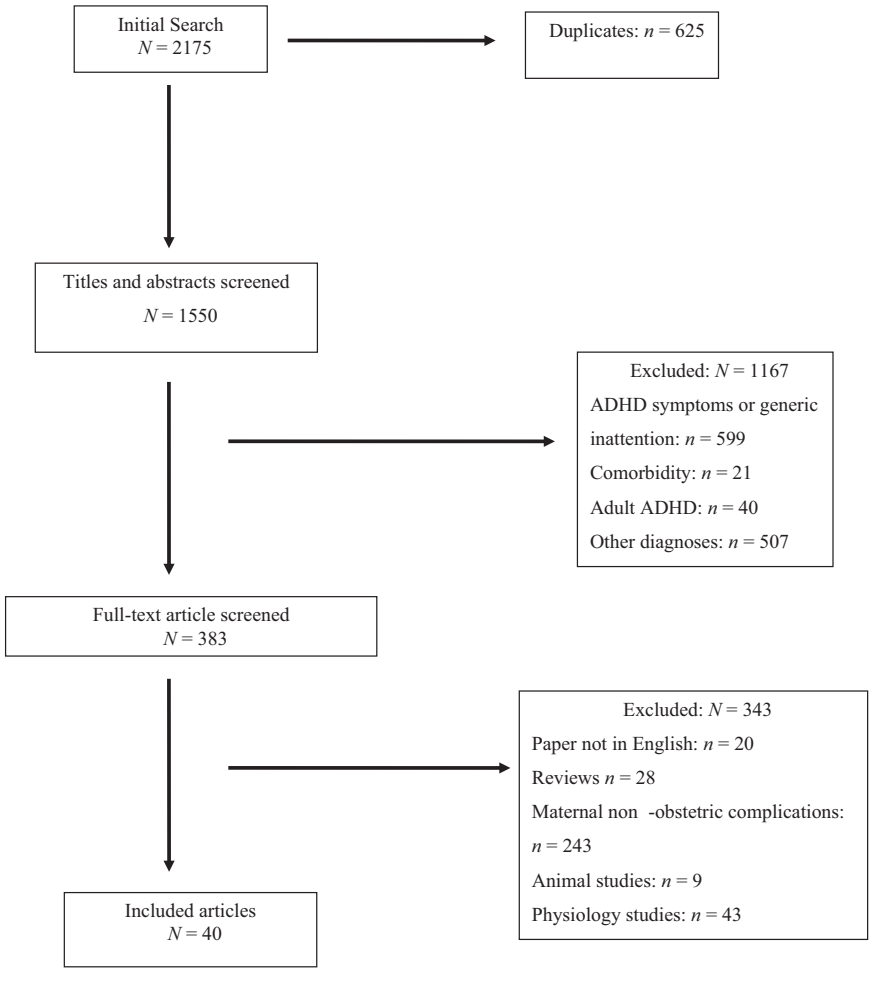

Figure 1 Prisma diagram for systematic reviews

significantly higher rates of neonatal complications (including LBW) in children with ADHD compared with their unaffected siblings (p = .99)(Ben Amor et al., 2005). Stein, Siegel and Bauman (2006), in a population-based study, found that moderately LBW children had more ADHD cases and health need than offspring with normal birth weight (OR: 1.77; CI: 1.07–2.9). A prospective twin study by Hultman et al. (2007) reported that LBW was a risk factor for ADHD symptoms also after controlling for genetic influence. Of note, another study reported differences in birth weight in discordant twins for ADHD (p = .031)(Lehn et al., 2007). In addition, LBW was associated with ADHD diagnosis in a study by Martel, Lucia, Nigg and Breslau (2007) (p < .01), while Langley, Holmans, van den Bree and Thapar (2007) failed to find an association between birth weight and ADHD (p = .40). A subsequent longitudinal study confirmed that SGA together with LBW was significantly associated with a higher risk of ADHD (OR: 3.60; CI: 1.63–7.95) (Heinonen et al., 2010). These results were replicated by a subsequent research showing that ADHD children had a significantly higher rate of prematurity and LBW with respect to controls in a Taiwan sample (p = .003) (Chu et al., 2012). A subsequent Swedish retrospective research confirmed the role of LBW in increasing the risk of ADHD (1.54; CI: 1.44–1.65)(Class, Rickert, Larsson, Lichtenstein & D'Onofrio, 2014). Murray et al. (2016) compared risk factors for ADHD in United Kingdom and Brazil, finding an association between LBW and ADHD in British sample (OR: 2.29; CI: 1.09–4.8), but not in Brazilian one (OR: 0.78; CI: 0.34–1.8).

ADHD and preterm birth

A register study based on a Swedish national cohort reported that children with an extreme preterm birth (≤28 weeks) were at risk to develop ADHD (OR: 3.3; CI: 1–10.5) (Lindström, Lindblad, & Hjern, 2011). Another Swedish large-sample research confirmed the result that VP birth was a risk factor for future development of ADHD (OR: 3.05; CI: 1.39–6.71) (Gustafsson & Källén, 2011). A subsequent large population-based prospective cohort study further supported that preterm birth (<35 weeks) was associated with ADHD (OR: 3.42; CI: 1.41–8.32)(El Marroun et al., 2012). Finally, Treyvaud et al. (2013) evaluated VP (<30 weeks) children at 7 years reporting borderline stastically significant difference in the prevalence of ADHD between VP offspring versus controls (10% vs. 3%; UOR: 4.09; CI: 0.93–18).

ADHD and asphyxia

Perna and Cooper (2012) reported an association between perinatal cyanoses and ADHD ($p = .05$). Finally, Getahun et al. (2013) reported that in utero exposure to ischemic-hypoxic conditions was a risk factor for future development of ADHD (OR: 1.16; CI: 1.11–1.21).

ADHD and Apgar score

A nationwide population-based cohort study found an association between low Apgar score at 5 min and ADHD, being the risk higher in children with Apgar scores from 1 to 4 (AHR: 1.75; CI: 1.15–2.66)(Li, Olsen, Vestergaard & Obel, 2011). Similarly, Apgar scores below 7 at 5 min were found to be significantly associated with ADHD (OR: 2.17; CI: 0.93–5.06)(Gustafsson & Källén, 2011). In contrast, low Apgar scores were not identified as a risk factor for ADHD in a study by Silva et al. (2014). Finally, a very recent study found low Apgar score to be the highest predictive perinatal risk factor for ADHD onset in males (Hanć et al., 2016).

ADHD and neonatal seizures

Pineda et al. (2007) reported an association between neonatal seizures and ADHD in a genetic high-risk group for this disorder (AOR: 5.6; CI: 1.4–22.5).

Conclusions

Perinatal complications represent an important, but modifiable risk factor for the future development of ADHD.

Considering the individual perinatal complications, oxytocin-induced labour does not seem to be associated with subsequent ADHD diagnosis, as showed by the only large-sample study on this topic (HR: 1.42; CI: 1.12–1.80) (Henriksen et al., 2015). Similarly, only one study (though with a large sample) found that cord prolapse is a risk factor for ADHD in females, and therefore this result must be confirmed by future research (OR 2.83) (Silva et al., 2014). Results are also contrasting for emergency delivery so that further studies must confirm this finding.

Low birth weight (<2.5 kg) can be considered the risk factor with the evidence of its association with ADHD. Of note, ten independent researches for a total of 3,640,305 subjects (Breslau et al., 1996; Chu et al., 2012; Class et al., 2014; Hultman et al., 2007; Lehn et al., 2007; Martel et al., 2007; Mick et al., 2002; Murray et al., 2016; Sasaluxnanon & Kaewpornsawan, 2005; Stein et al., 2006) found LBW to be a major risk factor of future diagnosis of ADHD (Cohen's *d* effect size range: 0.31–1.64) (McGough & Faraone, 2009). Only a low-quality study failed to find an association between LBW and ADHD (Langley et al., 2007). In addition, the study with the highest effect size ($d = 1.64$) is one among those with the best quality of methodology and largest sample size (OR: 19.6; CI: 1.44–266) (Hultman et al., 2007). Future studies will have to figure out what is the specific role of preterm birth versus inflammation during pregnancy in determining the LBW of ADHD-risk patients. This question is necessary considering that increased inflammation during pregnancy is one of the determinants of LBW (Niu et al., 2016) and it is associated with mothers' psychiatric conditions (Serati, Redaelli, Buoli & Altamura, 2016) including those (e.g. bipolar disorder) (Buoli et al., 2016) which are considered as a risk factor for ADHD in the offspring (Axelson et al., 2015). Some authors have raised the question if severe LBW further increases the risk of ADHD in the offspring. Four studies (Astbury et al., 1987; Botting et al., 1997; Boulet et al., 2011; Singh et al., 2013) confirmed that VLBW is a risk factor for ADHD, but the effect sizes are comparable to those that have been extrapolated for LBW (effect size *d* range: 0.28–0.84). Similar considerations can be done for studies with ELBW (<1 kg) subjects, although in this case the sample sizes are even smaller than in the case of VLBW (Hack et al., 2009; Szatmari et al., 1990; Van Lieshout et al., 2015). Of note, three papers (Breeman et al., 2016; Jaekel et al., 2013; Schieve et al., 2016) considered the combination of VP and VLBW as a risk factor for ADHD, but the effect size range (0.25–0.56) was smaller than that of the studies considering only VLBW. However, two of these studies (Breeman et al., 2016; Jaekel et al., 2013) showed a specific association with ADHD-IA: the cumulative effect of multiple risk factors might be associated with specific ADHD subtypes, respectively (2.8; CI: 1.6–5) (RR: 2.76; CI: 1.46–5.19). Taken as a whole these data indicate that LBW is an important predictor of ADHD, without being a clear proportional relationship between weight reduction and increased risk of illness for birth weights below 2,500 g.

All researches for a total of 1,217,773 subjects (El Marroun et al., 2012; Gustafsson & Källén, 2011; Lindström et al., 2011) reported a statistically significant association between preterm birth and ADHD diagnosis with medium effect sizes (range *d*: 0.41–0.68), with the exception of one small sample-size research (Treyvaud et al., 2013) which reported a borderline statistically significant difference in the prevalence of ADHD between VP subjects versus controls, despite the medium- large effect size ($d = .76$), perhaps as a consequence of the small sample size ($N = 242$). Taken as a whole the available data indicate preterm birth as an important risk factor for future diagnosis of ADHD, although the different studies used different definition of preterm birth.

With regard to Apgar scores three (Gustafsson & Källén, 2011; Hanć et al., 2016; Li et al., 2011) of

four researches found a significant association with future ADHD diagnosis, however, the studies were heterogeneous about the cut-off of Apgar scores and the effect sizes were smaller than those about LBW and preterm birth (Cohen's *d* range: 0.31–0.43). Further studies will confirm if Apgar scores have a predictive value for the future diagnosis of ADHD.

Regarding perinatal cyanosis and neonatal seizures, data are too scanty to draw definitive conclusions about the association between these factors and ADHD.

Taken as a whole these considerations indicate that:

1. Mental and physical health of women (Serati, Buoli & Altamura, 2015) is crucial for limiting the risk of ADHD in the offspring;
2. PB and LBW children should be carefully monitored for an early diagnosis of ADHD;
3. Parents should be informed about the risk of LBW and preterm child to develop future ADHD (Rommel et al., 2017).

Limits of the present review are represented by:

1. the selection of articles only in English;
2. most of articles have been conducted retrospectively and with family/teacher reports
3. the heterogeneity of methods of the selected articles that prevented to perform a metanalysis of the results;
4. the variability of the definition of LBW in the different papers;
5. the variability of the definition of preterm birth in the various researches;
6. the fact that some register-based studies used the same nationwide sample so that results may be overlapped
7. the use of different ADHD assessment tools within the different studies

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Key points

- It is well-known that complications during the perinatal period together with neonatal environment have significant implications on child's physical and mental health development.
- According to the last studies ADHD prevalence is about 8% and in some countries <1% and it is caused by gene and environment interplay.
- The aim of the present systematic review is to synthesize the literature related to obstetric and neonatal complications and the risk of developing ADHD from birth until 12 years of age.
- Results indicate that: PB and LBW children should be carefully monitored for an early diagnosis of ADHD; parents should be informed about the risk of LBW and preterm child to develop future ADHD.

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What do childhood attention deficit/hyperactivity symptoms in depressed adults tell us about the bipolar spectrum?

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ABSTRACT

Background: This study aims to establish if adult patients with major depressive disorder (MDD) and childhood Attention Deficit/Hyperactivity disorder (ADHD) symptoms would be more frequently within the bipolar spectrum than depressed patients without childhood ADHD.
Methods: This study was carried out in outpatients recruited by psychiatrists in private practice, with 3963 participants being included in the final sample. Clinicians filled out questionnaires about current depressive symptoms in their patients, lifetime bipolar symptoms, global assessment of functioning and parental history of both major depression and bipolar disorder. Patients assessed current level of anxiety and depressive symptoms and antecedents of childhood ADHD symptoms.
Results: Depressed adults with significant childhood ADHD symptoms had a specific pattern of their major depressive episode compared to depressed patients without such symptoms. Subjects with childhood ADHD symptoms were more likely to report lifetime symptoms of mania/hypomania and to have a parent with type I or II bipolar disorder. The developmental trajectories of familial risk for lifetime bipolar symptoms showed that parental bipolar disorder influenced lifetime bipolar symptoms both through a direct pathway and an indirect pathway involving childhood ADHD symptoms. Childhood ADHD and number of depressive symptoms both made direct contributions to lifetime bipolar symptoms.

1. Introduction

Links between externalized and mood disorders have been documented throughout development in both clinical and population based samples (Reef et al., 2011). Attention Deficit Hyperactivity Disorder (ADHD), a chronic neurodevelopmental condition characterized by high levels of inattention, impulsivity and hyperactivity has shown significant comorbidity with major depressive disorder (MDD) (Meinzer et al., 2014) and dysthymia (Elia et al., 2008). Relations between ADHD and bipolar disorder (BD) have been also documented, but yield inconsistent results across developmental stages, study design and definition of bipolar phenotypes (Marangoni et al., 2015).

Studies in referred samples of adults with ADHD show higher current and lifetime prevalence of affective disorders in ADHD compared with controls (Biederman et al., 1994, 1993; Secnik et al., 2005; Shekim et al., 1990; Sobanski et al., 2007). In a study of adults with a primary diagnosis of major depression, full or sub-threshold criteria for childhood ADHD were documented in 16% and ADHD symptoms persisted in adulthood in 12% (Alpert et al., 1996). In clinical samples of children and adolescents, high rates of comorbidity between ADHD and depressive disorders have also been found (Biederman et al., 1991; Brown et al., 2001; Cantwell, 1996; Gau et al., 2010; Jensen et al., 1997; Spencer, 2006). Although co-occurrence between ADHD and mood disorders is generally highest in clinical samples and retrospective data, lifetime and present mood disorders are also overrepresented in adults and children with ADHD in epidemiological samples and birth cohorts (Fayyad et al., 2007; Kessler et al., 2006; Meinzer et al., 2014; Smalley et al., 2007).

ADHD has been identified as a prevalent condition in adults with BD. The US National Comorbidity Survey Replication study showed

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that 31,4% of adults with any type of BD also had a diagnosis of lifetime ADHD (Merikangas et al., 2007). In the STEP-BD study, 9.5% of adults with BD met criteria of lifetime ADHD and 62% of this group had persistent ADHD at the time of assessment (Nierenberg et al., 2005). In a sample of BD outpatients in remission, co-occurrence of ADHD was 18% for a lifetime- and 10% for a current diagnosis (Bernardi et al., 2010) and a similar rate (e.g. 19,8%) of both current and lifetime ADHD was found in 96 adults with BD (Perugi et al., 2013). When adults with ADHD were compared with controls, higher levels of BD (4.5% vs 0.6%) were reported in the group with ADHD (Secnik et al., 2005).

Longitudinal studies of ADHD and BD show conflicting results. Early studies found no elevated risk of BD in follow-up studies of ADHD (Hazell et al., 2003; Mannuzza et al., 1998) and other studies with positive associations between ADHD and subsequent BD used a broad definition of juvenile BD (Biederman et al., 2009b, 2010). This broad BD phenotype, characterized by non-episodic irritability (Wozniak et al., 1995) has high rates of co-occurring ADHD compared to narrowly-defined BD (i.e. distinct manic episodes with euphoria) (Carlson and Klein, 2014). In a recent nationwide cohort of Taiwanese patients with ADHD, the risk of later BD defined by ICD-10 categories was significantly increased (ADHD: 2.1% vs 0.4%) (Wang et al., 2015) and ADHD also predicted BD in adolescents and young adults with major depression (Chen et al., 2015). A 14 year follow-up of participants in the Multimodal Treatment Study of ADHD showed that as young adults (aged 21–24 years) they had no greater risk for developing BD than the comparison group, but showed higher rates of BD symptoms, especially non specific manic symptoms (Elmaadawi et al., 2015).

Comorbid ADHD/BD has been associated with early-onset of the first affective episode, a severe course of the illness, higher levels of mood symptoms and poor adaptive functioning (Ryden et al., 2009). In patients with BD, lifetime ADHD elevates the risk of early onset of mood episodes, diagnosis of BD I rather than BD II. They also have more substance abuse, social phobia and post-traumatic stress syndrome than BD patients without lifetime ADHD (Nierenberg et al., 2005).

As suggested from available data, ADHD is both an antecedent and a comorbid condition of mood disorders. To date, the developmental links between ADHD symptoms in childhood and adult MDD are poorly understood. In particular, it is unclear whether childhood ADHD symptoms may inform about bipolar spectrum symptoms in adulthood. The present study addresses this issue in adults diagnosed with a current major depressive episode (MDE) and treated in community care. In this population, developmental ADHD symptoms are likely to be prevalent, and their identification may have clinical and therapeutic implications as regards early identification of bipolar symptoms and associated features. We therefore made the hypothesis that adult depressive patients with childhood ADHD would be more frequently within the bipolar spectrum, therefore with (1) greater severity of depression (earlier onset of depression, higher severity of the current episode, higher recurrency rates) and lower level of functioning, (2) more lifetime bipolar symptoms and/or more familial history of BD.

2. Methods

2.1. Participants

This study was carried out in outpatients recruited by psychiatrists in private practice. One thousand six hundred eleven psychiatrists of a national contact list held by the study's sponsor were contacted via mail for participation, 867 agreed and 840 (52%) finally contributed to the study. Psychiatrists were asked to recruit adult patients with a current episode of major depression. The patients were required to be above 18 years of age, to be affiliated to a social security system and to speak fluent French. The participants gave written informed consent after receiving a detailed description of the study. Five thousand five hundred and fifty-eight patients participated in the study. Among the questionnaires returned, 5485 (98,68%) clinician-rated questionnaires and 5411 (97,35%) patient-rated questionnaires were usable and included in the initial database.

2.2. Instruments

Clinicians filled out questionnaires about current depressive symptoms in their patients, lifetime bipolar symptoms, and global assessment of functioning. They also assessed parental history of MDD and BD.

The diagnosis of a major depressive episode (MDE) relied on clinical diagnosis and a check-list of corresponding DSM-IV-TR items. The presence of five or more symptoms along with duration and impairment criteria was requested for the diagnosis of a MDE according to DSM-IV-TR criteria. The assessment also included questions relative to the duration of the current episode, number of past episodes, current age and age or the first MDE. Lifetime bipolar symptoms were assessed by the mania/hypomania screening items of the Diagnostic Interview for Genetic Studies (Nurnberger et al., 1994; Preisig et al., 1999). Presence of elated mood (not only irritability) was required for a positive screening on lifetime bipolar symptoms. Elated mood needed to be present for an entire day or if intermittent, during a minimum of two days.

Current adaptive functioning was assessed with the Global Assessment of Functioning (GAF) (American Psychiatric Association, 1994). Familial history of depression and BD was investigated with the appropriate items from the French version of the Family Interview for Genetics Studies (FIGS) (NIMH genetics initiative, 1992).(Fig. 1).

Patients were given auto-questionnaires about current level of anxiety and depressive symptoms and about antecedents of childhood attention-deficit/hyperactivity symptoms. To assess current anxiety and depression symptom severity patients filled out the Hospital Anxiety and Depression Scale (HAD) (Zigmond and Snaith, 1983), a self-report instrument consisting of two subscales each containing seven items on a 4-point Likert scale. Patients reported childhood ADHD symptoms using the French version of the Wender-Utah Rating Scale (WURS) (Bayle et al., 2003), a 25-items self-report questionnaire used for retrospective screening of ADHD symptoms. According to the literature, a score of 46 and above was used to define a positive childhood history of ADHD symptoms.

2.3. Inclusion criteria

The following criteria had to be fulfilled to include a patient in final analyses:

-both clinician-rated and patient-rated questionnaires returned.

-presence of DSM-IV-TR criteria of a current MDE (presence of 5 or more items, with impairment) (n=42 subjects excluded).

-duration criteria: 2 weeks of duration minimum (n=56 excluded).

-depressive symptoms not accounted for by bereavement or drug use (n=200 excluded).

-depressive sub-scale of HAD < 8 (n=348 excluded).

-WURS and HAD completed (n=634 excluded for incomplete WURS, n=94 for HAD).

The clinical database was further checked for inconsistencies, errors and incomplete information. Data from 3963 participants were included in the final sample for statistical analysis.

2.4. Statistics

Variables were examined for the normality of distribution before using parametric tests. Given the sample size, rejection of a normal distribution was expected for all variables with the Kolmogorov-

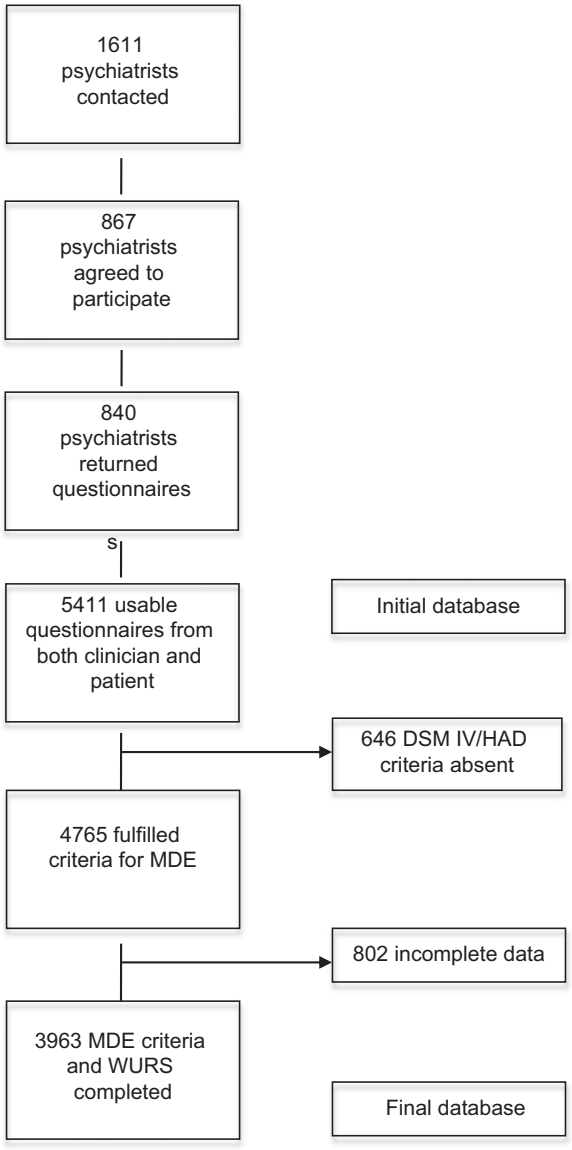

Fig. 1. Flow chart. HAD: Hospital anxiety and depression scale. MDE: Major depressive episode.

Smirnov test. Thus, Q-Q plots (quantiles) were used to assess the distribution of WURS scores and major covariables. The graphical assessment showed that WURS scores and major covariables (age, total number of depressive symptoms, functioning, HAD anxiety and depression scores) were close enough to normal distribution. One-way ANOVAs were used to test for differences in demographic and clinical characteristics according to childhood ADHD status. Relations between categorical variables were assessed with chi-square tests. We then used multivariate analyses to examine whether the presence of childhood ADHD symptoms predicted lifetime bipolar symptoms. To assess predictors of possible bipolar spectrum symptoms in our sample, independent variables significantly associated with lifetime bipolar symptoms were retained in the logistic regression model. Age at first episode (related to number of MDE) as well as anxiety and depression scores (related to severity/number of symptoms) were not retained in the final model. In all analyses a probability level of $p < 0.05$ was used to indicate statistical significance.

Finally, structural equation modeling was used to further analyze the respective role of clustered variables on lifetime bipolar symptoms. The variables and the direction of the effects where chosen a priori according to a hypothetico-deductive approach. Possible developmental antecedents of lifetime bipolar symptoms were entered in the model: C-ADHD, number of MDE and parental BD. Structural equations models have been estimated with the lavaan function of the R software. Weighted least-squares routines were used to deal with ordered and binary variables.

3. Results

Women comprised 67.13% of the final sample and on average age participants were 45.78 years old (SD=12.95). The mean duration of the MDE was 14.37 weeks (SD=29.72). The average number of depressive symptoms was 6.97 (SD=1.20). The current MDE was a first episode for 32.44% of patients and the mean number of MDEs in the sample was 3.05 (SD=3.36). The first MDE occurred at an average age of 32.82 (SD=12.26). The mean level of functioning in the entire sample was 49.96 on the GAF scale graded from 0 to 100. Lifetime symptoms of mania/hypomania were present in 19.45% of the total sample and parental BD (type I or II) was documented in 9.46%. Parental MDE were found in 30.12% of the sample and in 2,3% the parents had at least one mood episode with psychotic features.

In our sample of adults with a current MDE presence of significant childhood ADHD symptoms (C-ADHD+) compared with absence of significant ADHD symptoms (C-ADHD-) was associated with younger age, a greater proportion of men, a higher number of previous MDE, a younger age at occurrence of the first episode and greater anxiety levels (Table 1). Duration of the current episode was shorter in C-ADHD+ relative to C-ADHD-. Severity of current MDE was greater in C-ADHD + according to clinician's ratings (number of DSM-IV-TR symptoms) but there was no significant difference between the two groups in the self-rated depression sub-score of HAD.

Subjects with C-ADHD+ also had a lower level of functioning compared to those without significant retrospective ADHD symptoms (mean GAF 50.64 vs 48.35; F1, 3846=40.23; $p < 0.0001$). The linear regression model showed that the level of adaptive functioning was significantly predicted by lifetime BD symptoms and childhood ADHD symptoms. Indicators of severity of MDE (i.e. number of depressive

Table 1
Clinical characteristics of patients with major depression according to status of childhood ADHD symptoms.

	C-ADHD- Mean (SD) N=2793	C-ADHD+ Mean (SD) N=1124	df	F	p value
Age	46.85 (13.22)	43.21 (11.92)	1	63.62	< 0.0001
Number of symptoms	6.92 (1.18)	7.12 (1.22)	1	22.26	< 0.0001
Number of episodes	2.87 (3.30)	3.40 (3.47)	1	14.23	< 0.0001
Duration of current episode	15.09 (32.73)	12.65 (20.76)	1	5.43	0.02
Age at first episode	34.45 (12.55)	29.27 (10.80)	1	116.69	< 0.0001
GAF	50.64 (9.94)	48.35 (10.82)	1	33.16	< 0.0001
HAD anxiety	13.47 (3.23)	14.80 (3.20)	1	139.31	< 0.0001
HAD depression	14.15 (3.36)	14.17 (3.33)	1	0.02	0.89
HAD total	27.63 (5.23)	28.97 (5.28)	1	53.25	< 0.0001
	C-ADHD- N (%)	C-ADHD+ N (%)	df	chi-square	p value
Sex (men)	870 (31.40)	422 (36.38)	1	9.20	0.001
Mania/Hypomania LT	447 (16.00)	324 (27.69)	1	71.89	< 0.0001
Parental BD	195 (6.98)	180 (15.38)	1	67.96	< 0.0001
Parental depression	762 (27.57)	413 (36.32)	1	29.34	< 0.0001
Parental psychotic features	53 (1.90)	38 (3.26)	1	6.76	0.009

C-ADHD-: absence of significant childhood ADHD symptoms (WURS < 46); C-ADHD+: presence of significant childhood ADHD symptoms (WURS ≥46), GAF: Global Assessment of Functioning, Mania/Hypomania LT: lifetime symptoms of mania/hypomania. Parental BD: parental bipolar disorder (type I or II).

symptoms, HAD depression sub-score), current anxiety level as measured by the HAD anxiety sub-score and number of MDE, also showed negative predictive value for current level of functioning (details in the supplementary table).

Subjects with C-ADHD+ were more likely to report lifetime symptoms of mania/hypomania and to have a parent with BD type I or II. They also had a greater proportion of parents with a history of MDE and with at least one depressive episode with psychotic features. Variables associated with lifetime bipolar symptoms (L-BD) in our sample of adults with a current major depressive episode were age ($F_{1,3839}=3.93$; $p=0.048$), number of depressive episodes ($F_{1,2582}=94.83$; $p < 0.001$), number of depressive DSM-IV-TR symptoms ($F_{1,3962}=10.86$; $p < 0.001$), age at first depressive episode ($F_{1,2913}=21.82$; $p < 0.001$), general functioning ($F_{1,3846}=28.05$; $p < 0.001$), anxiety sub-score of HAD ($F_{1,3942}=9.54$; $p=0.002$), depression sub-score of HAD ($F_{1,3962}=5.08$; $p=0.02$), presence of a BD in at least one parent (chi-square (1)=207.40; $p < 0.001$), depression with psychotic features in a parent (chi-square (1)=10.83; $p=0.001$), and, in accordance with our hypothesis, presence of childhood ADHD symptoms (chi-square (1)=71.87; $p < 0.001$). Sex, duration of the current episode and parental history of MDD were not associated with L-BD.

The overall logistic regression model including independent variables significantly associated with L-BD in the precedent analyses predicts the dependent variable L-BD (Table 2). Number of MDE, general level of functioning, parental bipolar disorder and C-ADHD+ were significant predictors of L-BD.

We further examined the respective role of clustered variables on lifetime bipolar symptoms through path analysis (Fig. 2 and supplementary table). No alternative models were estimated, because the fit between the model and the data was perfect: Normed Fit Index (NFI) =1 and Root Mean Square Error of Approximation (RMSEA)=0. The NFI compares the target model with the null model in which all measured variables are uncorrelated. Values for this statistic range between 0 and 1 with values greater than 0.90 indicating a good fit (Bentler and Bonnet, 1980). The RMSEA shows how well the model would fit the populations covariance matrix with values below 0.08 indicating a good fit (MacCallum et al., 1996).

The model examining the comparative strength of direct and indirect relationships among antecedents of L-BD shows that L-BD are significantly related to number of MDE, parental BD and C-ADHD +. Parental BD both influences L-BD through a direct pathway and an indirect pathway involving C-ADHD+. In our model, presence of C-ADHD+ is directly related to lifetime bipolar symptoms.

4. Discussion

Although a prospective relation between ADHD and depression has been demonstrated in the literature in referred and non-referred patients, the progression to depression in patients with ADHD is still not fully understood. A better comprehension of the mechanisms underlying the ADHD-depression relationship may be crucial for timely and targeted prevention strategies. The present study was addressed to explore rates of childhood ADHD in adults with depression followed in community care, and to describe possible clinical features of depression with childhood ADHD symptoms, with particular reference to hypomanic or manic features.

Table 2
Predictors of lifetime bipolar symptoms.

	B	SE	Exp (B)	p
Age	−0.004	0.004	0.99	0.42
Number of MDE	0.14	0.002	1.16	< 0.001
Number of symptoms	−0.01	0.04	0.98	0.78
GAF score	−0.01	0.005	0.98	0.02
Parental MDE/psychotic	0.21	0.28	1.23	0.45
Parental BD	1.34	0.14	3.83	< 0.001
C-ADHD+	0.45	0.11	1.57	< 0.001
Constant	−1.19	0.51	0.30	0.02

MDE: Major depressive episodes; GAF: General assessment of functioning; Parental MDE/psychotic: at least one depressive episode with psychotic characteristics in a parent, C-ADHD+: significant level of childhood ADHD symptoms.
Model statistics: Model chi-square (7)=229.36; $p < 0.001$; −2 log likelihood=2421.26; $R^2=0.14$

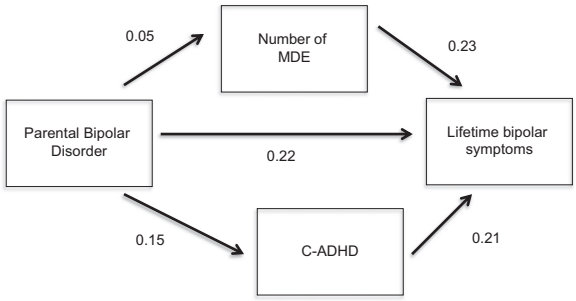

Fig. 2. Structural Equation Model for lifetime bipolar symptoms. Model statistics: RMSEA=0; NFI=1. Test of individual parameter estimates are significant $p < 0.001$ for all coefficients R command line: model < - ' manie ~nedm+atcdbpd+wurscat. wurscat ~atcdbpd. nedm ~atcdbpd. nedm ~~wurscat '. fit < - sem(model, data=dt, ordered=c("-manie","wurscat")). MDE: Major depressive episode; C-ADHD: childhood ADHD symptoms.

The sample included 3963 unselected adult patients diagnosed as depressed, 1124 (28.4%) presenting childhood ADHD symptoms (C-ADHD+). A previous study reported a prevalence rate of ADHD of 16% in a small sample of 115 adult patients with depression (Alpert et al., 1996), and a greater incidence, close to 50%, was reported in another study of adult outpatients with MDD (Ratey et al., 1992). Our sample presented a high number of depressive symptoms (7+/−1) suggestive of a moderate to high clinical severity, while the GAF score (50) indicated a moderate functional impairment.

Our findings support the notion that childhood ADHD is not only associated with a higher risk for presenting a depressive disorder, but may also represent a pathway for a specific depressive phenotype. Our depressed patients with C-ADHD+ showed a significantly greater number of lifetime (hypo)manic symptoms, compared with the C-ADHD- group. Additional features of the depressive disorder in patients with C-ADHD+ were an earlier onset of the first episode, a greater severity in terms of both clinicians' rated number of depressive symptoms and level of functioning, a higher number of previous MDE, higher rates of anxiety, more frequent psychotic symptoms, and more frequent familiarity for BD I or II (but also for psychotic depression). All these features were found to be possible predictors of a bipolar spectrum disorder in patients with current diagnosis of depression: earlier onset of depression (Geller et al., 2001; Sachs et al., 2000), higher recurrence of the depressive episodes (Smith et al., 2005), comorbid anxiety (Calabrese et al., 2005; Kessler et al., 2005), psychotic symptoms (Ruggero et al., 2011), and familial history for bipolar I or II (Wiste et al., 2014). Other findings relate to specificities of the BD phenotype in the presence of co-occurrent ADHD: some studies have found more atypical depression (Torres et al., 2015) and no support of a higher severity of the depressive episodes but higher severity in outcomes related to impulsivity (Carlotta et al., 2013).

The issue of a hidden bipolarity in depressed patients is still controversial. Previous research suggests that a subset of about a quarter of unipolar depressed patients in primary care settings had evidence of bipolarity after careful screening (Hirschfeld et al., 2005). Misdiagnosed patients typically experience depression as the first symptom of their illness; they seek treatment for depression, and not for mania or hypomania, especially in primary care settings. Lifetime or current ADHD may be one of the possible predictors that should alert physicians to the possibility of a bipolar/mixed depression in patients currently treated for major depression. Most of these patients are poor

responders to usual antidepressant treatments (Biederman et al., 2009b).

The path analysis model examining relationships between lifetime bipolar symptoms and personal and familial antecedents showed that parental bipolar disorder both had a direct impact on lifetime bipolar symptoms and an indirect influence through C-ADHD+. The trajectory relating parental BD, C-ADHD+ and lifetime bipolar symptoms is in line with the previously reported high prevalence of ADHD in offspring of BD parents. Indeed, some family studies examining children of parents with BD found high rates of ADHD compared to offspring of controls (Axelson et al., 2015; Chang et al., 2000; Hirshfeld-Becker et al., 2006) but other reports did not show elevated rates of ADHD diagnosis or symptoms in BD offspring (Hillegers et al., 2005). Rates of ADHD in offspring of BD parents and offspring of parents with non-BD symptoms have been found to be similar in some studies with mood symptoms more specifically found in children from parents with BD (Carlson and Weintraub, 1993). As there was no formal diagnostic assessment for ADHD in our study, a positive WURS score may be ADHD-specific but could also reveal early-onset emotional dysregulation, a frequent clinical feature of ADHD (Sobanski et al., 2010) but also of prodromal bipolar symptoms (Faedda et al., 2014).

Our model also identified a direct pathway between childhood ADHD symptoms and lifetime bipolar symptoms. This finding raises the question of the risk of mania in the course of ADHD, especially in case of co-occurrent depression. While previous reports have shown that the presence of ADHD significantly increases the risk for switching to BD type I in children with unipolar depression (Biederman et al., 2009b), more recently the same research group (Biederman et al., 2013) explored this issue in a sample of young adults with ADHD and depression, searching for possible specific predictors of bipolar switches in the context of depression. According to this study, emotional dysregulation and sub-threshold forms of BD type I disorder, similar to those reported in our study, increased the risk for switching from unipolar depression to BD type I disorder in young adulthood (57% vs. 21% in ADHD depressed patients with or without sub-threshold manic symptoms). Other longitudinal studies have not reported any significant association between childhood ADHD and later BD (Fischer et al., 2002; Hazell et al., 2003; Mannuzza et al., 1993; Weiss et al., 1985). Symptom overlap (e.g. motor restlessness, distractibility, irritability), differences in definition of BD phenotype (e.g. chronic irritability vs. episodic mania) and insufficient duration of follow-up may account for these inconsistent results (Skirrow et al., 2012). Another factor of confusion in the description of the juvenile BD phenotype is the possibility of rapid cycling (e.g. recurrent full-syndromal mood episodes) and ultradian cycling (e.g. mood fluctuation in the same episode) (Geller and Cook, 2000), the latter phenotype sharing characteristics of emotional lability occurring in the course of ADHD (Birmaher, 2013).

However, recent studies in population samples show heightened risk of subsequent BD in subjects with ADHD. A nationwide Danish follow-back study bipolar disorder has been associated with increased risk of preceding affective disorder and ADHD (Andersen et al., 2013). Similarly, ADHD independently predicted later BD among adolescents and young adults with major depression (Chen et al., 2015) and a recent systematic review of prospective studies was also in favour of ADHD being a risk factor for BD (Faedda et al., 2014). These findings emphasize the critical importance of considering sub-syndromal manifestations of BD and emotional dysregulation when evaluating, treating, and monitoring patients with ADHD and comorbid depression, especially when they are treated with antidepressants.

Although ADHD in adults also having depression with mixed features or bipolar spectrum disorder is associated with a worse course and greater burden of depression, dysregulation of impulse control, alcohol and substance abuse and dependence (Nierenberg et al., 2005), clinicians are hesitant to treat ADHD with pharmacotherapy (e.g., psychostimulants or atomoxetine) because of the fear of exacerbating the course of BD and provoking manic symptoms. Importantly, in contrast with the hypothesis that stimulant use could precipitate manic symptoms in bipolar ADHD/BD patients, two studies in children and adolescents reported that treatment with psychostimulants was not associated with worsening of manic symptoms (Biederman et al., 2008; Scheffer et al., 2005). Data on treatment response in adults with ADHD/BD are more limited, and in clinical practice, ADHD/BD patients are likely to be treated for BD only.

A frequently neglected component of the transition between ADHD and mood disorders (both MDD and BD) is a co-occurring anxiety disorder. According to our findings, anxiety was significantly more reported in depressed patients with childhood ADHD symptoms. Meinzer et al. (Meinzer et al., 2013) found that a lifetime history of an anxiety disorder as well as the onset of anxiety after mid-adolescence, were robust predictors of adult depression in non-referred patients with childhood ADHD. Jerrell et al. (2015) explored risk factors for developing a depression in a cohort including 22.452 cases diagnosed with ADHD at a mean age 7.8 years. Among these patients, 1259 (5.6%) cases received a diagnosis of depression at a mean age of 12.1 years, and the risk of developing depression was significantly associated with a comorbid anxiety disorder (aOR=3.53), as well as with disruptive behavior disorders (aOR=3.45), or a substance use disorder (aOR=2.31). Roy et al. explored the pathway from ADHD to depression, and particularly the role of anxiety and disruptive behavior disorders as mediators (Roy et al., 2014). Anxiety was more prevalent in girls, while disruptive behavior disorders were more prevalent in boys. Anxiety and disruptive behaviors mediated 32% of depression in ADHD. Recent findings from cross-sectional studies suggest that poor emotion regulation, a common feature of ADHD, anxiety disorders and some disruptive behavior disorders, may mediate the relationship between ADHD and depressive symptoms (Meinzer et al., 2012; Seymour et al., 2012; Skirrow and Asherson, 2013). If anxiety is a possible moderator in the phenotypic progression from ADHD to depression, it is also crucial in affecting the progression to bipolarity. About two-third of adult patients diagnosed with co-occurring ADHD and BD present a lifetime history of at least one anxiety disorder (Tamam et al., 2008). Anxiety disorders represent a possible pathway to bipolarity, both in children/adolescents (Masi et al., 2012, 2001) and in adults (Faedda et al., 2014).

Future research is needed to explore whether the successful treatment of comorbid anxiety may decrease the risk of subsequent depression. As anxiety symptoms in depressed patients with childhood ADHD may represent a further predictor of a superimposed bipolar spectrum disorder in patients with depression, this pattern of comorbidity should be actively explored for timely preventive interventions.

Our study should be considered in the light of several limitations. Firstly, ADHD symptoms were assessed on a retrospective basis, with no available information about the current diagnostic status as regards ADHD. Adult ADHD status was not assessed here because the primary focus of the study was to examine childhood and familial antecedents of depression. Unfortunately, it turned out to limit the significance of our findings because of possible shared features between ADHD with emotion dysregulation and BD. However, the identification of manic symptoms relied more heavily on elation than on irritability.

As retrospective self-report of childhood has shown low specificity of a diagnosis of ADHD, especially in males (Suhr et al., 2009), our study refers to symptoms of ADHD rather than to a diagnosis of ADHD. Furthermore, a potential overlap between hypomanic and ADHD symptoms cannot be excluded. It is still debated whether the persistence of ADHD symptoms into young adulthood might account for a substantial portion of the association between ADHD and depression onset. Emotional dysregulation and anxiety may be more significant when ADHD symptoms are persistent, thus the diagnosis of current adult ADHD may be even more important. As depression accounted for by substance abuse was an exclusion criteria in our study and as substance use was not assessed, co-occurent BD and ADHD, character-

ized by frequent substance abuse (Nierenberg et al., 2005; Torres et al., 2015) may be underrepresented in our sample.

Another limitation is the lack of information about specific ADHD treatments, preventing an examination of pharmacotherapy as a moderator of the association between ADHD and depression onset. Actually, the maintenance of an effective treatment for ADHD into early adulthood may lower the risk of a superimposed depression. Two longitudinal studies support a potential protective effect of ADHD treatment, as youth receiving pharmacotherapy for ADHD had subsequently lower rates of mood disorders compared to untreated ADHD youth (Biederman et al., 2009a; Daviss et al., 2008).

In conclusion, most adults with ADHD are not recognized and remain untreated, although a large portion of these individuals are diagnosed and treated for other comorbid mental disorders, such as MDD and BD. Taken together, our findings suggest that, consistent with previous research in referred samples, a positive history of ADHD in childhood has a significant impact on depression onset and phenotype with increased risk of bipolar spectrum features. As such, individuals with positive histories of ADHD should be routinely screened for depression and bipolar symptoms. Similarly, individuals with depression, namely with mixed features and/or treatment refractoriness, should be screened for current or lifetime ADHD. Adolescents or young adults with ADHD, co-occurring anxiety disorders and familial load for mood disorders may represent good candidates for depression prevention programs (Clarke et al., 2001; Jaycox et al., 1994). Regarding treatment options, a recommendation could be treating the most destabilizing illness (for example MDD or BD) first, and then continue in a step-wise fashion to manage all the comorbidities, including anxiety disorders, impulse dyscontrol, substance abuse, and first of all, ADHD.

In conclusion, most adults with ADHD are not recognized and remain untreated, although a large portion of these individuals are diagnosed and treated for other comorbid mental disorders, such as MDD and BD. Taken together, our findings suggest that, consistent with previous research in referred samples, a positive history of ADHD in childhood has a significant impact on depression onset and phenotype with increased risk of bipolar spectrum features. As such, individuals with positive histories of ADHD should be routinely screened for depression and bipolar symptoms. Similarly, individuals with depression, namely with mixed features and/or treatment refractoriness, should be screened for current or lifetime ADHD. Adolescents or young adults with ADHD, co-occurring anxiety disorders and familial load for mood disorders may represent good candidates for depression prevention programs (Clarke et al., 2001; Jaycox et al., 1994.

Conflicts of interest

Pr. Falissard reports personal fees from Pfizer, personal fees from Sanofi, personal fees from GSK, personal fees from BMS, personal fees from Lundbeck, personal fees from Janssen, personal fees from Roche, outside the submitted work.

Pr. Gorwood reports grants and personal fees from Eli Lilly, grants and personal fees from Servier, personal fees from AstraZeneca, personal fees from Biocodex, personal fees from Bristol-Myers-Squibb, personal fees from Janssen, personal fees from Lundbeck, personal fees from Naurex, personal fees from Otsuka, personal fees from Roche, personal fees from Sanofi Pasteur MSD, outside the submitted work.

Dr. Le Strat reports personal fees from Lundbeck, personal fees from Otsuka, personal fees from Takeda, personal fees from Janssen, outside the submitted work.

Dr. Masi reports grants and personal fees from Eli Lilly, grants and personal fees from Shire, personal fees from Angelini, personal fees from Otsuka, personal fees from Lundbeck, outside the submitted work.

Dr Porfirio reports no conflicts of interest.

Pr Purper-Ouakil reports personal fees from Shire, Otsuka, Janssen and Boiron outside the submitted work.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.psychres.2016.12.055.

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Associazione Italiana
Disturbi Attenzione e Iperattività
REGIONE TOSCANA
Sede Legale: c/o CTCC V.le Redi 127, 50125 Firenze
C/F: 94123070487 P.I. 05897680483
a.i.d.a.i. TOSCANA
Aidai.toscana@gmail.com www.aidaiassociazione.com

Concorso fotografico AIDAI TOSCANA 2017 – 17 III edizione

"D'IMPULSO"

FIRENZE 6 DICEMBRE 2017

A seguito del grande successo riscontrato per le edizioni precedenti, la sezione regionale Toscana dell'Associazione Italiana Disturbi dell'Attenzione e Iperattività (AIDAI TOSCANA) indice il III concorso fotografico a premi per bambini/ragazzi dai 3 ai 14 anni e per le scuole dell'obbligo (Scuola dell'infanzia, Primaria e Secondaria di primo grado) della regione Toscana. La terza Edizione avrà il sottotitolo "D'IMPULSO"

DESTINATARI

Il bando di concorso è aperto a tutti i bambini e ragazzi di scuola dell'infanzia, primaria e secondaria di primo grado della regione Toscana. E' possibile partecipare individualmente, come classe o gruppo.

FINALITA'

Promuovere una riflessione attiva sul tema dell'Impulsività

Attraverso il concorso si intende stimolare bambini, ragazzi, insegnanti e genitori a riflettere sul concetto di impulsività ed esprimere la loro opinione. L'atto del riflettere è un processo metacognitivo che promuove una migliore conoscenza del proprio

agire e il pensiero critico.

-

- ***Stimolare i processi di osservazione e la creatività.***

Il mondo che ci circonda offre una miniera inesauribile di fonti di ispirazione che aspettano solo di essere osservate. La struttura tipica della società attuale orienta l'individuo al "fare" e al "realizzare" e poco spazio viene lasciato all'otium così come veniva inteso nell'antica Roma. Il concorso fotografico di AIDAI TOSCANA, si propone di sostenere negli alunni e negli insegnanti, il piacere di osservare, la virtù del cercare, l'abilità dell'immaginare. Fotografare frutta verdura e in generale i vegetali che sono intorno a noi permette non solo di fermarsi ad osservare il contesto alimentare e naturale, ma immaginare come essa possa trasformarsi.

- **Promuovere metodologie di lavoro per una didattica inclusiva**

Le fasi del concorso (osservazione, ripresa fotografica, modifica artistica dell'immagine e produzione narrativa) offrono la possibilità ai partecipanti di contribuire in almeno una fase del processo di costruzione del prodotto finale. Le esperienze realizzate nel passato hanno messo in luce come il concorso possa rappresentare un valido strumento per promuovere una partecipazione attiva anche in alunni che presentino difficoltà negli apprendimenti curricolari

PROCEDURA

1. FOTOGRAFARE

I bambini/ragazzi dovranno **fotografare elementi vegetali** che contengano colori compresi nella gamma del rosso dall'arancione al viola (es. frutta verdura foglie, fiori) la cui forma o le cui sfumatura possano ispirare un collegamento con il concetto di **"IMPULSIVITA'"".** Possono essere forme o sfumatura che ricordano personaggi, animali, scene o quanto la fantasia del fotografo possa immaginare.

Al fine di rendere più comprensibile l'immagine, è possibile creare una seconda immagine e aggiungere sulla foto alcuni particolari che ne chiariscano il significato. Le foto possono essere modificate: a) con programmi al computer (es. Photoshop) b) con applicazioni per cellulari (es. Pixlr Express) c) direttamente su carta con penne o pennarelli, stoffe o altri materiali. Le modifiche dovranno limitarsi alla sola aggiunta di particolari. **IMPORTANTE**: è necessario inviare una copia dell'immagine **originale** e una copia dell'immagine **modificata** al computer oppure a mano. Le

immagini originali dovranno essere rinominate inserendo il titolo es. farfalla, quelle modificate aggiungendo al titolo la dicitura modifica es. farfalla modifica.

Qualora non sia possibile modificare l'immagine, può essere utile inviare una breve descrizione della foto affinchè sia comprensibile ciò che il fotografo intende descrivere.

2. COSTRUIRE UNA NARRAZIONE

Sulla base dell'immagine fotografata, i partecipanti dovranno produrre una breve storia ispirata al tema dell'IMPULSIVITA'. Sarà possibile, partendo dall'immagine, proporre **una breve frase, una descrizione, una filastrocca o un racconto** di massimo 200 parole. Il testo narrativo dovrà essere trascritto nella scheda narrativa (Allegato B) e **dovrà necessariamente fare riferimento all'IMPULSIVITA' oppure al suo contrario: la riflessione. Il racconto dovrà contribuire alla conoscenza del concetto di impulsività_ la sua utilità, il suo limite etc…**

Ad ogni fotografia dovrà essere attribuito un titolo da inserire nella scheda narrativa (Allegato B).

Alcuni esempi sono disponibili alla pagina Facebook di AIDAI TOSCANA digitando l'hashtag #D'IMPULSO

3. INVIARE IL TUTTO PER E- MAIL

Gli elaborati (Foto originale e foto modificata, scheda di iscrizione-Allegato A e scheda narrativa - Allegato B) e) dovranno essere inviati all'indirizzo e-mail: nuvole.aidai@gmail.com

MODALITA' DI ISCRIZIONE AL CONCORSO

L'iscrizione al Concorso è subordinata all'invio della scheda di iscrizione (Allegato A) da parte delle scuole e/o da parte dei singoli studenti, unitamente alle immagini partecipanti al concorso (Immagine originale e immagine modificata) e alla Scheda Narrativa (Allegato B). Nella scheda di iscrizione dovrà essere esplicitata la categoria di appartenenza:

Categoria A: Bambini o ragazzi che aderiscono individualmente al Concorso, eventualmente guidati dal loro genitori.

Categoria B: Classi o GRUPPI guidati dai lori insegnanti o tutor

Non saranno ammesse al concorso le foto prive della scheda di iscrizione.

REGOLAMENTO

Articolo 1

Ogni candidato può partecipare con un **massimo di due immagini** a colori o in bianco e nero (due immagini originali e due modificate). ***Tutte le fotografie dovranno essere inedite.***

Le immagini possono essere scattate con qualsiasi apparecchiatura fotografica (fotocamera digitale, cellulare etc) e dovranno essere presentate in formato digitale (per le immagini modificate manualmente si richiede la scansione tramite scanner). Sono ammessi i formati: jpeg, pdf, tiff. I file contenenti le immagini devono essere nominati indicando nome e cognome del bambino, la provincia di residenza, il nome della scuola, e il numero della foto. Il bambino Guido Rossi residente a Grosseto e frequentante la scuola Capponi nominerà quindi il file con la dicitura "Guido Rossi GR Capponi foto1". Le immagini inviate devono inoltre avere una risoluzione tale da consentire la migliore resa stampa possibile nei limiti delle potenzialità tecniche del mezzo con cui sono state realizzate.

Articolo 2

Le immagini verranno sottoposte all'insindacabile giudizio di una Giuria nominata dall'ente organizzatore.

La giuria di qualità sarà composta da fotografi, esperti di attenzione ed insegnanti. I criteri generali di valutazione saranno i seguenti:

• originalità nell'interpretazione del tema;

• efficacia espressiva dello scatto in relazione al tema;

• originalità del racconto sulla IMPULSIVITA''

La partecipazione al concorso comporta l'integrale accettazione delle norme contenute nel presente bando.

Articolo 3

La partecipazione al concorso è **gratuita** e le fotografie consegnate non saranno restituite. Le fotografie si intendono donate in favore dell'Associazione Italiana Disturbi dell'Attenzione e Iperattività (AIDAI) regione Toscana.

AIDAI TOSCANA si impegna, in caso di utilizzo pubblico delle opere, a citare l'autore. Tutto il materiale pervenuto potrà essere utilizzato dagli organizzatori in qualsiasi manifestazione e/o pubblicazione.

Ai sensi della Legge 675/96 si informa che i dati personali dei partecipanti saranno utilizzati unicamente ai fini del Concorso.

Articolo 4

L'assegnazione dei premi avverrà sulla base del risultato della votazione della Giuria. A tutti i vincitori verrà inviato un attestato di partecipazione.

SCADENZE

26 MARZO 2018 scadenza per l'invio delle foto

Il materiale dovrà essere inviato all'indirizzo e-mail: nuvole.aidai@gmail.com entro e non oltre LUNEDI 26 marzo 2018 (farà fede la data di invio telematico):

- 2 Foto: foto originale ed eventuale immagine modificata
- Scheda di Iscrizione (Allegato A)
- Scheda Narrativa (Allegato B)

6 APRILE 2018

Entro il 6 APRILE verranno analizzati i materiali inviati e assegnati i premi. La comunicazione avverrà per e-mail all'indirizzo indicato nella scheda di iscrizione.

SARA' INDIVIDUATA UNA DATA PER REALIZZARE UNA MOSTRA CON I MATERIALI PERVENUTI. LA DATA E LA SEDE DELLA MOSTRA SARA' RESA NOTA AI PARTECIPANTI TRAMITE MAIL.

SEGRETERIA

Il bando è disponibile sul sito www.aidaiassociazione.com. Per maggiori informazioni è possibile inviare una mail all'indirizzo dedicato al concorso : nuvole.aidai@gmail.com o telefonare al cell. 3397233435 (Chiara Vernucci).

PREMI

I premi saranno assegnati dalla giuria in base all'ordine di classificazione dei partecipanti.

Nel caso in cui ci sia uno o più premi che NON si desidera ricevere, si prega di barrare con una X la casella GRIGIA (colonna sulla destra).

PREMI

TIPOLOGIA PREMIO	DESTINATARI	ENTE	SITO INTERNET	NO
Parco ricreativo per bambini e ragazzi, inserito in un'oasi affiliata al WWF a Limestre (PT)	Per classi di scuola primaria e secondaria di primo grado	Associazione Dynamo Camp Onlus	www.dynamocamp.org	

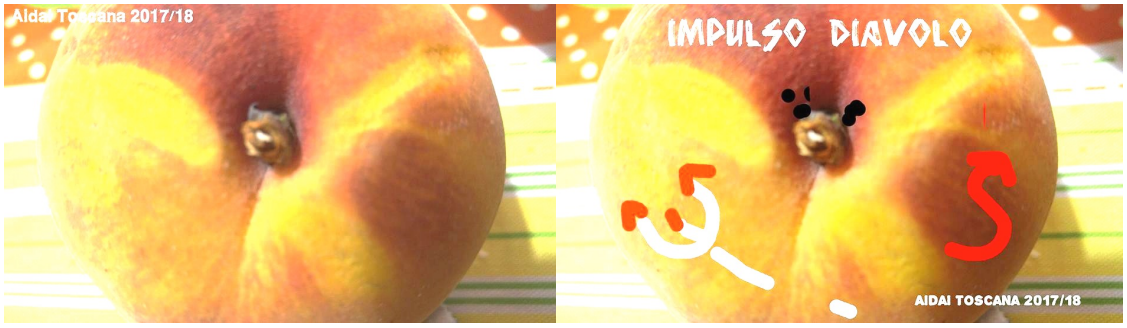
Ingresso gratuito al ParcoAvventura, percorsi sugli alberi TreeExperience Vincigliata, Vincigliata – Firenze	Premio individuale per bambini/ ragazzi dai 5 ai 14 anni	Treexperience	http://www.treeexperience.it/	
Museo Galileo. Istituto e Museo di Storia della Scienza a Firenze	Premio individuale	Museo della scienza Galileo	www.museogalileo.it	
Fondazione museo del calcio Firenze	Premio individuale	Museo del calcio	www.museodelcalcio.it	
- 1 mese di lezione per i bambini dai 3 ai 10 anni. Per la classe, due interventi in un mese presso la scuola con lezione di inglese di un'ora. - 3 lezioni aiuto compiti o preparazione al compito in classe per ragazzi dagli 11 ai 14 anni. Per la classe, due interventi in un mese presso la scuola con lezione di inglese di un'ora. Per Firenze e zone limitrofe.	Premio singolo e per le classi. Per bambini dai 3 anni fino ai 14.	Pingu's English	http://firenze.pinguseenglish.it/	
Giochi da tavolo	Per bambini/ ragazzi dai 3 ai 14 anni	Redglove Parpignol Asmodee Erickson	www.redglove.eu www.parpignol.info/ www.asmodee.it www.erickson.it	
Kit t-shirt per magliette colorabili	Dai 3 anni agli 11	Giokit	www.giokit.com	
Libri per bambini e ragazzi	Per bambini/ ragazzi dai 3 ai 14 anni	Erickson Giunti Scuola Libriliberi	www.erickson.it www.giuntiscuola.it www.libriliberi.com/	

Libri scientifico-divulgativi	Insegnanti	Il Mulino	www.mulino.it/	
Incontri di Attività Assistita con gli Asini (AAA) sia per le famiglie che per le scolaresche: presso la Fattoria di Ponte alle Catene Scarlino (GR), situato nel Patrimonio Agricolo Forestale Regionale “Bandite di Scarlino”(GR).	Premio sia individuale sia di classe. Per bambini /ragazzi	AsiniAmo	www.asiniamo.it	
Mattinata presso la scuderia del maneggio dove una istruttrice federale FISE parlerà della vita in scuderia, dei cavalli e delle loro abitudini. Possibilità di effettuare il battesimo del cavallo per i ragazzi che lo vorranno. Pacchetto di n.3 lezioni di equitazione svolto in maneggio.	Per classi di scuola primaria e secondaria di primo grado. Premi singoli per bambini dai 6 ai 14 anni.	Maneggio Granducato. Centro Ippico Granducato-Associazione Sportiva Dilettantistica	www.centroippicogranducato.it	
Pic-nic in fattoria (una giornata in cui i bambini, accompagnati dalle famiglie faranno attività con gli animali, giochi e lavoratori a tema). Presso Fattoria Didattica "A Spasso Con Ciuchino" Strada dell'Abate 19, Tavarnelle V.P. (Fi)	Premio individuale per bambini accompagnati dalla propria famiglia	A spasso con ciuchino	www.onoterapia.eu	

ESEMPIO

Si riportano due esempi di elaborazione. La prima immagine raffigura un fiore di Malva che è stato successivamente modificato al computer per diventare un Ninja

La seconda immagina ritrae una pesca trasformata in un diavoletto



ALL. A

SCHEDA DI ISCRIZIONE AL III CONCORSO FOTOGRAFICO AIDAI TOSCANA D'IMPULSO 2017/2018

Spett.le AIDAI TOSCANA

V.le Redi 127, 50127 Firenze

Indicare i dati del partecipante in base alla categoria:

□ *Categoria A*: Bambini o ragazzi che aderiscono individualmente al Concorso, eventualmente guidati dal loro genitori.

Nome	Cognome
Nato/a il	Nato/a a
Città	Via n
Provincia	Cap
Tel.	E-mail

Autorizzazione trattamento dei dati personali (firma di un genitore o chi ne fa le veci)
……

□ *Categoria B:* Classi o studenti guidati dai lori insegnanti. Indicare il nominativo del referente Insegnante/tutor)

Nome	Cognome
Classe	Istituto Scolastico
Città	Via n
Provincia	Cap
Tel.	E-mail
Nomi dei partecipanti:	

chiede di partecipare al III Concorso fotografico *AIDAI TOSCANA d'implso*, per la categoria indicata di seguito:

A tale proposito, dichiara sotto la propria responsabilità, quanto segue (cancellare ciò che non interessa):
a. partecipa come singolo concorrente;
b. partecipa come gruppo, del quale è referente e responsabile;
c. in caso di partecipazione come gruppo o classe di studenti, indica i nominativi di tutti gli altri

autori: _____
_____

d. la/e immagine/i inviata/e sono originali
e. esonera l'Ente promotore da qualsiasi responsabilità derivanti dall'utilizzo delle stesse immagini;
f. autorizza l'Ente promotore ad utilizzare le immagini nei termini previsti dal bando; g. ha letto e accettato le condizioni previste dal bando;
h. dichiara di avere letto l'informativa sulla privacy e di accettarne le condizioni.

Allega:
- n. ____ foto formato _____
- scheda narrativa (Allegato B)

Data

Firma _____

PREMI

I premi saranno assegnati dalla giuria in base all'ordine di classificazione dei partecipanti.

Nel caso in cui ci sia uno o più premi che NON si desidera ricevere, si prega di barrare con una X la casella GRIGIA (colonna sulla destra).

PREMI

TIPOLOGIA PREMIO	DESTINATARI	ENTE	SITO INTERNET	NO
Parco ricreativo per bambini e ragazzi, inserito in un'oasi affiliata al WWF a Limestre (PT)	Per classi di scuola primaria e secondaria di primo grado	Associazione Dynamo Camp Onlus	www.dynamocamp.org	
Ingresso gratuito al ParcoAvventura, percorsi sugli alberi TreeExperience Vincigliata, Vincigliata – Firenze	Premio individuale per bambini/ ragazzi dai 5 ai 14 anni	Treexperience	http://www.treeexperience.it/	
Museo Galileo. Istituto e Museo di Storia della Scienza a Firenze	Premio individuale	Museo della scienza Galileo	www.museogalileo.it	

Fondazione museo del calcio Firenze	Premio individuale	Museo del calcio	www.museodelcalcio.it	
- 1 mese di lezione per i bambini dai 3 ai 10 anni. Per la classe, due interventi in un mese presso la scuola con lezione di inglese di un'ora. - 3 lezioni aiuto compiti o preparazione al compito in classe per ragazzi dagli 11 ai 14 anni. Per la classe, due interventi in un mese presso la scuola con lezione di inglese di un'ora. Per Firenze e zone limitrofe.	Premio singolo e per le classi. Per bambini dai 3 anni fino ai 14.	Pingu's English	http://firenze.pinguseenglish.it/	
Giochi da tavolo	Per bambini/ ragazzi dai 3 ai 14 anni	Redglove Parpignol Asmodee Erickson	www.redglove.eu www.parpignol.info/ www.asmodee.it www.erickson.it	
Kit t-shirt per magliette colorabili	Dai 3 anni agli 11	Giokit	www.giokit.com	
Libri per bambini e ragazzi	Per bambini/ ragazzi dai 3 ai 14 anni	Erickson Giunti Scuola Libriliberi	www.erickson.it www.giuntiscuola.it www.libriliberi.com/	
Libri scientifico-divulgativi	Insegnanti	Il Mulino	www.mulino.it/	
Incontri di Attività Assistita con gli Asini (AAA) sia per le famiglie che per le scolaresche: presso la Fattoria di Ponte alle Catene Scarlino (GR), situato nel Patrimonio Agricolo Forestale Regionale "Bandite di Scarlino"(GR).	Premio sia individuale sia di classe. Per bambini /ragazzi	AsiniAmo	www.asiniamo.it	
Mattinata presso la scuderia del maneggio dove una istruttrice federale FISE parlerà della vita in scuderia,	Per classi di scuola primaria e secondaria di primo grado.	Maneggio Granducato. Centro Ippico Granducato-	www.centroippicogranducato.it	

dei cavalli e delle loro abitudini. Possibilità di effettuare il battesimo del cavallo per i ragazzi che lo vorranno. Pacchetto di n.3 lezioni di equitazione svolto in maneggio.	Premi singoli per bambini dai 6 ai 14 anni.	Associazione Sportiva Dilettantistica		
Pic-nic in fattoria (una giornata in cui i bambini, accompagnati dalle famiglie faranno attività con gli animali, giochi e lavoratori a tema). Presso Fattoria Didattica "A Spasso Con Ciuchi no" Strada dell'Abate 19, Tavarnelle V.P. (Fi)	Premio individuale per bambini accompagnat i dalla propria famiglia	A spasso con ciuchino	www.onoterapia.eu	

ALLEGATO . B

III CONCORSO FOTOGRAFICO AIDAI TOSCANA
2017/2018 D'IMPULSO

NOME DEL FILE IMMAGINE _____

SCHEDA NARRATIVA: AIUTACI A CAPIRE LA TUA/VOSTRA IDEA SULL'IMPULSIVITà

Partendo dall'immagine che hai scelto costruisci una frase, una filastrocca o un racconto che parli dell'IMPULSIVITA'

TITOLO DELLA STORIA _____

Autore/i : _____

E-MAIL_____

LA MORALE DELLA STORIA SULL'IMPULSIVITA' è

_____

_____

To take care of children with ADHD

a therapeutic diagnostic pathway

Milano il 23 Novembre 2017 - IRCCS Istituto di Ricerche Farmacologiche Mario Negri

17 differenti figure professionali e specialistiche presenti

1,4 milioni di record per 4477 pazienti nel registro regionale ADHD della Lombardia

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+160 visualizzazioni su YouTube

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, n. 778 del 05/02/2015, n. 5954 del 05/12/2016 e N. 1077 del 02/02/2017) 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